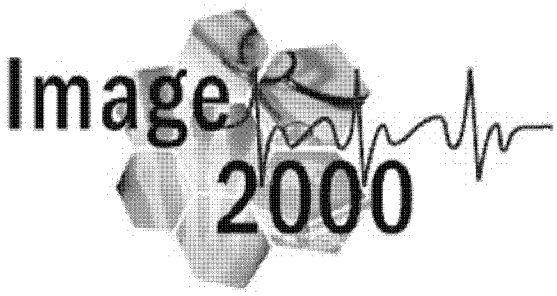


USER: RITCHWOOD, JASMINE M (jmr)

FOLDER: K983454 - 140 pages (FOI:08007513)

COMPANY: BREG, INC. (BREG)

PRODUCT: PUMP, INFUSION, ELASTOMERIC (MEB)

SUMMARY: Product: PAIN CARE 2000

DATE REQUESTED: Fri Sep 10 24:00:00 2010

DATE PRINTED: Wed Oct 27 10:17:05 2010

Note: Releasable Version

Table of Contents

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

DEC 16 1998

Ms. Kathleen Barber
Vice President of Regulatory Affairs
BREG®, Incorporated
2611 Commerce Way
Vista, California 92083

Re: K983454
Trade Name: PAIN CARE 2000
Regulatory Class: Unclassified
Product Code: MEB
Dated: September 29, 1998
Received: September 30, 1998

Dear Ms. Barber:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531

through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4692. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Timothy A. Ulatowski
Director
Division of Dental, Infection Control,
and General Hospital Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

STATEMENT OF INDICATIONS FOR USE

Intended Use

BREG's Pain Care 2000 is intended to provide patient controlled intermittent infusion of a local anesthetic into an intra-operative site for the post-operative management of pain. BREG's Pain Care 2000 provides a delivery mechanism of local anesthetic maintenance doses in order to sustain pain relief that is initially established by the bolus of local anesthetic that is injected intra-operatively (loading dose).

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓ OR Over-The-Counter Use _____

(Optional Format 1-2-96)

Patricia Cucuzzella
(Division Sign-Off)
Division of Dental, Infection Control,
and General Hospital Devices
510(k) Number K983454

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

AUG 23 2000

Ms. Kathleen Barber
Vice President
Quality Assurance/Regulatory Affairs
Breg, Incorporated
2611 Commerce Way
Vista, California 92083

Re: K983454
Device Name: PAIN CARE 2000
Dated: July 21, 2000
Received: July 24, 2000

Dear Ms. Barber:

We have reviewed the information dated July 21, 2000, regarding the 510(k) notification K983454 previously submitted for the device referenced above. Based solely on the information that you have provided, it does not appear that you have significantly changed or modified the design, components, method of manufacture, or intended use of the device referenced above (see 21 CFR 807.81(a)(3)). It is, however, your responsibility to determine if the change or modification to the device or its labeling could significantly affect the device's safety or effectiveness and thus require submission of a new 510(k). The information you have supplied will be added to the file.

Sincerely yours,

Timothy A. Ulatowski
Director
Division of Dental, Infection Control
and General Hospital Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date: 7/24/00

From: DMC (HFZ-401)

Subject: Premarket Notification Number(s): K983454/A5

To: Division Director: HO/DDIG-1

The attached information has been received by the 510(k) DMC on the above referenced 510(k) submission(s). Since a final decision has been rendered, this record is officially closed.

Please review the attached document and return it to the DMC, with one of the statements checked below.

__✓__Information does not change the status of the 510(k); no other action required by the DMC; please add to image file. (Prepare K-25)

_____Additional information requires a new 510(k); however, the information submitted is incomplete; (Notify the company to submit a new 510(k); [Prepare the K30 Letter on the LAN]

_____Additional information requires a new 510(k); please process. [THIS INFORMATION WILL BE MADE INTO A NEW 510(K)]

_____No response necessary (e.g., hard copy of fax for the truthful and accurate statement or 510(k) statement).

CLIA CATEGORIZATION refers to laboratory test system devices reviewed by the Division of Clinical Laboratory Devices (HFZ-440)

_____Information requires a **CLIA CATEGORIZATION**; the complexity may remain the same as the original 510(k) or may change as a result of the additional information (Prepare a CAT letter)

____Additional information requires a **CLIA CATEGORIZATION**; however, the information submitted is incomplete; (call or fax firm)

_____No response necessary

This information should be returned to the DMC within 10 working days from the date of this memorandum.

Reviewed by: [signature]

Date: 8/14/00

AUG 23 2000

K983454/A5

BREG

July 21, 2000

BY FEDERAL EXPRESS

Document Mail Center
Center for Devices and Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ - 401)
9200 Corporate Blvd.
Rockville, Maryland 20850

510(k) K983454
PAIN CARE 2000
Amendment #5

As the representative of Breg, Inc., Vista, CA I am supplying the following Amendment to 510(k) K983454, for the PAIN CARE 2000.

The amendment contains changes to the following page which were part of the original submission. The original page was not correct. Two copies are included.

- **Page 6** Correct the qty on catheter sets from 2 to 1
- **Page 6** Add certified statement

Please direct all correspondence regarding this submission to me at the above letterhead addresses. If you have any questions which may be appropriately answered by phone, then please telephone my office at (760) 599-5719 during the hours of 7:30AM - 5:00PM, PST. Thank you for your attention to this document.

Sincerely yours,

Kathleen Barber
Vice President
QA/RA

Enclosures: 2 copies - 510(k) Amendment, **Page 6**

RECEIVED
24 Jul 00 10 57
FDA/ORH/ODE/DRG

3

Sk-3

9.0 BIOCOMPATABILITY:

The components of the **PAIN CARE 2000** are listed on Diagram 1. These materials are identical to those used in the predicate device, the I-Flow PainBuster and are processed and sterilized in the same manner. All materials conform to the ISO-10993 biomaterial testing program for medical devices.

10.0 STERILITY ASSURANCE:

The type of sterilization is (b)(4) gamma radiation performed by (b)(4) (b)(4) to acheive a sterility assurance level of 10 to the -6. This process is equivalent to the I-Flow predicate device

The sterility validation methodology used to initially establish our dose requirements and our ongoing quarterly audits will comply with the following specifications: (1) USP Section 71; (2) ISO-11135; and (3) ANSI/AAMI Method 1.

Parts will be packed into industry recognized sterilazation pouches designed for radiation applications which are heat sealed prior to sterilization.

11.0 KITS, PACKS or TRAYS

The **Pain Care 2000** system is packed as a kit which contains the following elements:

- **1 Infusion Device**
- **1 16GA IV Catheter Needle**
- **1 16GA IV Epidural Catheter Set(s)**
- **1 Luer Y-adapter**
- **1 60cc Syringe**

The Infusion Device is the subject of this 510(k) submission and is discussed in detail.

The 16GA Epidural Catheter sets have been found to be SE through the premarket notification process for the uses in which the kit is to be intended. These catheters are purchased in bulk and reprocessed by the addition of luer connectors, defined lengths and drilled hole patterns and gamma sterilization.

For the other elements above, I certify that these devices have been found to be substanially equivalent through the premarket notification process for the uses for which the kit is to be intended. I further certify that these devices/components are not purchased in "bulk", but are purchased in finished form, i.e. they are packaged, labeled, etc., consistent with their premarket notification status.

Kathleen Sarb

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

NOV 3 1999

Ms. Kathleen Barber
Vice President of Regulatory Affairs
BREG, Incorporated
2611 Commerce Way
Vista, California 92083

Re: K983454
Device Name: PAIN CARE 2000
Dated: October 18, 1999
Received: October 19, 1999

Dear Ms. Barber:

We have reviewed the information dated October 18, 1999 regarding the 510(k) notification K983454 previously submitted for the device referenced above. Based solely on the information that you have provided, it does not appear that you have significantly changed or modified the design, components, method of manufacture, or intended use of the device referenced above (see 21 CFR 807.81(a)(3)). It is, however, your responsibility to determine if the change or modification to the device or its labeling could significantly affect the device's safety or effectiveness and thus require submission of a new 510(k). The information you have supplied will be added to the file.

Sincerely yours,

Timothy A. Ulatowski
Director
Division of Dental, Infection Control
and General Hospital Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food And Drug Administration

Memorandum

Date: 10-20-99

From: Document Mail Center (HFZ-401)

Subject: Premarket Notification Number(s): K983454/A4

To: Division Director: HO / DRIG

The attached information has been received by the 510(k) Document Mail Center (DMC), on the above referenced 510(k) submission(s). Since a final decision has been rendered, this record is officially closed.

Please review the attached document and return it to the DMC, with one of the statements checked below. Feel free to note any additional comments below.

Thank you for your cooperation.

✓ Information does not change status of the 510(k); no other action required by the DMC; please add to the image file. [THE DIVISION SHOULD PREPARE A CONFIRMATION LETTER - AN EXAMPLE IS AVAILABLE ON THE LAN (K25). THIS DOES NOT APPLY TO TRANSFER OF OWNERSHIP. PLEASE BRING ANY TRANSFER OF OWNERSHIP TO POS.]

_____ Additional information requires a new 510(k) however the information submitted is incomplete. Notify the company to submit a new 510(k). [THE DIVISION SHOULD PREPARE THE (K30) LETTER ON THE LAN.]

_____ Additional information requires a new 510(k); please process. [THIS INFORMATION WILL BE MADE INTO A NEW 510(k)].

_____ No response necessary (e.g., hard copy of fax for the truthful and accuracy statement or 510(k) statement).

This information should be returned to the DMC within 10 working days from the date of this memorandum.

Reviewed by: MN

Date: 11/1/99

BREG

K983454/149

October 18, 1999

BY FEDERAL EXPRESS

Document Mail Center
Center for Devices and Radiological Health
Office of Device Evaluation
Document Mail Center(HFZ-401)
9200 Corporate Boulevard
Rockville, MD 20850

510(k) K983454
PAIN CARE 2000
Amendment #4

Attn.: Irene Naveau

As the representative of Breg, Inc., Vista, CA I am supplying the following Amendment to 510(k) K983454, for PAIN CARE 2000.

The amendment contains changes to the following pages. Two copies are included.

- Page 4 Change text to 16 gauge epidural catheter
- Page 5 Change text to 16 gauge epidural catheter
- Diagram #1 – Updated
- Updated Labeling of Product

Please direct all correspondence regarding this submission to me at the letterhead address. If you have any questions which may be appropriately answered by phone, then please telephone my office at (760) 599-5719, during the hours of 7:30AM - 5:00PM, PST. Thank you for your attention to this document.

Sincerely yours,

Kathleen Barber
Vice President of Regulatory Affairs

Enclosures: 2 copies of 510(k) with cover letter attached

BREG, Inc.
2611 Commerce Way
Vista, CA 92083
(760) 599-3000
(800) 321-0607
FAX 598-6193

ISO 9001

48
39

3

hydrochloride and ropivacaine hydrochloride, have long been used for the immediate relief of pain following surgery. Drugs, such as these, have been shown to be safe and effective.[2,4,7]

Current research has shown that continuous intra-articular or local administration of non-narcotic anesthetics into the operative site through a catheter following surgery, can significantly prolong the patient's post-operative pain relief. This method has been shown to be safe and effective.[1,5,6,8,10] The main advantage of post-operative infusion of local anesthetics into the surgical site is that the patient experiences extended local pain relief, thereby reducing or eliminating supplemental systemic narcotic anesthetic usage and their inherent side effects.

BREG's new Pain Care 2000 is a device designed to provide patient controlled intermittent infusion of a local anesthetic into an operative site for the post-operative management of pain. It is substantially equivalent to the I-Flow PainBuster and the Sgarlato SurgiPEACE. The features are compared in Table II with promotional materials in Attachement 4. The noted Bibliography and scientific research noted are included in Attachment 5.

8. DESCRIPTION

BREG's Pain Care 2000 consists of a dispensing device that is connected via a Luer LOK connector to a standard 16 gauge epidural catheter. Included is a standard 16 gauge intravenous (IV) catheter insertion needle to assist in insertion of the standard 16 gauge epidural catheter into the operative site. A 60 cc syringe is also supplied to aid in filling the dispensing device with fluid (appropriate local anesthetic recommended by a licensed physician).

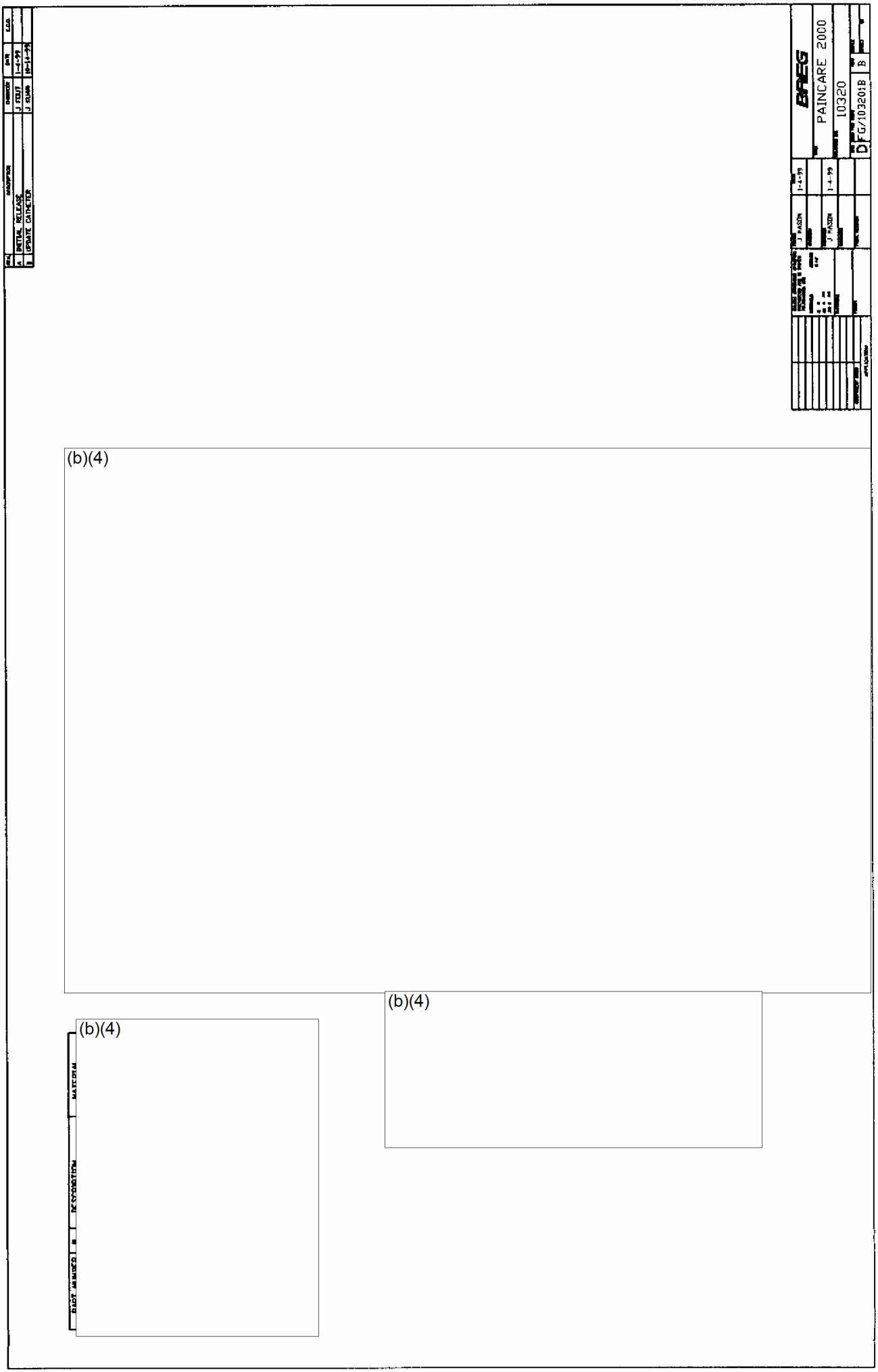
The dispensing device consists of fluid reservoir bag (approximately 50 cc), a spring loading 5 cc syringe, a flow control, an in-line particulate filter, and two valves. All internal dispensing device components are connected via Luer fittings and then housed in a plastic case.

The plastic case can be attached to a belt, clothing, or post-operative brace or sling via a metal clip fastened to the case. The plastic case has an exterior button enabling the user to depress the spring loading syringe, and thus injecting the fluid that has accumulated in the spring loading syringe through the catheter and into the operative site. The flow control is between the fluid reservoir and the spring loading 5 cc syringe. The flow control permits filling of the of the spring loading syringe at a rate, not to exceed, 16 cc per hour. A one way valve is located between the standard 16 gauge epidural catheter and the spring loading 5 cc syringe. The one way valve prevents aspiration of fluids from the standard 16 gauge epidural catheter to the dispensing device . The in-line particulate filter is in-between the fluid reservoir bag and the flow control and thus prevents clogging of the flow control.

There is a second one way Luer LOK fill port on the exterior of the case that is connected to the 50 cc fluid reservoir bag inside the case. This port permits injection of the fluid via the 60 cc syringe . The fill port also has a tethered removable cap to maintain sterility and to ensure that the proper pressure is maintained within the fluid reservoir and system. There is an outflow port that connects the dispensing device to the standard 16 gauge catheter. Fluid that has accumulated within the spring loading 5 cc syringe is injected through this port to the catheter and into the operative site by depressing the button on the case. (See Diagram 1 for complete configuration) The patient is able to dispense local anesthetic into the operative site as needed for pain relief. The design of the Pain Care 2000 permits administration of local anesthetic at a rate not to exceed 16 cc per hour. All components are provided in a sterile package.

MECHANICAL FUNCTION

- Fluid reservoir bag filled with fluid through the fill port.
- Fill port capped.
- Button is depressed (which depressed the spring loading 5 cc syringe) to prime system.
- Standard 16 gauge epidural catheter is connected to outflow port via Luer fitting.
- Spring loading 5 cc syringe creates an aspirating vacuum within the system (The spring that is attached to the syringe continually draws out the plunger of the syringe until maximum capacity is reached).
- Fluid from the fluid reservoir bag is aspirated through particulate filter .
- Fluid that passes through the particulate filter passes through the flow control and into the 5 cc spring loading syringe.
- The one way valve between 5 cc spring loading syringe and catheter prevents aspiration of fluids from the standard 16 gauge epidural catheter back to the syringe.
- As determined by the user's pain need, the button on the case is depressed.
- Plunger of 5 cc spring loading syringe is depressed via button.
- Fluid is injected through the one way valve, through the out port, through the catheter, and into the operative site.
- Flow control prevents injection of fluid back into the fluid reservoir.
- Cycle repeats.
- Patient depresses button as need for pain.
- Pain Care 2000 use is discontinued once fluid reservoir is empty
- The Pain Care 2000 will last for approximately 2-3 days of use, depending upon local analgesia duration prior to the next injection.
- Catheter is removed by day three.


PAINCARE 2000
10320
DFG/103201B
(b)(4)
(b)(4)
(b)(4)

BREG™

Breg, Inc., 2611 Commerce Way, Vista, CA 92083 U.S.A.

PART NO. 10320

CONTENTS / INHALT / CONTENU / CONTENIDO: 1

PAIN CARE™ 2000

Patient Controlled Local Anesthetic Infusion Device

50 ml Volume • 4 ml Volume per Dose

For Single Patient Use Only

STERILE

CONTENTS:
1 each - 50 ml Vol., 4 ml Infusion Device
1 each - Catheter Introducer Needle
1 each - 16 GA Catheter Set
1 each - Tube Extension Set
1 each - 60 cc Syringe

SEE DIRECTIONS FOR USE. CAUTION: FEDERAL LAW (U.S.A.) RESTRICTS THIS DEVICE TO SALE BY OR ON THE ORDER OF A HEALTHCARE PROFESSIONAL

E/U Authorized Representative
MDSS
Burckhardtstrasse 1
D-30163 Hanover
Germany

PATENT PENDING

P/N 1.01390 Rev. A 3/99

To Reorder Call:
(800) 321-0607
(760) 599-3000

CE

Lot #: 725210320

7

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

DEC 16 1998

Ms. Kathleen Barber
Vice President of Regulatory Affairs
BREG®, Incorporated
2611 Commerce Way
Vista, California 92083

Re: K983454
Trade Name: PAIN CARE 2000
Regulatory Class: Unclassified
Product Code: MEB
Dated: September 29, 1998
Received: September 30, 1998

Dear Ms. Barber:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531

through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4692. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Timothy A. Ulatowski
Director
Division of Dental, Infection Control,
and General Hospital Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

2

STATEMENT OF INDICATIONS FOR USE

Intended Use

BREG's Pain Care 2000 is intended to provide patient controlled intermittent infusion of a local anesthetic into an intra-operative site for the post-operative management of pain. BREG's Pain Care 2000 provides a delivery mechanism of local anesthetic maintenance doses in order to sustain pain relief that is initially established by the bolus of local anesthetic that is injected intra-operatively (loading dose).

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓ OR Over-The-Counter Use _____

(Optional Format 1-2-96)

Patricia Cucenbe

(Division Sign-Off)
Division of Dental, Infection Control,
and General Hospital Devices
510(k) Number K983454

3

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food And Drug Administration

Date: 12/11/98

F Memorandum

Reviewer(s) - Name(s) Irene Naveau

Subject: 510(k) Number K983454

To: The Record - It is my recommendation that the subject 510(k) Notification:

☐ Refused to accept.

☐ Requires additional information (other than refuse to accept).

☒ Accepted for review 10/14/98.

☐ Is substantially equivalent to marketed devices.

☐ NOT substantially equivalent to marketed devices.

De Novo Classification Candidate? ☐ YES ☐ NO

☐ Other (e.g., exempt by regulation, not a device, duplicate, etc.)

Is this device subject to Postmarket Surveillance?	☐ YES	☒ NO
Is this device subject to the Tracking Regulation?	☐ YES	☒ NO
Was clinical data necessary to support the review of this 510(k)?	☐ YES	☒ NO
Is this a prescription device?	☒ YES	☐ NO
Was this 510(k) reviewed by a Third Party?	☐ YES	☒ NO
Special 510(k)?	☐ YES	☒ NO
Abbreviated 510(k)?	☐ YES	☒ NO

This 510(k) contains:

Truthful and Accurate Statement ☐ Requested ☒ Enclosed
(required for originals received 3-14-95 and after)

☐ A 510(k) summary OR ☒ A 510(k) statement

☐ The required certification and summary for class III devices

☒ The indication for use form (required for originals received 1-1-96 and after)

☐ Material of Biological Origin ☐ YES ☐ NO

The submitter requests under 21 CFR 807.95 (doesn't apply for SEs):

☐ No Confidentiality ☐ Confidentiality for 90 days ☐ Continued Confidentiality exceeding 90 days

Predicate Product Code with class: Additional Product Code(s) with panel (optional):

80/MEB/Unclassified 880.5727

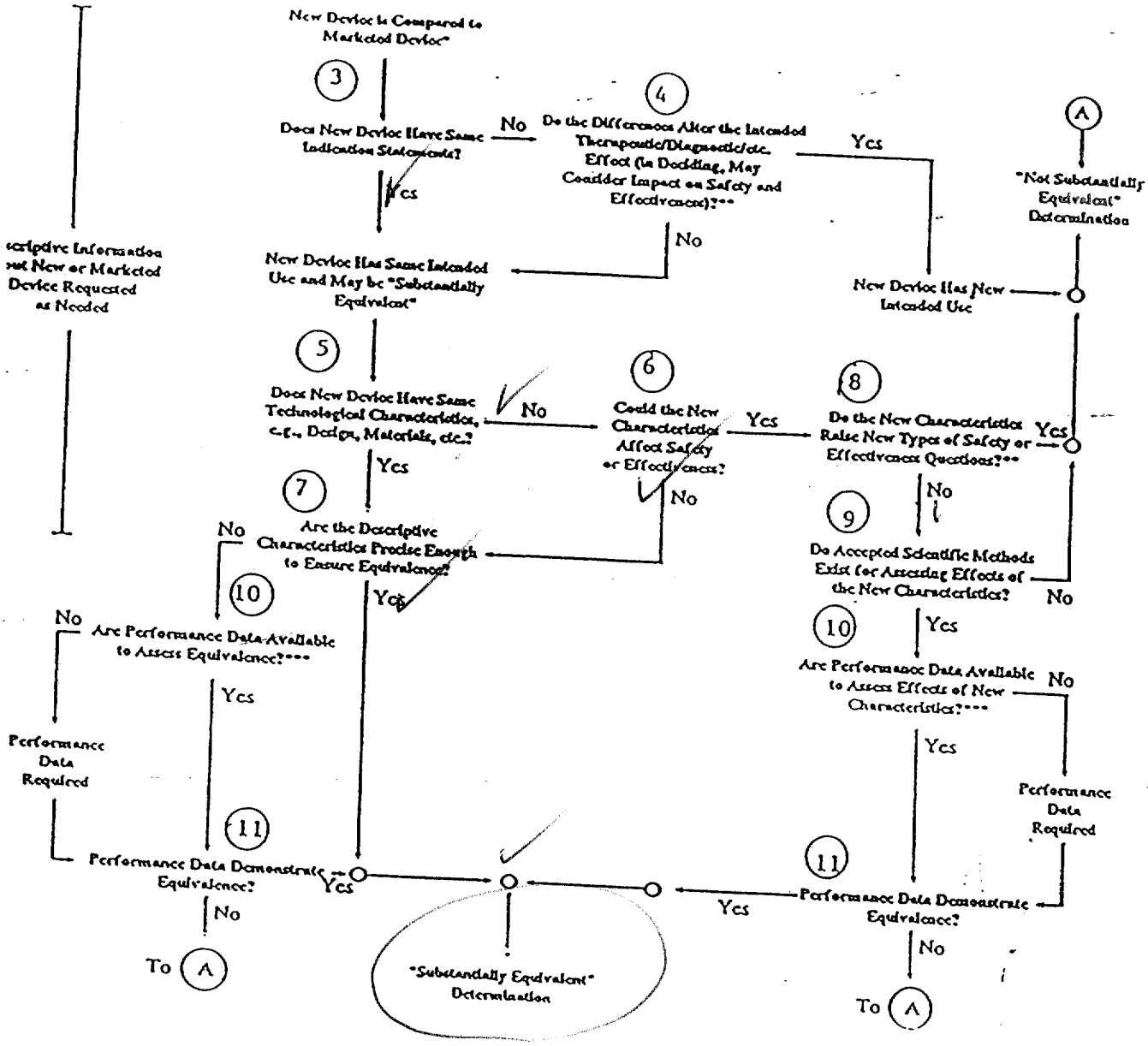
Rev Paulette Cicconetti HFZ-410 12-16-98
(Branch Chief) (Branch Code) (Date)

Final Review: [signature] 12/16/98
(Division Director) (Date)

4

Revised:6/2//98

510(k) "SUBSTANTIAL EQUIVALENCE" DECISION-MAKING PROCESS (DETAILED)



510(k) submissions compare new devices to marketed devices. FDA requests additional information if the relationship between marketed and "predicate" (pre-Amendments or reclassified post-Amendments) devices is unclear.

This decision is normally based on descriptive information alone, but limited testing information is sometimes required.

Data may be in the 510(k), other 510(k)s, the Center's classification files, or the literature.

Internal Administrative Form

	YES	NO
1. Did the firm request expedited review?		✓
2. Did we grant expedited review?		✓
3. Have you verified that the Document is labeled Class III for GMP purposes?		✓
4. If, not, has POS been notified?		✓
5. Is the product a device?	✓	
6. Is the device exempt from 510(k) by regulation or policy?		✓
7. Is the device subject to review by CDRH?	✓	
8. Are you aware that this device has been the subject of a previous NSE decision?		✓
9. If yes, does this new 510(k) address the NSE issue(s), (e.g., performance data)?		✓
10. Are you aware of the submitter being the subject of an integrity investigation?		✓
11. If, yes, consult the ODE Integrity Officer.		✓
12. Has the ODE Integrity Officer given permission to proceed with the review? (Blue Book Memo #I91-2 and Federal Register 90N0332, September 10, 1991.		✓

Screening Checklist
For all Premarket Notification 510(k) Submissions

Device Name: Pain Care 2000	K993454
Submitter (Company): Breg, Inc.	

Items which should be included *(circle missing & needed information)*	SPECIAL YES	SPECIAL NO	ABBREVIATED YES	ABBREVIATED NO	TRADITIONAL YES	TRADITIONAL NO	✓ IF ITEM IS NEEDED AND IS MISSING
1. Cover Letter clearly identifies Submission as: a) "Special 510(k): Device Modification" b) "Abbreviated 510(k)" c) Traditional 510(k)	GO TO # 2,4		GO TO # 3,4,5		✓ GO TO # 4,5		
2. "SPECIALS" - ONLY FOR MODIFICATIONS TO MANUFACTURER'S OWN CLASS II , III OR RESERVED CLASS I DEVICE							
a) Name & 510(k) number of legally marketed (unmodified) predicate device							
b) ***STATEMENT - INTENDED USE AND INDICATIONS FOR USE OF MODIFIED DEVICE AS DESCRIBED IN ITS LABELING HAVE NOT CHANGED****			* If no - STOP not a special				
c) ***STATEMENT - FUNDAMENTAL SCIENTIFIC TECHNOLOGY OF THE MODIFIED DEVICE HAS NOT CHANGED****			* If no - STOP not a special				
d) Design Control Activities Summary							
i) Identification of Risk Analysis method(s) used to assess the impact of the modification on the device and its components, and the results of the analysis							
ii) Based on the Risk Analysis, an identification of the verification and/or validation activities required, including methods or tests used and acceptance criteria to be applied							
iii) A declaration of conformity with design controls. The declaration of conformity should include:							
1) A statement signed by the individual responsible, that, as required by the risk analysis, all verification and validation activities were performed by the designated individual(s) and the results demonstrated that the predetermined acceptance criteria were met							
2) A statement signed by the individual responsible, that manufacturing facility is in conformance with design control procedure requirements as specified in 21 CFR 820.30 and the records are available for review.							

→ → → CONTINUE TO SECTION 4 ← ← ←

	SPECIALS		ABBREVIATED		TRADITIONAL		✓ IF ITEM IS NEEDED AND IS MISSING
	YES	NO	YES	NO	YES	NO	
3. ABBREVIATED 510(K): SPECIAL CONTROLS/CONFORMANCE TO RECOGNIZED STANDARDS							
a) For a submission, which relies on a guidance document and/or special control(s), a summary report that describes how the guidance and/or special control(s) was used to address the risks associated with the particular device type							
b) If a manufacturer elects to use an alternate approach to address a particular risk, sufficient detail should be provided to justify that approach.							
c) For a submission, which relies on a recognized standard, a declaration of conformity to the standard. The declaration should include the following:							
i) An identification of the applicable recognized consensus standards that were met							
ii) A specification, for each consensus standard, that all requirements were met, except for inapplicable requirements or deviations noted below							
iii) An identification, for each consensus standard, of any way(s) in which the standard may have been adapted for application to the device under review, e.g., an identification of an alternative series of tests that were performed							
iv) An identification, for each consensus standard, of any requirements that were not applicable to the device							
v) A specification of any deviations from each applicable standard that were applied							
vi) A specification of the differences that may exist, if any, between the tested device and the device to be marketed and a justification of the test results in these areas of difference							
vii) Name/address of test laboratory/certification body involved in determining the conformance of the device with applicable consensus standards and a reference to any accreditations for those organizations							
d) Data/information to address issues not covered by guidance documents, special controls, and/or recognized standards							

→ → → CONTINUE TO SECTION 4 ← ← ←

8

4. GENERAL INFORMATION: REQUIRED IN ALL 510(K) SUBMISSIONS	SPECIALS		ABBREVIATED		TRADITIONAL		✓ IF ITEM IS NEEDED AND IS MISSING
	YES	NO	YES	NO	YES	NO	
a) trade name, classification name, establishment registration number, address of manufacturer. device class					✓		
b) OR a statement that the device is not yet classified	FDA - may be a classification request; see coordinator						
c) identification of legally marketed equivalent device	NA				✓		
d) compliance with Section 514 - performance standards	NA				✓		
e) address of manufacturer					✓		
f) Truthful and Accurate Statement					✓		
g) Indications for Use enclosure					✓		
h) SMDA Summary or Statement *(FOR ALL DEVICE CLASSES)*					✓		
i) Class III Certification & Summary *(FOR ALL CLASS III DEVICES)*							
j) Description of device (or modification) including diagrams, engineering drawings, photographs, service manuals					✓		
k) Proposed Labeling:					✓		
i) package labeling (user info)					✓		
ii) statement of intended use					✓		
iii) advertisements or promotional materials					✓		
i) MRI compatibility (if claimed)							
m) Comparison Information (similarities and differences) to named legally marketed equivalent device (table preferred) should include:					✓		
i) labeling					✓		
ii) intended use					✓		
iii) physical characteristics							
iv) anatomical sites of use							
v) performance (bench, animal, clinical) testing	NA						
vi) safety characteristics	NA						
n) If kit, kit certification							
5. Additional Considerations: (may be covered by Design Controls)							
a) Biocompatibility data for all patient-contacting materials, OR certification of identical material/formulation:					✓		
i) component & material						✓	
ii) identify patient-contacting materials					✓		
iii) biocompatibility of final sterilized product						✓	
b) Sterilization and expiration dating information:						✓	
i) sterilization method						✓	
ii) SAL						✓	
iii) packaging						✓	
iv) specify pyrogen free						✓	
v) ETO residues						✓	
vi) radiation dose						✓	
c) Software validation & verification:						✓	
i) hazard analysis						✓	
ii) level of concern						✓	
iii) development documentation						✓	
iv) certification						✓	

Items shaded under "NO" are necessary for that type of submission. Circled items and items with checks in the "Needed & Missing" column must be submitted before acceptance of the document.

Passed Screening ✓ **Yes** ____ **No** **Reviewer:** _____

Date: OCT - 6 1998 **Concurrence by Review Branch:** _____

MEMO TO THE RECORD
510 (K) REVIEW

K983454

Date: December 11, 1998
From: Irene Naveau

Office: HFZ-480
Division: DDIGD/GHDB

COMPANY NAME: Breg, Inc.
DEVICE NAME: Pain Care 2000

"SUBSTANTIAL EQUIVALENCE (SE) DECISION-MAKING DOCUMENTATION"

NARRATIVE DEVICE DESCRIPTION

1. SUMMARY DESCRIPTION OF THE DEVICE UNDER REVIEW:

The Pain Care 2000 consists of a dispensing device, an 18 gauge epidural catheter, an 18 gauge IV catheter insertion needle, and a 60ml syringe to fill the device. The dispensing device, itself, includes a 50ml fluid reservoir bag, a spring loading 5ml syringe, a flow control, an in-line particulate filter, and 2 one-way valves, all of which are connected via luer fittings and seated in a plastic case. The plastic case has an exterior button that is initially pressed to prime the syringe. Thereafter, the amount of fluid accumulated in the syringe will be injected through the catheter to the operative site. The flow control, located between the fluid reservoir and the syringe, permits filling of the syringe at a rate not to exceed 16ml per hour.

A one-way valve between the 18 gauge epidural catheter and the spring loading 5ml syringe permits aspiration of fluids from the 18 gauge epidural catheter to the dispensing device. A second one-way luer lock fill port with a tethered cap to maintain sterility, and ensure maintenance of proper pressure with the reservoir and system, is located on the exterior of the case. The case is connected to the 50 ml reservoir bag inside the plastic case, and allows injection of the fluid via the 60 ml syringe. The in-line particulate filter between the flow control and the fluid reservoir bag prevents clogging of the flow control. When the fluid reservoir is emptied, the Pain Care 2000 is discontinued. The Pain Care 2000 lasts approximately 2-3 days. The catheter is removed by day 3 of the infusion.

2. INTENDED USE: To provide a delivery mechanism of local anesthetic maintenance dose in order to sustain pain relief that is initially established by the bolus of local anesthetic that is injected intraoperatively.

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3. DEVICE DESCRIPTION:

A. Life-supporting or life-sustaining: No
B. Implant (short-term or long term): No
C. Is the device sterile? Yes

Method	(b)(4) Gamma Radiation
Validation	ANSI/AAMI Method 1/ISO 11135/USP section 71
SAL	10^{-6}
Dosage	Being determined
Packaging	Heat sealed pouches

D. Is the device for single use? Yes
E. Is the device for prescription use? Yes; See labeling.
F. Is the device for home use or portable? Yes
G. Does the device contain drug or biological product as a component? No
H. Is the device a kit? Yes
If yes, and some or all of the components are not new, does the submission include a certification that these components were either preamendment or found to be substantially equivalent? Yes
I. Software-driven: No
J. Electrically Operated: No
K. Applicable standards to which conformance has been demonstrated (e.g., IEC, ANSI, ASTM, etc): N/A

L. Device (s) to which equivalence is claimed, manufacturer, and 510(k) number or preamendment status: PainBuster, I-Flow Corp., K980558; SugiPeace Pump System, Sgarlato Labs, Inc, K896422. (licensed under agreement with Burron for Burron Ambulatory Drug Delivery System)

M. Submission provides

comparative specification	a	Yes
comparative in vitro data	b	No
performance data	c	No
animal testing	d	No
clinical testing	e	No
biocompatibility testing	f	No

N. Provide a statement of how the device is either similar to and/or different from other marketed devices, plus data (if necessary) to support the statement. Provide a summary about the devices design, materials, physical properties and toxicology profile if important.

The Pain Care 2000 is similar to the predicate devices in intended use and performance, and its materials are identical to the I-Flow PainBuster. This device differs in that it is patient controlled with a spring loading syringe, with a flow restrictor for syringe filling vs I-Flow's continuous flow, elastomeric membrane, and flow restrictor. The SugiPeace Pump System also has continuous flow, with a compression spring on the syringe, and a flow restrictor. All devices vary in capacity and flow rate.

Performance testing consisted of a drop test, an environmental and stress test, and biocomatibility testing. The sponsor states that the device passed all tests. The sponsor certifies that the materials are identical to the I-Flow PainBuster, and is processed and sterilized in an identical manner. The sponsor also states that all materials conform to the ISO-10993 biomaterials standard.

The labeling is found to be adequate this device. It includes appropriate warnings and cautions, directions for filling the reservoir bag, placing and attaching the catheter, and starting the Pain Care 2000. (Attachment 2) Patient directions are clear re: how the device functions, and what the patient should do if any complication arose. Troubleshooting tips, common questions questions and answers, and removal of the Pain Care 2000 are included for the patient. (Attachment 3)

Additional correspondence with the sponsor on December 9, 1998 included a request for a change in the syringe size within the plastic case. Originally, it was listed as a 5 cc syringe, but was inadvertently changed to 4cc, which was incorrect. This error was corrected on pages 4, 5, and 17.

Based on the information provided in this premarket notification, I believe that this device is substantially equivalent to the I-Flow PainBuster, its predicate device, and that no new issues of safety and effectiveness exist for this device.

O. Does the submission include a summary of safety and effectiveness information upon which an equivalence determination is based? No If not, does the submission include a certification that such information will be made available to interested persons upon request? Yes

P. RECOMMENDATION:

I believe that this device is equivalent to: 80 MEB

Classification should be based on: Infusion Pump

880.5727 Class: Unclassified

Irene Naveau 12/11/98
Irene Naveau

12

"SUBSTANTIAL EQUIVALENCE" (SE) DECISION MAKING DOCUMENTATION

K983454

Reviewer: Irene Naveau

Division/Branch: DDIGD/GHDB

Device Name: Pain Care 2000

Product To Which Compared (510(K) Number If Known): PainBuster, I-Flow Corp., K980558; SugiPeace Pump System, Sgarlato Labs, Inc., K896422

		YES	NO	
1.	Is Product A Device	X		If **NO** = Stop
2.	Is Device Subject To 510(k)?	X		If **NO** = Stop
3.	Same Indication Statement?	X		If **YES** = Go To 5
4.	Do Differences Alter The Effect Or Raise New Issues of Safety Or Effectiveness?			If **YES** = Stop **NE**
5.	Same Technological Characteristics?		X	If **YES** = Go To 7
6.	Could The New Characteristics Affect Safety Or Effectiveness?		X	If **YES** = Go To 8
7.	Descriptive Characteristics Precise Enough?	X		If **NO** = Go To 10 If **YES** = Stop **SE**
8.	New Types Of Safety Or Effectiveness Questions?			If **YES** = Stop **NE**
9.	Accepted Scientific Methods Exist?			If **NO** = Stop **NE**
10.	Performance Data Available?			If **NO** = Request Data
11.	Data Demonstrate Equivalence?			Final Decision:

Note: In addition to completing the form on the LAN, "yes" responses to questions 4, 6, 8, and 11, and every "no" response requires an explanation.

1. Intended Use: To provide a delivery mechanism of local anesthetic maintenance dose in order to sustain pain relief that is initially established by the bolus of local anesthetic that is injected intraoperatively.

2. Device Description: Refer to SE Memo dated December 11, 1998.

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EXPLANATIONS TO "YES" AND "NO" ANSWERS TO QUESTIONS ON PAGE 1 AS NEEDED

5. Describe the new technological characteristics: The Pain Care 2000 consists of a dispensing device that contains a fluid reservoir bag, a spring loading syringe, a flow restrictor, an in-line particulate filter and two on-way check valves which are contained in a plastic case. By way of an 18 ga. epidural catheter that is connected via luer lock connector to the dispensing device, the patient, after pressing a button on the exterior of the plastic case, is able to dispense a local anesthetic into the operative site at a dosage pre-determined by the physician. The mechanism within the dispensing device prevents an overdosage of medication, yet provides the patient with the means for post-operatively pain relief, when needed.

6. Explain how new characteristics could or could not affect safety or effectiveness: The new characteristics do not affect safety or effectiveness. This device is equivalent to legally marketed devices with the same indications for use, and offer and increased assurance of sterility, and may ensure proper reservoir pressure with the spring loading syringe.

K983454 /A3

BREG

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10 DEC 98 13 22
FDA/CDRH/ODE/DMC

December 9, 1998

BY FEDERAL EXPRESS

Document Mail Center
Center for Devices and Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ - 401)
9200 Corporate Blvd.
Rockville, Maryland 20850

510(k) K983454
PAIN CARE 2000
Amendment #3

Attn.: Irene Naveau

As the representative of Breg, Inc., Vista, CA I am supplying the following Amendment to 510(k) K983454, for the PAIN CARE 2000. This document is submitted based upon our phone conversation of December 9, 1998.

The amendment contains changes to the following pages submitted as part of Amendment #2. The change was made in error and the initial reference to 5cc found in the preliminary submission was correct. Two copies are included.

- **Page 4** Change the text to 5cc syringe.
- **Page 5** Change the syringe size to 5cc.
- **Page 17** Change the text to the correct 5cc syringe measure

Please direct all correspondence regarding this submission to me at the above letterhead addresses. If you have any questions which may be appropriately answered by phone, then please telephone my office at (760) 599-5719 during the hours of 7:30AM - 5:00PM, PST. Thank you for your attention to this document.

Sincerely yours,

Kathleen Barber
Vice President
QA/RA

Enclosures: 2 copies - 510(k) Amendment, **Page , 4, 5, 17,**

ck-16

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■

hydrochloride and ropivacaine hydrochloride, have long been used for the immediate relief of pain following surgery. Drugs, such as these, have been shown to be safe and effective.[2,4,7]

Current research has shown that local administration of non-narcotic anesthetics into the operative site through a catheter following surgery, can significantly prolong the patient's post-operative pain relief. This method has been shown to be safe and effective.[1,5,6,8,10] The main advantage of post-operative infusion of local anesthetics into the surgical site is that the patient experiences extended local pain relief, thereby reducing or eliminating supplemental systemic narcotic anesthetic usage and their inherent side effects.

BREG's new Pain Care 2000 is a device designed to provide patient controlled intermittent infusion of a local anesthetic into an operative site for the post-operative management of pain. It is substantially equivalent to the I-Flow PainBuster and the Sgarlato SurgiPEACE. The features are compared in Table II with promotional materials in Attachement 4. The noted Bibliography and scientific research noted are included in Attachment 5.

8. DESCRIPTION

BREG's Pain Care 2000 consists of a dispensing device that is connected via a Luer LOK connector to a standard 18 gauge epidural catheter. Included is a standard 18 gauge intravenous (IV) catheter insertion needle to assist in insertion of the standard 18 gauge epidural catheter into the operative site. A 60 cc syringe is also supplied to aid in filling the dispensing device with fluid (appropriate local anesthetic recommended by a licensed physician).

The dispensing device consists of fluid reservoir bag (approximately 50 cc), a spring loading 5 cc syringe, a flow control, an in-line particulate filter, and two valves. All internal dispensing device components are connected via Luer fittings and then housed in a plastic case.

The plastic case can be attached to a belt, clothing, or post-operative brace or sling via a metal clip fastened to the case. The plastic case has an exterior button enabling the user to depress the spring loading syringe, and thus injecting the fluid that has accumulated in the spring loading syringe through the catheter and into the operative site. The flow control is between the fluid reservoir and the spring loading 5 cc syringe. The flow control permits filling of the of the spring loading syringe at a rate, not to exceed, 16 cc per hour. A one way valve is located between the standard 18 gauge epidural catheter and the spring loading 5 cc syringe. The one way valve prevents aspiration of fluids from the standard 18 gauge epidural catheter to the dispensing device . The in-line particulate filter is in-between the fluid reservoir bag and the flow control and thus prevents clogging of the flow control.

Amendment #3
K983454

There is a second one way Luer LOK fill port on the exterior of the case that is connected to the 50 cc fluid reservoir bag inside the case. This port permits injection of the fluid via the 60 cc syringe . The fill port also has a tethered removable cap to maintain sterility and to ensure that the proper pressure is maintained within the fluid reservoir and system. There is an outflow port that connects the dispensing device to the standard 18 gauge catheter. Fluid that has accumulated within the spring loading 5 cc syringe is injected through this port to the catheter and into the operative site by depressing the button on the case. (See Diagram 1 for complete configuration) The patient is able to dispense local anesthetic into the operative site as needed for pain relief. The design of the Pain Care 2000 permits administration of local anesthetic at a rate not to exceed 16 cc per hour. All components are provided in a sterile package.

MECHANICAL FUNCTION

- **Fluid reservoir bag filled with fluid through the fill port.**
- **Fill port capped.**
- **Button is depressed (which depressed the spring loading 5 cc syringe) to prime system.**
- **Standard 18 gauge epidural catheter is connected to outflow port via Luer fitting.**
- **Spring loading 5 cc syringe creates an aspirating vacuum within the system (The spring that is attached to the syringe continually draws out the plunger of the syringe until maximum capacity is reached).**
- **Fluid from the fluid reservoir bag is aspirated through particulate filter .**
- **Fluid that passes through the particulate filter passes through the flow control and into the 5 cc spring loading syringe.**
- **The one way valve between 5 cc spring loading syringe and catheter prevents aspiration of fluids from the standard 18 gauge epidural catheter back to the syringe.**
- **As determined by the user's pain need, the button on the case is depressed.**
- **Plunger of 5 cc spring loading syringe is depressed via button.**
- **Fluid is injected through the one way valve, through the out port, through the catheter, and into the operative site.**
- **Flow control prevents injection of fluid back into the fluid reservoir.**
- **Cycle repeats.**
- **Patient depresses button as need for pain.**
- **Pain Care 2000 use is discontinued once fluid reservoir is empty**
- **The Pain Care 2000 will last for approximately 2-3 days of use, depending upon local analgesia duration prior to the next injection.**
- **Catheter is removed by day three.**

Amendment #3
K983454

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COMMON QUESTIONS AND ANSWERS

1. **How does the Pain Care 2000^{TM} work?** *The Pain Care 2000^{TM} consists of a spring loading syringe that distracts the plunger in the 5 cc syringe. This creates a vacuum in the system. The vacuum cause the fluid from the fluid reservoir bag to pass through a flow control and into the 5 cc syringe. When the patient starts to experience pain, he/she depresses a button on the case of the Pain Care 2000TM that in-turn depresses the plunger of the 5 cc syringe. The local analgesic is then dispensed through the epidural catheter and into the affected surgical site.*
2. **How much medication does the device hold?** *The fluid reservoir bag holds approximately 50 cc of fluid.*
3. **How much medication is dispensed with each depression of the button?** *There will be 5 cc dispensed with each full depression of the button.*
4. **How long with the Pain Care 2000^{TM} run for?** *The length of time that the Pain Care 2000^{TM} will run for depends upon how often the user injects the 5 cc bolus through the catheter and into the operative site. Typically, the device will last for 2-3 days.*
5. **What is the filter size?** *The particulate filter is 1.2 microns. The air eliminating filter is 0.02 microns.*
6. **How can I tell when the pump is empty?** *Infusion is complete when the fluid reservoir bag is empty. The fluid reservoir bag can be viewed through the windows in the plastic case.*
7. **Can the pump be used on patients with latex sensitivity?** *There is no latex in the fluid pathway or in the external components, and therefore, is safe for patients with latex sensitivity.*
8. **How should the patient carry the Pain Care 2000^{TM} ?** *The Pain Care 2000^{TM} can be attached to a belt, waistband, brace, or sling by the metal spring clip that is part of the case.*
9. **How do I remove air from the Pain Care 2000^{TM} ?** *Prior to dispensing medication through the catheter, you need to prime the Pain Care 2000^{TM} by depressing the button completely prior with the catheter disconnected. This will eliminate all air from the system.*

How durable is the Pain Care 2000^{TM} ? *The Pain Care 2000^{TM} has been extensively tested to withstand a drop from 6 feet.*

Amendment #3
K983454

17
18

hydrochloride and ropivacaine hydrochloride, have long been used for the immediate relief of pain following surgery. Drugs, such as these, have been shown to be safe and effective.[2,4,7]

Current research has shown that local administration of non-narcotic anesthetics into the operative site through a catheter following surgery, can significantly prolong the patient's post-operative pain relief. This method has been shown to be safe and effective.[1,5,6,8,10] The main advantage of post-operative infusion of local anesthetics into the surgical site is that the patient experiences extended local pain relief, thereby reducing or eliminating supplemental systemic narcotic anesthetic usage and their inherent side effects.

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The dispensing device consists of fluid reservoir bag (approximately 50 cc), a spring loading 5 cc syringe, a flow control, an in-line particulate filter, and two valves. All internal dispensing device components are connected via Luer fittings and then housed in a plastic case.

The plastic case can be attached to a belt, clothing, or post-operative brace or sling via a metal clip fastened to the case. The plastic case has an exterior button enabling the user to depress the spring loading syringe, and thus injecting the fluid that has accumulated in the spring loading syringe through the catheter and into the operative site. The flow control is between the fluid reservoir and the spring loading 5 cc syringe. The flow control permits filling of the of the spring loading syringe at a rate, not to exceed, 16 cc per hour. A one way valve is located between the standard 18 gauge epidural catheter and the spring loading 5 cc syringe. The one way valve prevents aspiration of fluids from the standard 18 gauge epidural catheter to the dispensing device . The in-line particulate filter is in-between the fluid reservoir bag and the flow control and thus prevents clogging of the flow control.

Amendment #3
K983454

4 of 9

There is a second one way Luer LOK fill port on the exterior of the case that is connected to the 50 cc fluid reservoir bag inside the case. This port permits injection of the fluid via the 60 cc syringe . The fill port also has a tethered removable cap to maintain sterility and to ensure that the proper pressure is maintained within the fluid reservoir and system. There is an outflow port that connects the dispensing device to the standard 18 gauge catheter. Fluid that has accumulated within the spring loading 5 cc syringe is injected through this port to the catheter and into the operative site by depressing the button on the case. (See Diagram 1 for complete configuration) The patient is able to dispense local anesthetic into the operative site as needed for pain relief. The design of the Pain Care 2000 permits administration of local anesthetic at a rate not to exceed 16 cc per hour. All components are provided in a sterile package.

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- **Fluid from the fluid reservoir bag is aspirated through particulate filter .**
- **Fluid that passes through the particulate filter passes through the flow control and into the 5 cc spring loading syringe.**
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- **As determined by the user's pain need, the button on the case is depressed.**
- **Plunger of 5 cc spring loading syringe is depressed via button.**
- **Fluid is injected through the one way valve, through the out port, through the catheter, and into the operative site.**
- **Flow control prevents injection of fluid back into the fluid reservoir.**
- **Cycle repeats.**
- **Patient depresses button as need for pain.**
- **Pain Care 2000 use is discontinued once fluid reservoir is empty**
- **The Pain Care 2000 will last for approximately 2-3 days of use, depending upon local analgesia duration prior to the next injection.**
- **Catheter is removed by day three.**

Amendment #3
K983454

20 5

COMMON QUESTIONS AND ANSWERS

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3. **How much medication is dispensed with each depression of the button?** *There will be 5 cc dispensed with each full depression of the button.*
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8. **How should the patient carry the Pain Care 2000^{TM} ?** *The Pain Care 2000^{TM} can be attached to a belt, waistband, brace, or sling by the metal spring clip that is part of the case.*
9. **How do I remove air from the Pain Care 2000^{TM} ?** *Prior to dispensing medication through the catheter, you need to prime the Pain Care 2000^{TM} by depressing the button completely prior with the catheter disconnected. This will eliminate all air from the system.*

How durable is the Pain Care 2000^{TM} ? *The Pain Care 2000^{TM} has been extensively tested to withstand a drop from 6 feet.*

Amendment #3
K983454

21 17

BREG

2611 Commerce Way, Vista, CA 92083-8439

FAX

Date: 12/09/98 11:47 AM

Number of pages including cover sheet: 5

To

Irene Naveau

Device Evaluation

Phone:

Fax phone: 301-480-3002

301-594-1287

From:

Kathy Barber

BREG, Inc.

Phone: 800/321-0607, ext. 219

Fax phone: 760/598-6193

REMARKS: ☐ Urgent ☒ For your review ☐ Reply ASAP ☐ Please comment

Hello, Irene,

In response to your phone call of 12/4/98, I would like to let you know that BREG, Inc. Pain Care 2000 product has been tested in the following manner:

- Drop Testing — Passed all tests
- Environmental and stress testing — Passed all tests
- AAMI Sterilization Validation/Audit — Ongoing for the life of the product
- Biocompatability Testing of Components — Passed all tests

Also, the change made in Amendment 2 on pages 4,5, and 17 which identified the syringe as a 4cc instead of a 5cc, was not correct. I will send another amendment by overnight mail this afternoon.

Best Regards,

22

K983454/A2

December 2, 1998

BY FEDERAL EXPRESS

510(k) **K983454**
PAIN CARE 2000
Amendment #2

FDA/CDRH/ODE/DMC
98 DEC 10 P1:21
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Document Mail Center
Center for Devices and Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ - 401)
9200 Corporate Blvd.
Rockville, Maryland 20850

Attn.: Irene Naveau

As the representative of Breg, Inc., Vista, CA I am supplying the following Amendment to 510(k) K983454, for the PAIN CARE 2000. This document is submitted based upon our phone conversation of November 20, 1998.

The amendment contains changes to the following pages. Two copies are included.

- **Page 4** Removed the reference to intra-articular; corrected the text to 4cc to agree with page 17
- **Page 5** Corrected the syringe size from 5cc to 4cc to match the use and labeling
- **Page 7** Moved the Intended Use paragraph up; removed the references to specific medical procedures
- **Page 11** Corrected the labeling to read 4 ml to match the intended use: added "For Single Patient Use Only" to labeling
- **Page 13** Corrected the labeling to read 4 ml to match the intended use: added "For Single Patient Use Only" to labeling
- **Page 17** Corrected the text to refer to the correct 4cc measure

Additionally, I verbally confirmed to you that the spring loading device is permanently fixed into the case.

Please direct all correspondence regarding this submission to me at the above letterhead addresses. If you have any questions which may be appropriately answered by phone, then please telephone my office at (760) 599-5719 during the hours of 7:30AM - 5:00PM, PST. Thank you for your attention to this document.

Sincerely yours,

Kathleen Barber
Vice President
QA/RA

Enclosures: 2 copies - 510(k) Amendment, **Page , 4, 5, 7, 11,13, and 17**

SK-21

BREG, Inc.
2611 Commerce Way
Vista, CA 92083
(760) 599-3000
(800) 321-0607
FAX 598-6193

ISO 9001 Quality System

23

hydrochloride and ropivacaine hydrochloride, have long been used for the immediate relief of pain following surgery. Drugs, such as these, have been shown to be safe and effective.[2,4,7]

Current research has shown that local administration of non-narcotic anesthetics into the operative site through a catheter following surgery, can significantly prolong the patient's post-operative pain relief. This method has been shown to be safe and effective.[1,5,6,8,10] The main advantage of post-operative infusion of local anesthetics into the surgical site is that the patient experiences extended local pain relief, thereby reducing or eliminating supplemental systemic narcotic anesthetic usage and their inherent side effects.

BREG's new Pain Care 2000 is a device designed to provide patient controlled intermittent infusion of a local anesthetic into an operative site for the post-operative management of pain. It is substantially equivalent to the I-Flow PainBuster and the Sgarlato SurgiPEACE. The features are compared in Table II with promotional materials in Attachement 4. The noted Bibliography and scientific research noted are included in Attachment 5.

8. DESCRIPTION

BREG's Pain Care 2000 consists of a dispensing device that is connected via a Luer LOK connector to a standard 18 gauge epidural catheter. Included is a standard 18 gauge intravenous (IV) catheter insertion needle to assist in insertion of the standard 18 gauge epidural catheter into the operative site. A 60 cc syringe is also supplied to aid in filling the dispensing device with fluid (appropriate local anesthetic recommended by a licensed physician).

The dispensing device consists of fluid reservoir bag (approximately 50 cc), a spring loading 4 cc syringe, a flow control, an in-line particulate filter, and two valves. All internal dispensing device components are connected via Luer fittings and then housed in a plastic case.

The plastic case can be attached to a belt, clothing, or post-operative brace or sling via a metal clip fastened to the case. The plastic case has an exterior button enabling the user to depress the spring loading syringe, and thus injecting the fluid that has accumulated in the spring loading syringe through the catheter and into the operative site. The flow control is between the fluid reservoir and the spring loading 4 cc syringe. The flow control permits filling of the of the spring loading syringe at a rate, not to exceed, 16 cc per hour. A one way valve is located between the standard 18 gauge epidural catheter and the spring loading 4 cc syringe. The one way valve prevents aspiration of fluids from the standard 18 gauge epidural catheter to the dispensing device . The in-line particulate filter is in-between the fluid reservoir bag and the flow control and thus prevents clogging of the flow control.

There is a second one way Luer LOK fill port on the exterior of the case that is connected to the 50 cc fluid reservoir bag inside the case. This port permits injection of the fluid via the 60 cc syringe . The fill port also has a tethered removable cap to maintain sterility and to ensure that the proper pressure is maintained within the fluid reservoir and system. There is an outflow port that connects the dispensing device to the standard 18 gauge catheter. Fluid that has accumulated within the spring loading 4 cc syringe is injected through this port to the catheter and into the operative site by depressing the button on the case. (See Diagram 1 for complete configuration) The patient is able to dispense local anesthetic into the operative site as needed for pain relief. The design of the Pain Care 2000 permits administration of local anesthetic at a rate not to exceed 16 cc per hour. All components are provided in a sterile package.

MECHANICAL FUNCTION

- Fluid reservoir bag filled with fluid through the fill port.
- Fill port capped.
- Button is depressed (which depressed the spring loading 4 cc syringe) to prime system.
- Standard 18 gauge epidural catheter is connected to outflow port via Luer fitting.
- Spring loading 4 cc syringe creates an aspirating vacuum within the system (The spring that is attached to the syringe continually draws out the plunger of the syringe until maximum capacity is reached).
- Fluid from the fluid reservoir bag is aspirated through particulate filter .
- Fluid that passes through the particulate filter passes through the flow control and into the 4 cc spring loading syringe.
- The one way valve between 4 cc spring loading syringe and catheter prevents aspiration of fluids from the standard 18 gauge epidural catheter back to the syringe.
- As determined by the user's pain need, the button on the case is depressed.
- Plunger of 4 cc spring loading syringe is depressed via button.
- Fluid is injected through the one way valve, through the out port, through the catheter, and into the operative site.
- Flow control prevents injection of fluid back into the fluid reservoir.
- Cycle repeats.
- Patient depresses button as need for pain.
- Pain Care 2000 use is discontinued once fluid reservoir is empty
- The Pain Care 2000 will last for approximately 2-3 days of use, depending upon local analgesia duration prior to the next injection.
- Catheter is removed by day three.

STATEMENT OF INDICATIONS FOR USE

Intended Use

BREG's Pain Care 2000 is intended to provide patient controlled intermittent infusion of a local anesthetic into an intra-operative site for the post-operative management of pain. BREG's Pain Care 2000 provides a delivery mechanism of local anesthetic maintenance doses in order to sustain pain relief that is initially established by the bolus of local anesthetic that is injected intra-operatively (loading dose).

BREG

Breg, Inc., 2611 Commerce Way, Vista, CA 92083 U.S.A.

PART NO. XXXXX
CONTENTS / INHALT / CONTENU / CONTENIDO: 1

PAIN CARE™ 2000

Patient Controlled Local Anesthetic Infusion Device

50 ml Volume • 4 ml Volume per Dose

For Single Patient Use Only

STERILE

CONTENTS:
1 each - 50 ml Vol., 4 ml Infusion Device
1 each - 18 GA I.V. Catheter Needle
1 each - 18 GA I.V. Epidural Catheter Set
1 each - 16 GA Tube Extension Set
1 each - 60 cc Syringe

SEE DIRECTIONS FOR USE. CAUTION: FEDERAL LAW (U.S.A.) RESTRICTS THIS DEVICE TO SALE BY OR ON THE ORDER OF A HEALTHCARE PROFESSIONAL

E/U Authorized Representative
MDSS
Hauptster. 39
Wennigsen, Germany

CE
0123

PATENT PENDING

To Reorder Call:
(800) 321-0607

Lot # 700102000

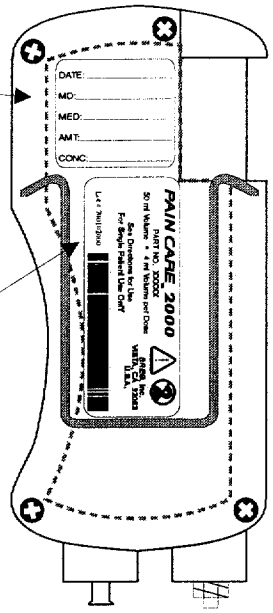
4.00"

6.00"

DATE:
MD:
MED:
AMT:
CONC:

1.13"

1.25"



PAIN CARE™ 2000
PART NO. XXXXX
50 ml Volume • 4 ml Volume per Dose
See Directions for Use
For Single Patient Use Only

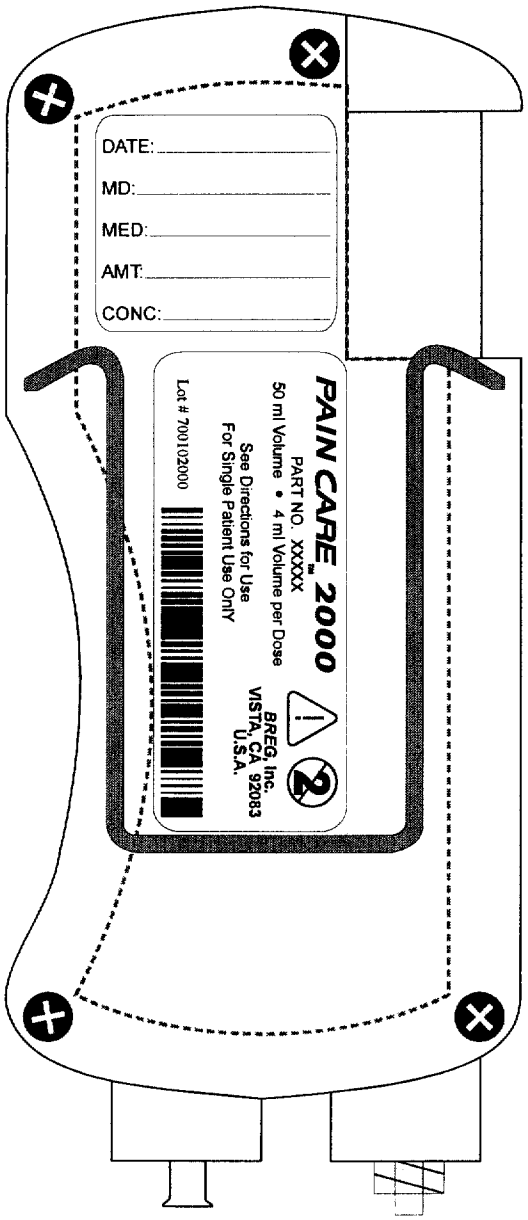
BREG, Inc.
VISTA, CA 92083
U.S.A.

Lot # 700102000

1.00"

2.50"

27 11


DATE:
MD:
MED:
AMT:
CONC:
PAIN CARE™ 2000
PART NO. XXXXX
50 ml Volume • 4 ml Volume per Dose
See Directions for Use
For Single Patient Use Only
Lot # 700102000
BREG, Inc.
VISTA, CA 92083
U.S.A.

COMMON QUESTIONS AND ANSWERS

1. **How does the Pain Care 2000^{TM} work?** *The Pain Care 2000^{TM} consists of a spring loading syringe that distracts the plunger in the 4 cc syringe. This creates a vacuum in the system. The vacuum cause the fluid from the fluid reservoir bag to pass through a flow control and into the 4 cc syringe. When the patient starts to experience pain, he/she depresses a button on the case of the Pain Care 2000TM that in-turn depresses the plunger of the 4 cc syringe. The local analgesic is then dispensed through the epidural catheter and into the affected surgical site.*
2. **How much medication does the device hold?** *The fluid reservoir bag holds approximately 50 cc of fluid.*
3. **How much medication is dispensed with each depression of the button?** *There will be 4 cc dispensed with each full depression of the button.*
4. **How long with the Pain Care 2000^{TM} run for?** *The length of time that the Pain Care 2000^{TM} will run for depends upon how often the user injects the 4 cc bolus through the catheter and into the operative site. Typically, the device will last for 2-3 days.*
5. **What is the filter size?** *The particulate filter is 1.2 microns. The air eliminating filter is 0.02 microns.*
6. **How can I tell when the pump is empty?** *Infusion is complete when the fluid reservoir bag is empty. The fluid reservoir bag can be viewed through the windows in the plastic case.*
7. **Can the pump be used on patients with latex sensitivity?** *There is no latex in the fluid pathway or in the external components, and therefore, is safe for patients with latex sensitivity.*
8. **How should the patient carry the Pain Care 2000^{TM} ?** *The Pain Care 2000^{TM} can be attached to a belt, waistband, brace, or sling by the metal spring clip that is part of the case.*
9. **How do I remove air from the Pain Care 2000^{TM} ?** *Prior to dispensing medication through the catheter, you need to prime the Pain Care 2000^{TM} by depressing the button completely prior with the catheter disconnected. This will eliminate all air from the system.*
10. **How durable is the Pain Care 2000^{TM} ?** *The Pain Care 2000^{TM} has been extensively tested to withstand a drop from 6 feet.*

DATE: November 19, 1998

MEMORANDUM OF TELEPHONE CONVERSATION

Between: Irene Naveau, Nurse Consultant
DDIG/GHDB, HFZ-480

Hung Trinh, Biomedical Engineer
DDIGD.GHDB, HFZ-480

And: Ms. Kathleen Barber
Vice President
QA/RA
Breg, Inc.

Hung and I initiated a telephone conversation with Ms. Barber to discuss, primarily, the indication for use for the Pain Care 2000 infusion pump. We explained to her that we had been clearing this type of pump for general surgical use. Ms. Barber's comparison table indicated that the indications for the Pain Care 2000 were similar to the indications for I-Flow Corporation's PainBuster, K980558. We have, however, not cleared the PainBuster for orthopedic surgical procedures, therefore, we suggested that the indications for orthopedic procedures be removed from the Indications for Use Statement. We also suggested that any reference to intra-articular and orthopedic procedures be deleted from this document. She agreed to do this.

The labeling included an international icon for single use, however we suggested that a statement, For Single Use Only, be included in the label.

There is some confusion regarding the amount of solution/medication which would be infused with each dose. The label on page 11, Attachment #1, states that there is 4ml volume per dose, while the label on page 13 states: 3ml (max) per hour. Again, there are statements, on page 17 in the questions and answers format that refer to 3ml as the volume. We suggested that this be clarified and that volume amounts be consistent in the label and on the device itself.

Page 4 of Amendment #1 states that the flow control permits filling of the spring loading syringe at a rate not to exceed 16cc per hour; Page 17 includes an answer statement that the syringe fills at a rate not to exceed 3cc per hour. We asked that she clarify these statements.

Ms. Barber was in agreement with our suggestions, and will forward the additional information.

Irene Naveau

Irene Naveau

BREG

K983454/A1

BY FEDERAL EXPRESS

October 10, 1998

Document Mail Center
Center for Devices and Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ - 401)
9200 Corporate Blvd.
Rockville, Maryland 20850

510(k) K983454
PAIN CARE 2000
Amendment #1

Attn.: Document Clerk

As the representative of Breg, Inc., Vista, CA I am supplying the following Amendment to 510(k) K983454, for the PAIN CARE 2000. This document is submitted to update labeling and correct reference errors in the original submission.

Please remove the following pages from the original submission and replace them with those included with this amendment. Two copies are included.

- **Page 2, 4, 5, 10, 11,13, and 17**

Please direct all correspondence regarding this submission to me at the above letterhead addresses. If you have any questions which may be appropriately answered by phone, then please telephone my office at (760) 599-5719 during the hours of 7:30AM - 5:00PM, PST. Thank you for your attention to this document.

Sincerely yours,

Kathleen Barber
Vice President
QA/RA

Enclosures: 2 copies - 510(k) Amendment, **Page 2, 4, 5, 10, 11,13, and 17**

SK-24

BREG, Inc.
2611 Commerce Way
Vista, CA 92083
(760) 599-3000
(800) 321-0607
FAX 598-6193

ISO 9001

AMENDMENT NOTIFICATION FOR

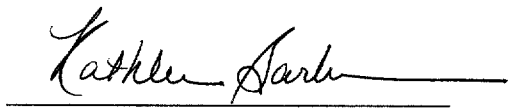
510(k) K983454

PAIN CARE 2000

Made by

BREG, INC.
2611 Commerce Way
Vista, CA 92083
Tel: (760) 599-3000
Fax (760) 598-6193

Document submitted by the official correspondent of
BREG, Inc.



Kathleen Barber
Vice President of Regulatory Affairs
BREG, Inc.

October 12, 1998

1. MANUFACTURER/FDA REGISTRATION

The manufacturer of the device is:

BREG, Inc.
2611 Commerce Way
Vista, CA 92083-8309
Tel: (760) 599-3000
Fax: (760) 598-6193

The FDA Registration Number is 2028253. Contract Sterilization will be provided by (b)(4)

2. DEVICE NAME

The common name of the device is "Infusion pump.".

The proprietary name of the product is **PAIN CARE 2000**.

3. CLASSIFICATION

Classification is found in **21 CFR 880.5725,** General Hospital Devices.

Infusion Pump:

(a) Identification. An infusion pump is a device used in a health care facility to pump fluids into a patient in a controlled manner. The device may use a piston pump, a roller pump, or a peristaltic pump and may be powered electrically or mechanically. The device may also operate using a constant force to propell the fluid through a narrow tube which determines the flow rate. The device may include means to detect a fault condition, such as air in, or blockage of the infusion line and to activate an alarm.

(b) Classification. Class II (performance standards)

Equivalent devices are listed under panel 80MEB, Pump, Infusion. A copy of similar products listed in this classification is included as Table 1.

BREG currently holds 510(k)s on the following products:

Polar Pump Model 500	**K913729**	**Polar Pad**	**K914434**
Polar Pad Sterile	**K920581**	**Polar Care Model 500/5000**	**K961855**
Polar Cub	**K942410**	**Polar Care 300**	**K963596**
Flexmate K500	**K950755**		

hydrochloride and ropivacaine hydrochloride, have long been used for the immediate relief of pain following surgery. Drugs, such as these, have been shown to be safe and effective.[2,4,7]

Current research has shown that continuous intra-articular or local administration of non-narcotic anesthetics into the operative site through a catheter following surgery, can significantly prolong the patient's post-operative pain relief. This method has been shown to be safe and effective.[1,5,6,8,10] The main advantage of post-operative infusion of local anesthetics into the surgical site is that the patient experiences extended local pain relief, thereby reducing or eliminating supplemental systemic narcotic anesthetic usage and their inherent side effects.

BREG's new Pain Care 2000 is a device designed to provide patient controlled intermittent infusion of a local anesthetic into an operative site for the post-operative management of pain. It is substantially equivalent to the I-Flow PainBuster and the Sgarlato SurgiPEACE. The features are compared in Table II with promotional materials in Attachement 4. The noted Bibliography and scientific research noted are included in Attachment 5.

8. DESCRIPTION

BREG's Pain Care 2000 consists of a dispensing device that is connected via a Luer LOK connector to a standard 18 gauge epidural catheter. Included is a standard 18 gauge intravenous (IV) catheter insertion needle to assist in insertion of the standard 18 gauge epidural catheter into the operative site. A 60 cc syringe is also supplied to aid in filling the dispensing device with fluid (appropriate local anesthetic recommended by a licensed physician).

The dispensing device consists of fluid reservoir bag (approximately 50 cc), a spring loading 5 cc syringe, a flow control, an in-line particulate filter, and two valves. All internal dispensing device components are connected via Luer fittings and then housed in a plastic case.

The plastic case can be attached to a belt, clothing, or post-operative brace or sling via a metal clip fastened to the case. The plastic case has an exterior button enabling the user to depress the spring loading syringe, and thus injecting the fluid that has accumulated in the spring loading syringe through the catheter and into the operative site. The flow control is between the fluid reservoir and the spring loading 5 cc syringe. The flow control permits filling of the of the spring loading syringe at a rate, not to exceed, 16 cc per hour. A one way valve is located between the standard 18 gauge epidural catheter and the spring loading 5 cc syringe. The one way valve prevents aspiration of fluids from the standard 18 gauge epidural catheter to the dispensing device . The in-line particulate filter is in-between the fluid reservoir bag and the flow control and thus prevents clogging of the flow control.

There is a second one way Luer LOK fill port on the exterior of the case that is connected to the 50 cc fluid reservoir bag inside the case. This port permits injection of the fluid via the 60 cc syringe . The fill port also has a tethered removable cap to maintain sterility and to ensure that the proper pressure is maintained within the fluid reservoir and system. There is an outflow port that connects the dispensing device to the standard 18 gauge catheter. Fluid that has accumulated within the spring loading 5 cc syringe is injected through this port to the catheter and into the operative site by depressing the button on the case. (See Diagram 1 for complete configuration) The patient is able to dispense local anesthetic into the operative site as needed for pain relief. The design of the Pain Care 2000 permits administration of local anesthetic at a rate not to exceed 16 cc per hour. All components are provided in a sterile package.

MECHANICAL FUNCTION

- Fluid reservoir bag filled with fluid through the fill port.
- Fill port capped.
- Button is depressed (which depressed the spring loading 5 cc syringe) to prime system.
- Standard 18 gauge epidural catheter is connected to outflow port via Luer fitting.
- Spring loading 5 cc syringe creates an aspirating vacuum within the system (The spring that is attached to the syringe continually draws out the plunger of the syringe until maximum capacity is reached).
- Fluid from the fluid reservoir bag is aspirated through particulate filter .
- Fluid that passes through the particulate filter passes through the flow control and into the 5 cc spring loading syringe.
- The one way valve between 5 cc spring loading syringe and catheter prevents aspiration of fluids from the standard 18 gauge epidural catheter back to the syringe.
- As determined by the user's pain need, the button on the case is depressed.
- Plunger of 5 cc spring loading syringe is depressed via button.
- Fluid is injected through the one way valve, through the out port, through the catheter, and into the operative site.
- Flow control prevents injection of fluid back into the fluid reservoir.
- Cycle repeats.
- Patient depresses button as need for pain.
- Pain Care 2000 use is discontinued once fluid reservoir is empty
- The Pain Care 2000 will last for approximately 2-3 days of use, depending upon local analgesia duration prior to the next injection.
- Catheter is removed by day three.

DIAGRAM 1

(b)(4)

#	DESCRIPTION	MATERIAL
1	(b)(4)	
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(b)(4)

ATTACHMENT 1

CONTENTS / INHALT / CONTENU / CONTENIDO: 1

BREG

PRODUCT NO. 01400

Breg, Inc., 2611 Commerce Way, Vista, CA 92083 U.S.A.

PAIN CARE™ 2000

Patient Controlled Local Anesthetic Infusion Device

50 ml Volume • 4 ml Volume per Dose

STERILE

CONTENTS:
1 each - 50 ml Vol., 4 ml Infusion Device
1 each - 18 GA I.V. Catheter Needle
1 each - 18 GA I.V. Epidural Catheter Set
1 each - 60 cc Syringe

SEE DIRECTIONS FOR USE. CAUTION: FEDERAL LAW (U.S.A.) RESTRICTS THIS DEVICE TO SALE BY OR ON THE ORDER OF A HEALTHCARE PROFESSIONAL

Lot #: 70011400

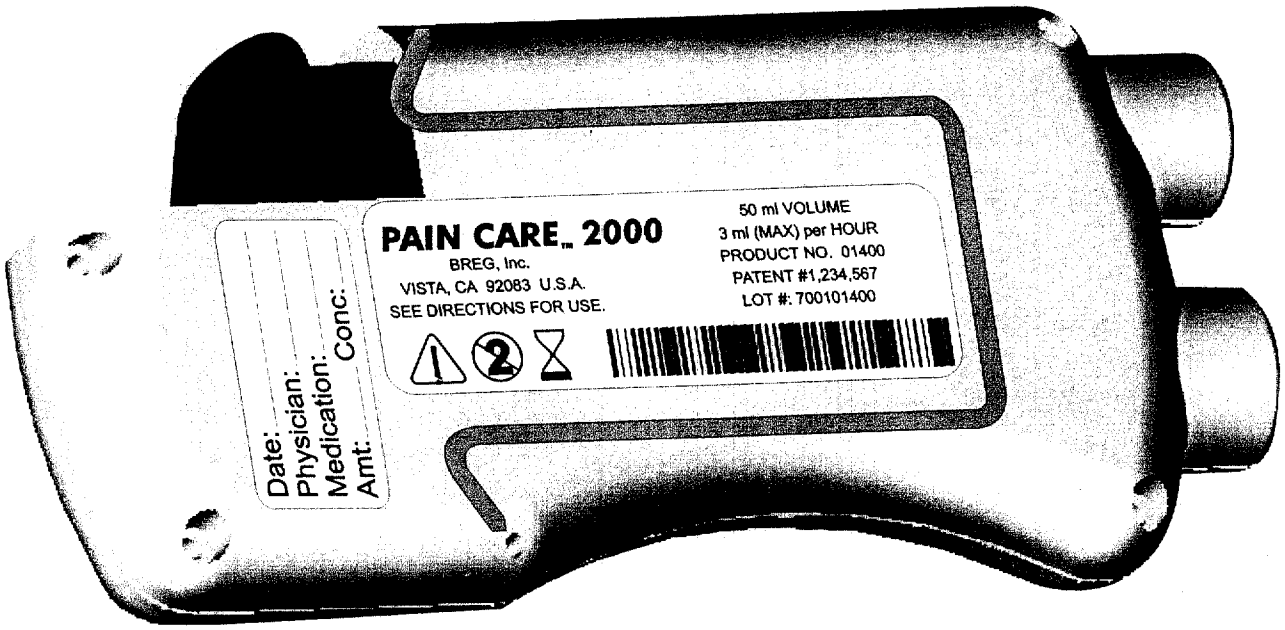
To Reorder Call:
(800) 321-0607

PATENT PENDING

3.75"

5.50"

Package Labeling


PAIN CARE™ 2000
BREG, Inc.
VISTA, CA 92083 U.S.A.
SEE DIRECTIONS FOR USE.
50 ml VOLUME
3 ml (MAX) per HOUR
PRODUCT NO. 01400
PATENT #1,234,567
LOT #: 700101400
Date:
Physician:
Medication:
Conc:
Amt:


BREG
0
1
2
3
4
PAIN CARE™ 2000

COMMON QUESTIONS AND ANSWERS

1. **How does the Pain Care 2000^{TM} work? The Pain Care 2000^{TM}** *consists of a spring loading syringe that distracts the plunger in the 5 cc syringe. This creates a vacuum in the system. The vacuum cause the fluid from the fluid reservoir bag to pass through a flow control and into the 5 cc syringe. The syringe fills at a rate not to exceed 3 cc per hour. When the patient starts to experience pain, he/she depresses a button on the case of the Pain Care 2000TM that in-turn depresses the plunger of the 5 cc syringe. The local analgesic is then dispensed through the epidural catheter and into the affected surgical site.*
2. **How much medication does the device hold?** *The fluid reservoir bag holds approximately 50 cc of fluid.*
3. **How much medication is dispensed with each depression of the button? Assuming that the syringe within the Pain Care 2000^{TM}** *has had enough time to completely fill (1 hour), there will be 3 cc dispensed with each full depression of the button.*
4. **How long with the Pain Care 2000^{TM} run for? The length of time that the Pain Care 2000^{TM}** *will run for depends upon how often the user injects the 3 cc bolus through the catheter and into the operative site. Typically, the device will last for 2-3 days.*
5. **What is the filter size?** *The particulate filter is 1.2 microns. The air eliminating filter is 0.02 microns.*
6. **How can I tell when the pump is empty?** *Infusion is complete when the fluid reservoir bag is empty. The fluid reservoir bag can be viewed through the windows in the plastic case.*
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10. **How durable is the Pain Care 2000^{TM} ?** *The Pain Care 2000^{TM} has been extensively tested to withstand a drop from 6 feet.*

DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, Maryland 20850

October 01, 1998

BREG, INC.
2611 COMMERCE WAY
VISTA, CA 92083
ATTN: KATHLEEN BARBER

510(k) Number: K983454
Received: 30-SEP-1998
Product: PAIN CARE 2000

The Center for Devices and Radiological Health (CDRH), Office of Device Evaluation (ODE), has received the Premarket Notification you submitted in accordance with Section 510(k) of the Federal Food, Drug, and Cosmetic Act (Act) for the above referenced product. We have assigned your submission a unique 510(k) number that is cited above. Please refer prominently to this 510(k) number in any future correspondence that relates to this submission. We will notify you when the processing of your premarket notification has been completed or if any additional information is required. YOU MAY NOT PLACE THIS DEVICE INTO COMMERCIAL DISTRIBUTION UNTIL YOU RECEIVE A LETTER FROM FDA ALLOWING YOU TO DO SO.

On January 1, 1996, FDA began requiring that all 510(k) submitters provide on a separate page and clearly marked "Indication For Use" the indication for use of their device. If you have not included this information on a separate page in your submission, please complete the attached and amend your 510(k) as soon as possible. Also if you have not included your 510(k) Summary or 510(k) Statement, or your Truthful and Accurate Statement, please do so as soon as possible. There may be other regulations or requirements affecting your device such as Postmarket Surveillance (Section 522(a)(1) of the Act) and the Device Tracking regulation (21 CFR Part 821). Please contact the Division of Small Manufacturers Assistance (DSMA) at the telephone or web site below for more information.

Please remember that all correspondence concerning your submission MUST be sent to the Document Mail Center (HFZ-401) at the above letterhead address. Correspondence sent to any address other than the Document Mail Center will not be considered as part of your official premarket notification submission. Because of equipment and personnel limitations, we cannot accept telefaxed material as part of your official premarket notification submission, unless specifically requested of you by an FDA official. Any telefaxed material must be followed by a hard copy to the Document Mail Center (HFZ-401).

You should be familiar with the manual entitled, "Premarket Notification 510(k) Regulatory Requirements for Medical Devices" available from DSMA. If you have other procedural or policy questions, or want information on how to check on the status of your submission (after 90 days from the receipt date), please contact DSMA at (301) 443-6597 or its toll-free number (800) 638-2041, or at their Internet address http://www.fda.gov/cdrh/dsmamain.html or me at (301) 594-1190.

Sincerely yours,

Marjorie Shulman
Consumer Safety Officer
Premarket Notification Staff
Office of Device Evaluation
Center for Devices and Radiological Health

40

K983454

BREG

2611 Commerce Way
Vista, CA 92083

BY FEDERAL EXPRESS

September 29, 1998

Document Mail Center(HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Boulevard
Rockville, MD 20850

Attn.: Document Clerk

As the representative of Breg, Inc., Vista, CA and as required by section 510(k) of the Food, Drug and Cosmetics Act as Amended, 1976 and the Safe Medical Devices Act of 1990, I hereby submit a 510(k) Premarket Notification (enclosed) indicating the intention of Breg, Inc. to manufacture and introduce into commercial distribution a medical device named the **PAIN CARE 2000**. The information required by 21 CFR807.87 is included in the enclosed 510(k) notification.

I believe this submission is subject to review and approval of the ODE, Division of General and Restorative Devices, Restorative Devices Branch.

Please direct all correspondence regarding this submission to me at the letterhead address. If you have any questions which may be appropriately answered by phone, then please telephone my office at (760) 599-5719, during the hours of 7:30AM - 5:00PM, PST. Thank you for your attention to this document.

Sincerely yours,

Kathleen Barber
Vice President of Regulatory Affairs

HO
II

Enclosures: 2 copies of 510(k) with cover letter attached

4K.24

41

510(k) NOTIFICATION

for the

PAIN CARE 2000

Made by

BREG, INC.
2611 Commerce Way
Vista, CA 92083
Tel: (760) 599-3000
Fax (760) 598-6193

Document submitted by the official correspondent of
BREG, Inc.

Kathleen Barber
Vice President of Regulatory Affairs
BREG, Inc.

September 29, 1998

TABLE OF CONTENTS

1. MANUFACTURER/FDA REGISTRATION

The manufacturer of the device is:

BREG, Inc.
2611 Commerce Way
Vista, CA 92083-8309
Tel: (760) 599-3000
Fax: (760) 598-6193

The FDA Registration Number is 2028253. Contract Sterilization will be provided by (b)(4)

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The proprietary name of the product is **PAIN CARE 2000**.

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Polar Pad Sterile	**K920581**	**Polar Care Model 500/5000**	**K961855**
Polar Cub	**K942410**	**Polar Care 300**	**K963596**
Flexmate K500	**K950755**		

4. STANDARDS

There are no mandantory or voluntary standards that govern the device under Section 514. Review of the Federal Register finds no proposed or ongoing process for development of standards at this time.

The Pain Care 2000-will be manufactured under QSR as well as ISO9001:1994 standards. Sterility and biocompatability are discussed separately.

5. LABELING/USE INSTRUCTIONS

Labeling is contained as Attachment 1, while Use Instructions are Attachement 2.

6. PROMOTIONAL MATERIAL

Promotional material is being designed. BREG, Inc. intends to make the following claims regarding the benefits and features of PAIN CARE 2000 in future brochures, advertising and materials for the sales force. See Attachment 3. Promotional materials for the SE device are Attachement 4.

- Decreased need for narcotic anesthetic pain medication following surgery.
- Direct local pain relief without the side effects of narcotics.
- Patient controlled local analgesia.
- Convenient for ambulatory use.
- Decreased incidence of breakthrough pain.
- Reduced hospital stay.
- Earlier ambulation .
- Improved range of motion (ROM).
- Improved rehabilitation.
- Improved recovery.

7. SUBSTANTIAL EQUIVALENCE

Pain is a well know symptom following surgery to the bone and joints. Narcotic pain medication is routinely prescribed by physicians to control post-operative pain. Historically, post-operative narcotic pain medication is administered via intra-muscular (IM) injections of systemic anesthetics, intravenous (IV) administration of patient controlled analgesia (PCA), and/or orally. The main side effects of narcotic pain medication, regardless of the mode of administration, is nausea, vomiting, constipation, respiratory depression, excessive sedation, and with extended use, physical addiction. Recently, a newer and more progressive method of post-operative pain management has gained popularity: continuous wound site infusion of non-narcotic anesthetics.[1,6,9,10] Intra-operative injection of local non-narcotic anesthetics, such as bupivacaine

hydrochloride and ropivacaine hydrochloride, have long been used for the immediate relief of pain following surgery. Drugs, such as these, have been shown to be safe and effective.[2,4,7]

Current research has shown that continuous intra-articular or local administration of non-narcotic anesthetics into the operative site through a catheter following surgery, can significantly prolong the patient's post-operative pain relief. This method has been shown to be safe and effective.[1,5,6,8,10] The main advantage of post-operative infusion of local anesthetics into the surgical site is that the patient experiences extended local pain relief, thereby reducing or eliminating supplemental systemic narcotic anesthetic usage and their inherent side effects.

BREG's new Pain Care 2000 is a device designed to provide patient controlled intermittent infusion of a local anesthetic into an operative site for the post-operative management of pain. It is substantially equivalent to the I-Flow PainBuster and the Sgarlato SurgiPEACE. The features are compared in Table II with promotional materials in Attachement 4. The noted Bibliography and scientific research noted are included in Attachment 5.

8. DESCRIPTION

BREG's Pain Care 2000 consists of a dispensing device that is connected via a Luer LOK connector to a standard 18 gauge epidural catheter. Included is a standard 18 gauge intravenous (IV) catheter insertion needle to assist in insertion of the standard 18 gauge epidural catheter into the operative site. A 60 cc syringe is also supplied to aid in filling the dispensing device with fluid (appropriate local anesthetic recommended by a licensed physician).

The dispensing device consists of fluid reservoir bag (approximately 50 cc), a spring loading 5 cc syringe, a flow restrictor, a in-line particulate filter, and two valves. All internal dispensing device components are connected via Luer fittings and then housed in a plastic case.

The plastic case can be attached to a belt, clothing, or post-operative brace or sling via a metal clip fastened to the case. The plastic case has an exterior button enabling the user to depress the spring loading syringe, and thus injecting the fluid that has accumulated in the spring loading syringe through the catheter and into the operative site. The flow restrictor is between the fluid reservoir and the spring loading 5 cc syringe. The flow restrictor permits filling of the of the spring loading syringe at a rate, not to exceed, 16 cc per hour. A one way valve is located between the standard 18 gauge epidural catheter and the spring loading 5 cc syringe. The one way valve prevents aspiration of fluids from the standard 18 gauge epidural catheter to the dispensing device . The in-line particulate filter is in-between the fluid reservoir bag and the flow restrictor and thus prevents clogging of the flow restrictor.

There is a second one way Luer LOK fill port on the exterior of the case that is connected to the 50 cc fluid reservoir bag inside the case. This port permits injection of the fluid via the 60 cc syringe . The fill port also has a tethered removable cap to maintain sterility and to ensure that the proper pressure is maintained within the fluid reservoir and system. There is an outflow port that connects the dispensing device to the standard 18 gauge catheter. Fluid that has accumulated within the spring loading 5 cc syringe is injected through this port to the catheter and into the operative site by depressing the button on the case. (See Diagram 1 for complete configuration) The patient is able to dispense local anesthetic into the operative site as needed for pain relief. The design of the Pain Care 2000 permits administration of local anesthetic at a rate not to exceed 16 cc per hour. All components are provided in a sterile package.

MECHANICAL FUNCTION

- Fluid reservoir bag filled with fluid through the fill port.
- Fill port capped.
- Button is depressed (which depressed the spring loading 5 cc syringe) to prime system.
- Standard 18 gauge epidural catheter is connected to outflow port via Luer fitting.
- Spring loading 5 cc syringe creates an aspirating vacuum within the system (The spring that is attached to the syringe continually draws out the plunger of the syringe until maximum capacity is reached).
- Fluid from the fluid reservoir bag is aspirated through particulate filter .
- Fluid that passes through the particulate filter passes through the flow restrictor.
- Fluid that passes through the flow restrictor passes into the 5 cc spring loading syringe.
- The one way valve between 5 cc spring loading syringe and catheter prevents aspiration of fluids from the standard 18 gauge epidural catheter back to the syringe.
- As determined by the user's pain need, the button on the case is depressed.
- Plunger of 5 cc spring loading syringe is depressed via button.
- Fluid is injected through the one way valve, through the out port, through the catheter, and into the operative site.
- Flow restrictor prevents injection of fluid back into the fluid reservoir.
- Cycle repeats.
- Patient depresses button as need for pain.
- Pain Care 2000 use is discontinued once fluid reservoir is empty
- The Pain Care 2000 will last for approximately 2-3 days of use, depending upon local analgesia duration prior to the next injection.
- Catheter is removed by day three.

9.0 BIOCOMPATABILITY:

The components of the **PAIN CARE 2000** are listed on Diagram 1. These materials are identical to those used in the predicate device, the I-Flow PainBuster and are processed and sterilized in the same manner. All materials conform to the ISO-10993 biomaterial testing program for medical devices.

10.0 STERILITY ASSURANCE:

The type of sterilization is (b)(4) gamma radiation performed by (b)(4) (b)(4) to acheive a sterility assurance level of 10 to the -6. This process is equivalent to the I-Flow predicate device

The sterility validation methodology used to initially establish our dose requirements and our ongoing quarterly audits will comply with the following specifications: (1) USP Section 71; (2) ISO-11135; and (3) ANSI/AAMI Method 1.

Parts will be packed into industry recognized sterilazation pouches designed for radiation applications which are heat sealed prior to sterilization.

11.0 KITS, PACKS or TRAYS

The **Pain Care 2000** system is packed as a kit which contains the following elements:

- **1 Infusion Device**
- **1 18 GA IV Catheter Needle**
- **2 18 GA IV Epidural Catheter Set(s)**
- **1 Luer Y-adapter**
- **1 60cc Syringe**

The Infusion Device is the subject of this 510(k) submission and is discussed in detail.

For the other elements above, I certify that these devices have been found to be substanially equivalent through the premarket notification process for the uses for which the kit is to be intended. I further certify that these devices/components are not purchased in "bulk", but are purchased in finished form, i.e. they are packaged, labeled, etc., consistent with their premarket notification status.

STATEMENT OF INDICATIONS FOR USE

Purpose

The purpose of BREG's Pain Care 2000 is to provide a delivery mechanism of local anesthetic maintenance doses in order to sustain pain relief that is initially established by the bolus of local anesthetic that is injected intra-operatively (loading dose).

Intended Use

BREG's Pain Care 2000 is intended to provide patient controlled intermittent infusion of a local anesthetic into an intra-operative site for the post-operative management of pain.

Applications

Orthopaedic surgical procedures including:
Arthroplasty procedures.
Arthroscopic procedures.
Reconstructive procedures.
Open reduction and internal fixation (ORIF) of fractures.
General open procedures.

TABLE I

SEARCH RESULTS

12 records were found in the **Product Classification Database** for **Device:** *Pump, Infusion*

#	Device Name	Regulation Number
1	PUMP, INFUSION OR SYRINGE, EXTRA-LUMINAL	876.5820
2	PUMP, INFUSION	880.5725
3	PUMP, INFUSION, IMPLANTED, PROGRAMMABLE	880.5725
4	PUMP, INFUSION, ANALYTICAL SAMPLING	880.5725
5	PUMP, INFUSION, INSULIN	880.5725
6	PUMP, INFUSION, ENTERAL	880.5725
7	PUMP, INFUSION, IMPLANTED, NON-PROGRAMMABLE	880.5725
8	PUMP, INFUSION, PCA	880.5725
9	PUMP, INFUSION, ELASTOMERIC	880.5725
10	PUMP, INFUSION, GALLSTONE DISSOLUTION	880.5725
11	PUMP, INFUSION, OPHTHALMIC	880.5725
12	ACCESSORIES, PUMP, INFUSION	880.5725

RETURN TO SEARCH | CDRH HOME PAGE | FDA HOME PAGE | SEND COMMENTS

(Database Updated September 8, 1998)

8 50

Comparative Analysis of Competitive Local Analgesic Infusion Pumps

Device Name	Manufacturer	Type	Capacity	Rate	Duration	Indications for Use	Contraindications	Performance
Pain Care 2000	Breg, Inc.	Patient Controlled, Spring Loading Syringe Injected, Flow Restrictor for Syringe Filling, Single Patient Use. Sterile	50 cc	4 cc per Injection	2-3 Days	Orthopedic procedures requiring local analgesic non-narcotic pain relief.	Not designed for epidural, subcutaneous or vascular drug delivery. Not for blood, blood products or TPN use.	Direct pain r narcotics, de pain, reduce ambulation a motion.
Pain Buster K980558	I-Flow	Continuous Flow, Elastomeric Membrane, Flow Restrictor, Single Patient Use. Sterile	100 cc	2 cc per Hour	2 Days	For orthopedic surgical procedures including: arthroscopy, arthroplasty, general open procedures. For post-operative patients requiring moderate to severe local pain relief.	Not designed for epidural, subcutaneous or vascular drug delivery. Not for blood, blood products or TPN use.	Direct pain r narcotics, de pain, reduce ambulation a motion.
SugiPEACE Pump System	Sgarlato Labs., Inc.	Continuous Flow, Compression Spring on Syringe, Flow Restrictor, Single Patient Use. Sterile	100 cc	0.5, 1, 2 cc per Hour	8, 4, 2 Days	For patients requiring slow continuous administration of local medication. System is indicated for the relief of pain in patients following surgery.	Not designed for rapid infusion of medications or intravenous infusion.	Pain treatme other forms for ambulato dependent, li stability and to Elastomer

TABLE II

51

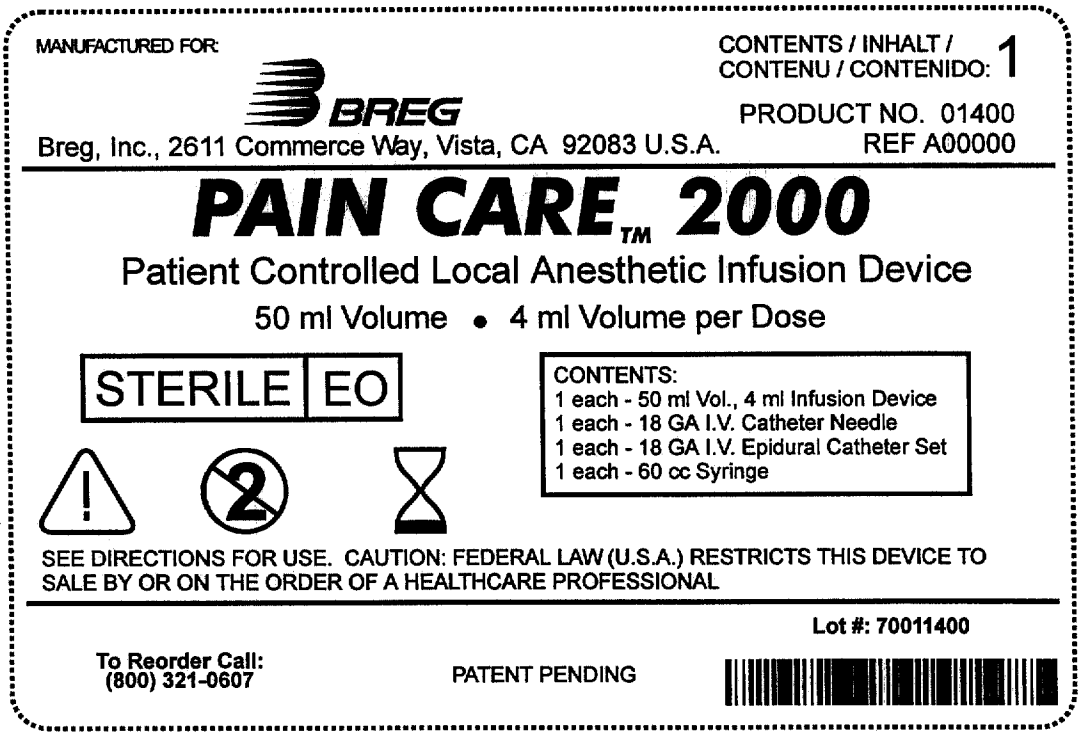
DIAGRAM 1

#	DESCRIPTION	MATERIAL
(b)(4)		

(b)(4)

(b)(4)

ATTACHMENT 1



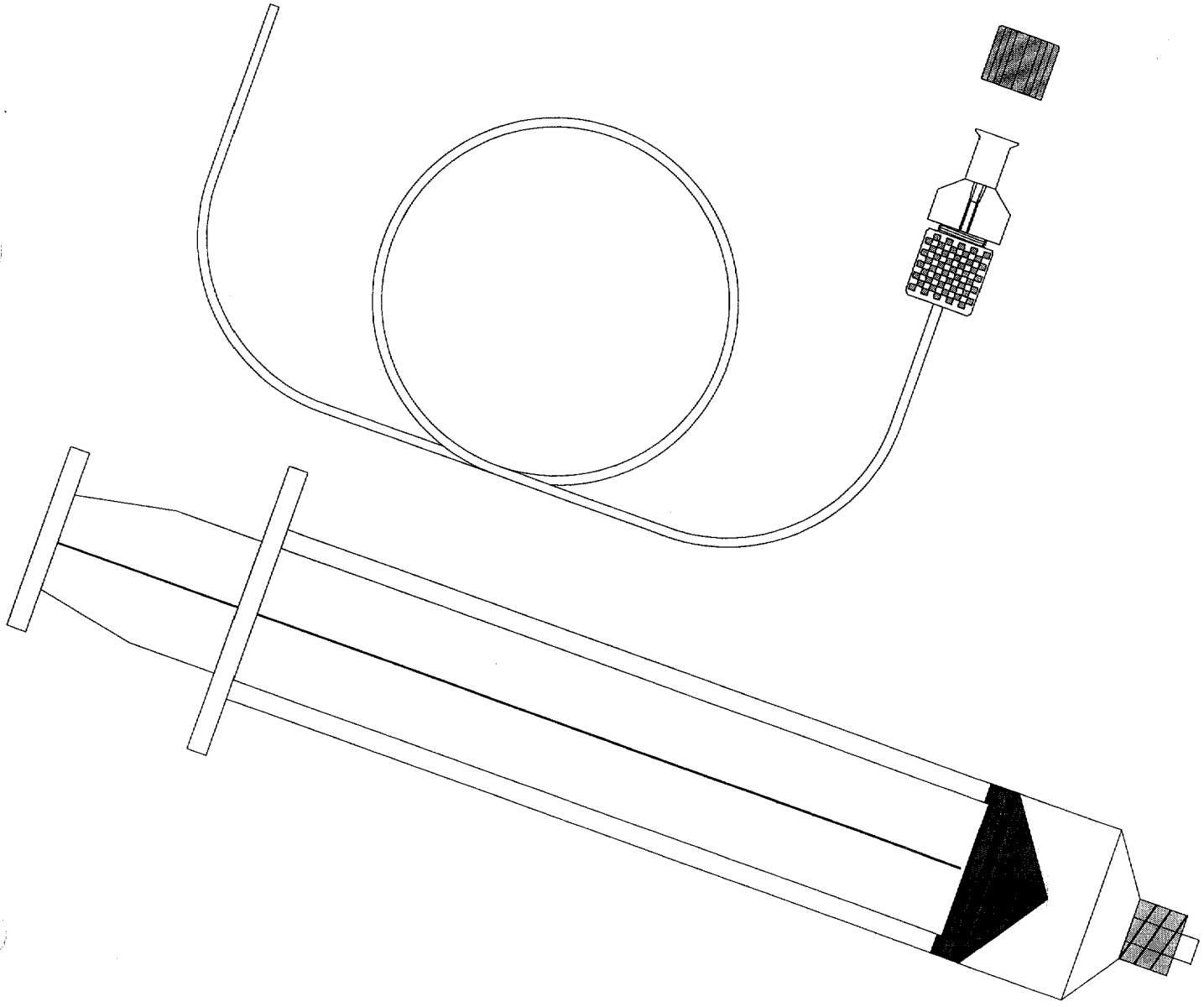
3.75"

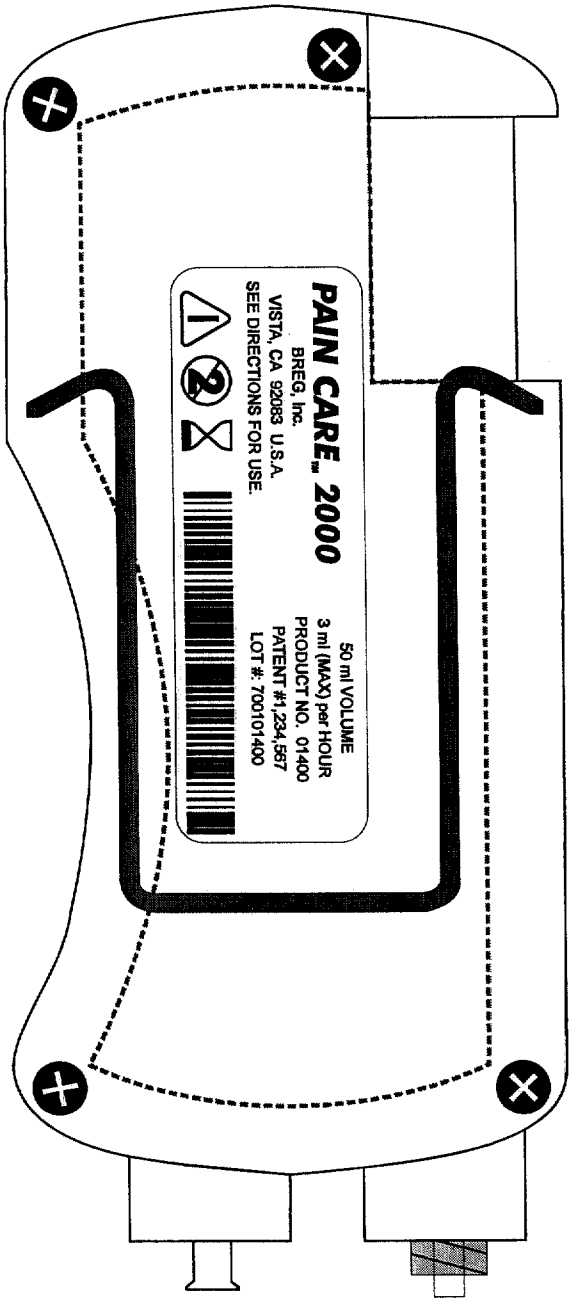
5.50"

Package
Labeling

53


OUT FLOW
PAIN CARE™ 2000
3
2
1
0
FILL PORT
BREG




PAIN CARE™ 2000
BREG, Inc.
VISTA, CA 92083 U.S.A.
SEE DIRECTIONS FOR USE.
50 ml VOLUME
3 ml (MAX) per HOUR
PRODUCT NO. 01400
PATENT #1,234,567
LOT #: 700101400

BREG **PAIN CARE™ 2000**

DIRECTIONS FOR USE

Intended Use

Breg's *Pain Care™ 2000* is intended to provide patient controlled intermittent infusion of a local anesthetic into an operative site for the post-operative management of pain.

Directions For Use

- **Use Aseptic Technique at All Times**

- **Filling the Fluid Reservoir Bag of *Pain Care™ 2000***
  1. Fill 60 cc syringe with 50 cc of local analgesic (e.g. 0.25% bupivacaine).
  2. Remove protective cap from fill port.
  3. Attach 60 cc syringe via Luer fitting to fill port.
  4. Inject 50 cc of the local anesthetic (as prescribed by the patient's physician) into fluid reservoir.
  5. Re-apply the protective cap to fill port.
  6. Depress the button on the *Pain Care™ 2000* to the prime system.

- **Placing the Catheter**
  1. Insert the 18 gauge introducer needle/insertion catheter through the skin (approximately 3-5 cm away from wound site). Then push introducer needle into the surgical site.
  2. Remove the introducer needle from the insertion catheter.
  3. Insert the marked end of the standard 18 gauge epidural catheter through the hub of the insertion catheter and into the wound site out of the bevel of the needle.
  4. Remove the insertion catheter while holding the standard 18 gauge epidural catheter tightly in place.
  5. Assure catheter placement in wound site.
  6. Cut catheter to desired length.
  7. Attach the Luer LOK catheter connector to the unmarked end of the catheter (Tighten until catheter cannot be removed from the Luer LOK catheter connector).
  8. Tape catheter securely in place.
  9. Apply appropriate dressing to catheter insertion site.
  10. The catheter "Y" adaptor *(optional)* may be used for infusion to two sites.

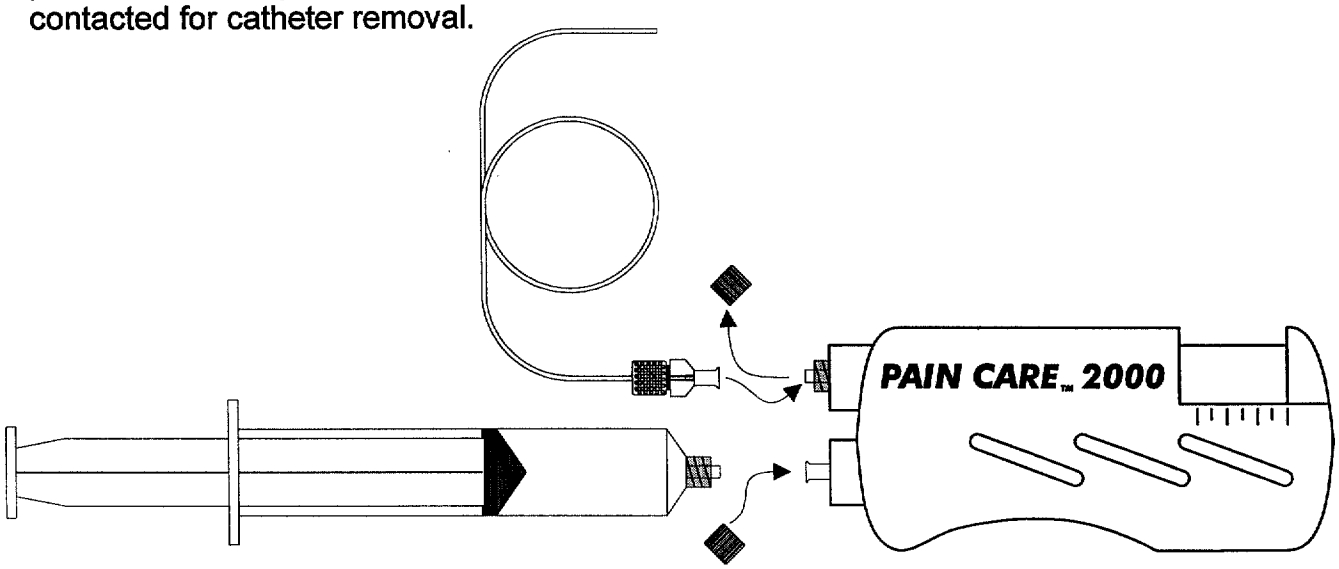
- **Attaching Catheter to *Pain Care™ 2000***
  1. Attach the Luer LOK catheter connector of the standard 18 gauge epidural catheter to the outflow port of the *Pain Care™ 2000* by twisting until secure.

- **Starting the *Pain Care™ 2000***
  1. Ensure all connections and caps are secure.
  2. Secure *Pain Care™ 2000* via metal clip to outer dressing, clothing, or brace/sling.
  3. Depress button to ensure proper flow.
  4. Depress button as needed for pain.

- **Infusion is complete when the *Pain Care™ 2000* is empty. The catheter should be removed at this time. For catheter removal, consult a licensed health care provider.**

WARNINGS

- The *Pain Care™ 2000* is designed to be applied by a licensed health care provider.
- All medication used in the *Pain Care™ 2000* is to be prescribed by a licensed physician.
- Patient education regarding proper use must be initiated by a licensed health care provider.
- Use sterile technique at all times during implantation of catheter, while connecting the catheter to the *Pain Care™ 2000* , while filling the fluid reservoir of the *Pain Care™ 2000* with the local analgesic, and upon removal of the catheter from the insertion site upon completion. If sterile technique is violated, a possible risk of infection exists.
- Disposable - Single patient use only.
- Discard/destroy after use.
- Only refill the device per physician's instructions.
- Do not re-sterilize the device
- Do not overfill fluid reservoir bag.
- Medications being used with the *Pain Care™ 2000* should be used in accordance with instructions provided from the drug manufacturer.
- If the Luer LOK catheter connector becomes disconnected from the *Pain Care™ 2000* or if the catheter becomes disconnected from the Luer LOK catheter connector after the surgical procedure is completed, do not re-connect it. A licensed health care provider must be contacted for catheter removal.



Caution
Federal (U.S.A.) law restricts this device to sale by or the order of a healthcare professional.

A PRODUCT OF

BREG

For Customer Service
Call: 1-800-321-0607

BREG, INC.
VISTA, CA 92083
U.S.A.

Patient Directions

Pain Care 2000™ Patient Instructions

The Pain Care 2000™ is a portable patient controlled infusion pump designed to deliver medication directly to the surgical site for management of pain.

How the Pain Care 2000™ Works

The Pain Care 2000™ administers local pain medication directly to the pain site via a tiny tube which is placed inside the wound by the physician during surgery. Pain relief is provided directly where needed. This is an alternative to other forms of therapy such as pain killers and narcotics taken orally which go throughout the entire body and sometimes cause side effects such as drowsiness, disorientation, nausea, constipation, and vomiting.

The Pain Care 2000™ is comprised of a dispensing device that permits you to administer pain medication as you need it. A very precise regulator is within the system to prevent injection of too much local pain medication. The device is filled by your physician with numbing pain medication at the time of surgery. A button on the Pain Care 2000™ is depressed when additional pain medication is needed. You will probably only have to depress the button every 4-6 hours or so. The rate at which medication is injected into the surgical site varies depending upon the surgery performed, individual pain tolerances, the effectiveness of pain medication used, and how much narcotic pain medication you take orally. The device should last 2-3 days. The system should remain intact for the entire duration of your therapy. Do not disconnect any part of the Pain Care 2000™ . Your therapy is completed when the fluid reservoir bag is empty. You can see this by looking through the window of the Pain Care 2000™ and into the fluid reservoir bag.

If Complications Arise

If you experience any problems with the Pain Care 2000™ unit such as leakage, the device becoming disconnected, the tube pulling out of the wound site, or if you experience discomfort or excessive pain, call your physician immediately. He/she may prescribe supplemental medication if necessary.

COMMON QUESTIONS AND ANSWERS

1. **How does the Pain Care 2000^{TM} work? The Pain Care 2000^{TM}** *consists of a spring loading syringe that distracts the plunger in the 5 cc syringe. This creates a vacuum in the system. The vacuum cause the fluid from the fluid reservoir bag to pass through a flow restrictor and into the 5 cc syringe. The syringe fills at a rate not to exceed 3 cc per hour. When the patient starts to experience pain, he/she depresses a button on the case of the Pain Care 2000TM that in-turn depresses the plunger of the 5 cc syringe. The local analgesic is then dispensed through the epidural catheter and into the affected surgical site.*
2. **How is the rate at which the dispensing syringe fills controlled?** *The 5 cc syringe filling rate is determined by a medical grade glass capillary, flow restricting orifice. The flow rate does not exceed 3 cc per hour.*
3. **How much medication does the device hold?** *The fluid reservoir bag holds approximately 50 cc of fluid.*
4. **How much medication is dispensed with each depression of the button? Assuming that the syringe within the Pain Care 2000^{TM}** *has had enough time to completely fill (1 hour), there will be 3 cc dispensed with each full depression of the button.*
5. **How long with the Pain Care 2000^{TM} run for? The length of time that the Pain Care 2000^{TM}** *will run for depends upon how often the user injects the 3 cc bolus through the catheter and into the operative site. Typically, the device will last for 2-3 days.*
6. **What is the filter size?** *The particulate filter is 1.2 microns. The air eliminating filter is 0.02 microns.*
7. **How can I tell when the pump is empty?** *Infusion is complete when the fluid reservoir bag is empty. The fluid reservoir bag can be viewed through the windows in the plastic case.*
8. **Can the pump be used on patients with latex sensitivity?** *There is no latex in the fluid pathway or in the external components, and therefore, is safe for patients with latex sensitivity.*
9. **How should the patient carry the Pain Care 2000^{TM} ?** *The Pain Care 2000^{TM} can be attached to a belt, waistband, brace, or sling by the metal spring clip that is part of the case.*
10. **How do I remove air from the Pain Care 2000^{TM} ?** *Prior to dispensing medication through the catheter, you need to prime the Pain Care 2000^{TM} by depressing the button completely prior with the catheter disconnected. This will eliminate all air from the system.*
11. **How durable is the Pain Care 2000^{TM} ?** *The Pain Care 2000^{TM} has been extensively tested to withstand a drop from 6 feet.*

12. **How will I know when to depress the button to inject the local analgesic?** *You need to press the button on the Pain Care 2000™ only when the pain starts to return. In general, when the last dose of local analgesic starts to wear off, you will experience some mild aching at the operative site. At this point, you should press the button again.*

13. **How often do I need to depress the button?** *Only depress the button when the pain starts to return. Generally, you will only have to dispense additional local analgesic every 6-8 hours.*

14. **Can the Pain Care 2000™ be re-filled again once it is empty to lengthen the duration of total pain relief?** *The Pain Care 2000™ is designed for single patient use. Consult your physician regarding increasing your total infusion duration.*

15. **What should be done if the catheter becomes detached from the Luer LOK catheter connector?** *The catheter should not be re-attached. Sterility has been broken. Risk of infection exists if the catheter is re-attached.*

Troubleshooting

The Pain Care 2000™ will not infuse medication through catheter upon depressing button.

1. Make sure the desired medication has been injected into the fluid reservoir bag via the fill port Luer LOK.
2. Make sure the Luer LOK cap has been replaced on the fill port.
3. Disconnect the catheter from the Pain Care 2000™ and prime the pump.
4. Make sure the Luer LOK catheter connector is properly connected to the Pain Care 2000™ .
5. Make sure the Luer LOK catheter connector is properly connected to the catheter.
6. Make sure the catheter is properly inserted into the operative site.
7. Make sure there are no kinks or bends in the catheter.
8. If all fails consult your physician.

Removing the Pain Care 2000*TM*

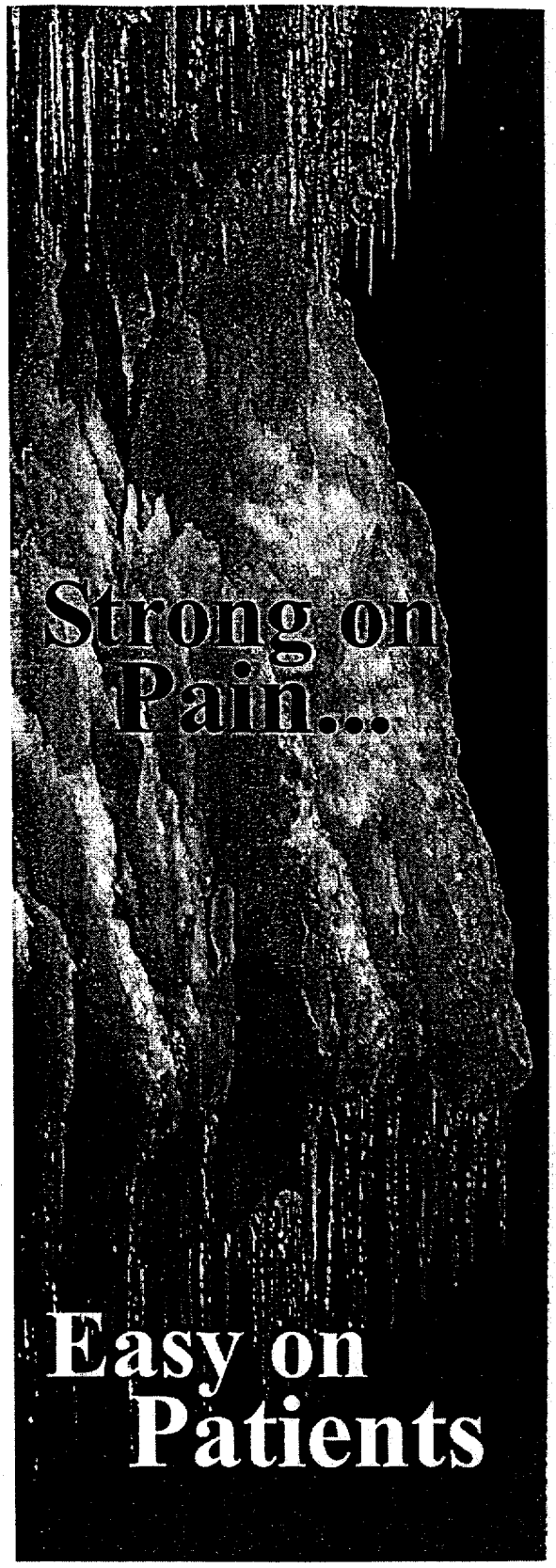
Once the Pain Care 2000™ has completely emptied (usually in 2-3 days), or per the physician's instructions, the catheter needs to be removed. Follow the instructions below.

1. Wash you hands.
2. Remove the surgical dressing and discard.
3. At this point, you will be able to see the catheter connected to the Pain Care 2000™ enter the incision. The catheter is NOT sutured in place, but simply held in place by several pieces of tape. Remove the pieces of tape and gently pull the catheter out. This should not be painful. Do NOT cut the catheter.
4. Apply the sterile 4x4 gauze pad over the tiny hole the catheter was removed from and hold slight pressure for a few minutes. A sterile bandage will be provided.
5. Do not wash the incision or put any ointment or lotion on it.
6. Apply the sterile bandage to cover the incision and tape it in place. If an arthroscopy was performed, apply Band-Aids over the 3-4 small portal incisions. Keep the bandages/bandaids dry.
7. Record the date and time that the catheter was removed.
8. If there are any questions or concerns regarding the Pain Care 2000TM , contact the attending physician.

The PainBuster System provides continuous infusion of a local anesthetic directly into the wound site.

Potential Benefits

- Direct pain relief without the side effects of narcotics
- Decreased incidence of breakthrough pain
- Reduced length of hospital stay
- Earlier ambulation and greater ROM



PainBuster™

I-FLOW®

THE FUTURE OF INFUSION TECHNOLOGY

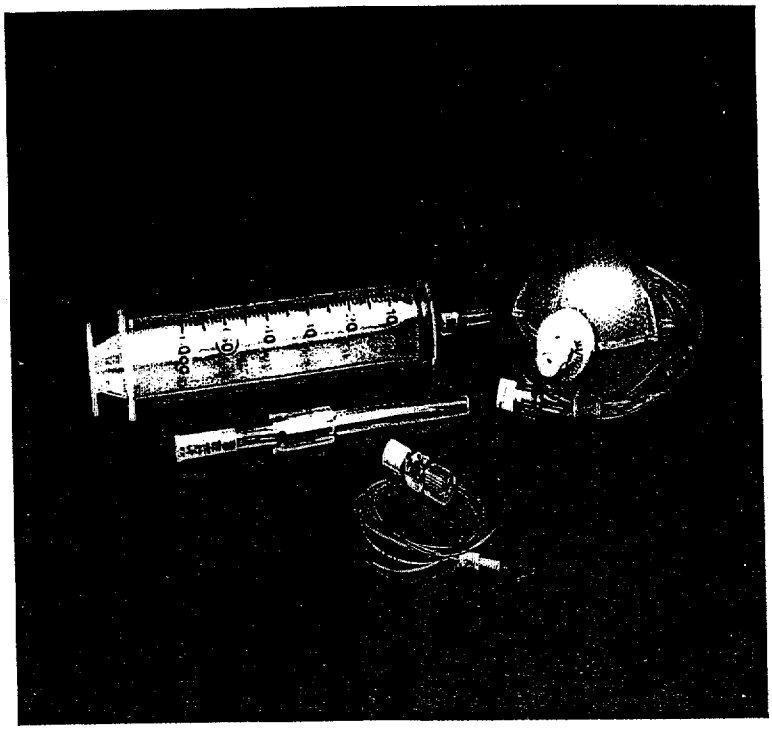
Postoperative Pain Management System

The PainBuster System provides continuous infusion of a local anesthetic directly into the wound site to alleviate the moderate to severe pain patients experience following many surgical procedures.

The PainBuster System includes an introducer needle, catheter, elastomeric infusion pump and other components for easy insertion and connection during surgery.

The infusion pump consists of a patented multi-layer elastomeric membrane, which provides positive pressure, pre-attached tubing, filter, on/off clamp and a flow restricting orifice, which controls the flow rate. This device can be filled with up to 100 mls of medication and infuses at 2 mls/hr providing a 48 hour infusion. The pump is compact and completely portable.

PainBuster System



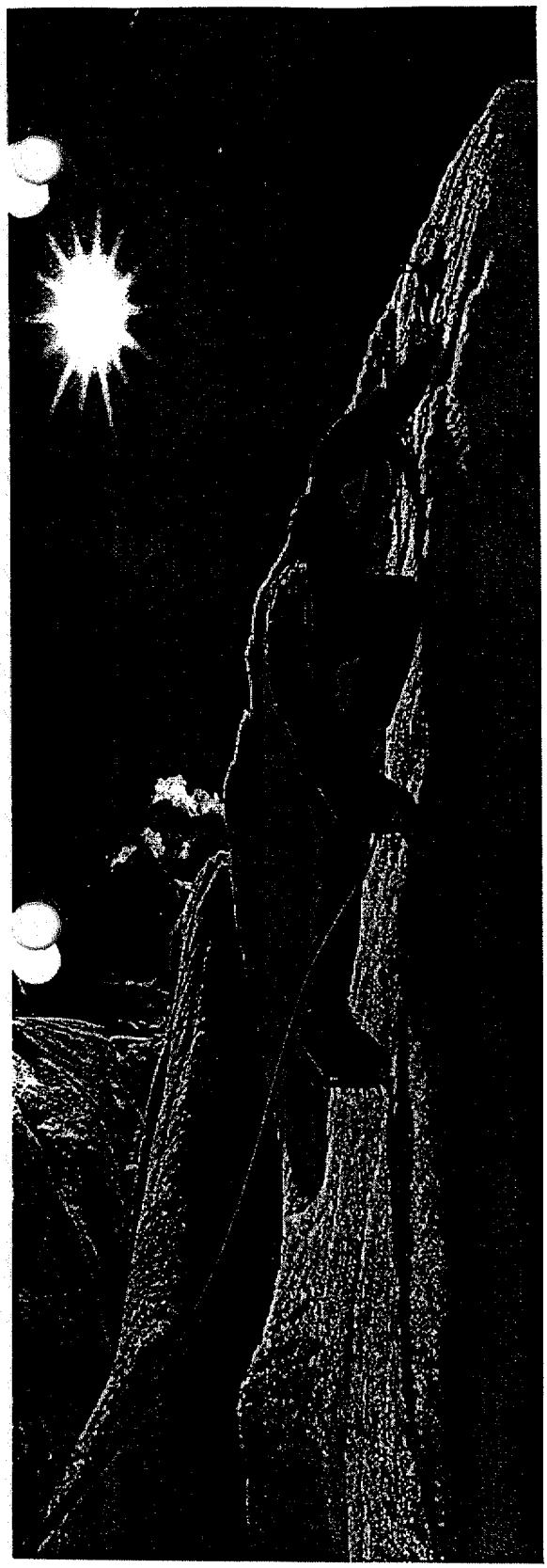
Model Description	Model Number
PainBuster Infusion Kit	P100020

Caution: Federal Law (U.S.A.) restricts this device to sale on the order of a healthcare professional.

For Customer Service: 800-448-3569

CE 0123

I-FLOW®
THE FUTURE OF INFUSION TECHNOLOGY
20202 Windrow Drive
Lake Forest, CA 92630 U.S.A.
Tel: 949-206-2700 Fax: 949-206-2600
www.i-flowcorp.com
1302056A 6/98



MANAGE POSTOPERATIVE PAIN WITHOUT NARCOTICS

Applications

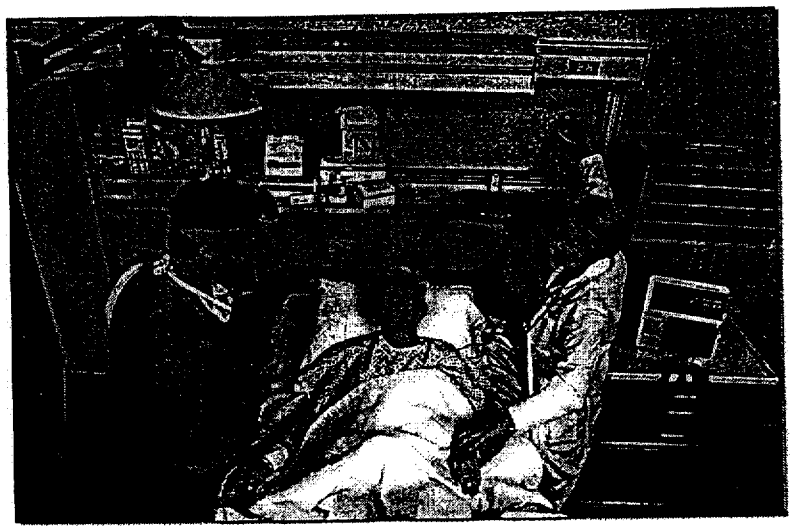
Orthopedic Surgery Including:

- Arthroplasty Procedures
- Arthroscopic Procedures
- General Open Procedures

I·FLOW®

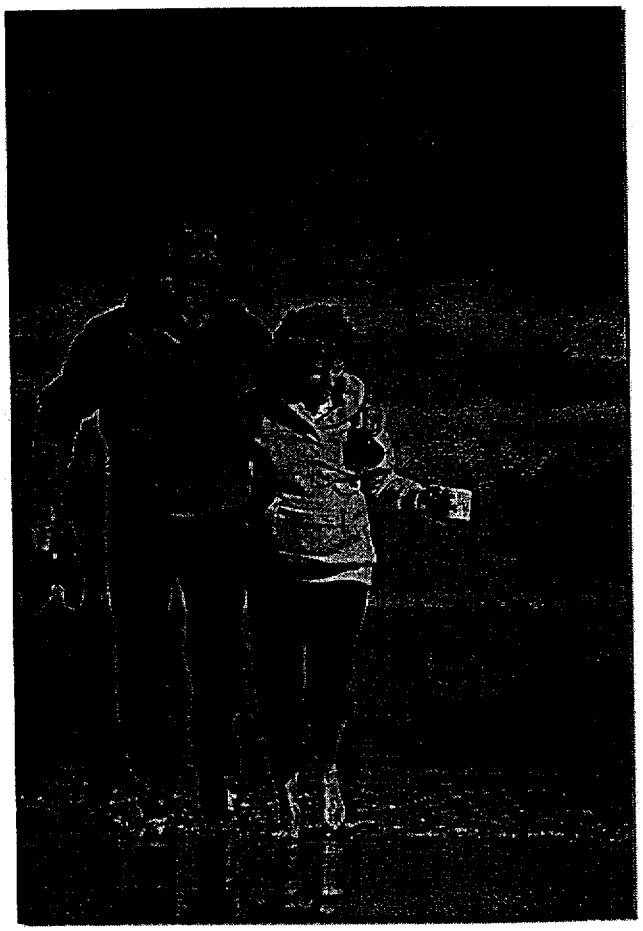
THE FUTURE OF INFUSION TECHNOLOGY

PainBuster™



From Surgery...

To Recovery



Optimal Pain Relief

PainBuster™

60

PainBuster™

INTENDED USE

The PainBuster is intended to provide continuous infusion of a local anesthetic directly into the intraoperative site for postoperative pain management.

CONTRAINDICATIONS

This system is not designed for epidural, subcutaneous or vascular drug delivery. Not for blood, blood products or TPN use. Not for chemotherapy drugs.

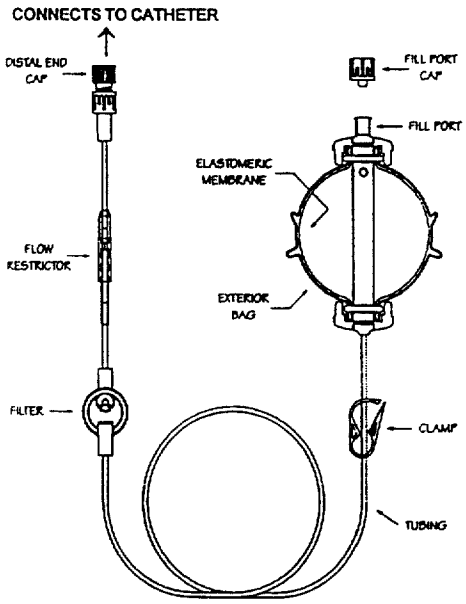
WARNINGS

- Single Use Pump. Do not refill. Discard after use.
- Do not overfill the pump.
- Medications being used with this system should be used in accordance with instructions provided from the drug manufacturer.

DIRECTIONS FOR USE

Use Aseptic Technique

Filling the Elastomeric Pump



1. Close clamp on tubing.
2. Remove protective cap from filling port.
3. Attach filled syringe to the fill port and inject fluid into pump. Repeat if necessary. Do not fill over 65ml or 125ml as applicable (refer to table below). Replace fill port cap.
4. To prime the tubing, open the clamp on the tubing and allow fluid to fill the tubing. Close clamp until ready for use.

Placing the Catheter

1. Insert introducer needle through the skin (approximately 3-5cm away from wound site) then push introducer needle into the surgical wound site.
2. Insert the marked end of the catheter through the hub of the introducer needle into the wound site out the bevel of the needle.
3. Remove introducer needle while holding catheter tightly in place. Assure catheter placement in wound site.
4. Cut catheter to desired length.
5. Attach the catheter connector to the unmarked end of the catheter. Tighten until catheter cannot be removed.
6. Attach the catheter connector to the pump tubing.
7. Tape catheter securely in place.
8. Apply appropriate dressing to catheter site.

Starting the PainBuster System

1. Open the clamp to begin delivering medication.
2. Secure flow restricter to skin and apply desired dressing.
3. Secure PainBuster Pump to the outer dressing with tape as desired.

Delivery Time Information for the PainBuster

	P065005	P100020
NOMINAL FLOW RATE (ml/hr)	0.5	2.0
NOMINAL VOLUME (ml)	65	100
MAXIMUM VOLUME (ml)	65	125
RETAINED VOLUME (ml)	<5	<5
	VOLUME (ml)	
APPROXIMATE DELIVERY TIME		
12 h		35
24 h/ 1 d		65
48 h/ 2 d	35	100
72 h/ 3 d	45	125
96 h/ 4 d	55	
120 h/ 5 d	65	
84 h/ 3.5 d		

Delivery accuracy is ±15% (at a 95% confidence interval) of the labeled infusion period when delivering saline at 88° F (31° C).

NOTES:

1. The infusion rate for each PainBuster Pump is indicated on each cap.
2. Actual infusion times may vary due to:
   -viscosity and/or drug concentration.
   -positioning the PainBuster pump above (increase) or below (decrease) the catheter site.
   -temperature: the PainBuster flow restricter (located distal to the filter) should be close to, or in direct contact with, the skin (31°C/88°F). Temperature will affect solution viscosity, resulting in shorter or longer delivery time. If the PainBuster is used with the flow restricter at room temperature (20°C/68°F), delivery time will increase by 25%.
3. This product uses DEHP plasticized PVC. Certain solutions may be incompatible with the PVC material used in the administration set. Consult the drug package insert and other available sources of information for a more thorough understanding of possible incompatibility problems.

Infusion is complete when the PainBuster Pump is no longer inflated.

CAUTION
Federal (U.S.A.) law restricts this device to sale by or the order of a healthcare professional.

For Customer Service
Call: 1.800.448.3569

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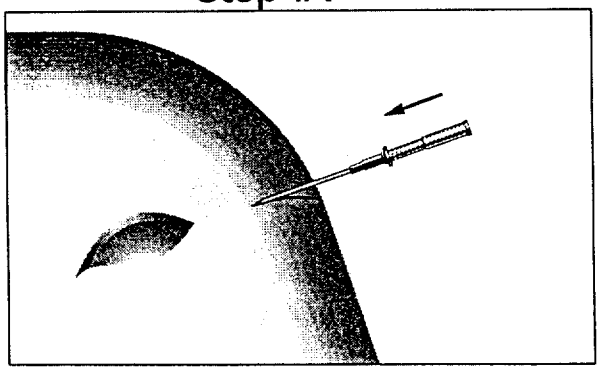
LAKE FOREST, CA 92630

Step #1



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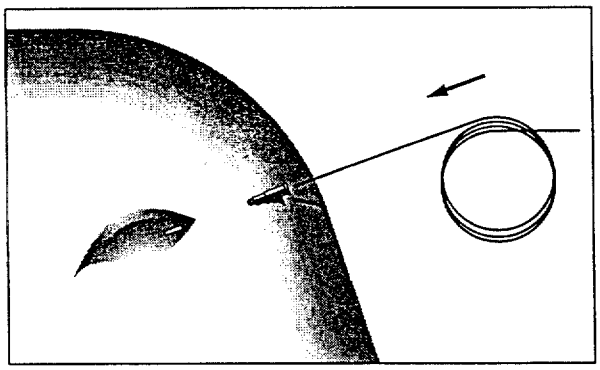

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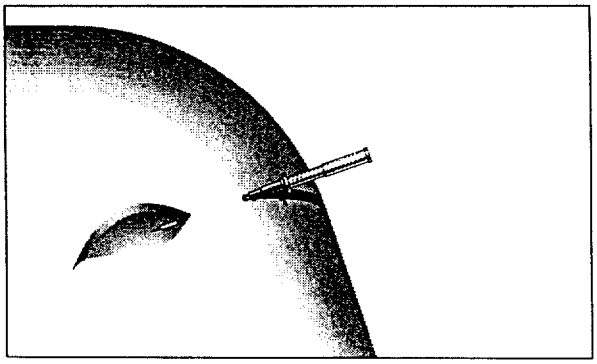

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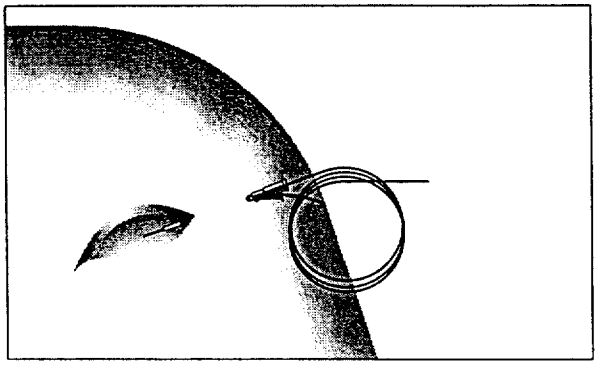

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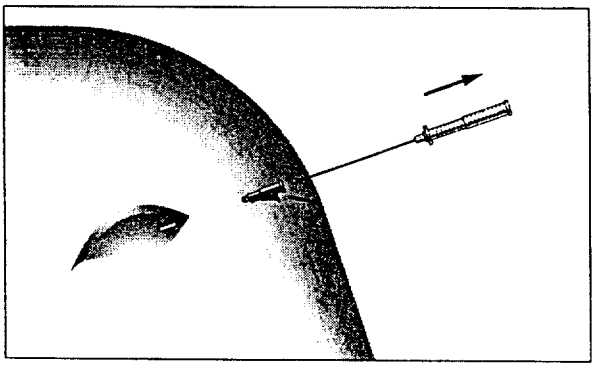

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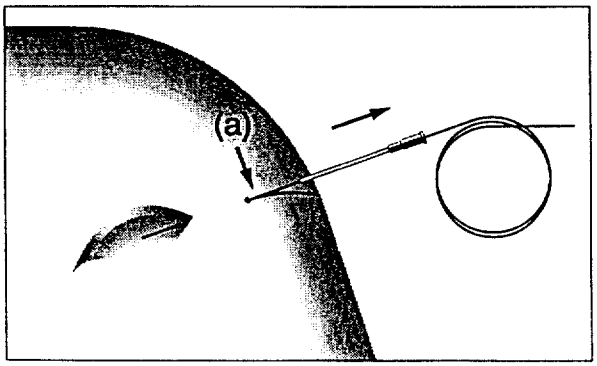

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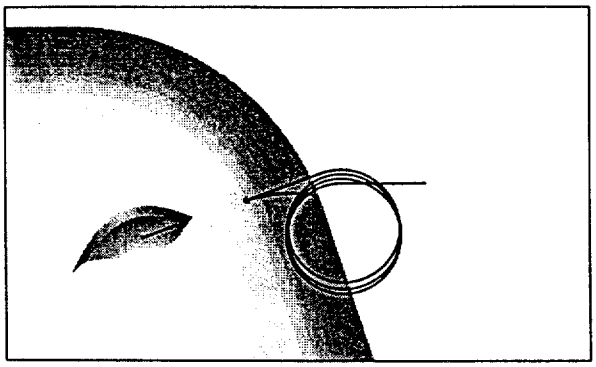

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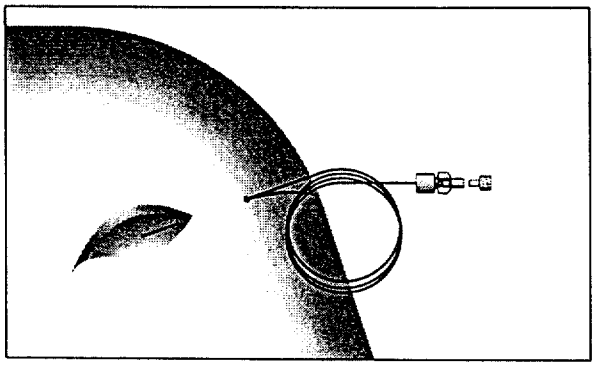

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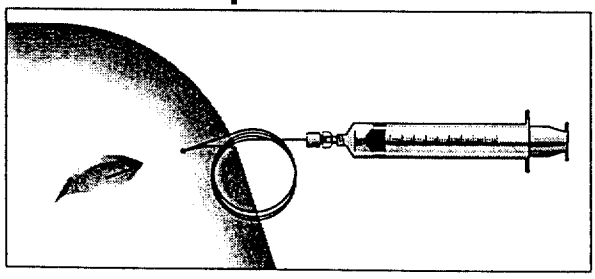

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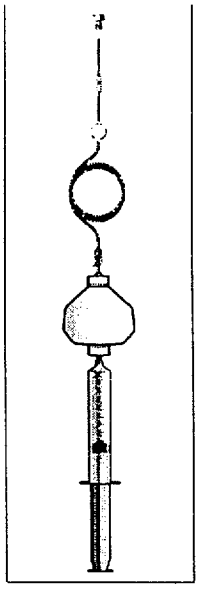

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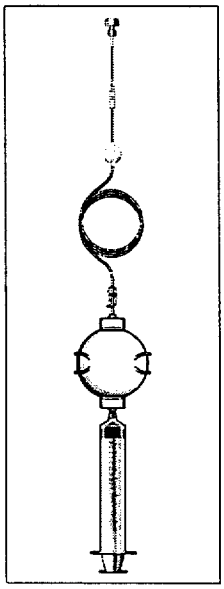

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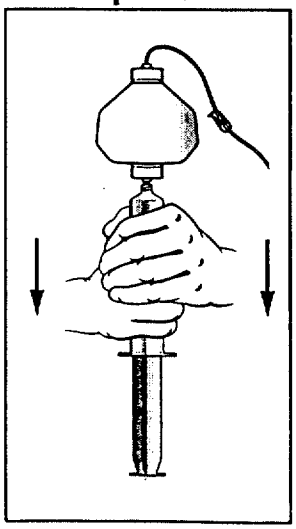

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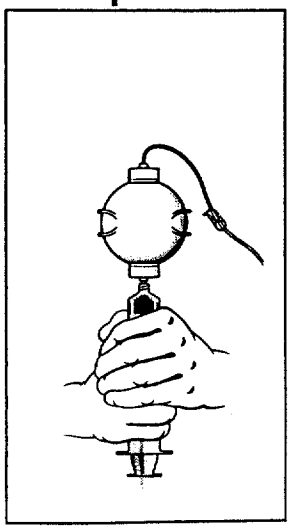

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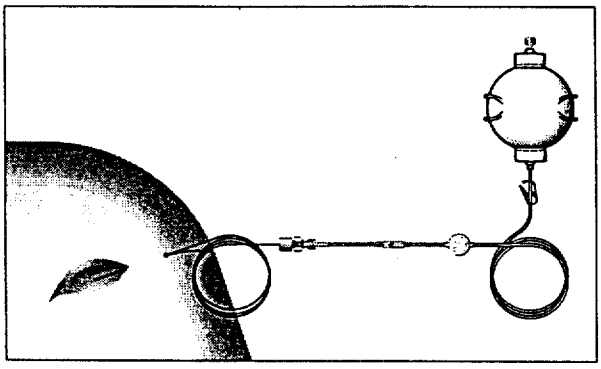

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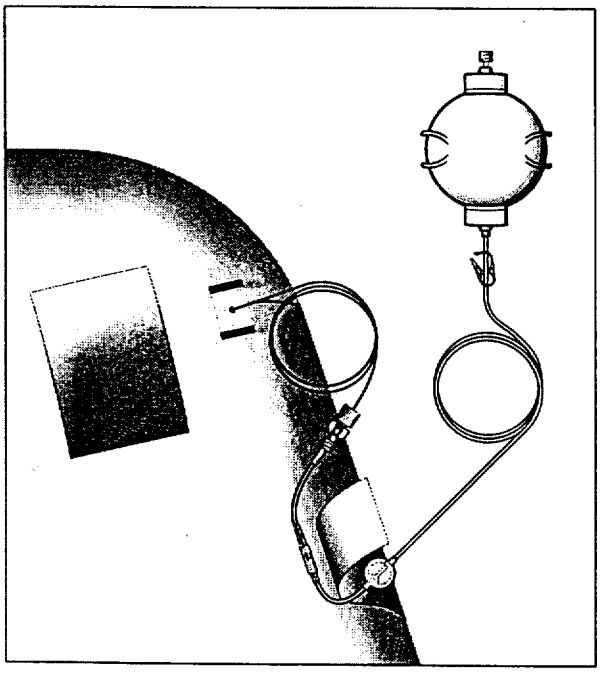
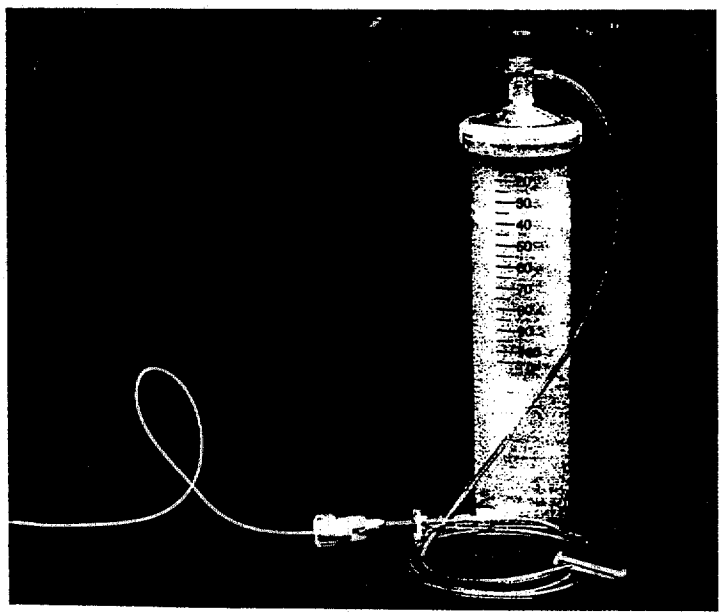


A Significant Improvement in Portable Infusion

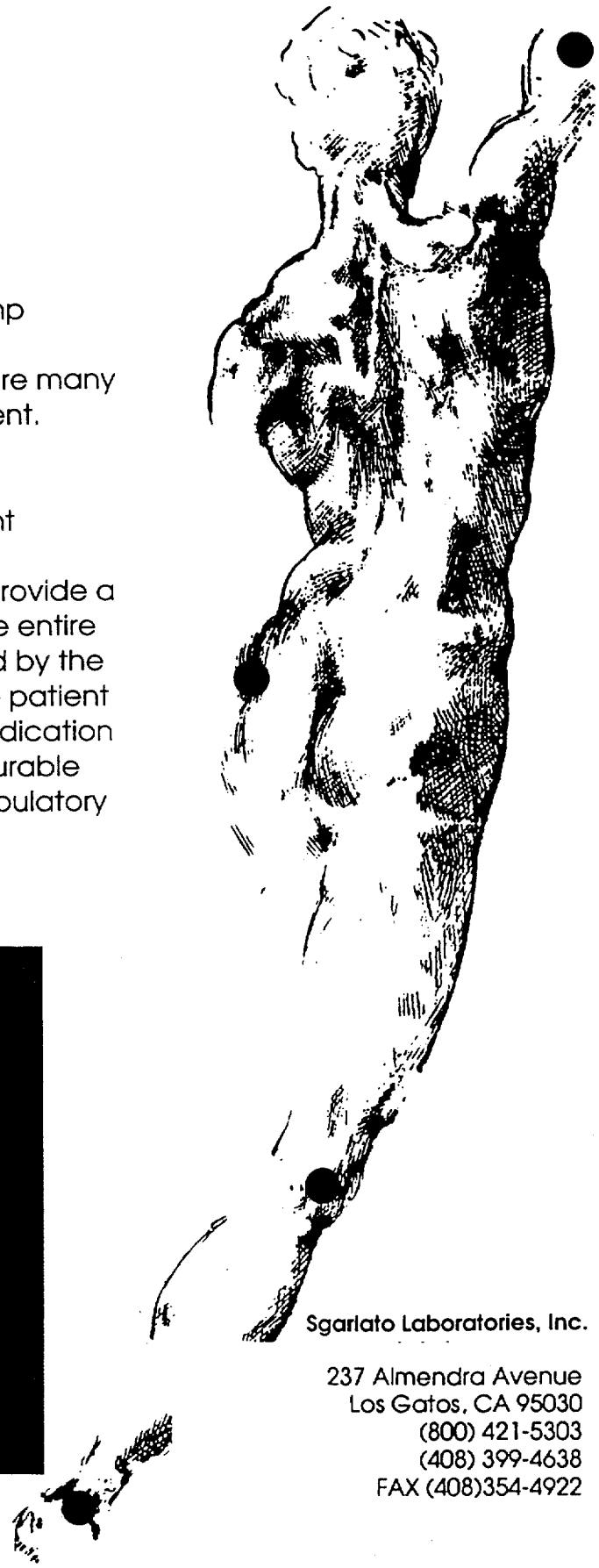
Take Aim at the Site of Pain

Now you can provide your patients with safe, reliable, and accurate continuous infusion via Sgarlato Lab's SurgiPEACE pump system. SP is suitable for delivery of local anesthetic directly to the pain site. There are many potential applications for pain management.

The SP system is a complete, lightweight disposable device which provides constant internal pressure via a unique precision compression spring and a flow resistor to provide a consistent infusion flow rate throughout the entire course of therapy. The flow rate is selected by the physician and cannot be changed by the patient thus ensuring safety and efficacy. The medication reservoir is constructed of a high quality durable and stable plastic which is suitable for ambulatory use. This simple and practical system is an excellent low cost option for many of your pain treatment needs.



Patent # 5,078,679 Patent # 4,997,420



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Safe and Accurate

- Consistent and reliable flow rate throughout therapy via a precision compression spring.
- Temperature stable design and unique flow restrictor prevent excess drug delivery and rate manipulation.
- Sterile, closed system design with integrated tubing reduces risk of contamination.
- Disposable after single use.

Simple and Practical

- Easy to use system is not gravity dependent and does not require complex counting, rate setting or electronic pump programming.
- Minimal patient and staff training.
- No cords, outlets, batteries or IV poles needed.
- Lightweight and compact design encourages patient compliance.

Flexible

Currently there are three flow rates available.

Model #	Flow Rate	Max Volume	Infusion Time
SP500	0.5 ml/hr	100 ml	8 days
SP1000	1 ml/hr	100 ml	4 days
SP2000	2 ml/hr	100 ml	2 days

Reliable and Durable

- Outer markings on barrel show exactly how much fluid is in the reservoir at any point in time.
- Durable hard plastic pump design minimizes possibility of pump being damaged or crushed, especially for long term use.
- All polypropylene housing provides for greater drug stability and less sensitivities compared to elastomeric pumps. Drug stability information is available.

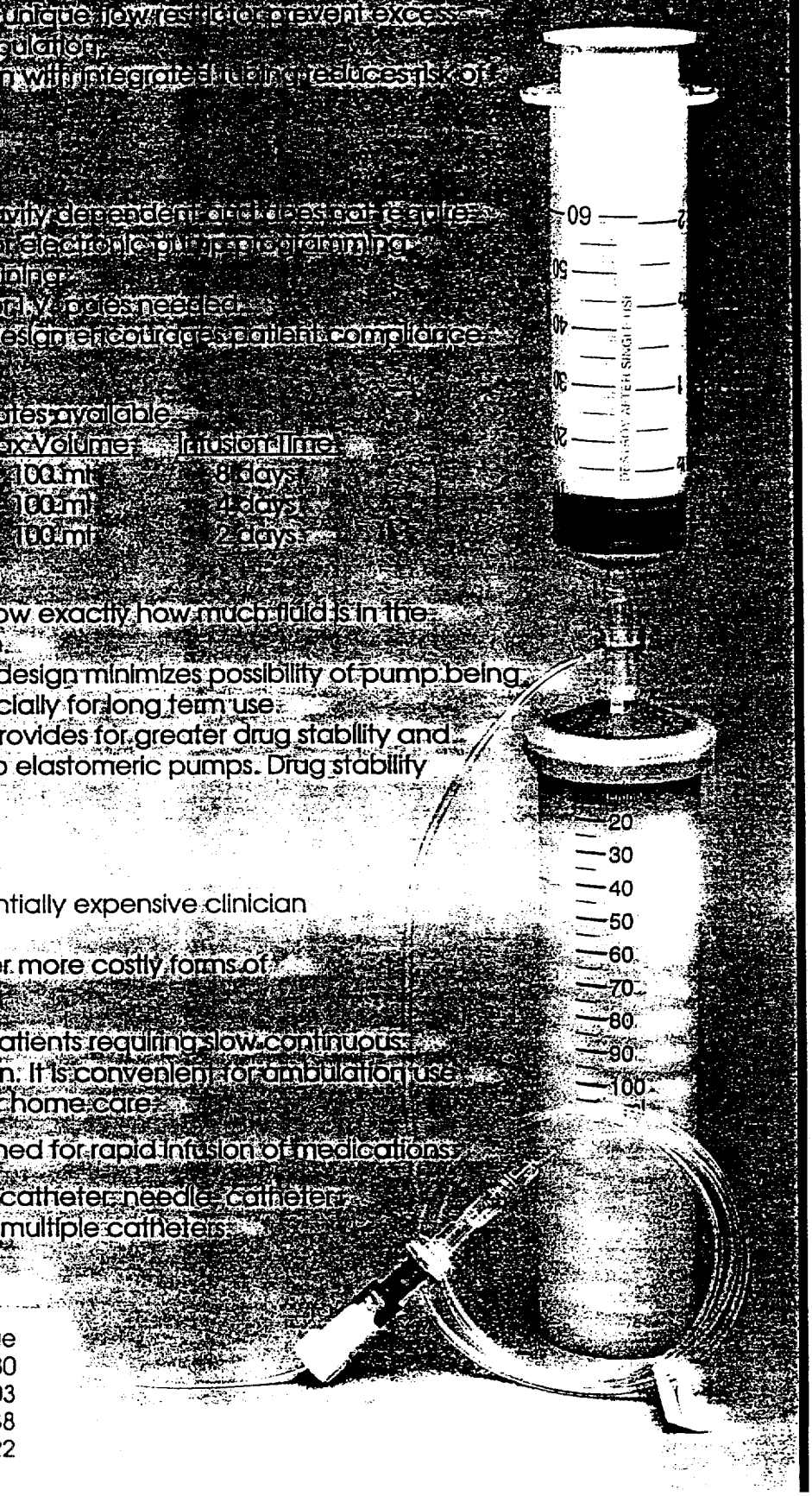
Cost Effective

- Low Cost
- Reduces or eliminates potentially expensive clinician intervention time.
- Low cost alternative to other more costly forms of pain treatment.

Indications and Usage: For patients requiring slow continuous administration of medication. It is convenient for ambulation use for inpatients, outpatients or home care.

Contraindications: Not designed for rapid infusion of medications.

Kit Options: Carrying harness, catheter, needle-catheter, connector, "Y" adapter for multiple catheters.



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Pain Control Infusion Pump

Pain Control System

DESCRIPTION

The Pain Control Infusion Pump is a complete, lightweight, disposable device which uses a constant internal pressure to infuse medication for control of pain. The system is designed to deliver medication continuously into the surgical wound site over the infusion period.

INDICATIONS

The system is indicated for the relief of pain in patients following surgery, by the continuous administration of medication into the wound site. It is convenient for use by ambulatory patients.

CONTRAINDICATIONS

Not intended for intravenous infusion.

WARNINGS

DISPOSABLE - Destroy after single use. Do not refill or resterilize.
Do not overfill device.
Follow drug manufacturer's instructions for the medication being used.

CAUTION

Federal (U.S.A.) Law restricts this device to sale by or on the order of a physician.

DIRECTIONS FOR USE:

Use Aseptic Technique.

FILLING RESERVOIR PUMP

1. Close on/off clamp of medication tubing.
2. Remove protective cover from female luer lock filling port and discard.
3. Attach 60 ml syringe without needle to filling port at the top of the Pump Reservoir (refer to figure 1.). Fill reservoir with up to 100 ml of medication.
4. Once filling is complete, remove syringe. Securely attach blue replacement cap to filling port to maintain a sterile filling port.

PRIMING SYSTEM (refer to figure 3a.)

1. Attach clear connector to medication catheter by pushing catheter into connector as deeply as possible. Twist connector as tightly as possible, use **MAXIMUM HAND FORCE** to screw connector components together to assure that the catheter will not pull out. It is almost impossible to constrict the catheter flow by maximum tightening.
2. Hold system reservoir and filter in upright position. Loosen proximal luer connector (green) to allow trapped air to exit.
3. Open on/off clamp (solution will automatically begin to flow into tubing and catheter). (Tighten proximal luer connector when fluid flow without air reaches connector.)
4. Hold the filter vertically and tap filter lightly to remove air bubbles.
5. Keep priming until all air has been purged from tubing, filter and catheter.
6. Allow 10 minutes before placing catheter in patient to see medication drops flow to the end of the medication catheter. If flow is not seen, attempt priming with 60 ml syringe filled with 10 ml or more of medication. Clamp off tubing with pinch clamp. Disconnect proximal luer connector and attach distal connection to syringe. Aspirate air bubbles and then force medication distally until drops of medication are seen at distal end of medication catheter. If flow is not seen, discard unit and repeat above steps with new Pain Control Infusion Pump unit. If flow is seen, reattach proximal connector and release pinch tubing clamp.

PLACING CATHETER (refer to figure 2.)

NOTE: Prime system completely prior to placing catheter.

METHOD A: FROM INSIDE THE WOUND

1. Push introducer needle from the surgical wound site subcutaneously and puncture through skin at a desired location away from the surgical wound site.
2. Thread open end of catheter through the tip of the catheter introducer needle at the puncture site until the catheter is seen in the surgical wound site.
3. Place the end of the catheter in an appropriate location (not in a vessel) within the surgical wound site.
4. Tape catheter to the skin to prevent the catheter from pulling out of the wound site. It is most effective to tape in a linear parallel manner to the catheter (refer to figure 3.)
5. Remove introducer needle from wound site leaving catheter in place and dispose of needle in accordance with institutional protocol.

METHOD B: INSERTION THROUGH SKIN

1. Puncture introducer needle through the skin at a desired location external to the surgical wound site; push the introducer needle subcutaneously into the surgical wound site.
2. The catheter is left free, unattached from the connector. Push catheter into the hub end of the needle and allow catheter to exit at the needle tip into the surgical wound site.
3. Remove introducer needle and tape catheter as described in Method A steps 4 and 5 above.
4. Attach catheter to clear connector per Priming System Procedure Step 1.

figure 1.

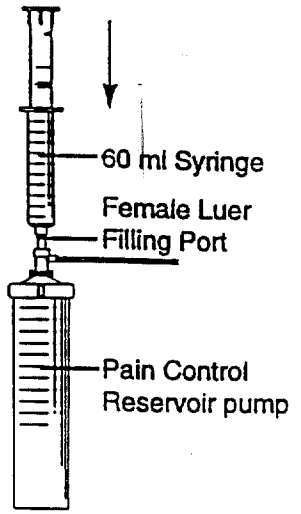


figure 2.

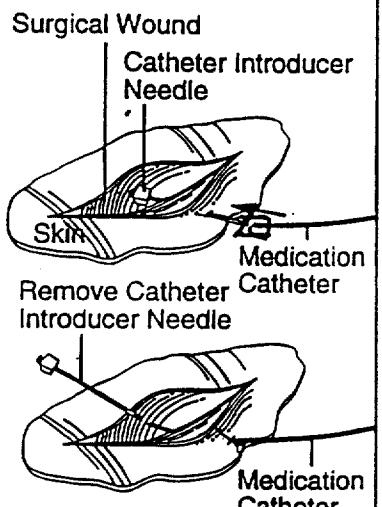
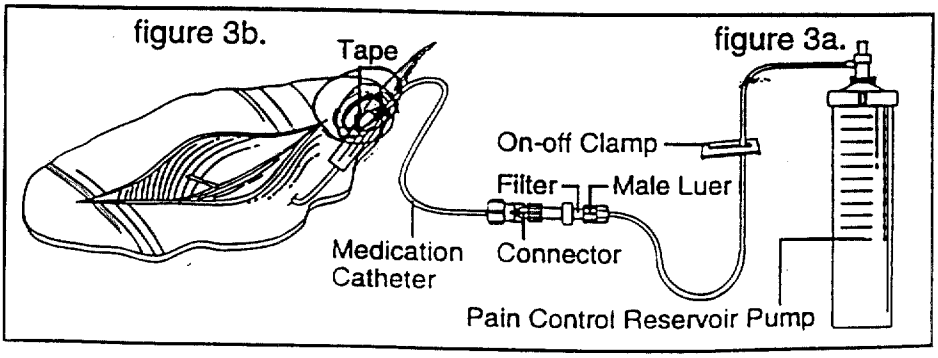


figure 3b.

figure 3a.



Manufactured for:
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A4806164 P-2143-3 REV. 1/97

PAIN CONTROL INFUSION PUMP Medical Necessity

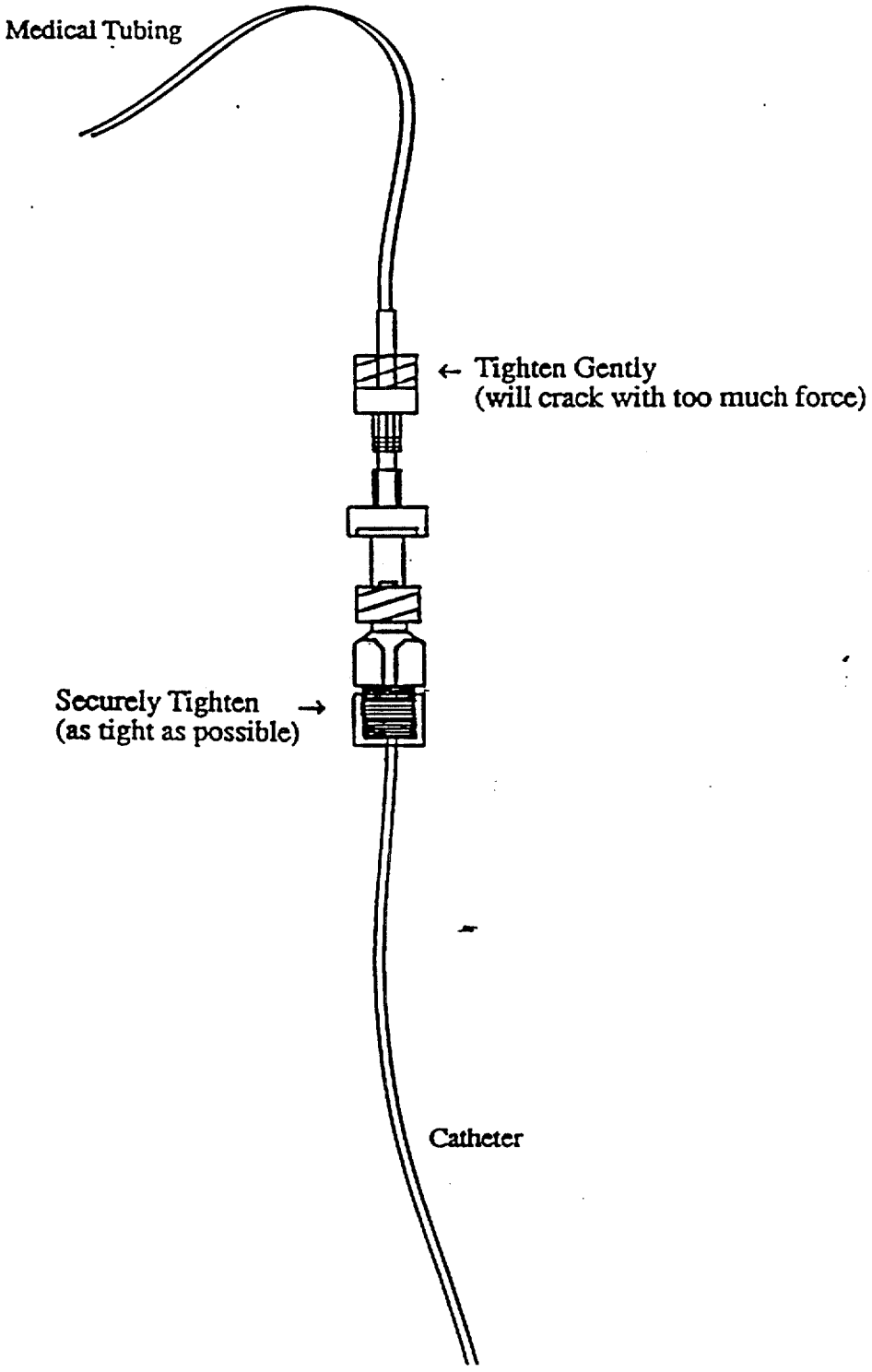
Postoperative pain management is an important concern for anesthesiologists and surgeons. Adequate pain control has been shown to reduce morbidity by improving mobility and decreasing the risk of developing deep venous thrombosis. Patient satisfaction is also increased with control of postoperative pain.

Systemic drugs such as narcotics can provide analgesia but often have side effects such as respiratory depression, excessive sedation nausea and vomiting. Regional anesthesia with local anesthetic reduces the need for systemic medications but requires a painful injection and repeated dosing.

Local infiltration of a surgical incision with a local anesthetic has been shown to provide adequate anesthesia. Techniques used include bathing the incision with local anesthetic prior to closure (provides limited duration of pain relief), repeated injections into the wound (painful, increased risk of wound infection and time-consuming) and placement of an epidural catheter into the wound to allow repeated boluses of local anesthetic. This last technique still requires additional time from the care given to provide the additional doses.

The PCIP medication infusion pump is a cost effective ambulatory, disposable, spring activated pump designed to continuously deliver a local anesthetic (Bupivacaine 0.25%). It has been developed to produce analgesia for the control of excruciating postoperative pain.

Special Instructions: Please Review



ABBREV. PAIN CONTROL INFUSION PUMP INSTRUCTIONS

Additional information is provided inside the sterile kit.

IMPORTANT: Use aseptic technique.
RECOMMENDED: Administer prophylactic antibiotic.

FILLING RESERVOIR PUMP:

1. Disconnect flow regulator from tubing at green male luer.
2. Close on/off clamp at the very end of tubing (next to green male luer).
3. Draw medication into 60 ml syringe. Remove air bubbles.
4. Remove and discard protective cap on top of reservoir filling port.
5. Attach 60 ml syringe without needle to reservoir filling port and load up to 100 ml of medication.
6. Remove syringe and attach blue replacement cap to filling port.
7. Prime reservoir and tubing by briefly opening clamp to let air bubbles out.
8. Connect flow filter to tubing. Do not tighten excessively. Open clamp.

PLACEMENT OF CATHETER:

1. Puncture blue introducer needle through the skin external to the surgical wound site. Push needle subcutaneously into the wound cavity.
2. Feed micro catheter through needle and allow catheter to exit at the needle tip into the wound at the desirable surgical plane.
IMPORTANT: Do not put catheter in blood vessel.
3. Remove and discard needle, leaving catheter in place.
4. Tape catheter to body very near to the insertion site utilizing the 3-4 loop technique in order to keep catheter securely in place.
5. Insert catheter as deeply as possible (apx. 1/2 inch) into connector. Twist connector as TIGHTLY AS POSSIBLE to assure that catheter will not pull out.
6. Tape connector below patient's knee (if procedure is below the knee). RECOMMENDED: Place gauze pad between body and connector for comfort.
7. Attach carrying harness to reservoir. Patients can wear or carry device however they prefer.

PAIN CONTROL INFUSION PUMP PATIENT INSTRUCTIONS

The PCIP Pain Control System is a portable infusion pump designed to deliver medication directly to the surgical site for management of pain.

How the System Works

PCIP administers local pain medication directly to the pain site via a tiny tube which is placed inside the wound by the physician during surgery. Pain relief is provided directly where it is needed. This is an alternative to other forms of therapy such as pain killers and narcotics taken orally which go throughout the entire body and sometimes cause side effects such as drowsiness, disorientation, nausea or other adverse reactions.

PCIP is comprised of a reservoir with internal spring pressure, tubing and a very precise flow regulator. The device has been filled with medication to flow continuously for a specific period of time. The system should remain completely intact for the duration of the period. Do not remove the blue cap or disconnect the device in any way.

If Complications Arise

If you experience any problems with the PCIP unit such as leakage, the device becoming disconnected, the tube pulling out of the wound site, or if you experience discomfort or excessive pain, call your physician immediately. He/she may prescribe supplemental medication if necessary.

There is a white clamp on the thicker tubing to restrict the fluid flow if necessary. This should be done only upon the direction of your doctor. As a general rule, you do not have to do anything with the unit because it is fully self contained and automatic.

Background and Significance of Pain Control Infusion Pump - "PCIP"

Post-operative pain management is an important concern for anesthesiologists and surgeons. Adequate pain control has been shown to reduce morbidity by improving mobility and decreasing the risk of developing deep venous thrombosis. Patient satisfaction is also increased with control of post-operative pain.

Systemic drugs such as narcotics can provide analgesia but often have side effects such as respiratory depression, excessive sedation, nausea and vomiting. Regional anesthesia with local anesthetic reduces the need for systemic medications but requires a painful injection and repeated dosing.

Local infiltration of a surgical incision with a local anesthetic has been shown to provide adequate anesthesia. Techniques used include bathing the incision with local anesthetic prior to closure (provides limited duration of pain relief), repeated injections into the wound (painful, increased risk of wound infection and time-consuming) and placement of an epidural catheter into the wound to allow repeated boluses of local anesthetic. This last technique still requires additional time from the care giver to provide the additional doses.

The PCIP medication infusion pump is a cost effective ambulatory, disposable, spring activated pump designed to continuously deliver a local anesthetic (Bupivacaine 0.25%). It has been developed to produce analgesia for the control of excruciating post-operative pain.

PCIP is assembled aseptically in a Clean Room (Class 100). It consists of simple assembly of components already used in medical devices. A spring is mounted on a syringe plunger and capped by an outer shell. Medical grade PVC tubing is connected to the syringe. A micro-glass cannula is placed in the end of the PVC tubing exiting the connector. A catheter is connected to the end of the PVC tubing. A "Y" connector may be added to add a catheter for more than one delivery site.

When medication is injected into the injection port, it flows into the syringe, pushing the syringe plunger against the spring. As the syringe reservoir is filled, the spring produces more pressure on the plunger, providing pressure on the medication fluid. The medication then flows through the micro-glass cannula which controls the rate of flow (in a fail-safe manner). The fluid exits the system via the epidural catheter. Any break in the system will result in reduced or no drug delivery to the patient.

Clinical experience demonstrates that excruciating post-operative pain decreases over time in most patients. This observation is further demonstrated by the patient's diminishing need for narcotic analgesia to control pain. Continuous infusion of local anesthetic should provide analgesia and reduce the need for systemic medications with little risk to the patient.

ATTACHMENT 5

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Regional Anesthesia 22(4):351–356, 1997

Local Anesthetic Infusion Through Nerve Sheath Catheters for Analgesia Following Upper Extremity Amputation

Clinical Report

F. Kayser Enneking, M.D.,* Mark T. Scarborough, M.D.,† and Ellyn A. Radson, R.N.*

Background and Objectives. Reports about the efficacy of local anesthetic perfusion of nerve stumps following lower extremity amputation are conflicting. We report our experience with this technique following amputation of the upper extremity. *Methods.* Six consecutive patients undergoing proximal upper extremity amputations (four forequarter amputations and two shoulder disarticulations) for malignancy were prospectively observed. In all patients, catheters were placed within the amputated nerve sheaths at the conclusion of the procedure. Bupivacaine, 0.25%, was administered through each catheter as a bolus and then as a continuous infusion for at least 72 hours after surgery. Narcotic usage, level of pain as reported verbally, and presence of phantom limb pain during the infusion were recorded. For at least 1 year after operation, data were gathered on the presence of phantom limb pain and its intensity during each follow-up visit. *Results.* Complete analgesia was achieved in all patients by postoperative day 2. Narcotic usage was low. Three of the six patients reported phantom limb pain during follow-up evaluation. *Conclusions.* Continuous local anesthetic perfusion of amputated nerves via a catheter placed under direct vision provided excellent postoperative analgesia. The incidence of phantom limb pain for cancer patients did not differ from that previously reported but was easily managed pharmacologically. The technique may also be efficacious for traumatic amputations. *Reg Anesth 1997: 22: 351–356.*

Key words: amputation, postoperative analgesia, nerve sheath catheters, phantom limb.

Phantom limb pain is a devastating complication of amputation. It occurs in 83% of patients within the first 4 days of amputation. Patients describe classic neuropathic pain as "knifelike," "sticking," "shooting," "burning" (1). In a retrospective chart review of upper extremity amputations in our institution from 1978 to 1992, 50% of patients had phantom limb pain requiring narcotic analgesics during follow-up evaluations. All these patients received general endotracheal anesthesia and intravenous narcotics postoperatively for pain control; all patients were followed for at least 1 year. Because the review was retrospective and the patients were not specifically asked about

From the Departments of *Anesthesiology and †Orthopaedics, University of Florida College of Medicine, Gainesville, Florida.

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No reprints. Correspondence: Editorial Office, Department of Anesthesiology, University of Florida College of Medicine, Box 100254, Gainesville, FL 32610-0254.

phantom pain, the number of patients who experience phantom pain is probably greater than 50%, as phantom limb pain is frequently underreported by patients and underdocumented by care givers (1,2).

The role of preemptive analgesia and its timing in the prevention of phantom limb pain are unknown. Examination of the literature reveals the lack of rigorous, well controlled studies of this difficult problem. Bach et al. (3) reported on a small series of patients undergoing lower extremity amputations who had epidural analgesia initiated 72 hours before surgery; these patients received either narcotics, local anesthetics, or both before surgery in this nonblinded study. Their postoperative pain was treated with intravenous narcotics and nonsteroidal antiinflammatory medications. The incidence of phantom limb pain in this study was 27% during the first week, 0 at 6 months, and 0 at 1 year; in the control group of 14 patients, the incidence of phantom limb pain was 64%, 38%, and 27%, respectively. Another study by Fisher and Meller (4) on 11 patients, who received no preoperative interventions for lower extremity amputations but who did receive postoperative nerve sheath infusions of local anesthetics up to 1 year postoperatively, reported a total absence of phantom limb pain in these patients; however, two patients had nonpainful paresthesias, similar to those found in our study. This, too, was a nonblinded study and the length of follow-up evaluation was not specified.

Woolf and Chong (5), in their review of preemptive analgesia, point out that in 22 of 24 studies comparing a preemptive intervention with no intervention, an analgesic effect could be demonstrated in the patients who received preemptive intervention. However, in studies comparing interventions made before versus after surgery, a preemptive effect could only be demonstrated in half the cases. There is no clear evidence as to when preemptive intervention of phantom limb pain should be initiated.

Initial reports of continuous nerve sheath infusion of local anesthetic described excellent pain control and decreased risk of phantom limb pain following lower extremity amputation (4,6). In a more recent report, however, analgesic use and the incidence of phantom limb pain did not differ between patients undergoing lower extremity amputation followed by continuous bupivacaine nerve sheath infusions and control patients (7). To our knowledge, no other investigators have applied this strategy to upper extremity amputation, a much rarer operation. This report describes the use of this technique for postoperative analgesia in six patients undergoing upper extremity amputation. The efficacy of analgesia and the incidence of phantom limb pain were examined.

Materials and Methods

With institutional review board approval, data were gathered prospectively in consecutive patients undergoing upper extremity amputation for malignancy at our institution between 1992 and 1995. All patients underwent general inhalational anesthesia with fentanyl, up to 5 μg/kg. With the forequarter amputations, the nerves were transected at the cord level and either two or three catheters were placed. The shoulder disarticulations were at the terminal branch level, and the catheters were placed in the median, ulnar, and radial nerve branches. In each case, the nerves were sharply transected proximal to the level of amputation. No clips or sutures were used on the nerve ends, and the nerves were cut at 5–10 cm proximal to the wound edges. After amputation, 20-gauge polyamide closed-tip catheters (Burron Medical, Bethlehem, PA were threaded between the epineurium and the severed nerve under direct visualization by the surgeon (Fig. 1). The technique for catheter placement involves transection of the nerves, identification of the epineurium, and placement of the catheter between the epineurium and the nerve. The catheter was typically threaded as far as it could be easily introduced, 2–5 cm proximal to the transection level. Two or three catheters were placed for each patient because at least two catheters enabled a greater volume of local anesthetic to be delivered if necessary. This strategy resulted from our experience with a patient who was not included in the study group because of extensive chest wall excision. Only one catheter was placed in this patient, and she complained of persistent pressure paresthesia when the rate of analgesic infusion was increased from 6 to 8 mL/h.

The catheters were secured with a suture to the epineurium and brought out at a site distant from the wound closure. After the catheters were secured, bupivacaine, 0.25%, was administered through each catheter, first as 10-mL boluses and then, when the patient reached the recovery room, as continuous infusions beginning at 4 mL/h by means of infusion pumps (Bard MedSystems, North Reading, MA). The rate of the infusions through all the catheters was adjusted to a combined maximum of 0.5 mg/kg/h as needed to achieve analgesia, and the infusions were main-

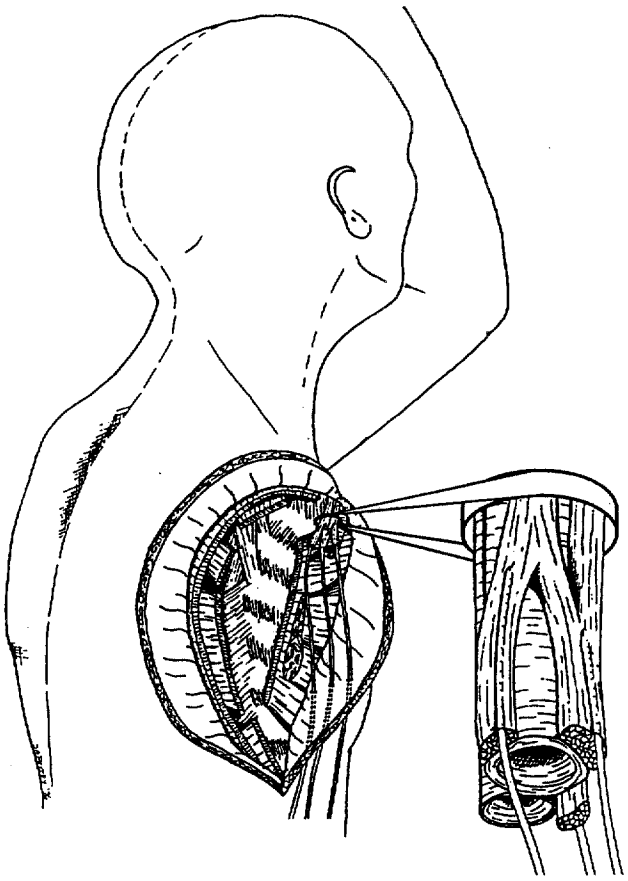

Fig. 1. Schematic drawing of nerve sheath catheters threaded between the epineurium and the nerve following shoulder disarticulation. All catheters are brought out to the skin and secured with a suture.

tained for a minimum of 72 hours. Morphine sulfate, 1 mg every 6 minutes maximum, was available to patients as needed by means of a patient-controlled device. The analgesic regimen was switched after the first postoperative day to oral narcotics, to be given at the patient's request.

Twice daily during infusions, patients were questioned about the following symptoms of local anesthetic toxicity: tinnitus, perioral numbness, metallic taste, and sedation. The amount and type of supplemental analgesics (morphine sulfate equivalents) used postoperatively were recorded. Pain and phantom limb sensation were assessed as follows. Before and twice daily for 3 days after amputation, patients were asked to assess the degree of pain in the affected upper extremity by means of a verbal scale ranging from 0 (no pain) to 10 (worst pain). At all postoperative follow-up visits, patients were asked whether they had any sensations in the phantom limb. These follow-up visits were scheduled at 2 weeks, at 1 month, and every 3 months for the first year and then every 6 months thereafter. Data are reported as mean ± SD.

Results

Six patients were studied (Table 1), three women and three men with a mean age of 59.5 years (range, 20–84). Their mean pain score preoperatively was 4.5 ± 3.8. Complete analgesia was achieved in all patients by postoperative day 2, the mean pain scores on postoperative days 0 to 3 being 3.8 ± 4.1, 1.8 ± 1.6, 0 ± 0, and 0 ± 0 respectively. After 24 hours of patient-controlled morphine, most patients received oral narcotics on request. The amount of morphine sulfate equivalent administered during the entire hospitalization averaged 20 mg, and for postoperative days 0 to 3, it was 10.4 ± 11.0 mg, 3.1 ± 4.2 mg, 1.1 ± 1.7 mg, and 4.9 ± 7.7 mg, respectively. For three patients who rated pain as 3 or higher and had an initial dose of bupivacaine of 4 mL/h, the infusion rate

Table 1. Demographic Data and Diagnoses for Patients Who Underwent Upper Extremity Amputation for Malignancy at One Institution in 1992–1995

Patient	Sex	Age (y)	Diagnosis	Area of Amputation	Follow-up Period (months)	Outcome
1	M	45	Recurrent osteosarcoma of the proximal humerus	Forequarter	15	Dead of disease
2	M	20	Osteogenic sarcoma of the proximal humerus	Shoulder disarticulation	41	Alive, no evidence of disease
3	F	82	Malignant fibrous histiocytoma of the proximal humerus	Forequarter	21	Alive, no evidence of disease
4	F	61	Angiosarcoma of the arm	Forequarter	22	Alive, no evidence of disease
5	F	65	Malignant fibrous histiocytoma of the proximal humerus	Shoulder disarticulation	27	Alive with disease
6	M	84	Metastatic adenocarcinoma with a humeral nonunion	Shoulder disarticulation	26	Alive, no evidence of disease

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was increased by 2 mL/h. The average rate of bupivacaine administration was 6 mL/h per catheter, with a range of 4–8 mL/h per catheter. Only one patient, a 90-kg, 20-year-old, received the maximum infusion rate, for a total of 45 mg/h over 80 hours. No patient exhibited any symptoms of local anesthetic toxicity.

During the infusion period and at subsequent follow-up visits throughout the study, all six patients reported nonpainful phantom sensations. Three patients reported phantom limb pain. In one of these patients, the infusion of bupivacaine was delayed by 90 minutes, and pain was rated as 10 on emergence from anesthesia. The patient was given additional boluses of 0.25% bupivacaine, and his infusion rates were increased to the maximum. He was also given morphine sulfate and ketorolac intravenously. His pain decreased to 4 on postoperative day 1 and to 0 by postoperative day 2. Phantom limb pain developed 2 weeks after amputation, which he described as "exactly what it felt like when I woke up." He received oxycodone, amitriptyline, and mexiletine for 10 weeks and has subsequently been free from phantom limb pain for 28 months. In a second patient, numbness in the phantom extremity was rated as 2 out of 10, but she took no medication 15 months after the amputation. In a third patient, pain was rated as 10 before the amputation and as 0 immediately afterward. At 1 month following surgery, intermittent phantom limb pain developed and gradually worsened. This patient has refused all pharmacologic interventions, and he rated pain as 8 out of 10 at 16 months after the amputation.

Discussion

All patients in this study underwent amputation of an upper extremity for malignancy. This analgesic technique may also be applicable to amputations for other indications, although this study did not examine other patient populations.

Although continuous infusion of local anesthetics via catheters placed percutaneously into nerve sheaths has provided effective analgesia following many types of extremity surgery (8–11), this is the first clinical report of analgesia following amputation of the upper extremity that was obtained by infusing local anesthetic through nerve sheath catheters. Our data suggest that (1) peripheral nerve sheath catheters can be used to infuse local anesthetic directly onto nerves of amputated limbs and (2) this technique can be used to obtain successful analgesia following upper extremity amputation. Although the number of patients we studied was small, our results are clinically valuable because of the limitations imposed by any study of upper extremity amputation; it is a rare operation, and phantom limb pain is such a devastating complication, both physically and emotionally, that studies using intravenous narcotic analgesia, with its known lack of efficacy, would be difficult to justify.

Local anesthetic block of peripheral nerves may reduce the nociceptive impulses from the periphery to the spinal cord and thus may prevent spinal cord hyperexcitability, which can lead to chronic phantom limb pain. Other techniques that would provide afferent block of impulses to the central nervous system should be equally efficacious in providing analgesia and possibly preventing phantom limb pain. To our knowledge, no other investigators have reported the use of continuous cervical epidural or interscalene block for analgesia following upper extremity amputation. The possible advantages of this technique over percutaneously placed catheters are that (1) catheters are known to be correctly placed, because they are placed under direct vision, and (2) these catheters cannot be pulled out or dislodged during surgery. The obvious disadvantage is that catheters are placed following surgery, when spinal cord hyperexcitability may have already occurred.

In one study, patients undergoing lower extremity limb salvage or amputation who received bupivacaine through a nerve sheath catheter placed during surgery under direct vision had substantially decreased postoperative narcotic analgesic requirements (6). No catheter-related complications or side effects secondary to the bupivacaine were reported. The incidence of phantom limb pain was not specified by Malawer et al.; however, none of the 12 amputees has since developed phantom limb pain (personal communication, 1994).

Other studies of the incidence and severity of phantom limb pain following lower extremity amputation have so far been conflicting. In one study (4) postoperative narcotic usage by a prospective, nonblinded series of 11 patients, who underwent lower extremity amputation and received a continuous infusion of local anesthetic through a catheter placed directly into the amputated stump of the sciatic or posterior tibial nerve, was compared with that by a retrospective control group who underwent a similar procedure. Mean narcotic use differed significantly between the groups. Also, phantom limb pain was totally absent at 1 year in the nine surviving patients who received a continuous local anesthetic infusion. In

contrast with those positive results, no difference in narcotic usage was reported in a retrospective review of 59 patients undergoing lower extremity amputation, 19 bupivacaine-treated patients and 40 control patients (7). When 9 of the bupivacaine-treated patients and 12 control patients were subsequently interviewed to assess their phantom limb pain, seven of the 9 bupivacaine-treated patients (77%) and half of the control patients reported this complication. A number of factors may influenced the different outcomes of the two comparison studies; for example, patient selection was dissimilar. All the patients in the positive study had peripheral vascular disease, compared with 32% in the negative study. The total mass of bupivacaine administered and the way it was administered also differed between the two studies: 25 mg/h by continuous infusion in the positive study, compared with 7.8 mg/h with intermittent boluses in the negative study.

Our technique more closely resembled that used in the positive study namely, continuous infusion of local anesthetic at a much larger volume (up to 45 mg/h). We followed the recommendations of Malawer et al. (6), who used a maximum infusion rate of 0.5 mg/kg/h and the same technique in their study. The reported serum bupivacaine levels ranged from undetectable to 1.1 μg/mL. In our study, only one patient received the maximum infusion rate of bupivacaine. In patients with hepatic or renal disease, the maximum infusion rate of bupivacaine should be reduced because bupivacaine clearance may be impaired.

The patients in both the positive and negative study differed from ours, all of whom had cancer. The incidence of phantom limb pain in patients undergoing amputation for cancer has been reported to be as high as 90% within the first year (2). Factors that place a patient at risk for developing phantom limb pain include preoperative pain level and coping strategy used (12,13). In oncology patients, pain is the most common presenting symptom. The combination of pain with the psychologic traumatization of the patient given a devastating diagnosis of cancer may lead to a higher incidence of phantom pain in oncology patients than in trauma patients. Krane and Heller (2) and Smith and Thompson (14) reported phantom limb pain to be more common in pediatric oncology patients than in pediatric trauma patients. In our series, phantom limb pain occurred during the first year in only three of the six patients, and only one patient, who refused further treatment, had significant pain at 1 year follow-up evaluation. On the basis of our experience with local anesthetic infusion through nerve sheath catheters following upper extremity amputation, we recommend the following:

- Two or more nerve sheath catheters should be placed within the amputated brachial plexus during surgery if at all possible.
- Bupivacaine should be administered through each catheter as a bolus followed by an infusion of at least 20 mg/h to the brachial plexus (based on the minimum effective infusions in our study and the positive experimental study [4]).
- A strategy for pain-free emergence from anesthesia should be developed, including timely delivery of local anesthetic and addition of other analgesic modalities as needed. Phantom pain should be treated aggressively if it develops.

Although this report is not conclusive, it suggests that continuous infusion of local anesthetic via nerve sheath catheters provides excellent postoperative analgesia following upper extremity amputation. The incidence of phantom limb pain did not differ from the retrospectively reviewed histories of other patients undergoing this procedure without this intervention. Combining this technique with preoperative nerve block may improve the immediate postoperative analgesia and may reduce the incidence of phantom limb pain. However further studies are needed to delineate the role of analgesia, whether preemptive or postoperative, in preventing phantom limb pain.

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Intraarticular Morphine, Bupivacaine, and Morphine/Bupivacaine for Pain Control after Knee Videoarthroscopy

George F. Khoury, M.D., Andrew C. N. Chen, Ph.D.,† Douglas E. Garland, M.D.,‡ Christoph Stein, M.D.§*

Evidence has accumulated that opioids can produce potent antinociceptive effects by interacting with opioid receptors in peripheral tissues. This study sought to compare the effects of morphine with those of bupivacaine administered intraarticularly upon pain following arthroscopic knee surgery. In a double-blind, randomized manner, 33 patients received either morphine (1 mg in 20 ml NaCl; n = 11), bupivacaine (20 ml, 0.25%; n = 11), or a combination of the two (n = 11) intraarticularly at the completion of surgery. After 1, 2, 3, and 4 h and at the end of the 1st and 2nd postoperative days, pain was assessed by a visual analogue scale, and supplemental analgesic requirements were recorded. Pain scores were significantly greater in the morphine group than in the other two groups at 1 h. There were no significant differences at 2 and 3 h. From 4 h until the end of the study period, pain scores were significantly greater in the bupivacaine group than in the other two groups. Analgesic requirements were significantly greater in the morphine group than in the other groups at 1 h but were significantly greater in the bupivacaine group than in the other groups throughout the remainder of the study period. We conclude that intraarticular morphine produces an analgesic effect of delayed onset but of remarkably long duration. The combination of these two drugs results in satisfactory analgesia throughout the entire observation period. (Key words: Analgesics, opioid: morphine. Anesthetics, local: bupivacaine. Anesthetic techniques: intraarticular. Pain: postoperative.)

OPIOID ANALGESIA has been associated with activation of opioid receptors within the central nervous system. Evidence has also accumulated that exogenous[1–3] as well as endogenous[4,5] opioids can produce pronounced antinociceptive effects by interacting with opioid receptors in peripheral tissues. We have been able to differentiate the types of opioid receptors involved[6] and to demonstrate such receptors on peripheral terminals of primary afferent neurons functionally[7] and *in situ*.[5] Furthermore, we have shown that peripherally administered opioids can elicit significant analgesic effects in humans.[8,9] Thus, low doses of intraarticular morphine, injected at the completion of arthroscopic knee surgery, can produce relatively long-lasting postoperative analgesia apparently *via* activation of local opioid receptors in the knee joint.[9]

Postoperative analgesia after arthroscopy has also been examined after the intraarticular administration of conventional local anesthetics.[10,11] So far, however, the results are equivocal. Thus, in patients receiving intraarticular bupivacaine, Henderson *et al.*[10] found no effect, whereas Chirwa *et al.*[11] found significantly reduced pain reports and supplemental analgesic use compared to controls.

The present study was designed 1) to examine the analgesic effect of intraarticular administration of a small dose of morphine upon postoperative pain in patients who had undergone arthroscopic knee surgery; 2) to compare the effect to that produced by a conventional local anesthetic, bupivacaine; and 3) to examine the effect of a combination of morphine and bupivacaine.

Materials and Methods

PATIENTS

The project was institutionally approved, and informed consent was obtained from each patient before surgery. Thirty-three outpatients undergoing arthroscopic knee surgery were studied. Surgical procedures included diagnostic tissue excisions, partial or total meniscectomies, and lateral release, with approximately equal representation among the groups. The criteria for exclusion from the study were ASA physical status rating of 3 and greater[12] and the requirement for postoperative intraarticular drainage. All patients received meperidine (1 mg/kg intramuscularly) and midazolam (0.03 mg/kg intramuscularly) 1 h before surgery. Anesthesia was induced with thiopental (4 mg/kg). Succinylcholine (1 mg/kg) was administered to facilitate tracheal intubation, after which anesthesia was maintained with O_2/N_2O and isoflurane (0.8–2.0%).

EXPERIMENTAL DESIGN

At the conclusion of surgery but before the arthroscope was removed, patients received one of the following so-

* Adjunct Associate Professor of Anesthesiology, Department of Anesthesiology, University of California, Los Angeles; Staff Anesthesiologist, Long Beach Community Hospital.

† Associate Professor of Pediatrics, Department of Pediatrics, University of California, Los Angeles.

‡ Clinical Professor of Orthopedics, Department of Orthopedic Surgery, University of Southern California, Los Angeles; Medical Staff, Long Beach Community Hospital.

§ Consultant of Anesthesiology, Department of Anesthesiology, Ludwig-Maximilians University, Klinikum Grosshadern, München; Department of Neuropharmacology, Max-Planck-Institut für Psychiatrie, Martinsried, Federal Republic of Germany.

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Address reprint requests to Dr. Khoury: Department of Anesthesiology, UCLA School of Medicine, Los Angeles, California 90024-1778.

lutions intraarticularly in a double-blind, randomized manner: 1 mg morphine-sulfate in 20 ml NaCl (n = 11), 20 ml 0.25% bupivacaine (n = 11), or 1 mg morphine sulfate in 20 ml 0.25% bupivacaine (n = 11). These doses were chosen based on previous animal and human studies.[6,8,9,11] Thereafter, general anesthesia was terminated. Since previous studies had shown that both intraarticular morphine and bupivacaine were more effective than saline,[8,9,11,13] we did not use such a control group, for ethical considerations.

Pain Assessment

Postoperative pain was assessed using a 10-cm visual analogue scale (VAS)[14] ranging from "no pain" to "unbearable pain." Scores were taken at 1, 2, 3, and 4 h after drug injection and at the end of the 1st and 2nd postoperative days, respectively. Supplemental analgesic medication was available upon request and was recorded at the above intervals. In the recovery room, fentanyl was given in increments of 0.05 mg and titrated to the patient's subjective level of comfort. Upon discharge from the hospital, the patients were instructed to use 1 or 2 codeine tablets every 3 h when needed, and were given a sheet of paper that had two VAS and a space for analgesics. They were asked to rate their pain intensity over the preceding 24 h and at the end of each postoperative day on the VAS and to record their analgesic usage at the same time. These sheets were then mailed back to the hospital by about 70% of the patients in each group.

Data Analysis

Demographic data were analyzed by analysis of variance (ANOVA).[15] To score the VAS, the distance (in millimeters) from the "no pain" end to the mark provided by the patient was measured. To determine supplemental analgesic requirements, meperidine doses were converted into codeine equivalents based on an equianalgesic ratio of 1:1.6.[16] Each patient's total consumption during their stay in the recovery room (1st h), in the outpatient department (2nd–4th h), and at home (1st and 2nd postoperative days) was calculated. Comparisons of pain scores between groups were made using the Kruskal-Wallis test and Dunn's procedure for *post hoc* evaluation. Comparisons of analgesic consumption between groups were made using an ANOVA and Fisher's least significant difference (LSD) procedure for *post hoc* testing.[15] A P value ≤ 0.05 was considered significant.

Table 1. Demographic Data

	Age (yr)	Weight (kg)	Duration of Surgery (min)
Morphine (n = 11)	44.0 ± 9.5	76.2 ± 2.7	67 ± 12
Bupivacaine (n = 11)	45.2 ± 8.0	74.3 ± 3.6	59 ± 7
Morphine + bupivacaine (n= 11)	44.9 ± 6.5	73.1 ± 2.2	61 ± 8

Means ± SEM are given.

Results

There were no significant differences (ANOVA) in patient demographics (table 1) and preoperative pain scores (average 12.4 ± 4 mm).

VAS scores were not different between groups up to 3 h postoperatively ($P > 0.05$, Dunn's test) except for the 1st h, when the morphine group displayed significantly greater values than the other two groups ($P < 0.006$, Dunn's test). From the 4th postoperative hour until the end of the study period (2nd postoperative day), pain scores were significantly greater in the bupivacaine group than in the other two groups ($P < 0.05$, Dunn's test) (table 2).

Supplemental analgesic consumption was significantly greater in the bupivacaine group than in the other two groups throughout the study period ($P < 0.05$, LSD test) except for the 1st h, during which time the morphine group required significantly more than the other two groups ($P < 0.001$, LSD test) (table 3).

Discussion

In patients who have undergone arthroscopic knee surgery, intraarticular morphine produces more pronounced analgesia than intraarticular bupivacaine between the 4th h and the end of the 2nd postoperative day, whereas bupivacaine is a superior analgesic during the 1st h postinjection. The combination of both substances produces satisfactory analgesia throughout the entire study period.

The analgesic efficacy of these treatments is documented by a direct subjective measure of pain intensity, the VAS,[14,17] and an indirect indicator, supplemental analgesic requirements. Both measures appear to correlate well, in that during the 1st h both VAS scores and analgesic requirements were significantly greater in the group receiving morphine alone than in the other two groups, and between the 4th h and the end of the study period, both measures were greater in the group receiving bupivacaine alone than in the other two groups. Despite the larger amounts of requested additional analgesics, the respective differences in reported VAS scores remain quite distinct. These differences might have been even greater in the absence of additional medication, which, however, was impossible to withhold for obvious ethical reasons.

TABLE 2. Visual Analogue Scores

Time	1 h	2 h	3 h	4 h	1 day	2 days
Morphine (G1)	56.0 ± 10 24.15	28.3 ± 11 17.33	22.8 ± 7 12.33	13.9 ± 7 14.66	18.6 ± 6 12.72	13.9 ± 5 13.67
Bupivacaine (G2)	22.3 ± 9 12.18	26.5 ± 11 15.30	22.5 ± 6 16.95	32.8 ± 9 20.40	36.8 ± 7 21.23	28.6 ± 6 21.55
Morphine + bupivacaine	20.0 ± 4 13.86	14.3 ± 6 14.18	20.6 ± 5 16.77	8.6 ± 4 11.72	20.2 ± 3 13.46	13.0 ± 4 12.36
F value	10.07	0.74	1.74	5.71	5.76	6.67
P value	0.006	NS	NS	0.05	0.05	0.04
Post hoc Comparison	G1 > G2 G1 > G3			G2 > G1 G2 > G3	G2 > G1 G2 > G3	G2 > G1 G2 > G3

Means ± SEM (millimeters) and mean ranks are given. Data were analyzed by Kruskal-Wallis' and Dunn's procedures. NS = difference not significant.

The present data suggest that intraarticular bupivacaine produces an immediate analgesic effect of relatively short duration, while morphine produces a much longer-lasting effect but with a delayed onset. These characteristics agree with previous reports examining the intraarticular administration of bupivacaine,[10,11,18] or morphine.[8,9,18]

To discuss these time courses of action, one has to consider several aspects. First, the question arises as to the site of action of these drugs. It is generally accepted that local anesthetics exert their effects through an action upon peripheral nerves, and the duration of action of bupivacaine observed here is entirely consistent with previous studies.[11,13,19] In the case of opioids, however, such effects have been demonstrated only recently. Thus, low doses of peripherally administered opioids can produce potent antinociceptive effects mediated by peripheral opioid receptors in inflamed tissue of the rat.[3,6,20] Moreover, in humans, low doses of intraarticular morphine can significantly inhibit postoperative pain by an activation of peripheral opioid receptors within the joint.[9] Similar to the spinal application of opioids, the duration of analgesia after intraarticular morphine appears to be considerably longer than after systemic administration.[21] The remote possibility of a central action of this small dose of morphine, although not examined here, has been excluded in a previous study.[9] Other possible explanations are morphine's low lipid solubility[21] and its slow rate of absorption into the circulation resulting therefrom, or a relatively low blood flow to the articular area. In contrast, the relatively high lipophilicity of bupivacaine[19] could account for its faster uptake into the circulation and consequent removal from the joint. On the other hand, if one assumes sensory nerves to be the common site of action of these drugs (see below), these physicochemical characteristics could explain morphine's delayed and bupivacaine's immediate onset of action.

Second, the mechanisms of action of these drugs have to be taken into account. Local anesthetics are thought to produce their effects through inhibition of the generation and/or propagation of action potentials at the neuronal membrane and a resulting blockade of afferent nociceptive barrage.[19] In the case of opioids, two different peripheral mechanisms may result in a decreased nociception. On the one hand, morphine may diminish local posttraumatic inflammation through actions on leuko-

TABLE 3. Postoperative Analgesic Consumption

Time	Fentanyl (μg)	Codeine (mg)		
	1 h	2–4 h	Day 1	Day 2
Morphine (G1)	130.0 ± 16.7	45.0 ± 14.3	50.0 ± 21.0 (95.0 ± 14.5)	33.3 ± 21.6 (128.3 ± 13.9)
Bupivacaine (G2)	21.4 ± 6.4	105.0 ± 22.2	120.0 ± 26.6 (225.0 ± 23.9)	84.5 ± 23.2 (309.5 ± 21.2)
Morphine + bupivacaine (G3)	31.8 ± 10.1	36.0 ± 5.7	66.0 ± 11.8 (72.0 ± 6.6)	33.0 ± 6.6 (105.0 ± 5.8)
Value	24.54	5.73	2.92	6.51
Value	<0.001	0.008	0.049	0.005
Post hoc Comparison	G1 > G2 G1 > G3	G2 > G1 G2 > G3	G2 > G1 G2 > G3	G2 > G1 G2 > G3

The patients' total consumption during their stay in the recovery room (1 h), in the outpatient department (2–4 h), and at home (postoperative days 1 and 2) is given in means ± SEM. Data were analyzed by analysis of variance and Fisher's least significant difference procedure. Cumulative amounts of codeine are given in brackets.

cytes,[22,23] inhibition of bradykinin formation,[22] or inhibition of plasma extravasation.[24] On the other hand, opioid binding sites have been shown on primary afferent neurons.[25–27] We have demonstrated such receptors functionally[7] and immunohistochemically.[5] Conceivably, activation of these neuronal receptors can cause attenuation of the excitability or nociceptive input terminals[28–30] and/or inhibition of release of excitatory transmitters[31,32] and ultimately result in antinociception.

In summary, we have shown that in patients having undergone arthroscopic surgery, intraarticular bupivacaine yields postoperative analgesia of immediate onset but only of short duration (2–3 h), whereas intraarticular morphine produces an analgesic effect of delayed onset (about 2 h postinjection), but of remarkably long duration (as long as 2 days postoperatively). The combination of these two drugs results in satisfactory analgesia throughout the entire observation period.

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Original Research

REGIONAL ANESTHESIA IN FOOT AND ANKLE SURGERY

*Thomas H. Lee, MD**
Keith L. Wapner, MD†
Paul J. Hecht, MD†
Patrick J. Hunt, MD§

A B S T R A C T

A method of regional anesthesia use in forefoot and midfoot surgery is described. Careful identification of the peripheral sensory nerves allows for effective anesthesia using bupivacaine and lidocaine in addition to sedation for comfort. A review of 355 patients showed that 98% received an effective surgical block of the sensory nerves. Complications were found to be minimal and patient satisfaction was high. This method provides a safe and effective anesthesia alternative for foot and ankle surgery.

With the advent of more effective drugs for patient sedation, the role of regional anesthesia in foot and ankle surgery has increased. Traditionally, several types of anesthesia have been available, including general, spinal epidural, and Bier block. Local block with sedation, often referred to as MAC (monitored anesthesia care) has proven to be both safe and effective in surgical procedures of the foot and ankle. The use of an ankle block provides adequate anesthesia for midfoot and forefoot procedures.[1-4] Augmentation with sedation allows the use of a tourniquet while still permitting patient comfort. Sedation also reduces patient anxiety and significantly reduces the pain of the ankle block insertion, thus increasing patient acceptance of this technique. Sedation avoids the common after-effects of spinal or general anesthesia. This allows the patient to comfortably undergo surgical procedures with minimal systemic involvement.

The purpose of this article is to review our experience with regional ankle block and sedation for foot and ankle surgery. Specific technique and the pertinent anatomy are reviewed.

MATERIALS AND METHODS

From 1989 to 1992, regional anesthesia was used in 355 of the 382 foot and ankle cases performed by two authors (Wapner and Hecht). A detailed questionnaire and examination were obtained in 164 patients, and a thorough review of the hospital and anesthesia record was obtained for the remaining patients. Regional anesthesia was limited to forefoot and midfoot surgery. The ankle block was performed by two authors (Wapner and Hecht) in all cases. Ankle blocks were performed in the same standard way using established landmarks, as described below. Regional anesthesia was augmented by the anesthesiologist using propofol along with small amounts of fentanyl and midazolam in all cases. Cardiovascular and pulmonary status was monitored by the anesthesiologist in all cases. All blocks were performed at the commencement of the case, allowing 10 minutes for the anesthesia to take effect. Patients were routinely prepared for general anesthesia in the event of failure of the regional block.

Anatomy. The foot is innervated by five significant sensory nerves: posterior tibial, superficial peroneal, deep peroneal, sural, and saphenous. Each nerve is selectively blocked for complete sensory anesthesia. The posterior tibial nerve lies within the neurovascular tunnel on the posterior aspect of the tibia. It is bordered by the flexor hallucis longus tendon and its tendon sheath laterally and the flexor digitorum longus medially. At the level of the distal tibia, the neurovascular bundle lies nearly in the midline along the medial border of the Achilles tendon. A tangential line along the medial border of the Achilles at the medial malleolus would intersect the posterior tibial nerve and its more laterally placed posterior tibial artery. The posterior tibial nerve divides into the medial and lateral plantar nerve after it delivers the medial calcaneal

*From *the Orthopaedic Institute, Grant Medical Center, Columbus, Ohio; and †the Department of Orthopedic Surgery, Medical College of Pennsylvania and Hahnemann University; and §the Department of Anesthesiology, Jefferson Medical College of Thomas Jefferson University, Philadelphia, Pa.*

Reprint requests: Keith L. Wapner, MD, 219 W Broad St, 5th Floor, Philadelphia, PA 19102.

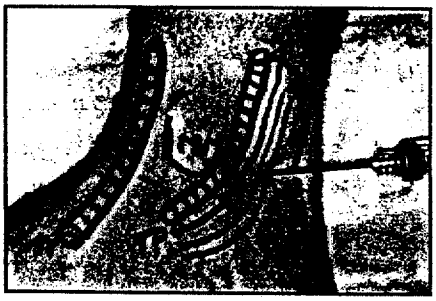

Fig 1: To block the posterior tibial nerve, the needle is introduced tangentially to the medial border of the Achilles tendon.

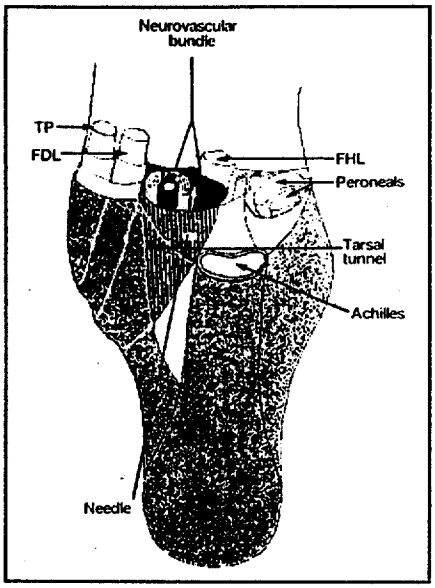

Fig 2: The point of the needle is aimed at the distal tibia and encounters the neurovascular bundle which is a midline structure. TP=tibialis posterior tendon, FDL=flexor digitorum longus tendon, FHL=flexor hallucis longus tendon.

plantar nerve lies between the abductor hallucis muscle and the flexor digitorum brevis muscle, where it gives off a medial branch to the great toe and finally divides at the base of the metatarsals to three plantar digital nerves. The sensory distribution is similar to the median nerve in the hand and includes the inner three and one half toes and their nailbeds. The lateral plantar nerve passes between the flexor digitorum brevis muscle and the abductor digiti minimi muscle before dividing into the deep and superficial branch. Its distribution is similar to the ulnar nerve in the hand and includes the lateral one and one-half toes and their nailbeds.

The deep peroneal nerve is located in the dorsum of the foot between and deep to the extensor tendons of the first and second toes. Fascia from the medial border of the extensor digitorum brevis extends over the nerve before coalescing with the extensor hallucis longus tendon. The deep peroneal nerve is lateral to the dorsalis pedis which provides a clear landmark. The deep peroneal nerve innervates the first webspace and provides sensory twigs to the first and second toe. Variations with the deep peroneal nerve are multiple.

The superficial peroneal nerve perforates the crural fascia on the anterior aspect of the distal two thirds of the leg, and runs subcutaneously along the lateral border of the foot and ankle. The superficial peroneal nerve with its medial and intermediate dorsal cutaneous branches innervate the foot centrally. These branches provide the dorsomedial hallucal nerve (anastomosis with the deep peroneal nerve in the first webspace) and the nerves to the second and third webspaces.

The sural nerve, arising as a coalescence of the tibial nerve and the common peroneal nerve, becomes subcutaneous distal to the midpoint of the leg. It merges with the short saphenous vein as it courses posteriorly and inferiorly to the lateral malleolus. The sural nerve innervates the lateral border of the foot and often can course more distally to innervate and include up to the fourth interspace. The sural nerve also provides the lateral calcaneal nerve, which provides the sensory innervation over this area.

The saphenous nerve, arising as a terminal sensory branch of the femoral nerve, becomes subcutaneous at the lateral aspect of the knee. It follows the great saphenous vein to run over the anterior superior aspect of the medial malleolus. The saphenous nerve terminates in the medial border of the foot with sensory distribution along the instep. It often can extend as far as the medial first metatarsophalangeal joint and communicates with the medial branch of the superficial peroneal nerve.

Pharmacology. The primary anesthetic used is 0.5% bupivacaine hydrochloride (Marcaine) without epinephrine. The maximum safe dose of Marcaine without epinephrine should not exceed 2.5 mg/kg of body weight. In a typical 70 kg adult, this comprises a maximum dose of 175 mg, or 35 mL of 0.5% Marcaine solution. The elimination half life is 2.7 hours, and the recommended dose is once every 3 hours. Often, 1% lidocaine hydrochloride without epinephrine is used to supplement the block because of its greater speed of onset. The maximum safe dose of lidocaine is 4.5 mg/kg of body weight and should not exceed 300 mg. For a typical 70 kg adult, this would be 30 mL of lidocaine. The effects of bupivacaine (Marcaine) and lidocaine are additive. Proportionate uses of these two compounds should not exceed the proportionate maximum dosages.

Block of the Posterior Tibial Nerve. The patient is approached in the supine position. The lower extremity is externally rotated, with the knee flexed and the foot supported on the contralateral leg. The foot is held in 90° of dorsiflexion by the assistant. At the level of the distal tip of the medial malleolus, a 22-ga needle is introduced tangentially to the medial border of the Achilles tendon (Fig 1). The point of the needle is aimed at the distal tibia and is advanced until the distal tibia is felt (Fig 2). The needle is withdrawn slightly, and 10 mL of bupivacaine 0.5% without epinephrine is injected after aspiration to assure that the needle is not in a vessel.

Block of the Superficial Peroneal and Sapheneous Nerves. Just anterior to the injection side of the posterior tibial nerve, a wheal of bupivacaine is raised. The ring block is performed subcutaneously with 0.5% bupivacaine without epinephrine along the anterior ankle joint to include the superficial peroneal and saphenous nerve. Care is taken to remain superficial to the long extensor tendons.

Block of the Sural Nerve. The needle is introduced 1 cm distal and anterior to the lateral malleolus. A skin wheal is elevated, and the needle is advanced in a ring block fashion toward the plantar surface. Care is taken to avoid the lesser saphenous vein and t

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Fig 3: To block the deep peroneal nerve, the needle is introduced into the interval between the extensor hallucis longus and the extensor digitorum longus tendon.

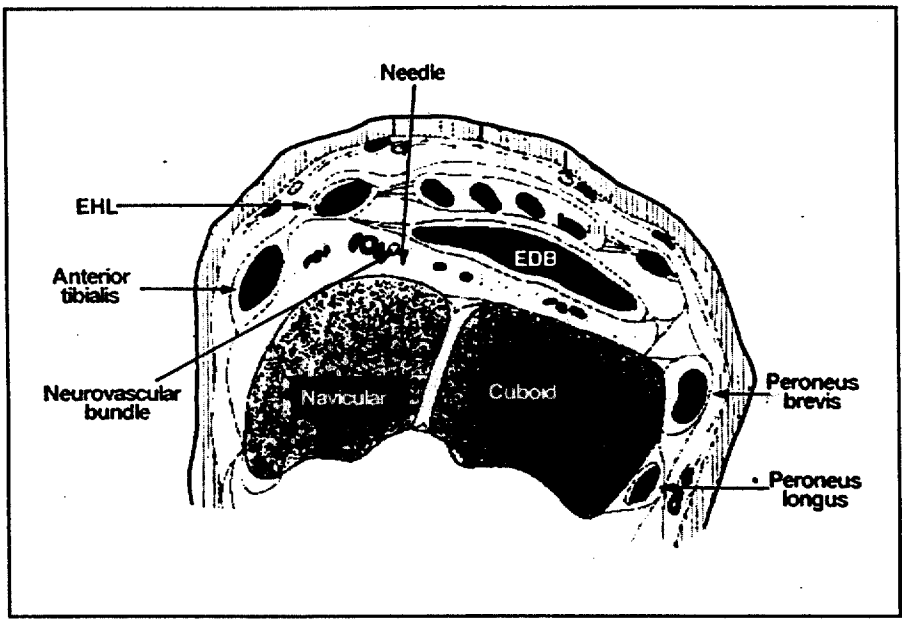

Fig 4: The needle is introduced perpendicular to this interval and advanced beyond the level of the deep ligaments. The fascia from the medial border of the extensor digitorum brevis extends over the nerve. EHL=extensor hallucis longus.

ficial to the peroneal tendons.

Block to the Deep Peroneal Nerve. The interval between the extensor hallucis longus tendon and the extensor digitorum longus tendons of the second toe is marked at the level of the midtarsus (Fig 3). The dorsalis pedis is palpated within this interval. The needle is introduced perpendicular to this interval and advanced beyond the level of the deep ligaments (Fig 4). After initial operation, 3 mL of bupivacaine is injected.

Postoperatively, close neurovascular examination was performed routinely. At the patient's first dressing change, the ankle was closely inspected for hematoma, neuroma formation, discoloration, and swelling. Patients were followed up after complete recovery with a detailed questionnaire.

RESULTS

In 382 total cases performed by the senior authors, 355 patients underwent regional anesthesia for forefoot and midfoot surgery. The Table lists the procedures that underwent successful regional block. Regional anesthesia was found to be successful in 352 patients, and the surgery was successfully completed without conversion to general anesthesia. Two patients could not tolerate the regional anesthesia and had no anesthesia despite near maximal Marcaine and lidocaine dosage. One patient had incomplete anesthesia and, due to the patient's anxiety, required conversion to general anesthesia. Surveys from 164 patients were evaluated. Of this group, 3.6% complained of minor pain at the operative site during the surgery; one patient stated the pain occurred at the end of the case. All patients stated the degree of pain did not affect their level of satisfaction with the technique of regional anesthesia. Another 3.0% of patients complained of sensation of pulling or pressure felt at the operative site. Six patients complained of discomfort at a site other than the operative site, most notably at the site of the tourniquet. Intravenous sedation during the case was well tolerated in 98% of patients. The sedation did have several postoperative complications in 16 patients. Ten patients complained of nausea, 3 patients complained of intravenous infiltration leading to bleeding and ecchymosis, 3 complained of dizziness, and 1 of slight laryngospasm with difficulty breathing.

No patients complained of vasovagal response or of postoperative neuritis secondary to the injection. No patients experienced postoperative hematoma formation after discharge from the hospital, and there were no postoperative wound infections from the injection sites. One hundred sixty-two of the 164 patients responding to the survey stated they would prefer to have the surgery performed in the same fashion.

Table

SUMMARY OF PROCEDURES WITH SUCCESSFUL REGIONAL BLOCKS

Forefoot Cases (eg, hallux valgus correction, first MTP fusion, interdigital neuroma, cheilectomy, lesser toe correction)	285 patients
Midfoot Cases (eg, midfoot fusion, midfoot osteotomy, hardware removal, tendon reconstruction)	41 patients
Hindfoot Cases (eg, excision ankle osteophyte, calcaneal osteotomy, ankle arthrotomy, osteochondritis dessicans of talus)	26 patients

DISCUSSION

It is the goal of the orthopedic surgeon to perform surgery with minimal risk to the patient. By using a technique of regional ankle block and sedation, the anesthetic risk of the surgery is markedly reduced.[5] There are higher risks to patients with underlying medical conditions such as diabetes mellitus, rheumatoid arthritis, and hypertension with the use of general anesthesia and in spinal or epidural anesthesia.[3] Ankle blocks tend to be preferable to Bier block in that it avoids intravenous lidocaine[3] and tourniquet pain, and the adjustment to postoperative discomfort is more gradual. Deaths are also noted in the use of general and spinal anesthesia and also in Bier block anesthesia.[6]

Regional ankle block anesthesia with sedation has several distinct advantages. The sedation allows the patient to comfortably tolerate the discomfort of the thigh tourniquet, which lies in an unanesthetized area. The tourniquet provides for a bloodless field and avoids excessive intraoperative bleeding. This completely obviates postoperative transfusions. The decreased anesthesia preparation time allows for early mobilization of the patient postoperatively and avoids common postoperative complications associated with general anesthesia (eg, nausea, vomiting, sore throat, difficulty with urination, and ileus).[2] Early mobilization allows for shorter hospitalizations, avoids complications of bedrest, and allows the patient a sense of wellness.[5]

Our technique consists of two discrete blocks of the posterior tibial nerve and the deep peroneal nerve in addition to a subcutaneous ring around the ankle. It utilizes well-demarcated anatomic landmarks to provide a safe, effective, and reliable block of all known sensory branches. Patient satisfaction is high, and patients report a high degree of comfort with minimal anxiety after thorough preoperative counseling and little postoperative complication related to the block. Three patients required conversion to general anesthesia despite maximal doses of anesthetic. Despite carefully placed injections, variations in the anatomy may occur which will lead to incomplete anesthesia. Our own experience shows this to occur, but rarely. The use of this foot and ankle block technique has been effective in our experience, and is highly recommended for use in the increasing role of ambulatory surgery.

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Analgesic Effects of Intra-articular Morphine During and After Knee Arthroscopy: A Comparison of Two Methods

Olof Lundin, M.D., Bengt Rydgren, M.D., Leif Swärd, M.D., Ph.D., and Jon Karlsson, M.D., Ph.D.

Summary: The objective of this study was to compare the analgesic effects of intra-articularly administered bupivacaine with bupivacaine/morphine during and after therapeutic knee arthroscopy. In a prospective, randomized study, 50 patients with clinical signs of medial meniscal injury were allocated to two groups, A and B. The patients in group A received 40 mL of 0.25% bupivacaine while the same dose of bupivacaine combined with 1 mg of morphine sulphate was administered in group B. Pain was estimated using the visual analogue scale (VAS) during surgery and at 2, 4, 6, and 24 hours after the operation was completed. Supplementary analgesic requirements were also registered, as well as the patients' overall rating of the entire procedure. The pain scores were significantly lower in Group B throughout the whole postoperative observation period. However, no significant differences were found between the two groups in terms of intraoperative pain scores, supplementary analgesic requirements, or the overall rating of the procedure. This study provides evidence that arthroscopic surgery can be performed in a safe manner after intra-articularly administered bupivacaine with or without low-dose morphine. The combination of low-dose morphine and bupivacaine did, however, produce a superior postoperative analgesic effect during the 24 hours following knee arthroscopy compared with bupivacaine alone. **Key Words:** Knee arthroscopy—Local anaesthesia—Analgesia—Morphine.

Several studies[1-3] report that knee arthroscopy can be performed effectively and safely after combining the subcutaneous and intra-articular administration of local analgesic agents. Keading et al.[4] reported satisfactory pain relief during arthroscopic knee surgery using intra-articular bupivacaine. However, this analgesic effect has been shown to last for only 2 to 4 hours[5] or less.[6] Satisfactory postoperative pain relief after intra-articularly administered local anesthetics at the end of arthroscopic knee surgery performed under general anesthesia has also been reported in several studies.[7] Intra-articularly administered morphine has been shown to produce prolonged postoperative analgesia after arthroscopic knee surgery.[7] These findings correspond well with the study by Karlsson et al.[8] in which the analgesic effects of bupivacaine and/or morphine administered intra-articularly at the end of arthroscopic anterior ligament reconstruction were investigated.

However, contradictory findings have been presented by other investigators. Hughes[9] and Milligan et al.[10] did not find that any significant analgesic effect was produced by intra-articular bupivacaine and Ates et al.[11] found both prilocaine and bupivacaine to be ineffective as postoperative analgesia after arthroscopy. White et al.[12] found short but insignificant pain relief after the subcutaneous and intra-articular administration of prilocaine combined with adrenalin. To further analyse the potential analgesic effect of intra-articular morphine, the aim of this study was to compare intra-articularly administered bupivacaine with bupivacaine/morphine during and after arthroscopic knee surgery in a homogeneous group of patients.

From the Departments of Orthopaedics and Anesthesiology (B. R.), Östra University Hospital, Göteborg, Sweden.
Address correspondence and reprint requests to Jon Karlsson, M.D., Ph.D., Department of Orthopaedics, Östra University Hospital, S-416 85 Göteborg, Sweden.

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PATIENTS AND METHODS

Fifty patients with clinical signs of medial meniscal injury were included in this study. Informed consent was obtained from all patients before surgery and the study was approved by the Ethics Committee at Göteborg University. The study was prospective, randomized, and controlled by an unbiased observer. The patients were randomly allocated (using closed envelopes) to two groups with 25 patients in each.

Surgical Procedure

Twenty minutes before the start of the operation, all patients received 8 mL of 0.25% bupivacaine subcutaneously in the anteromedial and anterolateral arthroscopic portals and 32 mL of 0.25% bupivacaine intra-articularly. In group B, the local anesthetic was combined with 1 mg of morphine sulphate. All the operations were performed by one of three experienced arthroscopic surgeons. A standard 5-mm arthroscope connected to a video camera and a television monitor was used. A pressure-monitored pump without continuous drainage was used. No further drugs were administered into the joint after the completion of surgery. All the patients were operated on as day cases. No specific surgical complications were seen.

Anesthetic Regimen

Before the administraion of bupivacaine/morphine, all patients received 0.5 mg of atropine intravenously to minimize the risk of bradyarrhythmia and 2 mg of midazolam (Dormicum; Roche, Basel, Switzerland) intravenously for sedation. Blood pressure, electrocardiogram (ECG), and pulse oximetry were continuously monitored during the operation. There were no anesthetic complications.

Pain Assessment

The intraoperative and postoperative pain scores were assessed using the visual analogue scale (VAS), a 10-cm scale ranging from 0 (no pain at all) to 10 (worst possible pain).[13] Pain scores were evaluated intraoperatively during the removal of the meniscus or some other intra-articular procedure. Pain scores postoperatively were evaluated at 2, 4, 6, and 24 hours after the operation was completed. The 24-hour pain score was mailed by the patient to the independent observer. The overall rating of the procedure was estimated during the 24 hours after surgery using the VAS scale from 0 (best possible) to 10 (worst possible). Supplementary analgesic medication was available on request and was also registered during the first 6 hours after the operation, while the patient was still on the day-care ward. All pain scores were administered by an independent observer not involved in the surgical procedure. None of the surgeons was involved in the administration of the VAS tests.

Statistics

All values are given as median (range). The Mann Whitney-U nonparametric two-tailed test was used in the independent comparisons of the treatment groups; $P < .05$ was considered statistically significant.

RESULTS

Eight patients were excluded from the study, six in group A and two in group B. Three were excluded because of intraoperative pain that required general anesthesia, two in group A and one in group B (not significant). In these patients, however, the intra-articular findings did not differ from those of the rest of the patients. Two patients had to be withdrawn because of technical errors, incorrect pressure in the pressure-monitored pump, and failure of the video apparatus, respectively. Furthermore, one patient was excluded after nonsteroidal anti-inflammatory drugs were given preoperatively and two patients did not complete the 24-hour follow-up. In all, 19 patients in group A and 23 in group B completed the study.

There were no significant differences between the groups in terms of patient demographics, such as sex and age (Table 1). The intraoperative findings were homogeneous, as were the surgical procedures. In group A, partial meniscectomy was performed in 11 patients, shaving of joint cartilage degeneration in two and in six patients the procedure was diagnostic. In group B, partial meniscectomy was performed in 13 patients, shaving of joint cartilage degeneration in five, removal of a loose body in one and in four patients the procedure was diagnostic.

TABLE 1. *Demographic Data for Patients in Both Groups*

	Group A Bupivacaine	Group B Bupivacaine/ Morphine
Sex ratio (M:F)	15:4	18:5
Age (y)	47 (25-71)	41 (24-66)
No. of surgical procedures	13	19
No. of diagnostic procedures	6	4
Duration of operation (min)	19 (7-35)	17 (8-30)
No. of patients withdrawn due to pain	2	1
No. of patients withdrawn for other reasons	5	—

During the operation, there was no difference in VAS scores between the groups (Table 2). VAS scores were registered at the moment of meniscal removal, shaving or abrasion of the joint cartilage or removal of a loose body. If only diagnostic arthroscopy was performed, the registration of pain was made when the arthroscope was moved inside the joint.

During the next 24 hours of the postoperative period, the pain scores were registered at rest. The pain scores were significantly lower in group B throughout the entire postoperative period, i.e., 2, 4, 6, and 24 hours after the completion of surgery (Table 2).

The consumption of supplementary analgesics was small in both groups and there was no significant difference. All patients were discharged from hospital the same day. There was no difference between the two groups in terms of the overall experience of the entire procedure. No pharmacological side effects were registered.

DISCUSSION

In several studies, peripheral opiate receptors have been assumed to mediate the analgesic effect of intra-articularly administered morphine during arthroscopic knee surgery.[8,14-16] Low doses of peripherally administered opioids have been shown to produce relatively long-lasting postoperative analgesia. This effect is thought to depend on the interaction with nociceptive afferents in the joint synovia.[7] These findings have been supported by Heard et al.[17] and Raja et al.[18] Moreover, Joshi et al.,[16] when studying the plasma profiles of morphine and its metabolites after the local administration of low-dose morphine, thought that the magnitude of these profiles was too low to produce effective, centrally mediated analgesia.

TABLE 2. *Pain Scores Assessed With VAS Peroperatively and 2, 4, 6, and 24 Hours Postoperatively*

	Group A Bupivacaine	Group B Bupivacaine/ Morphine	*P* Values
Intraoperative	2.0 (0-6) (2.4 ± 1.8)	1.5 (0-6) (2.1 ± 2.0)	.6
2 hours postoperative	0.5 (0-4) (1.3 ± 1.3)	0.0 (0-2) (0.3 ± 0.6)	.0082
4 hours postoperative	0.5 (0-5) (2.1 ± 2.4)	0.0 (0-9) (0.4 ± 0.7)	.0068
6 hours postoperative	2.0 (0-7) (2.6 ± 2.5)	1.0 (0-7) (0.8 ± 1.1)	.0089
24 hours postoperative	2.0 (0-8) (2.4 ± 2.1)	1.0 (0-7) (0.7 ± 0.9)	.0083
Overall experience	1.5 (1-5) (1.5 ± 1.5)	2.0 (0-7) (2.1 ± 1.7)	.16

NOTE. The patients' overall rating is also estimated by the use of VAS. All values are median (range). Mean values ± SD are shown in brackets.

The beneficial postoperative analgesic effect of intra-articular bupivacaine has previously been shown in patients undergoing diagnostic arthroscopy of the knee or medial and/or lateral meniscal resection.[4,5,19] No harmful effects by the drugs on the articular cartilage have been seen.[20] Most of the studies on this theme have been performed on patients receiving the local anesthetic agent after surgery under general anesthesia. Therefore, the pain score estimates have been made postoperatively.[1,2,4] However, there are a few studies in which plain local anesthesia has been used with pain score estimations both perioperatively and postoperatively.[22,23] The primary finding in this study was more complete postoperative analgesia during the first 24-hour postoperative period, when a local anesthetic was combined with an opioid, rather than being used alone.

Ekblom et al.[23] showed that the majority of knee arthroscopies can be safely performed under local anesthesia. They also found that 200 mg of intra-articularly administered pethidine exerted a significantly better analgesic effect postoperatively than prilocarpine. However, they found no peroperative difference in pain scores between pethidine and prilocarpine. These findings are in line with those of the present study.

Recent studies have shown and confirmed that opioid agonists have a pronounced peripheral antinociceptive effect in inflamed tissue.[16,24-27] The existence of such peripheral receptors has been shown in vivo by immunohistochemical methods.[26,28] In accordance with this, several authors have shown that intra-articularly administered opioids can exert good pain control during and after arthroscopic knee surgery. However, few controlled studies have been performed to assess the analgesic effect of an intra-articularly administered local anesthetic in combination with an opioid.[4,15,16,29] When studying three groups of patients (20 in each group) who received intra-articular meperidine (50 mg), morphine (5 mg), or placebo at the completion of surgery, Lyons et al.[30] found lower requirements for supplementary postoperative analgesics in the groups which received opioids. Jaureguito et al.[31] studied three groups of patients receiving morphine, bupivacaine, or placebo intra-articularly, and the morphine group reported significantly lower pain scores 24 hours postoperatively. This finding is in line with our results, which show an

extended analgesic effect when low-dose morphine is added.

The duration of analgesic action of bupivacaine is approximately 2 to 4 hours.[4,5,15] Both Stein et al.[7] and Khoury et al.[15] have reported an extended analgesic effect when bupivacaine was combined with low-dose morphine. Karlsson et al.[8] confirmed this finding in patients undergoing arthroscopic cruciate ligament reconstruction. Allen et al.[32] found less pain during the first 24 hours postoperatively when using bupivacaine/morphine than with bupivacaine alone. In a similar study, Boden et al.[33] found fewer requirements for supplementary analgesics in the bupivacaine/morphine group than in the bupivacaine group; however, there was no significant difference in the pain scores. Stein[34] suggested that the analgesic effect obtained by intra-articualar morphine might result from its anti-inflammatory effect. He also suggested that the relatively poor vascularization of the articular cartilage might indirectly contribute to the analgesic effect by diminishing the systemic absorption of the drug and thereby increasing the drug concentration at the local site.

There are a few studies that have not confirmed any beneficial effect by intra-articular morphine. In a recent review, Flory and Gamulin[35] concluded that the beneficial analgesic effects of peripherally administered opiates in animals have not been effectively confirmed in humans. Hege-Scheunig et al.[36] used a patient-controlled device for the administration of peripheral morphine for postoperative pain control. They could not find any difference in supplementary analgesic requirements between patients who at the end of the operation had received 1 mg of morphine intra-articularly and those who received placebo.

In conclusion, the present study shows that when morphine was combined with bupivacaine as the intra-articularly administrated analgesic in arthroscopic knee surgery, it provided more effective postoperative analgesia than bupivacaine alone. However, the intra-articular morphine did not influence the peroperative pain rating. The combination of bupivacaine and morphine appeared to enhance postoperative pain control but did not appear to influence the perioperative pain. The potential positive effects of knee arthroscopy under local anesthesia compared with general anaesthesia are reduced risk, increased well-being directly after surgery, the possibility of earlier discharge, and earlier mobilization. All these factors require the most complete postoperative pain control possible. A combination of bupivacaine and low-dose morphine appears to be beneficial when it comes to increasing the therapeutic potential when dealing with knee problems like those described in the present study.

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CRITICAL CARE MEDICINE

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Clinical Investigations

A prospective, randomized trial of gauze and two polyurethane dressings for site care of pulmonary artery catheters: Implications for catheter management

DENNIS G. MAKI, MD; SUSAN S. STOLZ, MS; SUSAN WHEELER, BSN; LEONARD A. MERMEL, DO, ScM

Objectives: **To compare the safety of a conventional polyurethane transparent dressing and a novel highly permeable polyurethane dressing, as compared with standard gauze and tape, as site dressings for pulmonary artery catheters; and to rigorously determine the sources of bloodstream infections deriving from these catheters.**

Design: **Prospective, randomized, clinical trial.**

Setting: **General adult intensive care units (ICUs) in a university hospital.**

Patients: **A total of 442 adult patients with pulmonary artery catheters were studied. Two thirds of the catheters had been inserted in the operating room and one third had been inserted in an ICU.**

Interventions: **Patients were randomized at the time of pulmonary artery catheter insertion to have one of three dressing regimens: a) sterile gauze and tape (control), replaced every 2 days; b) a conventional polyurethane dressing, replaced every 5 days; or c) a highly permeable polyurethane dressing, also replaced every 5 days.**

Measurements and Main Results: **The origin of each catheter-associated bloodstream infection was sought by quantitatively culturing the skin of the insertion site and all potential sources on the catheter, including the hub and infusate from each lumen of the introducer sheath and the pulmonary artery catheter, and intravascular segments of the introducer sheath and pulmonary artery catheter. Bloodstream infection was confirmed by demonstrating concordance between isolates from the device and blood cultures by pulsed-field electrophoresis of genomic DNA, digested with low-frequency-cleavage, restriction endonucleases.**

One hundred thirty catheters were randomized to be dressed with sterile gauze and tape (control), 127 with the conventional polyurethane dressing, and 185 with the highly permeable polyurethane dressing. Patients and catheters in the three dressing groups were very comparable.

Ninety-six (21.7%) of the 442 catheters studied showed colonization of the introducer sheath or the pulmonary artery catheter, and five (1.1%) catheters caused bloodstream infection. Catheter-related bloodstream infections were associated with concordant cutaneous colonization of the insertion site (n = 2), a contaminated catheter hub or infusate (n = 3), contamination of the extravascular segment of a repositioned catheter beneath the external protective plastic sleeve (n = 1), or hematogenous colonization of the catheter (n = 1). All pulmonary artery catheter-related bloodstream infections occurred with catheters (introducers) in place for ≥5 days ($p < .001$).

Cutaneous colonization under the dressing at catheter removal was lowest with gauze ($10^{1.3}$ colony-forming units), intermediate with the

From the Section of Infectious Diseases, Department of Medicine, University of Wisconsin Medical School (Dr. Maki); the Infection Control Department (Drs. Maki and Mermel, Ms. Stolz and Ms. Wheeler), and the Center for Trauma and Life Support (Dr. Maki), University of Wisconsin Hospital and Clinics, Madison, WI.

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Address requests for reprints to: Dennis G. Maki, MD, Department of Medicine, University of Wisconsin Hospital and Clinics, H4/574, 600 Highland Avenue, Madison, WI 53792.

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new highly permeable polyurethane dressing ($10^{1.8}$ colony-forming units; $p < .01$), and highest with the conventional polyurethane dressing ($10^{2.0}$ colony-forming units; $p < .001$). There were no significant differences in catheter colonization (20.0 to 25.2 cases per 100 catheters) or catheter-related bloodstream infection (0.8 to 1.6 cases per 100 catheters) between the three groups.

Conclusions: **The incidence of pulmonary artery catheter-related bloodstream infection has decreased over the past 5 yrs. Pulmonary artery catheter-related bloodstream infections originate from multiple sources, indicating that measures to prevent bacteremic infections of these devices must focus both on reducing cutaneous colonization at the insertion site and averting contamination of infusate and catheter hubs. Efforts should be made to limit the duration of catheterization with pulmonary artery catheters (including the introducer) to no longer than 4 days. The polyurethane dressings studied appear to be safe for use with pulmonary artery catheters and may be left on for up to 5 days between dressing changes. (Crit Care Med 1994; 22:1729–1737)**

KEY WORDS: **bacteremia; cross-infection; hospital-acquired infection; nosocomial infection; pulmonary artery catheterization; sepsis; intensive care unit; catheterization, intravenous**

Bacteremia or fungemia is the major life-threatening complication of vascular access (1). Considerable evidence indicates that most central venous catheter-related bloodstream infections begin with invasion of the transcutaneous catheter tract by microorganisms from the patients' cutaneous microflora (2–6). The importance of floral suppression with an effective antiseptic before insertion of an intravascular device cannot be overemphasized (6). However, extrinsic nosocomial contaminants or regrowth of the suppressed endogenous cutaneous flora can later invade the catheter insertion site and cause catheter-related bloodstream infection. The purpose of a catheter dressing is to prevent trauma to the wound and the cannulated vessel, to secure the device, and to prevent extrinsic contamination.

Transparent polyurethane film dressings have come into wide use. Some studies (7, 8) of these dressings, particularly with central venous catheters, have shown that when the dressing is left on for prolonged periods, buildup of cutaneous flora beneath the dressing may occur, potentially increasing the risk of catheter-related infection. In a prospective study (9) of 2,106 peripheral venous catheters, heavy cutaneous colonization of the insertion site and visible macroscopic moisture under the dressing were found to be independent predictors of catheter-related infection, suggesting that dressings for vascular catheters should be designed to keep the site as dry as possible.

There are substantial differences between different manufacturers' polyurethane dressings (10). A new polyurethane dressing (IV3000, Smith and Nephew, Hull, UK) has shown a permeability to cutaneous water vapor that is three to eight times greater than other transparent dressings on the market (moisture-vapor transmission rate 3000 vs. 422 to 839 g/m²/day) (11). The utility of such a dressing is supported by a study (11) in healthy volunteers showing substantially less accumulation of moisture and lower levels of cutaneous colonization beneath the dressing.

Balloon-tip, flow-directed, pulmonary artery catheters are widely used to guide the hemodynamic management of critically ill patients with shock or other disorders of oxygen transport. In the United States, these catheters are also commonly used for monitoring high-risk patients perioperatively. Approximately 2 million pulmonary artery catheters are sold in the United States each year.

There are numerous routes for microorganisms to gain access to a pulmonary artery catheter and, ultimately, the patient's bloodstream. Skin organisms from the insertion site can invade the transcutaneous tract and colonize the introducer sheath and pulmonary artery catheter extraluminally. Microorganisms can contaminate one or more of the three hubs of the pulmonary artery catheter, the hub of the introducer sheath, or the fluid column of one of the four lumens and enter the bloodstream directly. Microorganisms from the hands of a caregiver handling the pulmonary artery catheter can contaminate the extravascular portion and gain access if the catheter is withdrawn or advanced through the introducer sheath to reposition it. The intravascular portion of the introducer sheath or pulmonary artery catheter can become colonized hematogenously from a remote site of infection, such as the urinary tract. The device or infusate might even become contaminated from its manufacture (intrinsic contamination), which fortunately is rare (1). To reliably identify the source of microorganisms causing an intravascular catheter-related bloodstream infection in prospective studies, in order to develop more effective protective strategies, it is necessary to culture all of these potential sources at the time of catheter removal. If the results of these cultures appear to link a bloodstream infection with microorganisms isolated from one or more portions of the device, efforts

need to be made to conclusively establish concordance, beyond speciation and antimicrobial susceptibility profile using one or more molecular subtyping systems, such as multilocus enzyme analysis, plasmid profile, or restriction-fragment analysis of genomic DNA (1).

Since there are as yet unanswered questions regarding the best dressing regimens for central venous catheters, and since there has been only one small published trial of polyurethane dressings involving pulmonary artery catheters (12), and because there are little published data on the sources of bloodstream infection with pulmonary artery catheters, we undertook a prospective study to determine the following information: a) the performance and safety of a widely used, conventional transparent dressing and the new highly permeable polyurethane dressing with pulmonary artery catheters, as compared with standard gauze and tape; and b) the sources of pulmonary artery catheter-related bloodstream infection, using molecular subtyping.

MATERIALS AND METHODS

Sources of Clinical Data. The University of Wisconsin Hospital and Clinics is a 450-bed, tertiary referral center, which is air conditioned. Heparin-bonded, pulmonary artery catheters made of polyvinyl chloride (Thromboshield™, Baxter Edwards Critical-Care, Añdsco, Puerto Rico) were inserted into the subclavian or internal jugular vein through an indwelling, percutaneous, Teflon introducer sheath (Arrow International, Reading, PA) by supervised house officers using sterile gloves, gowns, and drapes. The sheath and a protective plastic sleeve covering the extravascular portion of the pulmonary artery catheter were used to prevent contamination, if the catheter later needed to be repositioned.

Patients >18 yrs of age who were scheduled to receive a pulmonary artery catheter were informed of the nature and purpose of this study, in accordance with the guidelines of the University of Wisconsin-Madison Human Subjects Committee, which approved the study, before written consent to participate was requested. Immediate family members or guardians were informed of the nature and purpose of the study if the patient was unable to provide consent. Consenting patients, and patients whose family members or guardians gave consent, were randomized to receive one of three dressing regimens: a) sterile gauze (Hermitage Hospital Products, Niantic, CT) and tape (Transpore™, 3M, St. Paul, MN), replaced every 2 days; b) a conventional polyurethane dressing (Tegaderm™, 3M), replaced every 5 days; or c) the new, highly permeable, polyurethane dressing (IV3000, Smith and Nephew), also replaced every 5 days. Before disinfection of the insertion site, the site was cultured quantitatively (3). Sites were disinfected with 10% povidone-iodine (Betadine®, Purdue Frederick, Norwalk, CT). No topical antimicrobial ointments were used.

Details of the protocol used for monitoring patients and their catheters in our studies of intravascular devices have been previously published (3, 5, 6, 9, 13). For each catheter, the patient was seen daily by a member of a team of research nurses. At this time, the patient was queried about pain, tenderness, or pruritus at the insertion site. Whenever the dressing adhered poorly or was scheduled to be changed or the patient reported pain or discomfort at the insertion site, the dressing was removed, the site was inspected, recleansed, and redressed. At all dressing changes and at the time of catheter removal, the condition of the dressing was assessed and scored, and the site was quantitatively scored for visible moisture, pain, pruritus, tenderness, erythema, purulence, and swelling (13).

The decision to remove a catheter was made independently by the patient's physicians. At the time of catheter removal, the site was scored for inflammation and cultured. Cultures were obtained from the hub of each lumen of the pulmonary artery catheter, the introducer sheath, and from the infusate in each lumen. The introducer sheath and pulmonary artery catheter were aseptically removed and cultured (5). Blood cultures were obtained from patients with fever or other signs of infection, and also from patients who had inflammation at the catheter insertion site.

Microbiological Methods. Methods for quantitative culture of the insertion site, the introducer sheath, pulmonary artery catheter, infusate, catheter hubs, and the extravascular portion of the pulmonary artery catheter inside the external protective sleeve have been previously published (5). Although it was not possible to blind users or the research nurses to the dressings used, the research microbiologists who processed all cultures were blinded to each catheter's dressing group.

Isolates from colonized insertion sites, introducers, pulmonary artery catheters, and positive blood cultures were subtyped by speciation and by pulsed-field (field inversion) electrophoresis of genomic DNA. The isolates were also digested with low-frequency-cleavage restriction endonucleases (14).

Definitions. The following definitions were used in determining catheter-related infection.

Local Catheter-Related Infection. Local catheter-related infection was defined as a positive, semiquantitative culture of the introducer sheath or pulmonary

artery catheter (>15 colony-forming units). A positive culture of either the introducer sheath or catheter was considered synonymous with colonization of the intravascular portion of the device (5).

Catheter-Related Bloodstream Infection. A bloodstream infection was defined as catheter-related when the following two criteria were fulfilled: a) a positive semiquantitative culture of the introducer sheath or pulmonary artery catheter and one or more percutaneously drawn blood cultures positive for the same strain, as determined by speciation and molecular subtyping, with negative cultures of hubs and infusate; and b) clinical features consistent with bloodstream infection.

Bloodstream Infection Due to a Contaminated Hub. A bloodstream infection was defined as due to a contaminated hub when the following two criteria were fulfilled: a) hub and separate percutaneously drawn blood cultures showed the same strain, and a semiquantitative culture of the introducer sheath and pulmonary artery catheter was negative for the infecting organism; and b) clinical features consistent with bloodstream infection.

Bloodstream Infection Due to Contaminated Infusate. A bloodstream infection was defined as due to a contaminated infusate when the following two criteria were fulfilled: a) infusate and one or more percutaneously drawn blood cultures showed the same strain, and semiquantitative cultures of the introducer sheath and pulmonary artery catheter were negative for the infecting organism; and b) clinical features were consistent with bloodstream infection.

Device-Related Bloodstream Infection. A bloodstream infection was defined as due to the device when the following two criteria were fulfilled: a) catheter, hub, or infusate showed the same strain as one or more percutaneously drawn blood cultures; and b) clinical features were consistent with bloodstream infection.

Statistical Methods. The significance of differences between groups was determined using chi-square or Fisher's exact test for categorical data and Student's *t*-test for continuous data. All *p* values reported are based on two-tailed levels of significance.

RESULTS

Characteristics of the Study Population. Over 90% of patients invited to enroll in this trial consented to participate. Patients and catheters in the three dressing groups were comparable in terms of risk factors predisposing to nosocomial infection (Table 1). Approximately two thirds of the catheters in each group had been inserted in the operating room in patients scheduled to have major surgery, usually open-heart surgery. The remaining one third of the catheters had been inserted in patients requiring hemodynamic monitoring in an intensive care unit (ICU). Three fourths of all catheters in each group were inserted in an internal jugular vein, and most of the remaining catheters were inserted in a subclavian vein. Baseline skin cultures before catheter insertion showed ~$10^{2.5}$ colony-forming units/mL in each group (Table 1; Fig. 1). Introducer sheaths and catheters remained in place for an average of 3 days in each group.

Effectiveness as Protective Barriers. All three dressings provided satisfactory coverage in the majority of patients, although gauze and tape did not adhere quite as well as the two polyurethane dressings; approximately one half of the dressings in each group showed some loss of adherence (Table 2).

Table 1. Comparability of patients and catheters in the three groups

	Gauze 2 Days (n = 130)	Conventional Polyurethane 5 Days (n = 127)	Highly Permeable Polyurethane 5 Days (n = 185)
Age (yr)	61 ± 14[a]	63 ± 13	61 ± 14
Host Risk Factors (%)			
Trauma	7	2	3
Postsurgery	74	73	77
Azotemia	18	17	20
Diabetes	19	28	21
Therapeutic Risk Factors (%)			
Other vascular catheters	100	98	99
Urinary catheters	99	98	99
Mechanical ventilation	92	92	92
Antimicrobial therapy	96	95	96
Corticosteroids	24	28	35
Laboratory Parameters			
Hematocrit (%)	30 ± 3[a]	30 ± 3	29 ± 3
	0.30 ± 0.03[a]	0.30 ± 0.03	0.29 ± 0.03
Glucose (mg/dL)	255 ± 102[a]	257 ± 100	249 ± 94
(mmol/L)	14.2 ± 5.7[a]	14.3 ± 5.6	13.7 ± 5.2
Albumin (g/dL)	3.1 ± 0.8[a]	2.9 ± 0.6	3.1 ± 0.7
(g/L)	31 ± 8[a]	29 ± 6	31 ± 7
Insertion in an old site, over a guidewire (%)	18	13	15
Difficult insertion (%)	3	2	3
Site of Catheter			
Subclavian vein	18	25	18
Internal jugular vein	81	73	81
Femoral vein	1	1	1
Colonization of insertion site, before disinfection	2.4 ± 0.3[b]	2.5 ± 0.3	2.6 ± 0.3
No. of hrs catheter in place	80 ± 44[a]	77 ± 41	74 ± 42

Differences between the three treatment groups are not significant.

[a]Mean ± SD; [b]mean log colony-forming units ± SEM.

Patient Tolerance. Visible moisture on the site was detected in 49% of the conventional polyurethane dressings, in 40% of the highly permeable polyurethane dressings, and in 21% of the gauze and tape dressings; the differences between these dressing groups in terms of visible moisture were significant (Table 3). Approximately one fourth of the patients in each group showed one or more markers for inflammation at the catheter insertion site. However, quantitative scoring of inflammation showed no significant differences between the three groups.

Microbiological Findings. Microbiological findings are described below.

Cutaneous Colonization. Cutaneous colonization under the dressing at the time of catheter removal occurred most often with coagulase-negative staphylococci. However, site colonization by *Staphylococcus aureus*, enterococci, Gram-negative bacilli, or yeasts was found with 3% to 5% of the catheters in each group. The quantitative level of colonization was lowest under the control gauze dressing ($10^{1.3 \pm 0.3}$ colony-forming units), intermediate under the highly permeable polyurethane dressing ($10^{1.8 \pm 0.3}$ colony-forming units [$p < .01$ as compared with gauze]), and highest under the conventional polyurethane dressing ($10^{2.0 \pm 0.3}$ colony-forming units [$p < .001$]) (Fig. 1). Two catheter-related bloodstream infections, one with *Candida albicans* and one with *Enterobacter aerogenes*, were associated with concordant cutaneous colonization of the insertion site.

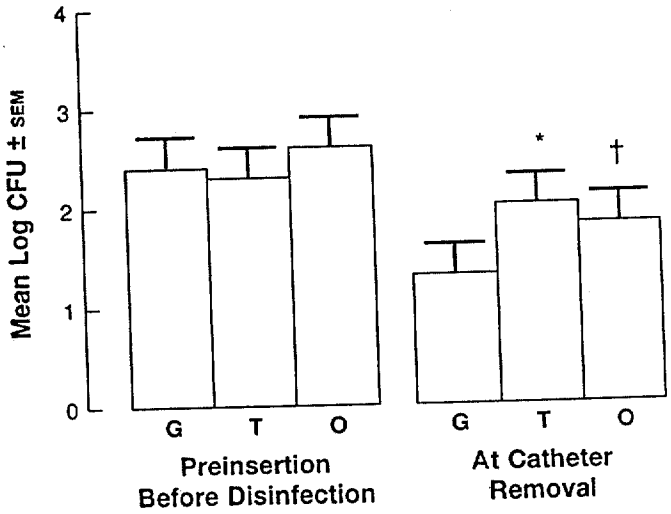

Figure 1. Cutaneous colonization (geometric mean colony-forming units [*CFU*] ± SEM) under the dressing at the time of catheter insertion and at catheter removal in the three dressing groups: *G*, gauze; *T*, conventional polyurethane dressing; *O*, highly permeable polyurethane dressing. *T vs. G ($p < .001$); †O vs. G ($p < .01$).

Contamination of Catheter Hubs. One of the four pulmonary artery catheter hubs (3, pulmonary artery catheter; 1, introducer sheath) was contaminated with >10 colony-forming units in 7.0% to 7.6% of catheters in each group, most frequently with coagulase-negative staphylococci. Three catheter-related bloodstream infections (one with *Staphylococcus epidermidis*, one with *Enterobacter cloacae*, and one with *C. albicans*) were associated with concordant contamination of the introducer or pulmonary artery catheter, hub, and infusate.

Contamination of Infusate. Infusate from one of the four lumens was contaminated with >10 colony-forming units/mL in 3.2% to 7.6% of catheters in each group (NS), again, most frequently with coagulase-negative staphylococci. In three cases, the contaminated infusate was associated with concordant contamination of a pulmonary artery catheter hub and catheter-related bloodstream infection.

Contamination of the Extravascular Portion of the Pulmonary Artery Catheter. The extravascular portion of the pulmonary artery catheter, inside the external protective sleeve, was contaminated with >10 colony-forming units at catheter removal in 7.8% to 12.3% of catheters in each group (NS), again most commonly by coagulase-negative staphylococci. The contaminated extravascular portion of the pulmonary artery catheter

Table 2. Condition of dressings during course

Condition	Gauze 2 Days (n = 130)	Conventional Polyurethane 5 Days (n = 127)	Highly Permeable Polyurethane 5 Days (n = 185)
Totally adherent	44	48	44
Edges up	30	35	35
Areas of focal nonadherence	25[a]	13	17
Completely nonadherent	2	4	3

[a]Compared with conventional polyurethane dressing group (odds ratio 2.1; 95% confidence interval 1.1–4.3; $p = .03$).

Table 3. Condition of insertion sites at catheter removal

Parameter	Gauze 2 Days (n = 130)	Conventional Polyurethane 5 Days (n = 127)	Highly Permeable Polyurethane 5 Days (n = 185)
Moisture visible	21[a]	49	40
Pruritus	4	8	5
Pain	12	12	10
Erythema	14	18	21
Tenderness	23	23	23

[a]Compared with the other two groups (odds ratio 0.3; 95% confidence interval 0.1–0.5; $p < .001$).

was associated with one pulmonary artery catheter-related bacteremia caused by *S. epidermidis*.

Device-Related Infection. Local catheter-related infection (>15 colony-forming units) occurred with 26 catheters (20.0%) in the control gauze and tape group, in 32 (25.2%) catheters in the conventional polyurethane dressing group, and in 38 (20.5%) catheters in the highly permeable polyurethane dressing group (Table 4). Two (1.5%) catheters in the gauze and tape group, one (0.8%) catheter in the conventional polyurethane dressing group, and one (0.5%) catheter in the highly permeable polyurethane dressing group caused device-related bloodstream infection, based on molecular subtyping that implicated the device in the genesis of the patient's bacteremia or candidemia (Fig. 2). None of these differences approached statistical significance.

Coagulase-negative staphylococci accounted for the majority of colonized catheters, including one bacteremia in each of the two polyurethane dressing groups. Two bacteremias in the gauze and tape group were caused by Gram-negative bacilli, and one catheter-related candidemia occurred in the highly permeable polyurethane dressing group (Table 4).

All five device-related bloodstream infections occurred with catheters in which the introducer sheath, with or without the pulmonary artery catheter, had been in place for ≥5 days ($p < .001$) (Fig. 3).

Sources of Organisms Causing Device-Related Bloodstream Infection. Five catheter-related bloodstream infections were identified, each associated with heavy colonization of the tip of the introducer sheath (three cases) or pulmonary artery catheter (two cases). Efforts to identify all possible sources of organisms colonizing catheters and producing catheter-related bloodstream infection (Table 5) show that skin of the insertion site was the probable source of infecting organisms in two cases and contamination of a catheter hub or infusate appear to have been the source in three cases (Fig. 2). Contamination of the extravascular portion of the pulmonary artery catheter inside the external protective sleeve and hematogenous colonization of the catheter may have been co-sources in one case each.

Table 4. Catheter-related infection in the three dressing groups

No. of Catheters	Gauze 2 Days	Conventional Polyurethane 5 Days	Highly Permeable Polyurethane 5 Days
Total studied	130	127	185
With local infection	26 (20.0)[a]	32 (25.2)[a]	38 (20.5)[a]
With bloodstream infection[b]	2 (1.6)[a]	1 (0.8)[a]	2 (1.1)[a]
Coagulase-negative staphylococci	17	28 [1][c]	27 [1][c]
Staphylococci aureus	1	—	2
Gram-negative bacilli	5[d] [2][c]	—	2
Enterococcus	1	1	—
Candida species	2	3	7 [1][c]

[a]Value in parentheses indicates percent; [b]concordance between device isolate and or isolates and blood culture isolate by DNA restriction-fragment polymorphism pattern; [c]value in brackets indicates number of bloodstream infections; [d]$p < .05$ compared with the conventional polyurethane dressing group.

DISCUSSION

The importance of the cutaneous microflora in the pathogenesis of intravascular device-related infection suggests that the dressing applied to the catheter insertion site could have considerable influence on the risk of catheter-related bloodstream infection (1).

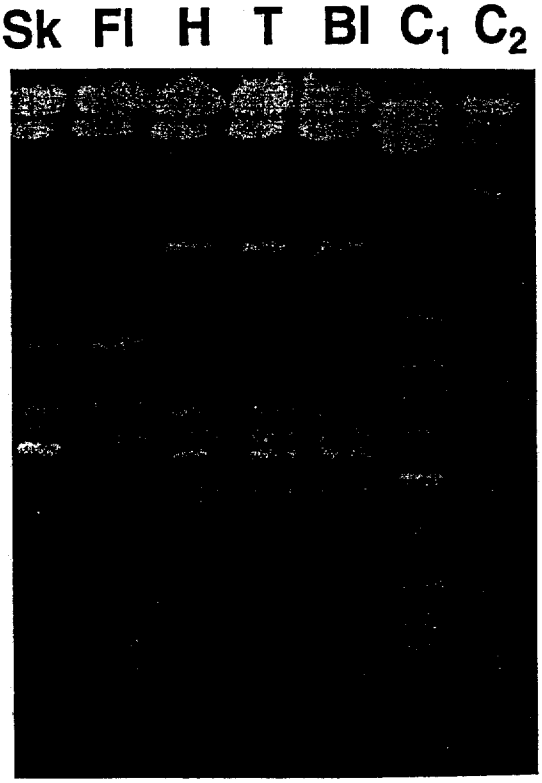

Figure 2. Restriction-fragment polymorphism patterns of genomic DNA of isolates of *Staphylococcus epidermidis* from all potential sources of infection with one infected catheter causative of bacteremia, subjected to *SmaI* endonuclease digestion. The isolates from the hub (*H*) of the introducer, the introducer tip (*T*), and blood (*Bl*) are concordant and differ from the isolates from skin (*Sk*) and fluid (*Fl*). C_1 and C_2 are unrelated control strains. The presumed pathogenesis is hub to introducer tip to blood.

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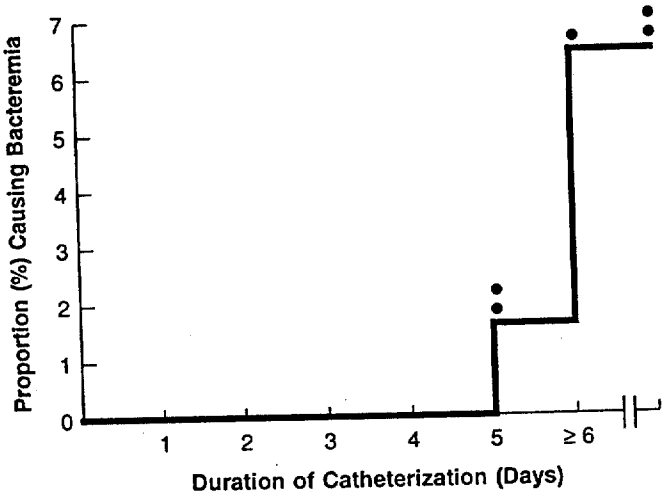

Figure 3. Cumulative (Kaplan-Meier) risk of pulmonary artery catheter-related bloodstream infection. Each *closed circle* indicates a case of catheter-related bloodstream infection.

Table 5. Potential sources of five pulmonary artery (PA) catheter-related bloodstream infections

	Gauze 2 Days	Conventional Polyurethane 5 Days	Highly Permeable Polyurethane 5 Days	Overall
Total no. of catheter-related bloodstream infections	2	1	2	5
Microbiologic Concordance with source				
Intravascular segment of introducer or PA catheter	2	1	2	5
Skin	1	—	1	2
Hub	1	1	1	3
Infusate	1	1	1	3
Extravascular portion of PA catheter, beneath external protective sleeve	—	—	1	1
Hematogenous, from remote source	—	—	1	1

Unfortunately, there have been few studies examining the specific aspects of site care for vascular catheters, until transparent polyurethane films for dressing vascular catheters became available. When used on vascular catheters, polyurethane dressings permit continuous inspection of the site, secure the device reliably, and are generally more comfortable than gauze and tape. Moreover, polyurethane dressings permit patients to bathe and shower without saturating the dressing. Clinical trials of these dressings have been prompted by the knowledge that cutaneous occlusion with tape or impervious plastic films results in an explosive increase in cutaneous microflora, with overgrowth by Gram-negative bacilli and yeasts (15). Although polyurethane dressings are semipermeable—impervious to extrinsic microbial contaminants and liquid phase moisture, and variably permeable to oxygen, CO_2, and water vapor—and studies in healthy volunteers have shown that these dressings have little effect on the cutaneous flora (16), clinical reports (17, 18) and a recent meta-analysis of published trials (19) have raised concern that these dressings could increase cutaneous colonization and the risk of catheter-related bloodstream infection.

At the present time, many manufacturers produce and market a polyurethane dressing. Whereas these products are almost indistinguishable on gross inspection, there are substantive differences in physical properties, particularly moisture vapor transmission rate, oxygen transmission, and cutaneous adherence (10), that may influence cutaneous floral populations beneath the dressing (11). Polyurethane dressings are more expensive than gauze and tape and, to contain cost and for convenience, many users leave these dressings on for prolonged periods (≥7 days). It has been questioned whether this practice might increase the risk of infection.

Studies (7, 8, 12, 20–23) of polyurethane dressings on short-term, noncuffed, central venous catheters have yielded conflicting results, in part reflecting differences in study protocols—such as the use of topical antimicrobial ointments under the dressing in the control gauze group but not in the transparent dressing group (20)—and the different dressings studied. A trial by Conly et al. (8) found a much higher rate of catheter-related bloodstream infection with catheters dressed with a conventional polyurethane dressing than with catheters dressed with gauze and tape. However, a similar but much larger trial in ICU patients found no significant differences in catheter-related infection with a conventional polyurethane dressing, as compared with gauze, when the transparent dressing was changed every 2 days (7), as is done in most U.S. hospitals with gauze and tape. Other prospective comparative trials (12, 20–23), which, in aggregate, encompass >1,000 patients with central venous catheters, did not find an increased risk of catheter-related bloodstream infection associated with transparent dressings left on for ≤7 days, as compared with gauze and tape replaced every second or third day.

Although there have been a number of published trials of polyurethane dressings with central venous catheters, most of these trials did not evaluate cutaneous colonization beneath the dressing. Only two trials

(7, 12) studied polyurethane dressings in ICU patients, who are at highest risk for catheter-related infection. Our ICU patients were highly susceptible to nosocomial infection (24, 25), as reflected by a mean age of 61 yrs, a high frequency of hypoalbuminemia and hyperglycemia, and nearly uniform exposure to surgery, mechanical ventilatory support, other invasive devices, and antimicrobial therapy during the period the study catheter was in place (Table 1).

The results of this prospective study of site care for pulmonary artery catheters, which were in place for an average of 3 days, showed that all three dressings were well tolerated and provided satisfactory protection of the insertion site. The effect of the highly permeable polyurethane dressing on the microflora (Fig. 1) was closer to the effect of the control gauze and tape dressing than was the standard polyurethane dressing, and can be considered a technological advance for site care of intravenous catheters. Neither of the polyurethane dressings studied was associated with an increased risk of device-related infection (Table 4), compared with gauze and tape, even when left on for ≥5 days. We conclude that both polyurethane dressings are safe for use with pulmonary artery catheters. Lower trends in moisture under the dressing and levels of site colonization were observed with the new highly permeable polyurethane dressing. These findings are consistent with the accumulating evidence (9, 11) that dressings for vascular catheters should be designed to reduce the accumulation of cutaneous moisture under the dressing and keep the site as dry as possible. With a polyurethane dressing, the goal should be a high moisture-vapor transmission rate.

The findings of this study are consonant with several recent studies examining the risk of infection with pulmonary artery catheters (5, 12, 26). The frequency of catheter-related bloodstream infection was low (~1%) in all three groups. We believe that the frequency of pulmonary artery catheter-related bloodstream infection has decreased substantially in recent years for the following reasons: a) greater attention to aseptic technique when inserting pulmonary artery catheters, as compared with other short-term central venous catheters; b) insertion of pulmonary artery catheters through an introducer made of Teflon, a material more resistant to microbial adherence than polyvinyl chloride (27); c) shorter durations of placement for pulmonary artery catheters, as compared with other central venous catheters (mean of 3 days in this study); and d) the wide use of heparin-bonded pulmonary artery catheters, which we have recently found exhibit surface antimicrobial activity against a wide range of potential pathogens, including *Candida* (28).

This study is the largest and most rigorous to date to prospectively seek to identify the sources and mechanisms of infection of pulmonary artery catheters. This study shows that whereas microbial cutaneous colonization of the insertion site is the major source of organisms colonizing the intravascular introducer sheath and pulmonary artery catheter (accounting for approximately one half of the related bloodstream infections), pulmonary artery catheters—which are heavily manipulated and which have many more potential sites for microbial access than other intravascular catheters—may be more vulnerable than other central venous catheters to nosocomial bloodstream infection deriving from contamination of the infusate or catheter hubs (Fig. 2). Moreover, pulmonary artery catheters may be more vulnerable to hematogenous colonization from distant, unrelated sites of infection. Precautions to prevent pulmonary artery catheter-related infection must focus on measures to further reduce skin colonization at the insertion site (1, 6, 29) and also on precautions to prevent contamination of infusate, stopcocks, and catheter hubs (1, 29). The risk of pulmonary artery catheter-related bloodstream infection should be very low if the device does not remain in place for >4 days (Fig. 3).

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The effects of incisional bupivacaine on postoperative narcotic requirements, oxygen saturation and length of stay in the post-anesthesia care unit

B. L. PARTRIDGE and B. E. STABILE

Departments of Anesthesiology and Surgery, University of California, San Diego and San Diego VA Medical Center, San Diego, California, USA

We compared postoperative pain and narcotic requirements, oxygen saturation (Sao_2) and length of stay in the post-anesthesia care unit (PACU) in patients who received 30 ml of either 0.25% bupivacaine (B) or saline placebo (S) infiltrated into the operative incision. Twenty ASA I–III patients undergoing abdominal surgery were studied in a double-blinded randomized prospective trial. Study and control groups were not different in patient age, procedure, intra-operative narcotics administered or preoperative Sao_2. In the PACU, patients receiving B had significantly lower analog pain scores (6.0 vs 8.3, $P=0.02$). They had lower respiratory rates (15.6 b/min vs 19.1, $P=0.02$), required significantly less narcotic (4.5 mg morphine sulphate vs 11.0, $P=0.03$) and were discharged from the PACU almost an hour sooner than patients receiving S ($P=0.02$). Patients receiving B had significantly higher minimum Sao_2 than those receiving S (93.3 % vs 89.9, $P=0.04$). Discharge pain scores, Sao_2 and respiratory rates were not significantly different between B and S groups. Finally, mean requirements for narcotics for the first 24 h were reduced by approximately 30% (from 406.9 mg meperidine to 255.5 mg, $P=0.006$). This study demonstrates that infiltration of a long-acting local anesthetic lowers initial pain scores and requirement for narcotics in the PACU. The effect can be seen for at least the first 24 h. A lower requirement for postoperative narcotics is accompanished by faster wake-up, more alert patients, and, most importantly, higher Sao_2 and shorter PACU stay. This may have a significant effect on pulmonary morbidity following abdominal operations.

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Key words: Analgesia: postoperative; anesthetic techniques: infiltration; complications: postoperative; local anesthetics: bupivacaine; pain: postoperative analgesia; pulse oximetry; recovery: recovery room stay.

Postoperative pain is frequently undertreated (1, 2). Inadequately treated incisional pain, however, may lead to splinting, loss of sighing and reduction of vital capacity (3, 4). These, in turn, may contribute to postoperative pulmonary morbidity. Thus upper abdominal operations, in particular, are associated with a high incidence of postoperative pulmonary complications. Several approaches for the treatment of postoperative pain have been advocated, including epidural and intrathecal narcotics (5), intrapleural anesthetics (6, 7) and patient-controlled analgesia (PCA) (2, 5, 8). The most commonly employed method of postoperative pain control, however, remains intramuscular or intravenous injection of narcotics.

Considerable attention has been focused upon the respiratory depression induced by narcotic analgesics. In the immediate postoperative period, narcotic administration may be particularly dangerous, since narcotics depress the ventilatory response to carbon dioxide and may impair consciousness and protection of the airway at a time when residual anesthetics are still present (8–10). An alternative may be to employ local anesthetics to provide immediate postoperative analgesia (11–13). First suggested in the 1950s, incisional infiltration of local anesthetic has experienced renewed popularity with the development of long-acting local anesthetics such as bupivacaine hydrochloride.

Previous studies have not examined the immediate postoperative period, nor have they controlled for intraoperative narcotic administration (11–13). The purpose of this study was to compare postoperative pain and narcotic requirements, oxygen saturation (Sao_2 = oxygen saturation measured by pulse oximetry) and length of stay in the post-anesthesia care unit (PACU) in patients receiving either 0.25% bupivacaine or saline placebo infiltrated into the operative incision.

Table 1
Criteria for PACU nurse assessment of patients.

Nausea: 0 = none, 1 = mild, 2 = moderate, 3 = severe, with emesis
Alertness: 0 = unresponsive, 1 = responds to pain, 2 = responds to voice, 3 = follows commands, 4 = spontaneous speech
Hypertension: defined as systolic bp > 160, diastolic bp > 100 or either value greater than 20% greater than pre-op.

MATERIAL AND METHODS

After Human Subjects Committee approval and informed consent, 20 ASA I–III patients aged 30–70 years were enrolled in the study. The subject population was selected from patients scheduled to undergo abdominal surgery (cholecystectomy, ventral herniorraphy, staging laparotomy, or colostomy closure) under general anesthesia. Most patients had a history of smoking, but none was receiving medications for respiratory disease. Patients were introduced to a visual analog pain scale ranging from zero (no pain) to ten (maximum pain imaginable) the night before surgery and informed that they would receive as much pain medicine as they needed postoperatively. Patients received no premedication. Induction was accomplished with thiopental (4–6 mg/kg) plus succinylcholine (1.5 mg/kg) or vecuronium (0.1 mg/kg) for intubation. Maintenance was with a balanced anesthetic of isoflurane, oxygen, nitrous oxide and i.v. fentanyl. In order to approximate most closely the usual anesthetic practice, administration of the anesthetic was left to the individual anesthesiologist in charge of each case but did not include any intrathecal or epidural medications. Intraoperative narcotics were administered as considered appropriate by the anesthesiologists, but none were given in the last 20 min of the procedure. Ten minutes before the end of the procedure, just prior to skin closure, 30 ml of either 0.25% bupivacaine or non-preservative normal saline were infiltrated into the subcutaneous tissue, muscle and fascia of the surgical incision. Choice of medication or control was assigned randomly by the pharmacist preparing the medication, based upon a random table created in advance. The patient, surgeons, anesthesiologists and PACU personnel were all blinded as to the identity of the injected solution.

All study patients were cared for by one of two PACU nurses. In the PACU, as soon as a patient was capable of responding, he was asked to gauge his pain on the visual analog pain scale. If he reported any pain, morphine sulphate (MS) was injected i.v. in 2–4 mg increments at 5–10-min intervals until he was comfortable. (The decision whether or not to medicate was left to the two PACU nurses, who followed their normal criteria for postoperative medication.) Discharge criteria from the PACU followed standard protocol for the hospital, and required patients to be alert and pain-free, and for 30 min to have elapsed since any i.v. medication. Prior to discharge from the PACU, the patient was asked to gauge his pain on the visual analog scale once more. Total narcotic administered intraoperatively and in the PACU, analog pain scores, time spent in the PACU and the length of time before the patient was able to respond to the visual analog scale were recorded. PACU nurses made a subjective assessment on a five-point scale of the patient's degree of alertness on arrival and discharge from the PACU (Table 1). Similarly, nausea and vomiting were recorded on a four-point scale (Table 1). Because postoperative hypertension sometimes results from inadequate pain control, hypertension, defined as systolic or diastolic pressure greater than 120% of preoperative values or systolic pressures greater than 160 mmHg (21.3 kPa) was recorded if present.

Sao_2 was measured preoperatively, and continuously both during the operation and in the PACU. It is the practice in our institution to provide supplemental oxygen (Fio_2 35% by mask) to all patients in the PACU. Room air saturation was measured in study patients by removing the oxygen mask for 3 min and continuously observing the oxygen saturation. If the oxygen saturation fell to less than 90%, the patient's mask was repositioned so that he received supplemental oxygen, and thus no patient was allowed to become hypoxic. Sao_2 was measured for each patient within 5 min of arrival in the PACU and again when the patient was comfortable. Minimum Sao_2 and per cent change in Sao_2 from preoperative values were recorded for each patient upon arrival in the PACU, after medication, and just prior to discharge from the PACU.

All patients' charts were later reviewed for evidence of postoperative complications. Although not part of the original study design, a record was made of all narcotics administered in the first 24 h postoperatively. Five patients (two from the bupivacaine group and three from the saline group) received patient controlled analgesia (PCA), and were excluded from the analysis because totals were not available.

Data were analyzed by non-parametric Mann Whitney U-test with $P < 0.05$ considered significant.

RESULTS

Study and control groups were not different in patient age, operative procedure, or length of surgery (Table 2). The time from discontinuation of anesthesia until the patient was able to respond to verbal commands and the time from awakening until the first spontaneous complaint of pain were also not significantly different between groups (Table 3). Upon arrival in the PACU, patients in the two groups were equally alert (Table 3); however, patients receiving bupivacaine had significantly lower analog pain scores ($P =$

Table 2
Characteristics of patient groups.

Characteristic	Saline	Bupivacaine	Significance
N	10	10	ns
Age	54.6 ± 4.0 yr*	55.4 ± 4.5 yr	ns
Procedures (n)	cholecystectomy (5) ventral hernia repair (3) pelvic node dissection (1) staging laparotomy (1)	cholecystectomy (5) ventral hernia repair (2) nephrectomy (1) staging laparotomy (2)	
Length of surgery	204 ± 24 min	232 ± 27 min	ns

* mean ± standard error.

0.02, Table 3). Their initial respiratory rate was significantly less (15.6 ± 1.48 for the bupivacaine group vs 19.1 ± 1.64 for the saline group, $P = 0.02$).

Total intraoperative narcotics were not different between groups. Patients receiving incisional bupivacaine required significantly less narcotic in the PACU, however (4.4 ± 1.26 mg MS vs 11.4 ± 1.7, $P = 0.003$), and were discharged from the PACU *almost an hour* sooner than patients receiving saline ($P < 0.02$, Table 3). In addition, retrospective analysis of narcotics used in the first 24 h postoperatively showed that patients who were randomized to bupivacaine infiltration received an average of approximately 30% less narcotic than those in the saline group (255.1 ± 61 mg meperidine compared to 406.9 ± 50, $P = 0.006$). Narcotic orders for these patients were for 75 mg meperidine up to every 4 h, as required for pain, so patients had to request pain medication.

With respect to arterial oxygen saturation, two effects were seen. First, there was a negative correlation between age and preoperative Sao_2 ($r = -0.51$, $P < 0.05$, Fig. 1a). This correlation was no longer seen postoperatively (Fig. 1b). Second, although preoperative values were not different between the two study groups, patients receiving bupivacaine had significantly higher minimum Sao_2 values in the PACU than those receiving saline (Fig. 2, $P < 0.05$, Table 3). A similar result was seen when the change in Sao_2 from preoperative values was calculated. The difference was striking, even though supplemental oxygen was provided for any patient whose Sao_2 fell to 90% while the patient was breathing room air. This occurred in four patients in the saline group and two patients in the bupivacaine group. At the time of discharge from the PACU, oxygen saturation was no longer significantly different ($P = 0.16$, Table 3). Two patients in the saline group and no patients in the bupivacaine group were discharged from the PACU with supplemental oxygen.

In this study, postoperative morphine requirements were unrelated to patient age (Fig. 3a). Total morphine dose administered in the PACU, however, showed a significant correlation with the lowest Sao_2 values recorded ($r = -0.52$, $P < 0.05$, Fig. 3b).

Patients were medicated until comfortable in the PACU. Discharge pain scores and respiratory rates were not significantly different between bupivacaine and saline groups. Mild nausea was observed in one patient in the bupivacaine group and in two patients in the saline group. Hypertension was observed in a single patient in each group. No postoperative complications were noted in either group.

Table 3

Effects of incisional bupivacaine vs saline.

Characteristic	Saline	Bupivacaine	Significance
Recorded times (min)			
Time to awaken	12.5 ± 1.4*	7.5 ± 0.9	ns
Time to 1st complaint	21.5 ± 2.1	19.8 ± 2.6	ns
Time to PACU discharge	204.5 ± 40.8	145.3 ± 14.1	$P = 0.02$
Alertness score			
PACU arrival	2.7 ± 0.3	2.7 ± 0.2	ns
PACU discharge	4.0 ± 0.0	3.8 ± 0.1	ns
Respiratory rate (breaths/min)			
PACU arrival	19.1 ± 1.6	15.6 ± 1.5	ns
PACU discharge	16.3 ± 0.7	16.4 ± 1.1	ns
Narcotic administered			
Intra-op (μg fentanyl IV)	615.0 ± 89	775.0 ± 156	ns
PACU (mg morphine IV)	11.0 ± 1.8	4.5 ± 1.3	$P = 0.003$
Next 24 h (mg meperidine IM)	406.9 ± 50	255.5 ± 61	$P = 0.006$
Oxygen saturation (Sao_2, per cent)			
Pre-op	97.0 ± 0.7	97.3 ± 0.5	ns
Lowest intra-op	97.9 ± 0.5	97.0 ± 0.8	ns
Lowest post-op	89.9 ± 0.9	93.3 ± 0.9	$P = 0.04$
Change from pre-op	7.5 ± 0.9	4.3 ± 0.7	$P = 0.02$
PACU discharge	93.3 ± 0.8	95.2 ± 0.9	ns
Analog pain score			
PACU arrival	8.3 ± 0.6	6.0 ± 0.6	$P = 0.02$
PACU discharge	4.8 ± 0.8	4.5 ± 0.7	ns

* mean ± standard error.

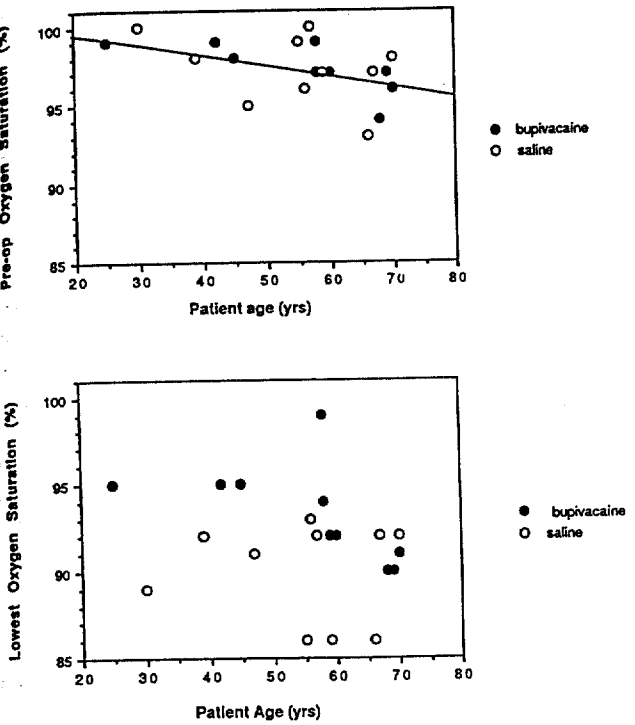


Fig. 1a. Correlation of preoperative oxygen saturation with patient age ($r=0.52$, $P<0.01$). Darkened circles represent patients in the bupivacaine group, open circles represent controls. b: Relationship of lowest postoperative saturation with patient age. The correlation demonstrated preoperatively is no longer seen, presumably because of the significant differences in narcotics received by different patients. (Symbols as in Fig. 1a.)

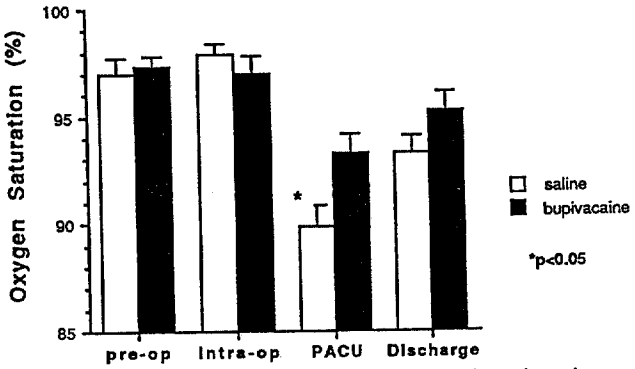
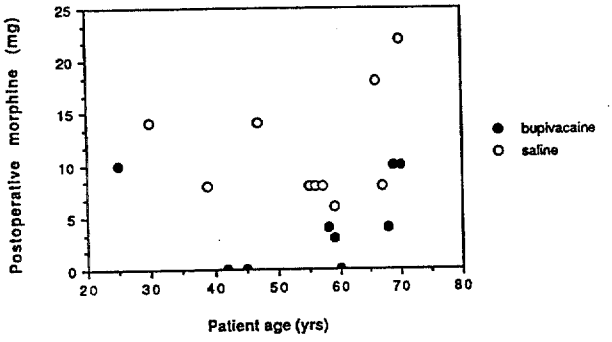


Fig. 2. Comparison of oxygen saturation measured by pulse oximeter in patients receiving bupivacaine (darkened bars) or saline (open bars). Shown are mean values ± standard error for preoperative Sao_2, lowest intraoperative measurement, lowest Sao_2 in the PACU and Sao_2 at discharge from the PACU. Significant differences between bupivacaine and saline groups are seen for postoperative Sao_2.

DISCUSSION

Postoperative pain control remains a serious problem in modern anesthesia and surgery. Intrathecal and continuous epidural narcotics provide excellent postoperative analgesia, but are costly, may require extended patient monitoring (2) and, may not be superior to PCA (5) or regularly scheduled narcotics (14, 15). As a result, they are not available in many hospitals. In the immediate postoperative period, when patients are drowsy but experiencing pain, administration of narcotics poses a potentially dangerous dilemma. On the one hand, severe pain, associated with catecholamine release and hypertension may be deleterious, but, on the other hand, administration of narcotics to a drowsy patient increases the risk of respiratory depression and loss of airway reflexes. This study demonstrates that incisional infiltration of a long-acting local anesthetic significantly lowered initial pain scores and requirement for narcotics in the PACU. The lower requirement for postoperative narcotics was accompanied by higher oxygen saturation in the PACU and shorter PACU stays.

The effects of infiltration with bupivacaine may be even greater than recorded here. In the interests of



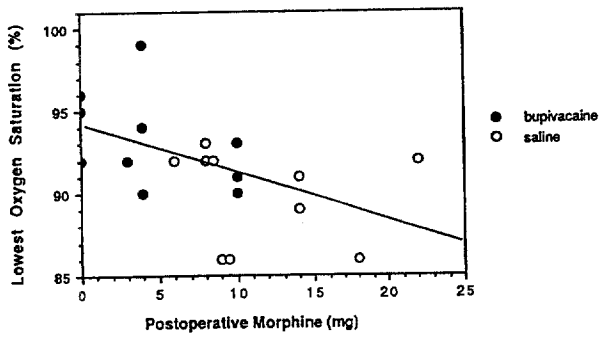


Fig. 3a. Narcotic administered in the PACU as a function of patient age. No significant correlation is seen between narcotic requirement and patient age. Patients in the bupivacaine group (darkened circles) required significantly less narcotic than those in the saline group (open circles). b: Postoperative Sao_2 as a function of narcotic administered in the PACU. A significant correlation is seen between the total morphine dose and lowest Sao_2 recorded in the PACU ($r=0.51$, $P<0.1$, symbols as in Fig. 3a).

patient safety, we immediately provided supplemental oxygen to any patient whose Sao_2 fell to 90% during the 3-min tests of breathing room air. Nonetheless, Sao_2 continued to fall in some patients before it rose in response to provision of supplemental oxygen. Thus minimum Sao_2 values recorded were sometimes below 90%. It is likely that Sao_2 would have fallen even further in those patients had we not provided supplemental oxygen, accentuating the difference between control subjects and those receiving bupivacaine.

Previous studies on the effect of local anesthetic injection into the operative incision on postoperative narcotic requirements have yielded conflicting results. Some previous studies have found decreased narcotic requirements after abdominal surgical procedures, similar to those reported here (16, 17). Those studies examined the period after discharge from the PACU, however, and no measurement was made of oxygen saturation or length of PACU stay. Results from studies performed after inguinal herniorraphy have been equivocal. Hashimi & Middleton (18) found significantly decreased narcotic requirement after infiltration with bupivacaine. Another, unblinded, study, however, reported no difference between control and treated patients (19). In that study, injection of bupivacaine into a deep-lying indwelling catheter in patients following inguinal herniorraphy appeared to have no effect, and was associated with some evidence of wound infection (19). The difference between studies may lie in technique: superficial infiltration appears efficacious; deep infiltration of underlying muscle does not.

Moss et al. (17) compared a group of 43 patients who received 40–50 ml 0.5% bupivacaine infiltration into the incision at the time of cholecystectomy with a historical control group of previously operated patients and found greatly reduced narcotic requirements. No description is given of intraoperative anesthetic technique or narcotic administration, however, and significant differences in patient instruction, surgical technique and postoperative care make it difficult to determine what role the bupivacaine played. In a double-blind study of bupivacaine vs saline in cholecystectomy patients, Patel et al. (16) reported a 36% decrease in narcotic requirements over the first 3 postoperative days, a value in complete agreement with that observed here. Patel et al. did not report on anesthetic technique or examine narcotic requirements in the PACU. They did examine pulmonary function and demonstrated a smaller decrement in forced vital capacity and forced expiratory volume on the first postoperative day. No significant differences were seen, however, in arterial blood gases drawn on the second postoperative day.

One recent study advocated intraperitoneal (IP) administration of bupivacaine to control pain and to reduce postoperative ileus after abdominal operations (20). Scott et al. (21) investigated the effect of continuous IP infusion of bupivacaine in patients receiving both upper and lower abdominal procedures and found no effect on the stress response (as measured by serum levels of cortisol and glucose) or on pulmonary function. Interestingly, they also noted very poor pain control in their patients, suggesting that a major part of postoperative pain was incisional and not visceral in nature.

It was not the aim of this study to examine outcome variables of morbidity and mortality, since to do so would have required a much larger sample size. Nonetheless, it seems reasonable to assume that the higher postoperative Sao_2 seen in the bupivacaine group should result in reduced morbidity from respiratory complications. Splinting from incisional pain after upper abdominal operations is associated with a higher incidence of postoperative pulmonary complications (3, 4). Control of pain with narcotics may cause drowsiness and interfere with cooperation in deep breathing (11). This notion is supported by evidence of a reduced incidence of postoperative atelectasis in patients receiving incisional bupivacaine (16). The optimal dose of incisional bupivacaine remains to be determined. Studies employing 0.5% bupivacaine have claimed reduced narcotic requirements lasting several days (16, 17).

Thus the benefits of incisional bupivacaine compared to placebo include lower analog pain scores upon awakening from anesthesia, lower narcotic requirements in the PACU and lasting up to 24 h and improved pulmonary function. Patients in the bupivacaine group experienced less pain in the PACU and required a shorter PACU stay which should reduce hospital costs.

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Address:
Dr. *B. L. Partridge*, MD, DPhil.
Department of Anesthesiology
(VA-125) VA Medical Center
3350 La Jolla Village Drive
San Diego, Ca., 92161
USA

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Comparison of Postoperative Analgesic Effects of Intraarticular Bupivacaine and Morphine Following Arthroscopic Knee Surgery

Srinivasa N. Raja, M.D.,* Ross E. Dickstein, M.D.,† Carl A. Johnson, M.D.‡

Recent studies have shown that, in the presence of inflammation, the local administration of opioids results in analgesia. The analgesic efficacy of local anesthetics and morphine administered intraarticularly was compared in patients undergoing arthroscopic knee surgery under epidural anesthesia. We compared postoperative pain scores (VAS) and opioid requirements among 47 patients receiving, in a randomized, double-blinded fashion, one of three intraarticular medications (20 ml): normal saline with 100 μg epinephrine (group 1, n = 16); 0.25% bupivacaine with 100 μg epinephrine (group 2, n = 15); and 3 mg morphine sulfate and 100 μg epinephrine in normal saline (group 3, n = 16). VAS scores were similar in the groups preoperatively and on arrival in the recovery room. At the end of the first postoperative hour, the residual sensory blockade was minimal in all three groups (mean = 3.8–4.1 segments) and almost total recovery occurred in all three groups before the second postoperative hour. The VAS in group 3 was not significantly different than group 1 at any time interval. Intraarticular bupivacaine (group 2) provided significantly better analgesia than did saline or morphine (group 1 or 3) in the first 2 postoperative hours (ANOVA, $P < .05$). Subsequent VAS scores were not significantly different in the three groups. While no patient in group 2 requested analgesics during the first postoperative hour, nine patients in group 3 required systemic analgesics ($P < .01$). We conclude that no evidence for a peripheral opiate-receptor mediated analgesia could be demonstrated in patients undergoing arthroscopic knee surgery under epidural anesthesia. (Key words: Analgesics, opioid: morphine. Anesthetics, local: bupivacaine. Pain: postoperative. Receptors: opioid. Surgery: arthroscopy.)

THE RECENT GROWTH in outpatient surgery has presented new challenges in the field of postoperative pain management. Difficulties in adapting common methods of acute postoperative pain management in hospitalized patients to outpatients has resulted in inadequate treatment of pain following outpatient surgery.[1,2] Thus, the search continues for an ideal analgesic technique that is site specific, long-lasting, easily administered and has a high therapeutic safety index.

Arthroscopic surgery of the knee is a common outpatient procedure. Although intraarticular injection of bupivacaine following arthroscopy has been demonstrated to be safe[3–5] and effective[6,7] in providing postoperative analgesia, the mean duration of analgesia is only 2 h.[7] In a recent report, intraarticular morphine resulted in prolonged analgesia following arthroscopic knee surgery.[8] Intraarticular injection of opioids theoretically has the potential to fulfill several of the above-listed criteria of an ideal analgesic following arthroscopy.

Contemporary research has focussed on "peripheral sites" in the region of tissue injury as potential targets of analgesic drugs. For example, the traditional view that opioids produce analgesia solely by action on opiate receptors in the central nervous system has been challenged by evidence for peripheral opiate receptor-mediated analgesia.[9–12] Russell and coworkers[13] demonstrated in an electrophysiologic study in cats that close arterial injection of opioids inhibited the spontaneous discharges of a majority of the small diameter afferents from inflamed knee joints in a dose-dependent manner. This effect was naloxone reversible, suggesting an opiate receptor-mediated mechanism.

The present study was designed to determine whether intraarticular administration of opiates results in postoperative analgesia following arthroscopic surgery. In addition, the analgesic effect of an intraarticular opioid was compared to that of local anesthetics.

Material and Methods

Patients (ASA physical status 1–3) scheduled for elective outpatient arthroscopic surgery of the knee performed by a single surgeon (C. A. J.) were enrolled in the study. The study protocol was approved by the Joint Committee on Clinical Investigation of The Johns Hopkins Medical Institutions. Informed consent was obtained from all patients. Patients younger than 18 yr or with cruciate ligament tears were not included in the study. Exclusion criteria were acute traumatic injury to the knee, the use of oral narcotics preoperatively, history of allergy to any study medication, and the refusal of epidural anesthesia. Surgical procedures were similar in the three groups and included debridement of fat pad and adhesions, synovectomies, and partial or total meniscectomies.

* Associate Professor, Department of Anesthesiology and Critical Care Medicine.
† Instructor, Department of Anesthesiology and Critical Care Medicine. Current position: Medical Director, Ambulatory Surgery Center, Department of Anesthesiology, Sinai Hospital, Baltimore, Maryland.
‡ Assistant Professor, Department of Orthopedic Surgery
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Address reprint requests to Dr. Raja: Department of Anesthesiology and Critical Care Medicine, Johns Hopkins Hospital, Osler 304, 600 North Wolfe Street, Baltimore, Maryland 21287-5354.

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TABLE 1. Patient Profiles

	Group 1	Group 2	Group 3	P Value
N	16	15	16	
Age (yr)	46 ± 4	44 ± 3	35 ± 3	.08
Recovery room time (h)	2.8 ± 0.3	2.7 ± 0.2	2.4 ± 0.1	.4
Volume of epidural lidocaine (ml)	15.6 ± 0.5 (13–20)	16.5 ± 0.4 (15–20)	17.1 ± 0.6 (13–20)	.14
No. of dermatomes anesthetized (intraoperatively)	12.3 ± 0.4	11.0 ± 0.8	10.3 ± 1.0	.23
No. of anesthetized dermatomes (1 h postoperation)	3.8 ± 1.1	4.1 ± 1.0	3.9 ± 1.3	.97
Surgical time (h)	1.5 ± 0.1	1.5 ± 0.1	1.6 ± 0.1	.76

Values are mean ± SEM with ranges in parentheses.

Patients did not receive any medication prior to coming to the operating room.

Patients were randomized prospectively to one of three groups. Patients were asked to mark the intensity of their ongoing knee pain on a 10-cm visual analog pain scale (VAS) prior to the start of the anesthetic. The VAS was anchored at 0 (no pain) and 10 (most intense pain). The VAS has been validated for both clinical and experimental pain by previous studies.§[14] The anesthetic regimen consisted of lumbar epidural anesthesia using 2% lidocaine hydrochloride with 1:200,000 epinephrine (range 13–20 ml). The mean dermatomal level of analgesia to pinprick was T_{10} (range T_8–T_{12}). Midazolam for sedation was titrated in increments of 1 mg (median dose 4 mg). Epidural and parenteral opioids were avoided pre- and intraoperatively. All patients underwent arthroscopic surgery after inflation of a thigh tourniquet to 300–350 mmHg.

At the conclusion of the procedure, the appropriate study drug was administered in a double-blinded, randomized manner from a coded syringe into the joint space *via* an 18-G needle. Patients in group 1 received 20 ml of normal saline and 100 μg epinephrine. Patients in group 2 received 20 ml 0.25% bupivacaine and 100 μg epinephrine, and patients in group 3 received 3 mg of preservative-free morphine and 100 μg epinephrine in a total volume of 20 ml of normal saline.

The tourniquet was deflated and the patient was taken to the postanesthesia recovery unit and subsequently to the Same Day Care Center prior to discharge. An observer blinded to the patients' group assignment obtained hemodynamic data, VAS scores, and noted the level of residual epidural block upon arrival in the recovery unit and each hour until discharge (3–6 h). The observer also recorded the time at which the patient first requested pain medication. Analgesic therapy in the immediate postoperative period was managed by a physician not directly involved in the study. The usual analgesic regimen was oral Tylox® (5 mg oxycodone hydrochloride and 500 mg acetaminophen, McNeil Pharmaceuticals, Fort Washington, PA). If pain was uncontrolled with oral opioids, iv fentanyl was administered with an initial bolus dose of 50 μg and additional doses titrated as needed.

All patients were discharged home with 20 capsules of Tylox® and a supply of VAS sheets. Patients were advised to take their analgesic medication on a 4-h as-needed basis and rate their pain intensity on the VAS scale at 6-h intervals. Patients were seen at follow-up by the surgeon at 48 or 72 h, at which time a final VAS was completed, the number of unused Tylox® capsules counted, the average 24-h use of opioid calculated, and the presence of any complications ascertained.

STATISTICS

A one-way analysis of variance was used to compare pain scores in the three groups, and the least significant difference method used for pairwise comparisons of means at each time point (Statistix v3.1, Analytical Software, St. Paul, MN). The time to first analgesic dose and the 24-hr analgesic requirement were analyzed using a one-way analysis of variance. A chi-square analysis of contingency table was used for comparison of categorized data such as ASA physical status and gender. Results are shown as mean ± SEM. A P value of $< .05$ was considered to be statistically significant.

Results

Forty-nine patients were enrolled in the study; one patient was lost to follow-up, and one patient was too sedated in the recovery unit to obtain measurements of postoperative pain. Data from these two patients were excluded from further analysis. There were no significant differences among the groups in ASA physical status, gender, height, or weight. The male/female ratios were similar in the three groups (M:F = 11:5, 12:3, 12:4 in groups 1, 2, and 3, respectively). Additional patient demographics, anesthetic doses, surgical time, and times for recovery from the epidural anesthetic for the 47 patients included in the study are given in table 1. No significant differences

§ Price DD, Harkins SW. Combined use of experimental pain and visual analogue scales in providing standardized measurement of clinical pain. Clinical Journal of Pain 3:1–8, 1987.

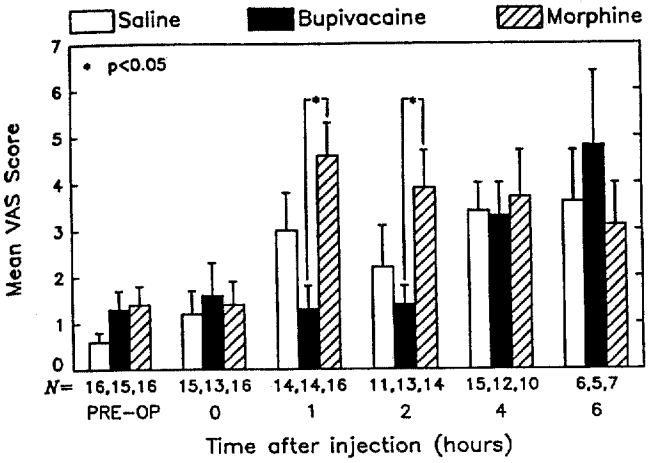

FIG. 1. Mean postoperative pain scores after arthroscopic knee surgery. Visual analog scores (VAS) of pain were obtained before and after the surgery. At the end of the surgery, patients were injected with 20 ml of one of the following three solutions intrarticularly: 100 μg epinephrine in 0.9% normal saline (saline); 0.25% bupivacaine and 100 μg epinephrine (bupivacaine); or 3 mg morphine sulfate and 100 μg epinephrine (morphine). The only significant differences were between the bupivacaine and morphine groups at the 1- and 2-h periods after the injection.

between the groups in any of the above-mentioned parameters (ANOVA, $P > .05$) were observed.

The preoperative and postoperative VAS scores during the first 6 h after surgery for the three groups are shown in figure 1. The difference in group scores are significant at the first and second postoperative hours. There are no other significant differences throughout the postoperative period. The lower number of patients during the sixth postoperative hour reflects that most patients were discharged prior to that time. The 24- and 48-hr VAS scores were 2.2 ± 0.6 and 1.9 ± 0.6 in group 1, 1.9 ± 0.6 and 1.5 ± 0.3 in group 2, and 2.2 ± 0.5 and 1.9 ± 0.6 in group 3 ($P > .8$).

Patients in group 3 (morphine) requested pain medication earlier than those in group 2 (bupivacaine; $P < .01$; table 2). Nine of 16 patients in the morphine group (group 3) and 2 of 16 patients in the control group (group 1) required supplemental analgesics during the first postoperative hour ($P < .05$). In contrast, none of the patients in the bupivacaine group required analgesics during the same hour ($P < .01$ compared to group 3). Despite the additional analgesic use in the morphine group, the VAS scores during the first 2 postoperative hours were higher in this group of patients compared to patients in the bupivacaine group ($P < .05$; fig. 1). Patients took pain medication *ad lib* over the first 2–3 postoperative days until follow-up. The Tylox® consumption per day did not differ by group (table 2).

Complications included two hemarthroses in each of the bupivacaine and morphine groups that resolved with either aspiration or conservative therapy and resulted in no long term sequelae.

Discussion

Our results indicate that, in patients undergoing arthroscopic knee surgery under regional anesthesia, intraarticular bupivacaine results in analgesia in the immediate postoperative period. In contrast, intraarticular morphine failed to provide significant analgesia during the same period. Our results are in agreement with those of earlier studies on the effects of intraarticular local anesthetics on postoperative analgesia in patients undergoing arthroscopy under general anesthesia.[7,15–17] Our observations of a lack of analgesic effect of morphine during the first 2 postoperative hours are also similar to the observations of Stein *et al.*[8] However, unlike in the reports of Stein *et al.*[8] and Khoury *et al.*,[17] we failed to observe a prolonged or perhaps delayed and prolonged analgesic effect with morphine. Our results are in agreement with those of Heard *et al.*,[18] who failed to demonstrate significant postoperative analgesia following intraarticular morphine in patients undergoing arthroscopic surgery either under general or regional anesthesia. The reasons for the discrepancy between the studies are not clear at present, but possible explanations are discussed.

Opiate receptors and endogenous opiates have been demonstrated not only in brain and spinal cord but in peripheral nerves and the dorsal root ganglia.[19,20] Neurophysiologic studies in uninjured skin have, however, failed to demonstrate an effect of opiates on response of cutaneous nociceptive afferent fibers innervating normal

TABLE 2. Postoperative Opioid Requirements

	Group 1 (Saline)		Group 2 (Bupivacaine)		Group 3 (Morphine)		
	n	Mean ± SEM	n	Mean ± SEM	n	Mean ± SEM	P
Time to first opioid dose (h)	13	2.9 ± 0.7	11	5.7 ± 1.6*	12	1.6 ± 0.7	.01
No. of opioid tablets per day	15	3.0 ± 0.6	14	2.5 ± 0.6	15	2.7 ± 0.4	.8

* Group 2 significantly greater than groups 1 and 3 ($P < .01$); group 3 not different from group 1 ($P > .05$).

skin in cat and monkey.[21,22] Several behavioral studies have demonstrated a site-specific analgesia by peripherally administered opiates in models of peripheral inflammation in rats.[10,12,23,24] It is possible that the activation of the peripheral opiate receptors depends on the presence of chemical mediators of inflammation. Behavioral and pharmacologic studies suggest a peripheral site of action of opiates in inflamed tissue. Joris *et al.* demonstrated that ethylketocyclazocine, a kappa opiate receptor agonist, and fentanyl, a mu receptor agonist, when injected subcutaneously blocked the thermal hyperalgesia induced by local inflammation of carrageenan in the rat paw. The same doses of opiate had no effect when given systemically. Opiates also inhibit cutaneous vasodilatation and extravasation induced by antidromic nerve stimulation[25,26] by inhibiting neuropeptide release from the sensory terminals. In addition, the peripheral release of substance P following C-fiber-strength stimulation of the peripheral nerve can be blocked by opioids.[27,28] The presence of periarticular opiate receptors also has been demonstrated in neurophysiologic studies in the cat following a chemically induced inflammation.[13]

Two possible explanations could account for the discrepancy between the results of this study and the recent reports of Stein *et al.*,[8] who observed a delayed, but prolonged, analgesic effect with intraarticular morphine. All patients in this study, including the control group, had intraarticular injection of epinephrine. If the local presence of epinephrine altered the inflammatory process, and thereby interfered with the activation of the opiate receptors, a peripheral opiate-receptor mediated analgesia may have been masked in our study. A second, more intriguing possibility pertains to the different anesthetic regimens in the two studies. Patients in this study underwent arthroscopy with epidural anesthesia, in contrast to the study by Stein *et al.*,[3] in which patients had general anesthesia. If the activation of the peripheral opiate receptors depends on neuroendocrine responses secondary to the afferent barrage of impulses along nociceptive pathways,[29–31] epidural anesthesia may prevent this activation. Recent reports indicate that protecting the nervous system from the noxious insults of surgery, using regional analgesic techniques, results in blunting of the neuroendocrine response[30,31] and confers long-term reduction in pain.[32,33] Thus, if the activation of peripheral opiate receptors is critically dependent on input to the central nervous system along nociceptive afferents, our anesthetic regimen would have precluded a peripheral opiate-receptor mediated analgesia. The observations by Heard *et al.*[18] that the patients who had regional anesthesia had lower VAS scores, irrespective of intraarticular drug treatment, compared to patients undergoing similar arthroscopic procedures under general anesthesia adds credence to this hypothesis.

The mechanism by which intraarticular morphine is associated with higher pain scores in the immediate postoperative period is obscure. Local histamine release or differences in pH may be contributory, though these factors were not analyzed in this study. However, increase in pain during the first 2 h following arthroscopy was also observed by Khoury *et al.*[17]

In conclusion, intraarticular bupivacaine provides better analgesia than does saline in the immediate postoperative period in this randomized prospective double-blind study. Our study fails to demonstrate functional opiate receptors in the knee joint in a clinical model of acute injury.

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LABORATORY REPORT

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Antimicrobial Activity of Bupivacaine and Morphine

Per H. Rosenberg, M.D., and Olli V. Renkonen, M.D.†*

Antimicrobial activity of bupivacaine and morphine against 10 microbial strains was studied with an agar dilution method. The strains tested were *Escherichia coli* (ATCC 25922), *Pseudomonas aeruginosa* (ATCC 27853), *Staphylococcus aureus* (ATCC 25923), and one of each of the clinical isolates of *Staphylococcus epidermidis* (a multiresistant strain), *Staphylococcus epidermidis* (a sensitive strain), *Streptococcus pneumoniae, Streptococcus pyogenes* (A), *Streptococcus faecalis, Bacillus cereus,* and *Candida albicans.* The antimicrobial effect of bupivacaine was tested at concentrations of 0.5, 1.25, 2.5, and 5 mg/ml (0.05% 0.125%, 0.25%, and 0.5%). Bupivacaine at a concentration of 2.5 mg/ml inhibited the growth of the sensitive *S. epidermidis* strain, *S. pyogenes,* and *S. pneumoniae,* and all of the others except *P. aeruginosa* at a concentration of 5 mg/ml. Morphine 0.2 and 2 mg/ml (0.02 and 0.2%) did not inhibit any of the strains. (Key words: Analgesics: morphine. Anesthetics, local: bupivacaine. Bacteria: antibacterial activity; growth rates.)

STRICTLY ASEPTIC TECHNIQUES for introducing and maintaining catheters for regional analgesia and the use of bacterial filters[1] may be the main reason why serious epidural infections[2–4] are so rare. In this respect, less attention has been paid to the potential bacteriostatic and bacteriocidal effect of local anesthetics[5–7] in protection against bacterial infections. The increasing popularity of continuous catheter techniques for the treatment of both acute and chronic pain, including home treatment of cancer pain,[8] has given rise to renewed speculation about infectious complications. We therefore studied the effect of two of the most common drugs used for epidural analgesia, bupivacaine and morphine, on the growth of 10 different microorganisms.

Material and Methods

The microorganisms tested were *Escherichia coli* (ATCC 25922), *Pseudomonas aeruginosa* (ATCC 27853), *Staphylococcus aureus* (ATCC 25923), and one of each of clinical isolates of *Staphylococcus epidermidis* (multi-resistant strain), *Staphylococcus epidermidis* (sensitive strain), *Streptococcus pneumoniae, Streptococcus pyogenes* (A), *Streptococcus faecalis, Bacillus cereus,* and *Candida albicans.* The growth medium was Mueller-Hinton agar supplemented with 5% heated horse blood. The inoculum added per plate contained about 10^5 colony forming units (CFU). The plates were examined after 18 h at 35° C. The result was scored negative if there was no visible growth on agar.

DRUGS

Bupivacaine hydrochloride was donated by Astra Pharmaceutical Company (Sodertalje, Sweden), and the concentrations tested were 0.5, 1.25, 2.5, and 5 mg/ml. Pure morphine hydrochloride was obtained from the pharmacy of the Helsinki University Central Hospital, and the concentrations tested were 0.2 and 2 mg/ml. Neither of the drugs contained any preservatives.

Results

Bupivacaine at 5 mg/ml inhibited the growth of all microorganisms tested, except for that of *P. aeruginosa* (table 1). At 2.5 mg/ml, bupivacaine still was able to inhibit the growth of *S. epidermidis* (sensitive strain), *S. pneumoniae,* and *S. pyogenes* (A), but 1.25 mg/ml had no effect. Morphine hydrochloride was totally ineffective at the concentrations tested. Morphine had no additional effect on the activity of bupivacaine when both drugs were tested in combination at their highest levels, 2 and 5 mg/ml, respectively.

Discussion

Kleinfeld and Ellis[6] reported that 5 mg/ml tetracaine inhibited the growth of *C. albicans, S. epidermidis,* and *P. aeruginosa.* The latter strain of bacteria was, however, resistant to 20 mg/ml lidocaine and procaine,[7] and to 5 mg/ml bupivacaine in the present study. Abouleish *et al.*,[9] using 5 mg/ml bupivacaine or 20 mg/ml chloroprocaine for epidural or caudal analgesia, found no bacterial growth in the fluid from inside the catheter. Bupivacaine at 2.5 mg/ml has inhibited the growth of clinical isolates of *S. epidermidis* and *Corynebacterium pyogenes.*[1] In the present study, *S. pneumoniae* and *S. pyogenes* (A) also were inhibited, but at 1.25 mg/ml, a concentration also commonly used for continuous epidural

* Associate Professor of Anesthesiology.

† Associate Professor of Clinical Microbiology.

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Address reprints requests to Dr. Rosenberg: Department of Anesthesia, Surgical Hospital, Helsinki University Central Hospital, SF-00130 Helsinki 13, Finland.

TABLE 1. Effect of Bupivacaine Hydrochloride and Morphine Hydrochloride on the Growth of Nine Bacteria and *Candida albicans*. Evaluation after Incubation for 18 h at 35° C.

	Bupivacaine 1.25 mg/ml	Bupivacaine 2.5 mg/ml	Bupivacaine 5.0 mg/ml	Morphine 2.0 mg/ml	Bupivacaine 5.0 mg/ml + Morphine 2.0 mg/ml
Staphylococcus aureus (ATCC 25923)	+	+	−	+	−
Staphylococcus epidermidis (multi-resistant strain)	+	+	−	+	−
Staphylococcus epidermidis (sensitive strain)	+	−	−	+	−
Streptococcus pneumoniae	+	−	−	+	−
Streptococcus pyogenes (A)	+	−	−	+	−
Streptococcus faecalis	+	+	−	+	−
Bacillus cereus	+	+	−	+	−
Escherichia coli (ATCC 25922)	+	+	−	+	−
Pseudomonas aeruginosa (ATCC 27853)	+	+	+	+	+
Candida albicans	+	+	−	+	−

+ = growth; − = no growth.

analgesia, bupivacaine was ineffective. The mechanisms of the antibacterial and antifungal actions of local anesthetics are not known but probably are related to interactions with cell surface macromolecules and cellular membranes.[10,11] Differences in cell membrane structure between *P. aeruginosa* and other bacteria‡ may explain the above sensitive differences. Morphine at 2 mg/ml, a concentration regularly used in epidural pain control, did not affect microorganism growth. Drugs of the morphine series, levallorphan in particular, have inhibited the growth of *Escherichia coli*.[12] Morphine at its limit of solubility had no effect on the growth of this strain, however.[12] It is concluded that high clinical concentrations of local anesthetic solutions may provide some protection against bacterial and fungal infections. Any benefit derived from the antimicrobial activity of local anesthetics may be offset by the fact that local anesthetics are potent inhibitors of phagocytosis and leukocyte metabolism.[13] However, after obtaining the results of the present study, when morphine is used for long-term intermittent epidural analgesia, we have considered it worthwhile filling the catheter with local anesthetic solution after each morphine injection to reduce the risk of intraluminal microorganism invasion.

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BUPIVACAINE INFUSION FOR ILIAC CREST DONOR SITES

R. A. WILKES, W. G. THOMAS

Pain is common after a bone graft has been taken from the iliac crest (Kurz, Garfin and Booth 1989). Local wound infiltration with bupivacaine at closure is effective, but relief lasts for only four hours (Todd and Reed 1991). We report a method of infusing bupivacaine which gives effective and lasting analgesia.

Patients and methods. Patients requiring iliac crest grafts were randomly selected to receive either bupivacaine infiltration at wound closure or bupivacaine infusion postoperatively.

For the infusion group, a fine-bore catheter was tunnelled into the wound between muscle and fat and used to infiltrate 0.5% bupivacaine solution at a rate of 5 ml/hour for 48 hours by a syringe driver. A drain was also used; drain and catheter were removed after two days.

For the infiltration group 10 ml of 0.5% bupivacaine solution was injected into the soft tissues by needle and syringe immediately before skin closure. A drain was used.

At 24 hours postoperatively, patients graded their pain on a visual analogue scale (Banos et al 1989; Campbell and Lewis 1990), taking zero as no pain and 10 as worst imaginable pain.

There were nine patients in the infusion group and seven in the infiltration group. The results were analysed by Student's *t*-test.

Results. All patients could distinguish iliac crest pain from that of other operation sites. The average pain score in the infusion group was 2.2 while that in the control group was 5.4 ($p < 0.01$).

Discussion. We have confirmed that infusion is a more effective method of pain relief than single infiltration. The technique is simple, but we recommend that the catheter is placed subcutaneously to reduce intraosseous absorption and the risk of toxicity (Gilman et al 1990).

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R. A. Wilkes, FRCS Ed, Orthopaedic Registrar
W. G. Thomas, FRCS, Consultant Orthopaedic Surgeon
Department of Orthopaedic and Trauma Surgery, Derriford Hospital, Derriford Road, Plymouth, Devon PL6 8DH, UK.

Correspondence to Mr R. A. Wilkes at 28 Pinewood Drive, Woolwell, Plymouth, Devon PL6 7SP, UK.

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Premarket Notification

510(k) Statement

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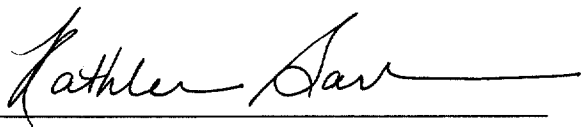

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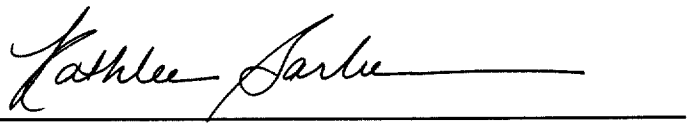

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