Postoperative Infusional Continuous Regional Analgesia
A Technique for Relief of Postoperative Pain Following Major Extremity Surgery

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A new technique using postoperative infusional continuous regional analgesia (PICRA) for postoperative pain relief was investigated in 23 surgical patients treated by amputation (12 patients) or by limb-salvage resection operations (11 patients). Bupivacaine was delivered into peripheral nerve sheaths via catheters placed therein at the time of surgery. Only patients in whom the nerves were easily accessible were treated. Catheters were placed in the axillary sheath, the lumbosacral trunk, and the femoral nerve sheaths of patients treated with shoulder girdle and pelvic procedures (resections and amputations), and within the sciatic nerve sheath of those treated with lower extremity procedures. The anesthetic agent was delivered at controllable rates. Regional analgesia was obtained in the operative site with minimal motor or sensory decrease. To assess the efficacy of this technique, the results of this study group were compared with those of a matched group of 11 patients receiving epidural morphine. Overall, the patients on PICRA had an 80% reduction of narcotic requirements when compared to the historical controls. The technique is reliable and can be performed by the surgeon, requiring about a ten-minute increase in operating time. It has potentially wide application in orthopedics in procedures in which the major nerves are easily accessible (e.g., pelvic fractures and revision hip surgery) and for patients with intractable pain of the extremities.

Experience with a relatively new infusional analgesic technique and its application to orthopedic surgery is described. The use of continuous postoperative infusions of bupivacaine (Marcaine, Winthrop, New York) into major nerve sheaths via catheters placed therein under direct vision at the time of surgery has expanded regional analgesia to make it amenable to major resections and other orthopedic procedures. Pain relief is obtained with minimal motor or sensory loss. This technique has been termed postoperative infusional continuous regional analgesia (PICRA).

Continuous infusional analgesia for postoperative pain relief using long-acting local anesthetic agents in the vicinity of peripheral nerves is a relatively new concept, although preoperative and intraoperative infusion techniques have been advocated recently.
This study attempted to use the infusion technique in the postoperative relief of pain. In the past, local anesthetic solutions were used during and after surgery for short-term pain relief. In general, administration involved delivering a bolus through a percutaneously placed catheter. However, percutaneous placement is not appropriate for major nerve plexuses in extended surgical procedures, and a single bolus can at best provide temporary relief. During most of the postoperative period, which may last many days, supplemental narcotics are also required. However, these problems are overcome with the use of PICRA. Moreover, because the catheter is placed intraoperatively by the operating surgeon under direct vision, reports of problems associated with blind needling of the neurovascular structures and the ensuing late fibrosis are avoided. \(^{16}\)

Until recently, the use of amide local anesthetic agents in postsurgical patients has been restricted to epidural administration. Whereas the efficacy of these agents in pain relief is undisputed, a number of complications have been reported in association with this route of administration. These have included spinal infections; inadvertent subarachnoid, subdural, or intravenous placement of the catheter; "dural" headaches; urinary retention; nausea; pruritis; paraplegia; phantom pain response; unmasking of respiratory depression from intraoperatively administered narcotics; and hypotension. In addition, the use of epidural techniques in patients receiving anticoagulant therapy remains controversial.\(^{6,11}\) Moreover, many centers require close monitoring in an intensive care unit for apneic episodes for all patients receiving epidural morphine. This adds tremendously to costs and seriously limits the routine applicability of such a modality.

By infusing local anesthetics directly into the operative site, the problems of epidural delivery of medication and of blind placements may be avoided and yet the advantages of these agents over narcotic administrations may be retained. The purpose of this paper is to describe this technique and clinical experience.

**MATERIALS AND METHODS**

Between November 1987 and November 1988, 23 consecutive patients, 14 males and nine females, with primary musculoskeletal neoplasms were entered into the study. All were treated with...
Amputations or limb salvage procedures and with PICRA. The histologic diagnoses were osteosarcoma in nine, parosteal osteosarcoma in two, chondrosarcoma in four, malignant fibrous histiocytoma in three, soft-tissue sarcomas in four, and other in one. The surgical stages (Musculoskeletal Tumor Society classification) were Stage IB (six), Stage IIB (15), Stage III B (one), and nonapplicable (one). The anatomic sites of the primary tumors were as follows: femur in 11 (mid, seven; distal, three; and proximal, one); pelvis in five; proximal humerus in two; proximal tibia in one; thigh-buttock in two; and other in two.

TECHNIQUE

Silastic catheters were placed into the nerve sheaths under direct vision at the time of surgery (Figs. 1 and 2). These placements were made only in patients in whom the nature of the surgical procedure necessitated exposure and dissection of the sheaths and plexuses. In patients treated with above-knee and below-knee amputations, the catheters were placed in the sciatic nerve above the level of the amputation, i.e., at the levels of the lesser trochanter and the popliteal space, respectively. These were placed by blunt dissection following traction on the nerves. The nerve sheaths were routinely opened. Following pelvic resections or hemipelvectomies, two catheters were employed: one along the lumbosacral trunk near the S I foramen and the other along the femoral nerve atop the psoas muscle.

The catheters were externalized through separate stab wounds made in the skin and stitched in place (Fig. 3). At the time of wound closure, a bolus dose of 10-20 ml of bupivacaine (0.25%-0.5%) was placed into the catheter and free flow into the tube was ensured. The timing was such that the patient would awaken just before the full effect of the bupivacaine, thus allowing neural integrity to be checked and yet ensuring that the patient would

FIG. 2. Proximal tibia resection. An intraoperative photograph showing a segmental custom prosthesis after a resection of a Stage IIB osteosarcoma and placement of a silastic catheter (large arrow) into the sciatic nerve sheath (small arrow) prior to wound closure. The gastrocnemius muscle will be transposed anteriorly to cover the prosthesis and knee joint. It is important to open the nerve sheath. All catheters are sutured to adjacent soft tissue with 4-0 chromic to avoid displacement. This permits easy removal. Excessive tortuous exit paths may cause difficulty in pulling the tube out.
FIG. 3. Below-knee amputation. This patient had a Stage IIB soft-tissue sarcoma of the leg. The silastic (Marcaine) catheter is placed as high as possible along the sciatic nerve. The catheter is seen externalized through a separate stab incision and sutured in place (arrow). At this stage, while staples are applied, a bolus of 10-20 ml of bupivacaine (0.25%) is injected.

not experience a period of pain in the recovery room. Because the average time of onset of bupivacaine is about 1 1 minutes,' the bolus was injected just before putting in the skin staples at wound closure (Fig. 2).

The tubes were attached to a standard intravenous infusion pump and the rate set at 2 ml per hour initially. With adults, a 0.5% solution was used, with children, a 0.25% solution. Five patients were not given the bupivacaine continuously but instead received it as timed boluses every four to five hours. If a patient experienced discomfort in the operative area, the rate was increased up to 4 ml per hour (up to a maximum of 2 mg/kg in any four-hour period in children). If the pain persisted despite this, then narcotics were not withheld. Note was made of any pain not originating from the site of surgery.

ANALYSIS

At the end of a 72-hour period, the total narcotic medication used in these cases in morphine sulfate-equivalent doses (MSE) was calculated. The period of 72 hours was defined as the day of the surgery and the following 72 hours.

For comparison, the data for 11 patients treated in the previous two years who were matched for type of surgery, diagnosis, age (in decades), hospital, and operating surgeon were reviewed. The method of pain control used in these 11 patients was epidural morphine and supplemental narcotics; none was treated by intramuscular narcotics alone. Administration of nonnarcotic analgesics and sedatives was also noted in both groups.

Catheter placement studies entailing the injection of nonionic, nonirritating radioopaque contrast material (Isovue, E. R. Squibb, Princeton, New Jersey) were performed in certain cases (Figs. 4-7). This was an excellent adjunct that could allay anxiety arising from possible extrusions or displacements. Bupivacaine levels were checked randomly to ensure safety; however, the titrations and dosage adjustments were based on clinical evaluation of the amount of pain rather than on pharmacologic studies.

RESULTS

The narcotic requirements of the two groups are summarized in Table 1. All calcu-
FIG. 4. Above-knee amputation. A contrast (Isovue) study performed through the nerve sheath catheter following a high above-knee amputation performed for a Stage IIB osteosarcoma. The nerve sheath had been opened and the catheter threaded up to lie as proximal as possible. Note the contrast extending to the sciatic notch (curved arrow). It is important to place the catheter as proximal as possible. The catheter can be visualized (small arrows).

lations are in MSE doses for a 72-hour period following the day of surgery as defined above.

Eleven (45.8%) of the patients on PICRA required no narcotic medication. Of the remaining 13 patients, the mean dosage was 47 mg of MSE. The overall average was 25 mg of MSE. The average dose for patients treated with amputations was 30 mg; the average dose for those treated by limb-salvage procedures was 18 mg.

Five hemipelvectomy, five above-knee amputations, and two below-knee amputations were performed. The average MSE required was 10 mg, 38 mg, and 61 mg, respectively. No narcotics were required by four of the five patients with hemipelvectomy, two of five patients with above-knee amputations, and one of two patients with a below-knee amputation.

Five pelvic resections (internal hemipelvectomies), four distal femoral/proximal tibia] resections, and two shoulder girdle resections were performed. The average MSE required was 11 mg, 35 mg, and 0 mg, respectively. No narcotics were required by one of five pelvic resection patients, one of four knee resection patients, and either of the two patients treated with shoulder resection.

There was no statistical difference in narcotic requirements between patients who received continuous infusion and those who received timed doses. Nineteen patients received delivery through pumps. Of these, eight required no narcotics, and the remainder required an average of 46 mg of MSE. As a group, the overall mean was 27 mg of MSE over 72 hours. Of the four patients receiving bupivacaine as timed boluses, two required no narcotics, and the other two averaged 51 mg of MSE. The overall average MSE was 26 mg.

No major complications were encountered. Bupivacine levels ranged from undetectable to 1.1 µl/ml of serum. Four patients had motor weakness (two had peroneal, one posterior tibial, and one femoral), indicative of partial motor blockade. All recovered following cessation of bupivacaine. There were no portal infections and only two minor complications related to catheters that extruded accidentally.

There were 11 patients in the matched control group, which was given epidural morphine and parenteral narcotics. The average dose was 123 mg of MSE during the first 72 postoperative hours. All patients required supplemental narcotics of some form. Epidurally delivered morphine diminished but did not eliminate the need for additional drugs. Three hemipelvectomy patients required an average of 110 mg, two pelvic resection patients required an average of 152 mg, and six patients treated with limb-salvage procedures of the lower extremity re-
FIGS. 5A AND 5B. Distal femoral resection. (A) An intraoperative photograph following a limb-sparing resection of a Stage 11B osteosarcoma reconstructed with a distal femoral, modular prosthesis. The silastic catheter (arrow) is being threaded into the sciatic nerve sheath (S). The catheter is placed several centimeters above the bone-prosthesis junction. (B) A postoperative contrast (Isovue) study done through the Marcaine catheter demonstrated filling of the sciatic sheath (arrows) and appropriate placement. The sciatic nerve sheath is routinely opened.

quired an average of 120 mg of MSE in the first 72 hours, respectively.

DISCUSSION

A simple and effective technique of pain management in the immediate postoperative period following major amputations and limb-salvage procedures is described. A silastic catheter is placed along the major peripheral nerves in the operative field before closure. This permits the continuous infusion of bupivacaine postoperatively for up to seven days. Performed by the operating surgeon, the technique entails only a five- to ten-minute increase in operating time. The clinical results in these 23 patients have been so dramatic that it was deemed justifiable to report these results as a single-arm study, i.e., a nonrandomized study with comparison to matched (historical) controls only. Nearly one half of the patients required no narcotic medications postoperatively. Overall, there was an 80% decrease in narcotic requirements when compared to historical controls treated by a combination of epidural morphine and supplemental narcotics. It is believed that this technique has wide application not only for musculoskeletal oncology but also for other orthopedic procedures such as amputations and hip revision surgery, in which the major nerves are exposed or easily accessible.

Pain and sensory fibers of mixed nerves have a lower threshold to the membrane-stabilizing action of local anesthetic agents than motor fibers because they are composed of slower conducting fibers of the A delta and C (unmyelinated) types. It may thus be possible to locate a level of anesthetic blockade that would allow pain relief while still allowing motor function and voluntary motor activ-
Partial motor blockade in the first 48 hours occurred in four patients, but because motor and sensory function were evaluated in the immediate postoperative period, this did not cause undue concern. Motor function returned on cessation of the infusion. (The half-life of bupivacaine is \(3.5 \pm 2\) hours).

Continuous sensory blockade for pain relief is a relatively new modality for the surgeon. The freedom from the systemic side effects of narcotics would certainly make the technique desirable. There is ample evidence that patients receiving continuous pain relief have a smoother postoperative period, better respiratory function, and less morbidity than those who receive narcotics." It is logical that these benefits would accrue to patients on similar regimens free from narcosis. Although respiratory studies were not carried out, the PICRA patients were in general more alert and complained less of nausea, constipation, and urinary difficulties than the patients receiving narcotic medications.

Other studies that have attempted continuous infusion techniques for postoperative relief have included direct wound irrigation, instillation into the abdomen, and continuous sciatic nerve block in one patient with gangrene." The efficacy of wound perfusion may to some extent be aided by a dilutional effect of the pain-mediating substance in the wound.

Interestingly, none of the patients in this series complained of significant phantom pain or sensations (among the amputees). This was true of all patients, regardless of the hip joint. This patient required only 5 mg of morphine postoperatively. Both the femoral and sciatic nerves are routinely catheterized following resections around the pelvis for optimal pain relief.
method employed. Given the small size of this series and the multifactorial etiology of the syndrome, it must await definitive evaluation to decide whether PICRA has a role to play in its prevention. Since early stump pain may contribute to the origin of phantom pain, and occasionally a single injection of local anesthetic may be curative, a significant reduction in its incidence may not be entirely unexpected.

Bupivacaine has a wide range in clearance and half-life. A two-point method that would allow early dose adjustments has therefore been recommended. In clinical practice, a factor as variable and prone to psychological modifications as pain may best be modified on an on-demand basis instead of on a strict mathematical approach. However, if blood levels are used as a guide to therapy, the true whole blood levels should be monitored rather than the plasma concentrations, because an artifactual error may be created by the hematocrit.

The possibility that bupivacaine might cause systemic cardio toxicities or neuro toxicities is remote, given the dosages employed. When compared to the large doses used in procedures such as caudal blocks (often doses between 75-150 mg repeated every three hours), the doses required by PICRA are
TABLE 1. Comparison of Narcotic Requirements of Patients Treated by PICRA (Group 1) Versus Matched Controls (Group 2)

<table>
<thead>
<tr>
<th>Type of Procedure</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Morphine Sulfate Required (Group 1 + 2) ≤ 100</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Dose</td>
<td>n</td>
</tr>
<tr>
<td>Hemipelvectomy</td>
<td>5</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Pelvic resection</td>
<td>5</td>
<td>11</td>
<td>2</td>
</tr>
<tr>
<td>Limb-sparing resection</td>
<td>6</td>
<td>35</td>
<td>6</td>
</tr>
<tr>
<td>Above-knee amputation</td>
<td>5</td>
<td>38</td>
<td>0</td>
</tr>
<tr>
<td>Below-knee amputation</td>
<td>2</td>
<td>61</td>
<td>0</td>
</tr>
<tr>
<td>Overall</td>
<td>23</td>
<td>25</td>
<td>11</td>
</tr>
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minimal (120-240 mg over 24 hours, calculated from 2-4 ml of 0.25% bupivacaine). Blood bupivacaine levels ranged from undetectable to 1.1 µg/ml, which is well below the recognized minimal toxic threshold of 4 µg/ml. Even with the bolus occasionally required, the dosage never exceeded the 400 mg/24 hours, which is considered within the safety levels in adults.

The explanation of the efficacy of this relatively low dosage probably lies in the peculiar anatomic environment. The action of amide anesthetics is concentration-dependent. Factors such as area, diffusion coefficient, thickness of the membrane, and the lack of a diluting influence of fluid in peripheral situations allow for the observed reduction in needed volumes. The local state of tissues, the pH, and the oxidation state modify this demand as well. Continuous blockade may result in augmentation, whereas repeated boluses, dependent on factors such as timing, may result in a decrease in effectiveness, a phenomenon known as tachyphylaxis. Clearly, larger studies and clinical trials are needed to ascertain the precise dosage, levels, and timings for each specific anatomic site in order to locate the optimal usage of PICRA.

For purposes of caution, it should be kept in mind that in disease states and at doses approaching the upper levels of systemic toxicity, signs that might appear include numbness of the tongue, lightheadedness, visual and auditory hallucinations, disorientation, and drowsiness, in addition to the better known objective excitatory signs such as shivering, unconsciousness, convulsions, or respiratory depression. It is, however, unusual to see any of these symptoms in patients whose plasma concentrations of bupivacaine are below 4 µg/ml. Additionally, direct effects on the cardiac and smooth muscles could occur. The dosage required for these is somewhat higher. The other systemic effects ascribed are expected to occur at doses far higher than in clinical practice with PICRA.

A final issue often discussed is the concern that amide anesthetics or their preservatives may exhibit local tissue toxicity. In clinical practice, this has not been evident to any significant degree even with extensive usage in potentially far more delicate anatomic areas. Thus, the only real aspect one may need to consider is an untoward or allergic reaction of the hypersensitivity or anaphylactic variety.

Some early observations and lessons learned from this study should be emphasized. (1) PICRA reduces, and in many cases eliminates, the need for large doses of narcotics. Supplemental medications such as acetaminophen or aspirin alone were sufficient for control of discomfort in these patients.

(2) Patients often complained of pain from sites other than the operative site. When pain of the primary site was well controlled, secondary sites would become the focus of complaints; for example, neck pain from awkward positioning at the operating table.
Additionally, there was an element of postoperative anxiety, which is normally dulled by narcotics. In the early part of the study, the nursing staff interpreted this as pain. Such problems are usually reduced by a sedative, especially on the first postoperative evening. (3) Sensory dulling may require above-average care in observing the neurovascular intactness of the patients postoperatively. Partial motor blockade may occasionally occur and may cause undue concern. The usual signs of pain, pallor, and parasthesia may be altered in patients receiving inadvertently tight casts. The first manifestation of bad plaster immobilization may be ulcers seen at the time of wound inspection. However, if this possibility is paramount in the mind of the surgeon then the complication need never occur. (4) PICRA patients with higher level resections (e.g., pelvic resection, hemipelvectomies, and shoulder resections) tend to have less postoperative discomfort than those who have been treated with more distal procedures (e.g., above-knee or below-knee amputations or resections). A percutaneous femoral catheter is now placed at the time of surgery in addition to the intraoperatively placed sciatic catheter in these patients. The data from these cases are not included in the present series but are promising. (5) The catheter tip may break during removal. To reduce the likelihood of breakage, it is recommended that excessively tortuous paths through muscle and fascial layers be avoided. Also, radioopaque tubes should be used and the length of the tube inside the wound should be marked and noted. (6) Certain segments of the nerve may be spared. It is suggested that a meticulous record of the dermatomes in which the pain is occurring be kept while experience is gained using PICRA. 

(7) To ensure uniformity, data are presented only on the first 72 postoperative hours. In practice (and as was done for several patients) the catheters can be left in for up to one week. The data in this situation are even more dramatic and convincing. Thus, potential application of the technique may extend beyond the 72-hour limit used in this study.

This study demonstrated the efficacy of continuous regional infusion of bupivacaine in decreasing postoperative narcotic requirements. It did not attempt to evaluate other important postoperative parameters, including patient preference, complications, or length of convalescence. It was the subjective view of the nursing and surgical staffs that these patients were more alert and comfortable and were mobilized earlier than patients receiving standard parenteral morphine regimens. Control studies evaluating these parameters are warranted. In addition, further studies to determine optimal dosage, rate of flow, timing (intermittent bolus versus continuous infusion), and location of catheters should be evaluated to determine optimal efficacy of PICRA.

REFERENCES

Pain Relief After Major Extremity Surgery


