Acute Pain Management

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The development of guidelines and requirements for inpatient pain continue to focus efforts to decrease acute pain in postoperative patients. Clearly, improvements in acute pain management must continue.[1] In the last few years, efforts in two aspects of acute pain management are likely to offer benefit in the near future. One is the pursuit of nonopioid analgesic adjuncts. The second is refined continuous regional analgesic techniques.

Opioids remain the standard drug for acute pain management and are the first choice for the treatment of moderate to severe acute pain. Given the narrow therapeutic window of opioids, we continue to use patient controlled analgesia for acute pain therapy and attempt to limit opioid related side effects. In an era of reduced nursing availability, patient controlled analgesia will continue. However, the efficacy of patient controlled analgesia may be no greater if nurses are given satisfactory time to assess pain and analgesic requirements, side effects, and administer an appropriate dose. The overall efficacy of parenteral opioids depends upon the amount of pain relief achieved and the side effects like nausea, vomiting, ileus, and respiratory depression.

Epidural analgesia. Epidural analgesia continues to be the emphasis of anesthesia-based acute pain services. Typically opioid-local anesthetic combinations are infused continuously for several days in the postoperative period. In general, most recent studies continue to demonstrate advantages (see below) of epidural analgesia if local anesthetics are using in combination with opioids. These advantages are:

- decreased pain particularly during mobilization[2-4]
- earlier return of bowel function after abdominal surgery[5,6]
- decreased pulmonary complications[4,7]

A recent multicenter study confirmed that even in a group of high-risk patients undergoing a wide variety of surgeries, epidural analgesia provided better pain relief at rest and with cough than parenteral opioids. Also, postoperative pulmonary complications were reduced. The benefits of regional anesthesia and analgesia compared to general anesthesia and parenteral opioids was also examined in a study comparing the outcome of patients undergoing abdominal aortic surgery[8]. Postoperative outcomes were similar among the treatments groups and adverse events were rare for all patients. In this particular setting, for these patients, epidural anesthesia and analgesia conferred no benefit. Overall, complications and morbidity were low.

The local anesthetic is critical for improved outcome using epidural analgesia. Choice of local anesthetic for epidural infusions include bupivacaine, ropivacaine, and levobupivacaine; the rate is usually 8 to 12 ml/hr. The advantages of using levobupivacaine and ropivacaine are quite small for thoracic epidural analgesia. For lumbar epidural analgesia, for instance, after lower extremity orthopedic procedures, there may be advantages to using ropivocaine because it is intended to reduce motor block. Levobupivocaine and ropivacaine may be useful when a concern for systemic toxicity is warranted. Rarely do epidural infusions cause levels of local anesthetics to approach the toxic range in adults.

To local anesthetic, either a lipid soluble opioid or a hydrophilic opioid is added. Although studies indicate that continuous treatment using lipophilic opioids like fentanyl administered epidurally or parenterally are equivalent in dosage requirements and quality of analgesia, epidural lipophilic opioids remain popular. Fentanyl tends to be rapidly absorbed systemically after epidural administration; however, the addition of modest doses of epinephrine, i.e., like 2 micrograms per ml, reduces the systemic effects of epidural fentanyl, likely prolonging and enhancing its spinal action.[9] Epinephrine may also have analgesic properties by itself. Epidural administration of hydrophilic opioids like morphine or hydromorphone reduces the dose required to produce equivalent analgesia compared to the intravenous route (Fig. 1).

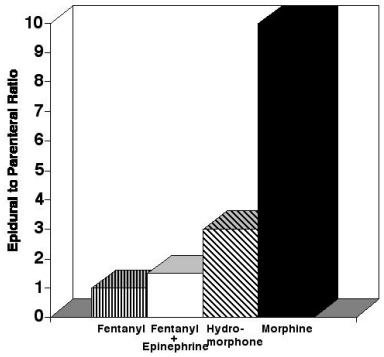

Fig. 1 Epidural to parenteral ratio for opioids

Clonidine is available in preservative-free formula and extensive basic science literature indicates its neuraxial analgesic properties. High doses of epidural clonidine are associated with hypotension and sedation[10]. Enthusiasm for the addition of small doses of clonidine to thoracic epidural analgesia with local anesthetics is modified by the increased incidence of hypotension associated with the sympatholytic effects of epidural clonidine. A study examining the combination of levobupivacaine and clonidine noted marked improvement in epidural analgesia when clonidine (8.3 mcg/ml) was added to levobupivacaine.[11]

Continuous nerve block. Recent systematic reviews conclude that preemptive analgesia by itself does not substantially contribute to acute pain management.[12] Duration and efficacy of each particular analgesic treatment rather than timing may be most important for outcome in acute pain management. Continuous nerve and plexus blocks for pain control in surgery on extremities are becoming more common and new approaches and equipment using these techniques may increase their utilization[13-17].

Table 1 Continous Plexus and Nerve Block

Surgery	Continuous Technique
Shoulder	Cervical Paravertebral
Shoulder	Interscalene
Elbow/Forearm	Axillary
Elbow/Forearm	Infraclavicular
Knee	Femoral
Foot	Sciatic

Non opioid analgesia. One mechanism to advance perioperative pain management is to develop non-opioid, acute pain therapy.[10] Typically, the efficacy of nonopioid analgesics are studied by examining opioid-sparing effects. For example, acetominophen may decrease morphine consumption in the first 24 hrs after surgery. This demonstrates the drug has an analgesic effects; however, this is not a definitive outcome measure. Improved outcome would be noted if pain was less (even with decreased morphine use), nausea and vomiting were decreased, ileus was shortened, costs were reduced or morbidity was decreased. Studies with opioid sparing treatments may improve[18] or not influence outcome[19]. Currently, acetaminophen and related drugs (like paracetamol and propacetamol) can be important components of pain therapy in the

postoperative period. Moore and Mcquay[20-22] have systematically reviewed single-dose, placebo-controlled, randomized trials assessing pain relief in patients with moderate or severe postoperative pain. Pain relief was converted into the number of patients with at least 50% pain relief which was used to calculate the number-needed-to-treat (NNT) for one patient to achieve at least 50% pain relief (Table 2).

Table 2 Data from systematic reviews of analgesic drugs for acute pain

DRUG	Number-Needed-to-Treat
Morphine 10 mg	2.9
Paracetamol 1000mg	3.6
Paracetamol 650mg	5.0
Ketorolac 30 mg	3.4
Ibuprofen 400 mg	2.7

Ten mg of parenteral morphine had an NNT of 2.9, i.e. one of every three patients with moderate or severe postoperative pain treated with 10 mg parenteral morphine received at least 50% pain relief (Table 1). An NNT of 3.6 for 1000 milligrams of paracetamol and 5.0 for a smaller doses. There is little evidence for toxicity of acetaminophen-related drugs in the perioperative period, occasionally hepato- or nephrotoxicity may be a concern. It must be recognized that the benefit of mild analgesics like these may depend on the particular surgery. For instance, pain after third molar extraction may be quite sensitive to drugs like acetominophen but in many major surgical cases, little benefit is noted. This may limit the interpretation of systematic reviews that include groups of patients like tooth extraction that do not generalize to the operating room.

NSAIDS block the synthesis of prostaglandins by inhibition of cyclooxygenase enzymes. In Table 2, NNT data from systematic reviews on NSAIDS and acute pain are shown. Again, the inclusion of dental trials in part limits the interpretation to how these drugs may best be used in the operating room, recovery room and hospital wards. Most studies demonstrating analgesic effects of NSAIDS have been measured in patients undergoing orthopedic, abdominal and gynecological surgery. Usually, a 20-30% opioid sparing effect is noted[23,24].

Precautions with NSAIDS:

- Gastric irritation/bleeding
- Surgical bleeding
- Renal insufficiency
- Heart failure/diuretic use
- Hypovolemia
- Bone graft healing?

Classically, NSAIDS inhibit both forms of cyclooxygenase, cyclooxygenase 1 (COX-1) and cyclooxygenase 2 (COX-2). Despite the demonstration of their analgesic effects, the use of NSAIDS has been limited by side effects and anticipated complications. The development of drugs specifically inhibiting COX-2 has heightened our interest in non-opioid analgesia. COX-2 is an inducible form of the cyclooxygenase enzyme although it is normally present in the central nervous system, kidney, and gastrointestinal tract. It is thought that the side effects of NSAIDS are largely related to COX-1 inhibition, particularly effects on platelets and the GI tract. Since COX-2 is present in the kidney, renal side effects of these drugs may occur with their use in the perioperative period. Table 3 summarizes results from recently published, randomized controlled trials of COX-2 inhibitors in acute pain.

Table 3 Clinical trials using COX-2 inhibitors for acute pain.

SURGERY	DRUG	OUTCOME
Spinal Fusion[25]	Celecoxib 200 mg Rofecoxib 50 mg	Lower pain scores
Total Knee Replacement [26]	Parecoxib 40 mg	Decreased pain
Total Hip Replacement[27]	Parecoxib 20 or 40 mg	Decreased vomiting
CABG[28]	Etodolac 300 mg	Decreased antiemetic use
Gynecologic Surgery[29]	Parecoxib 40 mg	No difference
Lumbar laminectomy[30]	Rofecoxib 50 mg	Decreased pain
Radical Prostatectomy[31]	Rofecoxib 50 mg	No difference
Otolaryngologic Surgery[32]	Celecoxib 200 mg	No difference
Otolaryngologic Surgery[33]	Celecoxib 200 mg Rofecoxib 50 mg	Decreased pain
Otolaryngologic Surgery[34]	Rofecoxib 50 mg	Decreased pain

It is anticipated that use of the COX-2 inhibitors in selective patients will likely produce less toxicity than conventional NSAIDS. The most vulnerable population of patients for adverse consequences caused by inhibition COX-2 may be patients with heart failure, renal insufficiency or moderate to severe hypovolemia in the perioperative period. There has been some controversy whether patients taking COX-2 inhibitors may be at increased risk for thromboses[35,36]; guidelines are suggested[37]. The effect of COX-2 inhibitors on bone healing is also controversial.

Precautions with COX-2 Inhibitors

- Renal insufficiency
- Heart failure/diuretic use
- Hypovolemia
- Thromboses?
- Bone graft healing?

NMDA receptor antagonists are another class of nonopioid analgesic drugs. The NMDA receptor has been implicated in pain memory and chronic pain. One drug that antagonizes NMDA receptors is ketamine. Ketamine produces marked analgesia that is limited by psychotomimetic side effects and amnesia. In low doses, ketamine has been is an adjunctive analgesic. The precise role of NMDA receptor antagonists and ketamine in the perioperative period is still under scrutiny.[38] Another NMDA receptor antagonist, dextromethorphan, has undergone multiple clinical trials. Only very modest analgesic effects are noted and thus its utility is limited.

Most practitioners limit the use of ketamine in acute pain management. If a trial is warranted, some suggestions from the literature include:[39]

- Parenteral infusions of 0.25 mg/kg/hr can be beneficial. Greater dosing is limited by psychotomimetic effects.
- Ketamine administration for several days may modify the development of persistent postoperative pain.
- There is little evidence to suggest that neuraxial ketamine should be administered in the perioperative period. Parenteral treatment produced greater analgesia.

- Ketamine may reduce pain and/or opioid requirements by reducing acute opioid tolerance[40].

Chronic pain after surgery. It is becoming increasingly clear that in some cases a large proportion of patients are developing chronic pain after surgery. The incidence of chronic pain after certain surgeries[41]:

- Limb Amputation 30-81%
- Breast Surgery 50%
- Gallbladder Surgery 3-56%
- Thoracotomy 29-67%
- Inguinal Hernia Surgery 0-37%

Preoperative pain for more than one month, repeated surgery and preoperative psychosocial factors contribute to chronic pain after surgery. Intraoperatively, risk of nerve damage is a factor; postoperatively, severity of acute pain, radiation therapy, chemotherapy and psychological factors influence the likelihood of chronic pain.
In most cases, surgery is a timed, controlled event. Thus, there is an opportunity to better understand factors that contribute to chronic pain and also test strategies to prevent its development.

Postoperative epidural analgesia and anticoagulation. Guidelines and suggestions have been made towards placement of epidural catheters and performance of neuraxial procedures in patients who are anticoagulated or at about to undergo anticoagulation [42]. Practitioners in acute pain services find themselves in unique situations in which postoperative hemostatic abnormalities occur and epidural catheters must be removed. Suggestions for maintaining and removing epidural catheters in patients with potential hemostatic abnormalities are made[43].

In conclusion, regional analgesic techniques and nonopioid adjuncts offer improvements in acute pain management in the near future. Along with surgeons effort to produce less invasive surgery, further improvement in perioperative care will continue with the development of new drugs aimed toward the specific etiology of incisional pain[44]. Future studies on the development of persistent pain after surgery will enhance our understanding of chronic pain.

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