Operative Anesthesia and Pain Control

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ABSTRACT

A comprehensive understanding of operative anesthesia and postoperative pain control is essential to the practicing colon and rectal surgeon. Most of the operations performed—particularly in the perineum—cause significant patient discomfort and often result in a lengthy recovery period. A variety of factors, including patient positioning in the operating room and patient expectations, influence the choice of operative anesthesia. Postoperatively numerous modalities and agents exist for pain control. With this variety of options at hand, surgeons should be educated and decisions should be individualized, with the ultimate goals of improving the patient experience and facilitating recovery.

KEYWORDS: Patient controlled analgesia (PCA), epidural, opioids

Objectives: On completion of the article, the reader should be able to summarize the options available for postoperative pain control.

OPERATIVE ANESTHESIA

Anesthesia for operations on the anorectum includes the following options: straight local infiltration (perianal block), local perianal block with intravenous sedation, regional (spinal, epidural, or caudal block), and general anesthesia (via bag and mask, endotracheal tube, or laryngeal mask airway). The chosen option depends on factors such as the specific operation performed, patient position, patient comorbidities, and patient preferences. Local infiltration anesthesia is sufficient for excision of a thrombosed external hemorrhoid, whereas transanal endoscopic microsurgery for a rectal tumor typically requires general anesthesia. Lack of access to the airway in the prone-jackknife position may dictate either general endotracheal anesthesia or regional anesthesia. Procedures performed in the lithotomy position allow for general anesthesia via bag and mask or laryngeal mask airway (LMA).

In principle and in practice, most outpatient anorectal procedures may be performed under anal canal block. Unfortunately, anal canal block itself is often too

noxious for the fully conscious patient to bear. The most commonly used sedation regimen, intravenous midazolam and fentanyl, carries with it the risk of respiratory depression and/or upper airway obstruction. Management of this complication in the prone patient is difficult. Our group at the University of Massachusetts/Memorial Medical Center has utilized a sedative technique that permits placement of the anal canal block without gross patient movement or contraction of the anal sphincter, yet allows the patient to maintain airway patency.¹ This alternative technique obviates the need for airway intervention, provides the surgeon adequate operating conditions, and allows transfer of the patient directly to the phase II recovery area, thereby bypassing the postanesthesia care unit (PACU) and increasing operating room (OR) throughput.

The essence of our technique combines the phenylcyclidine derivative ketamine with the polyphenolic compound propofol. Ketamine has a unique ability to provide intense analgesia while maintaining respiratory drive and upper airway muscle tone. Undesirable side

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effects include increased salivation and psychotomimetic effects characterized by vivid, sometimes unpleasant dream-like sensations. Propofol, usually used for the induction of general anesthesia, has amnestic and mildly euphoriant effects when administered in small doses. In our review of 422 cases of patients sedated with ketamine and propofol, we found that 93% were able to proceed directly to the phase II recovery area. There was a significant reduction in time spent in the OR (sedation group 27 minutes, general anesthesia group 40 minutes, $p = 0.001$) and time spent in the hospital (sedation group 217 minutes, general anesthesia group 273 minutes, $p = 0.002$).¹ Combining these drugs has allowed us to meet our objectives while maintaining a low complication rate.

PAIN CONTROL

Optimal postoperative acute pain control for colorectal and perineal procedures can be a formidable challenge. Proper management of postoperative pain can relieve suffering and lead to earlier mobilization, shortened hospital stay, reduced hospital costs, and increased patient satisfaction. Recently, a stronger emphasis has been placed on pain control, from increased exposure and education in medical school to the development of the subspecialty of pain medicine.

Surgery produces tissue injury with consequent release of histamine and inflammatory mediators, such as bradykinin, prostaglandins, neurotransmitters, and neurotrophins.² The release of inflammatory mediators activates peripheral nociceptors, which initiate the transduction and transmission of the nociceptive information to the central nervous system (CNS) where the signal is modulated and perceived.² The ultimate goal of the treating physician is to modulate these signals such that the sensation, discrimination, and perception of pain are minimized, if not eliminated.

This outline will cover many of the options currently utilized by surgeons and pain specialists, including systemic analgesics [opioids, nonsteroidal antiinflammatory drugs (NSAIDs), acetaminophen, tramadol, and Neurontin (Pfizer Pharmaceuticals, New York, NY)] and regional techniques (neuraxial and peripheral analgesics). Many of these medications can be delivered via oral, parenteral (intravenous [IV], intramuscular, and subcutaneous), transdermal, epidural, and/or intrathecal routes. Although several safe and effective options are available, a multimodal approach is often most useful, providing concurrent administration of different classes of analgesics.³ This approach allows each class of analgesic to inhibit pain at different sites of the pain pathway, working synergistically, and allowing the use of relatively smaller doses of each agent. The net effect results in accelerated recovery, decreased length of hospitalization, reduced

dosage of each individual agent, and lower frequency and severity of side effects.⁴

Patient-Controlled Analgesia

Opioid analgesics are one of the cornerstone options for the treatment of postoperative pain, generally exerting their analgesic effects through μ receptors in the CNS, directly modulating the nociceptive process. Patient-controlled analgesia (PCA) is one of the most commonly utilized means of delivering opioid analgesics after major abdominal surgery. A variety of narcotic medications including morphine, hydromorphone, meperidine, and fentanyl can be self-administered utilizing this reliable, programmable delivery system. A PCA device can be programmed for several variables, including demand (bolus) dose, lockout interval, and background infusion. Not only does PCA allow the patient to administer the pain medication "on command," but also in "real time," without lengthy delays between summoning the nurse and receiving medication. An additional advantage to this system is the sense of patient empowerment, with its associated psychological benefits. Pain control becomes one of the few aspects of their care that remain in their direct control, and this is not of minor significance. Additional benefits include reduced workload for the nursing staff and reduced chance for medication errors. Although some equipment-related malfunctions have been reported, the PCA device itself is relatively free of errors, and most problems related to PCA use result from user or operator errors.⁵

The incidence of opioid-related side effects from intravenous PCA is similar to other routes of administration.⁶ The analgesic efficacy of opioids is typically limited by the development of tolerance or opioid-related side effects such as nausea, vomiting, sedation, depression of brainstem control of respiratory drive, hypotension (more common in hypovolemic patients and following rapid injection), and urinary retention. Histamine release often follows morphine administration and may produce flushing, tachycardia, hypotension, pruritus, and bronchospasm. Gastrointestinal (GI) transit slows with prolonged administration, resulting in constipation and ileus in many patients. Peripheral μ -opioid receptor antagonists, such as alvimopan, have been studied as a means of counteracting this effect. In patients undergoing major abdominal surgery, alvimopan was well tolerated and accelerated GI recovery and time to discharge compared with placebo.⁷ Respiratory depression is also associated with intravenous PCA, but this is infrequent ($<0.5\%$).⁸ Factors that may be associated with the occurrence of respiratory depression with intravenous PCA include the use of a background infusion, advanced age, concomitant administration of sedative or hypnotic agents, coexisting pulmonary disease such as

sleep apnea, and errors in programming or administration.^{9,10} An understanding of opioid metabolism should be considered as well. Morphine is metabolized to morphine-3-glucuronide and morphine-6-glucuronide, which can accumulate in patients with renal impairment. Meperidine is metabolized to normeperidine, a toxic metabolite that can accumulate and cause seizures, particularly in the elderly, in dehydration, and in patients with renal impairment.

A background infusion was initially thought to improve analgesia, especially during sleep; however, benefit has not been demonstrated in recent studies, particularly in opioid-naïve patients.^{11,12} Many studies show that use of a background infusion only increases the analgesic dosage used and the incidence of side effects such as respiratory depression.^{6,12}

Epidural Route of Administration

Neuraxial routes of administration include the epidural and intrathecal (subarachnoid) routes, and require coordinated care with our anesthesiology colleagues. Both local anesthetics and narcotics can be administered on an intermittent or continuous basis through a tiny polypropylene catheter (19 or 20 gauge) inserted transcutaneously into the epidural space, at a variety of spine levels. Simply speaking, this blocks transmission of pain signals from the periphery to the spinal cord. The precise location of action of local anesthetics in the epidural space is not clear, and potential sites include the spinal nerve roots, dorsal root ganglion, or spinal cord itself.¹³ Although this form of anesthesia is particularly efficacious in childbirth and thoracic surgery, its utility in abdominal surgery tends to be less widely accepted. Patients must not be coagulopathic and must not be receiving antiplatelet or anticoagulant medication. Placement of an epidural catheter in the coagulopathic patient risks intraspinal bleeding and spinal hematoma formation, which can lead to severe neurologic injury. Catheters can be technically difficult to place due to variations in spinal anatomy, leading to ineffective analgesia. Infection may result from exogenous or endogenous sources. Serious infections including meningitis and spinal abscess are rare (<1 in 10,000),¹⁴ although some researchers report a higher incidence (~1 in 1000 to 2000),¹⁵ most likely the result of longer duration of use or the presence of a coexisting immunocompromising factor. Epidural catheter migration out of the epidural space and into the intrathecal, intravascular, or subcutaneous space decreases the effectiveness of this technique. The failure rate (i.e., earlier than anticipated discontinuation of the catheter for any reason) ranges from ~6 to 25%, with many centers reporting a rate between 10 and 20%.¹⁶⁻¹⁸

Epidural agents can be delivered by a single injection, intermittent injections, by continuous infusion, or via a patient controlled mechanism. Opioids and

local anesthetics are administered to achieve analgesia. When opioids are used alone, they do not generally cause motor block or hypotension from sympathetic blockade.¹⁹ An important determinant of opioid action when delivered using the neuraxial route is the drug's degree of lipid solubility. Morphine is hydrophilic, which accounts for its slow onset of analgesia, long duration of action, its ability to provide analgesia over a wide dermatomal distribution, and the risk for late respiratory depression (a result of rostral migration to the brain). Fentanyl is lipophilic, which accounts for its fast onset and short duration of action, its ability to provide segmental analgesia, and its limited risk of late respiratory depression.²⁰ Local anesthetics provide analgesia by blocking nerve conduction. In the epidural space, compared with the periphery, they are delivered at smaller and weaker concentrations. Compared with a local anesthetic or opioid alone, a local anesthetic-opioid combination infusion provides advantages including superior postoperative analgesia, limited regression of sensory block, and possibly decreased dose of local anesthetic administered (although the incidence of side effects may or may not be diminished).^{21,22}

Many medication-related (opioid and local anesthetic) side effects can occur with the use of postoperative epidural analgesia. In general, an Acute Pain Service sets institutional protocols, which allow nursing staff to monitor patients closely. These protocols include neurologic monitoring, treatment of side effects, and physician notification of critical parameters.

HYPOTENSION

Local anesthetics used in an epidural analgesic regimen may block sympathetic fibers and contribute to postoperative hypotension. Strategies to treat hypotension include decreasing the overall dose of local anesthetic administered (by decreasing the rate or concentration) or infusing an opioid epidural alone. At times, the associated hypotension can be corrected by increasing circulating volume with IV fluid administration or by supporting peripheral vascular tone with an α agonist such as phenylephrine.

MOTOR BLOCK

Use of local anesthetics for postoperative epidural analgesia may also contribute to lower extremity motor block in ~2 to 3% of patients.²³ Although motor block resolves in most cases after decreasing the concentration of local anesthetics or by stopping the epidural infusion for ~2 hours, persistent or increasing motor block should be promptly evaluated. Spinal hematoma, spinal abscess, and intrathecal catheter migration should be considered.¹⁹

NAUSEA AND VOMITING

Incidence may be as high as 45 to 80% and tends to be dose dependent.²⁴ This is thought to be related to the

cephalad migration of opioid within the cerebrospinal fluid (CSF) to the area postrema in the medulla.²⁵ Treatment options include the use of the lipophilic agent fentanyl alone or the addition of an antiemetic medication (i.e., ondansetron, droperidol).

RESPIRATORY DEPRESSION

The incidence of respiratory depression associated with neuraxial administration of opioids is dose dependent and typically ranges from 0.1 to 0.9%.^{26,27} As mentioned previously, lipophilic opioids are less likely to cause delayed respiratory depression than hydrophilic opioids. Patients with risk factors including increasing dose, increasing age, and concomitant use of systemic opioids or sedatives should be closely monitored. Although most large trials demonstrate relative safety on hospital wards, higher risk patients may be better monitored in an intensive care unit setting.

URINARY RETENTION

Opioids delivered via an epidural interact with the opioid receptors in the spinal cord, decreasing detrusor contractility, leading to urinary retention in as high as 70 to 80% of patients.²⁸ Epidural administration of local anesthetics is also associated with urinary retention, with a reported rate of ~10 to 30%.²⁹ Due to this high incidence, most surgeons leave a urinary catheter in place until the epidural catheter has been removed, particularly in elderly men with preexisting urinary dysfunction.

Benefits

The use of perioperative epidural anesthesia and analgesia, especially with a local anesthetic-based analgesic solution, can attenuate the pathophysiologic response to surgery and may be associated with a reduction in morbidity and mortality compared with analgesia with systemic (opioid) agents.³⁰ The use of epidural analgesia can decrease the incidence of postoperative GI, pulmonary, and possibly cardiac complications.³¹ Evidence suggests that postoperative thoracic epidural analgesia can facilitate return of GI motility, specifically when using a local anesthetic-based analgesic solution.³² It is theorized that this effect is mediated by inhibiting sympathetic outflow, decreasing the total opioid dose, and attenuating a spinal reflex inhibition of the GI tract. In addition, perioperative use of epidural analgesia with a local anesthetic-based regimen in patients undergoing abdominal and thoracic surgery has been shown to decrease postoperative pulmonary complications,³³ presumably by preserving postoperative pulmonary function by providing superior analgesia and attenuating a spinal reflex inhibition of diaphragmatic function. A meta-analysis of randomized data (141 trials enrolling 9559 subjects) demonstrated that perioperative use of neuraxial anesthesia and analgesia

(versus general anesthesia and systemic opioids) reduced overall mortality by ~30%.³⁴

PERINEAL PROCEDURES

Local anesthetics are routinely used when operating on the perineum and are particularly suited for anorectal procedures, as these tend to be performed on an outpatient basis. Local anesthetics work by blocking sodium transport and conduction in peripheral nerve fibers. There is evidence to suggest that the administration of local anesthesia prior to skin incision, by preemptively blocking nociceptors, leads to reduced conduction of pain signals to the CNS and an improvement of postoperative pain control. Some randomized trials have shown that local anesthetic injection around small incision sites reduces postoperative somatic pain.^{35,36}

Typically, short-acting agents (i.e., lidocaine) are administered with a long-acting agent (i.e., bupivacaine) to provide both immediate and long-lasting analgesia. Analgesia can be provided for 6 to 8 hours postoperatively when an adequate perianal block is applied particularly when epinephrine is administered concurrently. In addition to local injection, local anesthetics can be delivered as a continuous infusion, using a delivery system such as the OnQ pump (I-Flow Corporation, Lake Forest, CA). This is a self-contained repository of long-acting analgesic that is delivered through small catheters, which are inserted into the wound and anchored in the skin at the time of surgery. In the OR, this device can be placed within the abdominal incision or specifically positioned for anorectal procedures to block the pudendal nerves as they exit Alcock's canal. The delivery system is subsequently used on either an inpatient or outpatient basis. The infusion device is typically filled with 100 mL of 0.5% bupivacaine and infused for 48 hours after surgery.

The local anesthetics used at the time of surgery are often complemented by a variety of orally administered agents. Mild to moderate postoperative pain can often be managed with a NSAID, unless there is a contraindication to these agents. NSAIDs exert their analgesic effect through the inhibition of cyclooxygenase (COX) and synthesis of prostaglandins, which are important mediators of nociception. As an adjunct to systemic or neuraxial opioid analgesia, NSAIDs can improve postoperative analgesia and reduce opioid requirements by up to 50%.³⁷ The most commonly used NSAIDs are ibuprofen and diclofenac, which are typically given orally. Ibuprofen, particularly when delivered as a standing dose, provides additional analgesic and antiinflammatory effects. If oral medication is not tolerated, rectal administration is an alternative route. Ketorolac is the only NSAID approved for parenteral use, and so is particularly useful in the postoperative period. Administration of ketorolac can reduce narcotic

consumption by 25 to 45% and indirectly lower opioid side effects such as ileus, nausea, and vomiting.³⁸ After a loading dose of 30 mg IV, 15 to 30 mg IV every 6 hours can provide excellent analgesia, or supplement other analgesic techniques. Despite the analgesic benefits, perioperative use of NSAIDs is associated with several side effects, including decreased hemostasis, renal dysfunction, gastrointestinal ulceration/hemorrhage, and effects on bone healing and osteogenesis. Many of these side effects are related to inhibition of COX and formation of prostaglandins. After initial enthusiasm, selective COX-2 inhibitors are now rarely utilized due to concerns surrounding associated cardiac morbidity.

Weak opioids such as hydrocodone, oxycodone, dextropropoxyphene, and codeine are commonly combined with aspirin or acetaminophen. These are typically administered on an as needed basis, with decreasing requirements over time. Medications such as gabapentin (Neurontin) have been added to the postoperative armamentarium, with some benefit. Originally developed to prevent seizures, this centrally acting medication is particularly useful in treating neuropathic pain. Routine use is limited by delayed onset, side effects (including dizziness, drowsiness, and peripheral edema), expense, and animal studies suggesting increased incidence of adenocarcinomas. Oral medications that are considered nonnarcotic, and therefore may avoid postoperative constipation, include tramadol (Ultram; Ortho-McNeil Pharmaceutical, Raritan, NJ). Tramadol, although considered a non-opioid analgesic, has some opioid-like effects with weak μ -agonist activity. The advantages of tramadol for postoperative analgesia include the relative lack of respiratory depression, major organ toxicity, and depression of GI motility, as well as having a low potential for abuse. Tramadol should be used with caution in patients with seizures or increased intracranial pressure and in those taking monoamine oxidase inhibitors. Oral benzodiazepines such as diazepam can be added as well. The sedative effects are particularly helpful when taken at bedtime, whereas the skeletal muscle relaxant effects helps relieve the sphincter spasm that often results from anorectal procedures. A typical regime is to add low dose of diazepam (5 mg) at bedtime for the first 5 nights after surgery.

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