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Pain Management Techniques in Hip and Knee Arthroplasty: A Review of Literature

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Review Article

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Abstract

Adequate control of postoperative pain following hip and knee arthroplasty can be a challenging task [1,2]. Previous studies have shown that over 50% of patients undergoing surgery report postoperative pain as a major concern [3] .Inadequate control of pain may result in patient dissatisfaction, impaired patient rehabilitation, and prolonged hospitalizations [3]. The negative influence of postoperative pain on rehabilitation is particularly concerning for patients undergoing joint replacement. Functional recovery and return of muscle strength is dependent on the ability of these patients to comply with rehabilitation. The drawbacks of inadequate rehabilitation are especially cumbersome in hip and knee surgeries, since faster mobilization leads to quicker discharge from the hospital. Furthermore, studies have shown that recovery from knee arthroplasty is prolonged up to 50 days postoperatively, far greater than recovery from hip replacement [4]. Pain control is especially important for knee arthroplasty patients to allow recovery of range of motion and muscle strength for ambulation [5].

Keywords: Arthroplasty; Neurohumeral; Spinothalamic; Opioids; Periarticular

Introduction

Improvements in pain management techniques in the last decade have had a major impact on the practice of total hip and knee arthroplasty (THA and TKA). Although there are a number of treatment options for postoperative pain, a gold standard has not been established. However, there appears to be a shift towards multimodal approaches using regional anesthesia to minimize narcotic consumption and to avoid narcotic-related side effects. Over the last 10 years, we have used intravenous patient-controlled analgesia (PCA), femoral nerve block (FNB), and continuous epidural infusions for 24 and 48 hours with and without FNB.

Unfortunately, all of these techniques had shortcomings, not the least of which was suboptimal pain control and unwanted side effects. Our practice has currently evolved to using a multimodal protocol that emphasizes local periarticular injections while minimizing the use of parenteral narcotics. Multimodal protocols after THA and TKA have been a substantial advance; they provide better pain control and patient satisfaction, lower overall narcotic consumption, reduce hospital stay, and improve function while minimizing complications. Although no pain protocol is ideal, it is clear that patients should have optimum pain control after TKA and THA for enhanced satisfaction and function.

Multimodal Analgesia

Kehlet and Dahl first described the concept of combining multiple analgesic techniques in 1993 as a method of improving outcome following colon surgery [6,7]. Multimodal analgesia requires an understanding of the molecular mechanisms of pain pathways. Postoperative pain is a consequence of tissue injury, nerve irritation and the resulting cascade of neurohumeral events that follow. After a painful stimulus, chemical mediators such as prostaglandins (PGE2) and bradykinin are released at the site of tissue injury. These chemical mediators stimulate nociceptors, peripheral pain receptors that respond to trauma and high temperatures. These nociceptors form pain fibers that enter the spinal cord via the dorsal root ganglion. Pain receptors that are principally responsible for noxious stimulation in the dorsal horn of the spinal cord are N-methyl D-aspartate (NMDA) receptors. Painful stimulus is propagated by central NMDA receptors in the spinal cord by way of the spinothalamic tract to the brain. Through this complex pathway, the brain experiences pain after trauma inflicted to the site of tissue injury caused by surgery. The concept of multimodal analgesia relies on understanding these complex neurohumeral interactions. Analgesia after surgery can be achieved by using a combination of drugs that inhibit this complex pathway at multiple sites.

What is a Multimodal Approach?

Multimodal approach to pain control involves administration of combination and often multiple analgesics or modalities at various time points during the course of surgery that includes preoperative period. Pain control after knee and hip arthroplasty can be achieved with a combination of drugs used during the preoperative (NSAIDS, COX-2 inhibitors, anticonvulsants), intra-operative (opioids, local anesthetics), and the postoperative periods (opioids, NSAIDS, COX-2 inhibitors, α2-Agonists, NMDA antagonists, anticonvulsants, and centrally acting analgesics as acetaminophen).

Pre-operative Period

The pre-emptive strategy behind multimodal analgesia must begin in advance of the surgical incision.

NSAIDs and COX-2 Inhibitors

Use of non-opioid drugs during the preoperative period can reduce excess intra-operative opioid usage and the possible subsequent effect of opioid-induced hyperalgesia seen after surgery [8]. Opioid induced hyperalgesia is a complex phenomenon that can follow rapid escalation in opioids during or following surgical procedure which can paradoxically lower the pain threshold and result in greater opioid requirements. Research has shown that activation of NMDA receptors in the central nervous system results in hyperalgesia associated with opioids. This phenomenon may be minimized by limiting opioids and maximizing non-opioid drugs. The use of NSAIDs is recommended as a multimodal approach to management of pain as part of most acute pain management guidelines [9].

The use of preoperative NSAIDs and COX-2 inhibitors also has a significant effect on opioid requirements following surgery. This has been referred to as an "opioid sparing effect." The clinical significance of this may be the reduction of opioid related side effects, improved analgesia, and better patient satisfaction. The primary site of action of NSAIDs and COX-2 inhibitors are in the periphery where they inhibit prostaglandin synthesis and stimulation of nociceptors. Through this inhibition, they target peripheral pain pathways (peripheral sensitization). Recent findings show elevation of prostaglandins in the central nervous system which may also play a role in central sensitization syndrome [10]. Furthermore, the hypersensitivity of injured tissue may also produce a secondary hyperalgesic effect on the uninjured tissue [11]. Prostaglandins have been demonstrated to lower pain thresholds in both the central and peripheral nervous system. NSAIDS or COX-2 inhibitors can be used preoperatively to effectively reduce the occurrences of central and peripheral sensitization syndrome after surgery.

Preemptive treatments with the NSAIDs such as ketorolac and ibuprofen are shown to have the advantage of decreasing postoperative pain scores, opioid requirements, and postoperative nausea after surgery [12]. Some surgeons are concerned about the use of NSAIDS prior to surgery due to a decrease in platelet aggregation and potential increase in bleeding time [13]. Consequently NSAIDs are commonly discontinued 7-10 days before surgery to reduce perioperative bleeding, particularly with hip arthroplasty [14]. Other concerns associated with NSAIDS include gastritis and peptic ulcer disease, renal impairment, and poor wound and bone healing. Because of these concerns, COX-2 selective inhibitors may have advantages over NSAIDS in the acute postoperative setting.

COX-2 selective inhibition provides selective inhibition of prostaglandins thereby reducing bleeding and gastric side effects seen with NSAIDS. COX-2 selective inhibitors allow for dosage on an empty stomach prior to surgery with low risk of bleeding during surgery. Recently, COX-2 inhibitors have fallen out of favor because of concerns for potential increased risk of cardiovascular side effects with long term usage. Rofecoxib has been withdrawn from the market because of its cardiovascular side effects. However, the COX-2 selective inhibitors have not been implicated for cardiovascular side effects with short term use such as in postoperative analgesia. Many studies have demonstrated benefits of employing these agents in the perioperative setting.

One study using pre-surgical dosing of COX-2 inhibitors one hour before arthroscopic knee surgery showed significant reduction in pain scores as compared to placebo at 1 hr., 2 hr., and 24 hours after surgery [15]. These patients had a significantly longer duration postoperatively before requiring analgesics and the 24 hour consumption of opioids was significantly lower than patients who were offered the same drug post-operatively. Another study using rofecoxib 24 hours and 1 hour before surgery with continued postoperative drug administration for 14 days had better outcomes in total knee arthroplasty [16]. These patients showed reduced opioid requirements, faster time to physical rehabilitation, reduced nausea and vomiting, better sleep patterns and greater patient satisfaction after surgery. In addition, an opioid sparing effect has also been demonstrated with the preoperative use of celecoxib and rofecoxib after spinal fusion surgery [17]. In this study, rofecoxib 50 mg showed an extended benefit for 24 hours after surgery. Both NSAIDs and COX-2 inhibitors may also be continued after the patient is discharged from the hospital for optimal management of pain. Dosage recommendations for preoperative treatments are given in Table 1.

Drugs	Dose	Route of administration	Time Before Surgery	Time After Surgery
NSAID*				
Ketorolac	15-30 mg	PO/IV	1-2 Hour	15-30 mg 96 hrs
Ibuprofen	800 mg	PO	1-2 Hour	800 mg 96 hrs
COX-2 Inhibitors				
Celecoxib	400 mg	PO	1 hour	200 mg×12 hrs after surgery
Valdecoxib	40 mg	PO	1 hour	Bid
Anti-neuropathic				
Gabapentin	1200 mg	PO	1-2 hours	1200mg×1(24 hrs after surgery)
Pregabalin	150 mg	PO	1 hour	150mg×1(12 hrs after surgery)
Propacetamol	2g	PO/IV	15 Min	2g Every 4 hrs
Acetaminophen	1g	PO/IV	15 Min	1g every 4 hrs

Table 1: Dosage recommendations for individual non-opioidagents that may be administered as part of multimodal analgesia

Gabapentin and Pregabalin

In addition to NSAIDs and COX-2 inhibitors, anti-neuropathic drugs are playing a role in treatment of post-operative pain. Such drugs as gabapentin and pregabalin, intended for seizures and neuropathic pain syndromes, can inhibit central neuronal sensitization [18]. Studies have shown that preoperative administration of gabapentin leads to reduction in post-operative pain and morphine consumption [19-21]. Gabapentin administered one hour before surgery in patients undergoing knee surgery had significantly improved post-operative analgesia and better range of knee motion [22-24]. Synergistic benefits are seen up to 72 hours when COX-2 inhibitors and gabapentin are used together prior to surgery for lower abdominal and spinal fusion surgeries [19,25] Pregabalin was also found to have a synergistic effect with COX-2 inhibitors in clinical studies involving patient undergoing spinal fusion [26]. The combination of the two drugs reduced postoperative pain, morphine consumption at 24 hours, and opioid induced side effects. Improvements in outcome were greater when these drugs were used in combination than either of the drugs used alone.

Intraoperative Period

Spinal and Epidural Analgesia

Regional anesthesia is generally preferred over general anesthesia in the US. The merits of regional anesthesia are many. Regional anesthesia provides optimal surgical conditions and analgesia extending into the postoperative period. The motor block achieved by spinal anesthesia is unsurpassed by any other technique. The modest reduction in arterial blood pressure contributes to reduced surgical blood loss. Regional analgesia may also result in reduced postoperative nausea and vomiting, less respiratory and cardiac depression, and decreased risks of thrombo-embolisms [27-29]. Regional anesthesia has the advantage of blunting stress response in surgery and decreasing morbidity and mortality in high risk surgical patients [30-31]. Regional analgesia utilizes local anesthetics (such as bupivicaine, ropivicaine or tetracaine) as the primary agent for blockade of central sensory and motor receptors. The onset of analgesia is dependent on characteristics of the local anesthetic (lipid solubility, pKa, dosage and volume of anesthetic used), patient anatomy (age, weight, height, and gender), and technique used (site of injection, type of needle used, and the direction of the needle). Local anesthetics in regional anesthesia block nociceptive transmission in the peripheral (via peripheral nerve block) and central nervous system (via spinal/ epidural blocks). Some agents may be co-administered with local anesthetics in an attempt to enhance the quality of neural blockade. Agents commonly used include vasoconstrictors (epinephrine), opioids (morphine or fentanyl), α-2 receptor agonists (clonidine), NSAIDs (ketorolac), or COX-2 inhibitors [32]. While many studies have demonstrated a benefit to this practice, the use of some agents is equivocal. Also, the addition of some agents introduces other side effects. Hence the risk-benefit ratio must always be individualized to the specific patient.

Regional analgesia during the perioperative period involves the uses of spinal analgesia, combined spinal-epidural analgesia, or peripheral nerve blockade for pain control during and after surgery. Spinal anesthesia commonly used for total joint arthroplasty utilizes a spinal needle (Quincke, Sprotte, and Whitacre) to place drugs (local anesthetics) into the intrathecal (subarachnoid) space. The onset of spinal anesthesia is rapid since the cerebrospinal fluid (CSF) rapidly carries the drug to various sites in the spinal cord. The intensity and height of spinal blockade depends on the baricity (compared to spinal fluid) and the volume of the local anesthetic used. Opioids such as morphine and fentanyl may be added to the intrathecal mixture to prolong postoperative pain control. Fentanyl, because of its lipophilic properties, produces rapid onset (10-15 minutes) but short duration (2-4 hours) of analgesia, while morphine with its hydrophilic properties has a longer duration (18-24 hours) of action into the postoperative period [32]. Relatively small doses of intrathecal morphine (0.2 mg) are very effective for providing prolonged analgesia after hip arthroplasty. For optimal post-operative pain relief as part of multimodal analgesia, morphine has a higher degree of patient satisfaction due to prolonged analgesic effect. Randomized controlled studies with patients undergoing total hip replacement show significant reduction in postoperative intravenous morphine requirements for patients who received 0.1-0.3 mg of intrathecal morphine [33]. The same dose of morphine with total knee replacement did not significantly reduce the need for supplemental IV morphine in the postoperative period. The most common side effects of intrathecal morphine reported after the surgery was puritus, nausea/vomiting, and oxygen desaturation. Older patients undergoing hip arthroplasty may benefit from a more conservative dose of 100ug of morphine added to the spinal anesthetic, since serious side effects as over sedation and delayed respiratory depression are minimized [34]. Nonetheless, intrathecal morphine has a long track record of safety when moderate doses are employed and tailored to the specific patient.

In addition to the uses of morphine, the administration of clonidine with spinal local analgesics can also decrease the need for post-operative morphine consumption. Clonidine is a α2-adrenergic agonist which potentiates the sensory and motor blocks of local anesthetics in the spinal cord. The combination of clonidine and morphine to an intrathecal regimen has significant improvements in post-operative pain and decreased morphine requirements for 12 hours after total knee arthroplasty [35]. However, hypotension was reported in some of these patients.

Epidural anesthesia is preferred by some clinicians. Epidural anesthesia and analgesia requires placing a specially designed needle (Hustead, Tuohy, or Crawford) into the epidural space. Drugs may be injected directly through the needle or an epidural catheter may be inserted. Subsequent postoperative analgesia may utilize continuous drug infusion or injection of a single drug. A variety of other agents have been added to epidural infusions Epinephrine can induce a synergistic analgesic on the spinal cord as well as elicit vasoconstriction on the blood vessels for decreased absorption of local anesthetic [36]. Other multimodal approaches have utilized small doses of ketamine, an NMDA antagonist in the spinal cord, for sensory blockade and prevention of central sensitization of nociceptors [37].

Patients given a single epidural injection of extended-release epidural morphine (EREM) have demonstrated a 48 hour period of analgesia [38,39]. Patients given EREM in clinical trials after hip replacement had significant less supplemental opioid requirement after surgery than placebo [39]. Furthermore, the needs for rescue medications were minimal with less instances of hypotension. Other potential advantages of EREM include no epidural catheter or pump related issues which can create gaps in analgesia postoperatively. The absence of epidural and patient controlled analgesia pump technology theoretically reduces opportunities for medication errors and pump programming errors as well. The side effects of EREM are similar to other opioids including nausea, vomiting, constipation, and respiratory depressions. Ideally, the use of EREM in a multimodal analgesic approach and with appropriate patient selection may result in analgesia without the need for any tethering pump technology

The benefits of epidural analgesia and surgical outcomes have been well documented in the literature [38]. Compared with Parenteral opioid use after surgery, the utilization of continuous infusion with epidural analgesia provides superior relief in post-operative pain with few adverse outcomes. The limitations of epidural analgesia often involve failed or dislodged catheters, unilateral blocks, and incompatibility in patients who are anti-coagulated. There is a risk of spinal hematomas with patients who are receiving anti-coagulation with an indwelling epidural catheter. Other limitations related to local anesthetics include hypotension and motor impairment in these patients.

Some of these issues related to epidural catheters or the local anesthetics themselves may be addressed by

Peripheral Nerve Blocks

Peripheral nerve blocks (PNB) are an increasingly popular technique for anesthesia and pain management for total joint arthroplasty. Some clinicians prefer PNB in patients who will be anti-coagulated because of concerns for epidural hematomas. PNB may also reduce the incidence of arterial hypotension or urinary retention compared to spinal or epidural techniques. The psoas compartment block of the lumbar plexus is an effective analgesic block for total hip arthroplasty. Anesthesia for total knee arthroplasty requires block of both the lumbar plexus (femoral or psoas compartment) and the lumbosacral plexus (sciatic nerve).

However, adequate postoperative analgesia is usually achieved with block of the lumbar plexus alone. Peripheral nerve blocks can be achieved with single injection of a local anesthetic or with the use of a catheter that utilizes continuous infusion of a local anesthetic.

Some studies show that a continuous femoral nerve block has efficacy equal to epidural analgesia in patients undergoing total hip arthroplasty [40]. Although there were no significant differences between the two, some of the side-effects seen with epidural blocks as hypotension and spinal hematomas may be avoided with femoral nerve blocks. The authors concluded that peripheral blocks may be superior to epidural blocks due to decreased systemic side effects seen with these blocks.

In studies involving total knee arthroplasty, both epidural analgesia and continuous femoral nerve block had better pain relief and faster knee rehabilitation compared to IV PCA usage after surgery [41]. The efficacy of femoral nerve blocks alone is questioned by some since the sciatic nerve innervates the posterior and lateral aspect of the knee. While it is necessary to combine both femoral and sciatic nerve blocks for total knee arthroplasty anesthesia, adequate postoperative analgesia is usually achieved with femoral nerve block. Some studies have utilized a combination of continuous sciatic nerve block and femoral nerve block in patients undergoing total knee arthroplasty [42]. In one study, adding sciatic nerve block significantly decreased morphine requirements up to 36 hours. However one randomized study found minimal benefits of adding a sciatic nerve blocks to femoral nerve block [43]. There were no differences in morphine consumption with femoral blocks and the combined sciatic-femoral block. The authors concluded that sciatic innervations of the posterior knee may be a minor contributor of post-operative pain following total knee arthroplasty. Furthermore, the value of blocking the obturator nerve in a psoas block may also give limited benefit [44]. There was limited benefit in analgesic requirements in a psoas block and no difference in functional outcome when compared to femoral and sciatic blocks. No block is without risk, hence clinicians must carefully evaluate the individual risk/ benefit ratio of adding the sciatic block solely for postoperative analgesia.

All nerve blocks discussed above may be performed with a single injection of local anesthetic or with a continuous infusion through an indwelling catheter. The benefits offered by a continuous infusion may include better analgesia through the second postoperative day; however one study did not demonstrate a difference in length of hospital stay and functional recovery [45]. The limitations of a continuous catheter include additional time, cost, and skills required to manage the catheter. There are also potential risks of infections and nerve injury with continuous catheters. External infusion pump technology also introduces the potential for technical failures and requires additional surveillance. For these reasons, some clinicians avoid this approach.

Periarticular Injections

Injections given locally into and around the joint intra operatively have been extensively studied in arthroplasty patients. Different protocols have been reported based on the composition and dose of the injection, its location, and the presence of a catheter for continuous postoperative infusion; and results of well-designed studies have been conflicting. Given this significant heterogeneity, the literature should be critically assessed before the surgeon implements a change in clinical practice.

Local Anesthetics Alone

Two double-blinded randomized trials compared single periarticular injections of local anesthetic (ropivicaine and bupivicaine, respectively) with saline placebo in primary THA. No benefit was seen in pain scores or opioid consumption from ropivicaine with epinephrine injection in combination with a multimodal oral regimen. No improvement in pain scores was seen with bupivicaine injection; however, narcotic requirements were significantly lower in the first 12 hours postoperatively in the treatment group of one study. Several studies have compared postoperative local anesthetic infusions via catheter following TJA. Dobrydnjov, et al. conducted a randomized trial comparing the location of continuous ropivicaine infusion after THA and found that intra-and extra-articular delivery resulted in similar pain relief and narcotic requirements.

Multidrug Injections

Several randomized controlled trials have evaluated differing multidrug injections compared with placebo after TJA. Busch et al found that a periarticular injection of ropivicaine, epinephrine, and morphine resulted in lower 24-hour patient controlled analgesia requirements and pain levels; however, no effect on patient satisfaction was seen. In a trial comparing ropivicaine, ketorolac, and epimorphine injection with placebo after TKA, significant improvements in pain scores, narcotic consumption, and patient satisfaction were observed. Several randomized studies have compared periarticular multidrug injections to other pain management modalities. Parvataneni et al compared bupivicaine and morphine local injection with femoral nerve block in patients undergoing TKA and found no significant differences in pain scores. Two trials compared an injection of ropivicaine, ketorolac, and epinephrine with intrathecal morphine and epidural infusion, respectively, and both found improved pain control and length of stay in the injection groups.

Postoperative Pain Control

Intravenous Patient Controlled Analgesia (IV-PCA)

Intravenous PCA is the most widely utilized form of post-operative analgesia offered to patients after surgery [46]. PCA utilizes infusion pumps to deliver patient activated fixed and small doses of opioids based on demand and a lock out period with an hourly maximum dose. Opioids commonly utilized in PCA include morphine, hydormorphone, and fentanyl. For PCA to be successful, patients have to be willing to actively participate in their care. Patients must comprehend the operation of the devise and be able to give themselves bolus when needed. Effective PCA treatment involves initial clinician titration by bolus to establish analgesia. PCA is intended to maintain analgesia, not to achieve analgesia. Opioid related side effects are common. Elderly patients are particularly vulnerable to confusion and delirium after PCA use. Multimodal analgesia in combination with PCA may reduce opioid requirements resulting in better pain control and fewer side effects. The complexity of standard PCA pumps may consume valuable healthcare resources including nursing and pharmacist time and materials. PCA pumps have been implicated in medication errors and programming errors that may lead to patient harm. Hence, strict protocols need to be in place to prevent these harmful errors.

Transdermal PCA

Transdermal PCA is a novel approach to delivering opioids to the postoperative patient without venous access, external infusion pumps, or the potential for programming errors. Transdermal PCA utilizes iontophoresis technology to deliver drugs through the skin by use of an external electrical field [47]. The fentanyl iontophoretic transdermal system (fentanyl ITS) has recently been approved for treatment of post-operative pain [48-49]. This system consists of a preprogrammed, needle-free credit-card sized system that is applied to the patient's upper outer arm or chest for 24 hours. The system utilizes an on-demand delivery dose of 40 mcg of fentanyl for 10 minutes up to six doses an hour with a maximum of 80 doses. The system shuts down after 80 doses or 24 hours, whichever comes first. Randomized placebo controlled trials demonstrated that the fentanyl iontophoretic transdermal system was superior to placebo for pain control in the first 24 hours following surgery. Patients who received the fentanyl ITS had lower pain scores and fewer drug discontinuations compared to placebo. The side effect profiles were also similar between controls and those that received fentanyl ITS. Another randomized study conducted on patients undergoing abdominal and orthopedic surgeries in Europe showed fentanyl ITS to be just as effective as morphine PCA [50]. However, the iontophoretic system had greater ease of use and was less time consuming than traditional PCA. The fentanyl iontophoretic transdermal system may be particularly attractive for total joint arthroplasty patients as it eliminates the need for a bulky infusion pump and tethering IV tubing that may impede patient activity and participation in physical therapy. Further studies will be needed to identify the benefits of less invasive technologies.

Acetaminophen (Paracetamol)

Acetaminophen is a popular adjuvant to opioids as part of multimodal analgesia in acute post-operative pain management. It also has opioid sparing effect especially when used in combination with NSAIDs. Acetaminophen has no associated post-operative bleeding and is a cost-effective centrally acting analgesic. An intravenous formulation of acetaminophen is available in many parts of the world and is currently under development in the US. The intravenous acetaminophen formulation has been demonstrated to have great efficacy in patients undergoing total joint arthroplasty [51]. The use of the drug also resulted in reduced morphine requirements and was better tolerated in the elderly and high risk patients.

Conclusion

The use of multimodal pain regimens has revolutionized the type of perioperative care delivered to total joint arthroplasty patients. Although opioids remain common and effective in the treatment of post-operative pain, opioid medications are a component of the multimodal post-operative pain regimen and not the only medication available for pain control as once historically seen. Multimodal pain regimens include steroidal and non-steroidal anti-inflammatory medications, neuropathic pain agents, regional and local anesthetic blockade as well as psychosocial interventions. The decreased emphasis on opioid medications for the treatment of post-operative pain leads to decreased nausea and vomiting, better pain relief and shorter hospital stays. In the setting of a changing healthcare environment, multimodal pain regimens for patients undergoing TJA allows for improved care delivery and reduced costs for surgeons emphasizing patient-centered care.

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