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Review article

Perioperative pain management following total joint arthroplasty: A review and update to an institutional pain protocol

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ABSTRACT

As the rate of total joint arthroplasty increases with the aging population of the United States, new focus on decreasing opioid use through the development of multimodal pain regimens (MPRs) is becoming an important area of research. MPRs use different agents and modes of delivery in order to synergistically address pain at many levels of the pain pathway. MPRs include a combination of acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs), gabapentinoids, opioids (short- and long-acting), spinal/epidural analgesia, regional nerve blocks, and local anesthetics. This review summarizes the available literature on major components of MPRs shown to be effective in the total joint arthroplasty population. Finally, the authors' preferred method for pain control in the TJA population is reviewed.

1. Introduction

With the aging population of the United States, total hip (THA) and knee arthroplasty (TKA) volume is expected to increase significantly to reach an estimated 3.48 million per year by 2030.[1] As documentation of patient reported outcomes becomes routine and inpatient cost containment continues to be a priority, peri-operative analgesia has become a major focus for recent research. Furthermore, the opioid epidemic across the United States has led to the development of synergistic multimodal pain regimens aimed at achieving optimal analgesia and minimizing the risk of opioid abuse and addiction.

Multimodal approaches to pain control include the use of pre-operative spinal and epidural anesthesia, local nerve blocks, and peri-operative anti-inflammatories, narcotic based medications, as well as antiepileptic and neuropathic agents. This review will focus on the current trends in peri-operative pain control in the setting of THA and TKA, as well as the authors' preferred approach to this complex clinical challenge.

2. Multimodal pain regimen

In the past, peri-operative pain control was largely opioid-based. This model for pain control resulted in cognitive, gastrointestinal (GI), and urinary (GU) complications and more profoundly, a potential long-term dependence on chronic opioids for pain control.[2] Elderly patients (>65 years of age) are at increased risk for these potentially devastating side effects, and since total joint arthroplasty (TJA) patients are exhibiting increased longevity, it has become increasingly important to minimize the use of opioid analgesics to limit long-term adverse outcomes. Multimodal pain regimens (MPRs) have been introduced in an effort to decrease opioid use with the hope of also decreasing complications in the TJA population.

An MPR utilizes multiple classes and administrations of medications in order to achieve a synergistic response to treat varying etiologies of pain.[3] Pain pathways can be intercepted at multiple levels, from the local tissue inflammatory response to the central nervous system (CNS) via neurotransmission. An MPR attempts to address each of these pathways simultaneously with the primary aim being decrease in the overall use of narcotic medications.

Several key studies have shown the efficacy of MPRs in the TJA population.[4–10] The majority of MPRs include a combination of acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs), gabapentinoids, opioids (short- and long-acting), spinal/epidural analgesia, regional nerve blocks, and local anesthetics. The use of an MPR has been shown to decrease opioid consumption, improve peri-operative outcomes, and decrease length of stay in the TJA population.[4,5,7,8] Administration of NSAIDs both pre- and post-operatively has been shown to have the most profound effect on

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outcomes.[4] MPRs, with a special emphasis on NSAID use, are currently recommended as the standard of care by the American Society of Anesthesiologists Task Force on Acute Pain Management.[11]

3. Opioid analgesia

Opioids have classically been the workhorse of for the treatment of surgical pain. Opioids are effective through the binding of mu, kappa, and delta receptors at the dorsal root ganglion and CNS levels of the pain reception pathway.[3] Opioids are the pinnacle of the "Pain Relief Ladder" outlined by the World Health Organization that was created for the treatment of cancer pain.[12–14] In this model, non-opioids are the first-line drugs for post-operative pain, and opioids are added with the development of moderate to severe pain.

Opiates are extremely effective both in short- and long-acting formulations, but the efficacy of opiates may only be enhanced through route of delivery and higher doses of medication. Unfortunately, the administration of higher doses of opioid medications amplifies the side effect profile disproportionately to the degree of pain control. These unwanted side effects with high-dose narcotics led to the development of patient-controlled analgesia (PCA), in which patients self-administer frequent, small-dose demand doses of medication.

The use of a PCA results in a uniform plasma opioid concentration over time which differs for each individual patient. Variations in patient's pre-operative pain medicine use, pain tolerance, lag between perception of pain and medication administration, and variable absorption of medications due to kinetics and body habitus all contribute to poor pain control with one uniform approach for all patients.[15] Albert et al. showed that PCA is effective in the TJA population with 80% of patients reporting to be pain-free, comfortable, or in mild pain in the first 48 h after surgery.[16] While overall PCA has a favorable safety profile, side effects such as nausea, respiratory depression, and over-sedation can still be seen.[16–17] The side-effect profile can be accentuated when patient family members administer additional doses of the medication when they feel that the patient may be in pain.[18]

Wheeler et al. performed a comprehensive literature review focused on identifying adverse effects of narcotics when used in the post-operative setting.[19] Adverse effects were broken down into respiratory, GI, GU, dermatologic, and CNS side effects. While respiratory depression is the most severe complication of narcotic administration (2.8% of patients), GI complications (nausea, vomiting) are the most common (30% of patients). Urinary retention is another common side effect with post-operative opioids affecting over 17% of patients, especially patients receiving intrathecal opioids intra-operatively. Interestingly, urinary retention varies widely with form of administration of narcotics with retention occurring in 36% of patients receiving intrathecal opioids but only 16% of patients receiving systemic narcotics.[19]

Unfortunately, CNS side effects of opioid medications in the post-operative period are as common as GI side effects (above 30% of patients), yet the morbidity and mortality of these effects can be much more devastating. The effects of opioids alone on mental status is difficult to determine as many factors affect mental status, but many studies have shown the correlation between the administration of opioids and the development of hallucinations, nightmares, and delirium.[19] In a study aiming to predict post-operative delirium in the TJA population, Williams-Russo et al. found that 41% of elderly patients experience acute post-operative delirium.[20]

The review by Wheeler et al. in 2002 posited that the effects of opioids on mental status are idiosyncratic and not dose-related.[19] Nevertheless, the goal of post-operative pain control is to abate the negative effects of narcotics, and the authors maintain that the adverse sequelae of these medications can be minimized or eliminated through individualized pain regimens.

4. Non-opioid analgesia

4.1. Acetaminophen

Acetaminophen has widespread use as an antipyretic and analgesic agent. It is a non-opioid, non-NSAID agent that acts centrally as an analgesic.[21] Acetaminophen is available as an oral and recently as an intravenous agent, and it is commonly used in combination with opioid analgesics as part of an MPR. Efficacy of oral acetaminophen on pain control alone has not been studied in a controlled manner, likely due to its widespread use and over-the-counter availability. However, the efficacy of oral acetaminophen as part of an MPR was demonstrated by a study by Imasogie et al., which showed that the use of tramadol HCl/acetaminophen decreased opioid use in a small sample of total shoulder arthroplasty patients.[22]

A water-soluble prodrug of acetaminophen (propacetamol) has been shown to have similar analgesic efficacy to that of intravenous ketorolac in TJA patients.[23] The success of intravenous propacetamol as an analgesic agent lies in its ability to enter the cerebrospinal fluid within fifteen minutes of administration.[24] In non-orthopaedic populations, the use of intravenous acetaminophen was shown to decrease opioid use and lead to shorter time to extubation in the post-operative period.[25] Sinatra et al. demonstrated similar efficacy in the TJA population.[26] Furthermore, intravenous acetaminophen has been shown to be safe and effective in elderly patients for pain control following major orthopaedic procedures, which is particularly important in with the rising average age of patients with TJA.[27–29] Given the established safety profile and efficacy of acetaminophen, the addition of acetaminophen to an MPR is certainly warranted.

4.2. Non-steroidal anti-inflammatory drugs (NSAIDs)

Like acetaminophen, NSAIDs are widely prescribed and used for pre-operative pain control in patients with osteoarthritis. Non-selective NSAIDs and cyclooxegenase (COX) −2 inhibitors have antipyretic and analgesic effects similar to acetaminophen, but they also exert an anti-inflammatory effect at the tissue level acting against prostaglandin production through COX inhibition. However, NSAIDs have classically been held in the peri-operative period due to concern for increased bleeding. Traditional NSAIDs (such as ketorolac) act through COX-1 and COX-2 inhibition. Ketorolac can be given through many routes and does not have associated respiratory or CNS depressive effects seen with opioids.[30] A meta-analysis focusing on efficacy of ketorolac in the post-operative period showed that a single dose of ketorolac in the immediate post-operative period had opiate-sparing effects.[31] Another study showed a decrease in morphine consumption by 29% compared to placebo when ketorolac was used as part of an MPR. A decrease in post-operative nausea, vomiting and pruritis were observed as secondary outcomes.[32]

COX-1 is expressed systemically throughout the body whereas COX-2 is selectively expressed in inflammatory tissue. Selective COX-2 inhibitors (such as celecoxib) have grown in favor due to the dampening of effects seen with COX-1 inhibition, most notably GI effects.[4,33] Additionally, selective COX-2 inhibitors have minimal effect on the coagulation cascade and therefore are potentially valuable in this population where peri-operative bleeding is ideally minimized.

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