

Research Article

Perioperative Pain Management Following Total Joint Arthroplasty

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INTRODUCTION

Total Joint Arthroplasty (TJA) has proven to be very successful in the treatment of patients suffering from end-stage osteoarthritis of the hip and knee [1,2]. The demand for primary TJAs is expected to dramatically increase over the next several years due to more procedures being performed annually, younger patients being considered candidates for surgery, and patients exhibiting longer life expectancies. It is predicted that the number of Total Hip Arthroplasties (THAs) in the United-States is estimated to grow to 572,000 and Total Knee Arthroplasties (TKAs) to 3.48 million by the year 2030 [3]. The current healthcare cost containment environment in conjunction with a more patient-centered and clinical outcomes approach emphasizes both patient satisfaction and patient throughput [4].

Post-operative pain management continues to be a challenge for surgeons and anesthesiologists. In a telephone survey, 73% of patients requiring inpatient surgery reported pain prior to discharge with 88% of those reporting moderate to extreme pain [5]. Traditionally, intravenous opioids have been used to obtain rapid and complete post-operative pain relief [6]. The side effects of post-operative opioid analgesia, however, are common and can have deleterious effects on patient satisfaction and early post-operative outcome measures [7]. This review provides a summary of the major classifications of medications used in multimodal pain protocols for the treatment of post-operative pain following total joint arthroplasty. The author's preferred protocol for primary TJA is included at the end.

MULTIMODAL APPROACH

The multimodal approach to analgesia refers to the use of more than one medication, class of medications or delivery of medications to achieve pain control via multiple mechanisms [8]. The multimodal approach is utilized to achieve a synergistic effect in attaining optimal pain control. One such approach uses a validated "Pain Relief Ladder" for cancer pain [9-11]. In this approach, non-opioids are the first analgesic drugs given post-operatively. Opioids are added for moderate to severe pain. In addition to opioid and non-opioid medications the multimodal approach includes attenuation of psychosocial factors that contribute to post-operative pain [4,8].

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Modern Anesthesia Techniques for Total Joint Arthroplasty: from Blood Preservation to Modern Pain Control

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Several studies have demonstrated the benefit of a multimodal pain protocol following TJA. Methods used in TJA include epidural anesthesia, peripheral nerve blocks, oral analgesics, pericapsular analgesic injections and anticipatory discharge planning [4,12-16]. These approaches to post-operative pain control have been shown to improve perioperative outcomes, decrease adverse events and decrease hospital length of stay after TJA [4,13,14].

In a retrospective case-control study of patients undergoing TKA, a perioperative protocol including pre-operative patient education and discharge planning, pre-emptive pain management and nausea prevention resulted in decreased pain scores and decreased length of hospital stay. Under the protocol, patients attended a comprehensive interdisciplinary pre-operative TKA education class one week prior to surgery, addressing expectations including expected length of stay. Additionally, prior to surgery, the patients' discharge plans were coordinated. These non-medication related measures, in addition to pre-emptive pain and nausea intervention resulted in 0.26-day decrease length of stay, statistically significant lower Visual Analog Scale (VAS) pain scores with no increase in post-operative complications. The authors concluded that this decrease in length of stay, though modest in size, would allow an additional 43 admissions during a three-month period at their institution [4].

OPIOID ANALGESIA

Opioid analgesics have long been, and continue to be, part of the surgeon's armamentarium for the treatment of post-operative pain. Opiates, by definition, exert their effect by binding to opioid receptors. The three principal receptors are mu, kappa and delta. Opiates are very effective in the treatment of acute pain and their usefulness is only enhanced by the variety of routes through which they may be administered (oral, intravenous, subcutaneous, sublingual, rectal, epidural, intrathecal) and their relative inexpensiveness. Historically, opiates were the only medication

class utilized for post-operative pain. Patients continuing to feel pain following opiate administration were treated with higher doses of opiates, often resulting in an amplified effect of side-effects. However, opioids are often under-dosed due to concerns about side-effects including respiratory depression, urinary retention, gastrointestinal upset, Central Nervous System (CNS) depression and dermatologic effects.

Patient-Controlled Analgesia (PCA) became a common route of opioid administration in response to the under-dosing of opioid analgesics in hospitalized patients. Frequent demand doses, smaller than intermittent analgesia doses given by nursing staff on the floor, provide a more uniform plasma concentration. However, PCA use does not sustain a constant plasma concentration. Parker et al demonstrated in a randomized controlled trial that adding a basal rate of infusion in combination with PCA does not improve pain management compared to PCA alone in patients undergoing hysterectomy [17]. Albert et al demonstrated PCA to be a promising alternative to intermittent analgesia in a TJA population [18]. Patient-controlled analgesia exploits the hierarchy of pharmacologic effects seen with opioids whereby analgesia occurs at lower doses than sedation [19]. Nevertheless, side effects including nausea, respiratory depression and over sedation do still occur (Albert, 1990) [18,20]. Furthermore, any demand doses given by well-intentioned family members to assist with post-operative pain control can significantly increase the risk of serious complications [21].

A systematic review of the literature from 1990 to 2000 characterized opioid associated adverse events in post-operative patients. The most severe of these adverse sequela is respiratory depression. The respiratory effects are primarily dose related, but were found in the systematic review to be the least commonly reported category. A patient is said to be opioid tolerant when they have developed tolerance to the respiratory depression effects of opioids. In the United States, naloxone is the opioid antagonist most commonly used to treat acute opioid induced respiratory depression [7].

Wheeler et al. [7] found that gastrointestinal effects were the most frequently reported side effects with more than 30% of patients affected. The most common gastrointestinal symptoms reported were nausea and vomiting. Urinary retention, when reported, affected 17.5% of patients with intrathecal opioid administration being the biggest culprit (35.6%). The authors suggest this is likely under-reported due to the use of urinary catheters in the early post-operative period. Pruritis is a common complaint among patients treated with opioids (18.3%), with epidural analgesia associated with the highest incidence among routes of administration and Hydromorphone the most commonly associated opioid [7].

Post-operative delirium is common among elderly patients and can lead to prolonged hospital stays and delay rehabilitation as well as discharge from the hospital. Williams-Russo et al. reported an overall incidence of post-operative acute delirium in 41% of elderly patients undergoing bilateral TKA surgery [22]. In a systematic review by Wheeler et al. [7], central nervous depressive symptoms accounted for the second highest adverse event, reported in 30.3% of patients. Meperidine was the opioid most commonly associated with CNS depression, which appears

to be idiosyncratic and not dose related. Nevertheless, most of the adverse drug effects of opioids are dose related and the authors conclude that opioid limiting strategies are desirable [7].

NON-OPIOID ANALGESIA

Non-steroidal Anti-Inflammatory Drugs

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) are widely prescribed for patients with osteoarthritis, but are often held in the perioperative period due to concern for increased intra-operative bleeding. NSAIDs demonstrate reversible antiplatelet activity through inhibition of platelet production of thromboxane A₂. Non-selective NSAIDs, which inhibit both Cyclooxygenase (COX) 1 and 2 isoforms, have been shown in a systematic review to increase hemorrhage, requiring re-operation in patients undergoing tonsillectomy [23]. Ketorolac is a non-selective NSAID with potent analgesic effects that can be given intravenously, intramuscularly, orally and topically without respiratory or central nervous system depression effects [24]. A meta-analysis of thirteen randomized trials demonstrated that single dose systemic ketorolac decreased early post-operative pain and had opioid sparing effects. Additionally, the use of ketorolac as part of a multimodal pain strategy reduced post-operative nausea and vomiting [25]. Alexander et al. demonstrated that a single dose of pre-operative diclofenac or ketorolac reduced morphine consumption by 29% compared to placebo with an additional decrease in post-operative nausea, vomiting and pruritus in patients undergoing TJA [26].

Selective COX-2 inhibitors have minimal effect on coagulation and therefore are an attractive adjunct to the surgeon's post-operative pain protocol. Buvanendran et al [14] in a randomized, placebo-controlled, double blinded trial found that rofecoxib, a selective COX-2 inhibitor, given pre- and post-operatively to patients undergoing TKA decreased opioid consumption, decreased pain as reported on VAS score, decreased sleep disturbances, resulted in an increase in post-operative range of motion at discharge and at one month post-operatively. Similarly, patients receiving the selective COX-2 inhibitor reported higher satisfaction with anesthesia and analgesia at discharge. There were no bleeding complications requiring treatment in either group [14].

Similarly, Reist et al. found that rofecoxib administered pre-operatively as part of a multimodal pain therapy decreased pain scores and morphine consumption compared to placebo in patients undergoing spine, breast and orthopaedic surgery [27]. These findings were confirmed in a randomized, double-blinded trial where rofecoxib or placebo was given one hour before operation. The authors reported decreased post-operative pain scores, decreased morphine consumption and increased patient satisfaction [28].

Acetaminophen

Acetaminophen is a non-opioid, non-NSAID analgesic, which is frequently prescribed alone or in combination with opioid analgesics (ie. Percocet or Vicodin) as part of a multimodal post-operative pain regimen. In addition to its analgesic properties, acetaminophen has an antipyretic effect and a well-established safety profile. Because it is not soluble in water, acetaminophen

was until recently not available via an intravenous route. However, a water-soluble prodrug of acetaminophen, propacetamol, has been shown to have similar analgesic efficacy to ketorolac in patients undergoing TJA [29]. Propacetamol has been associated with rare cases of contact dermatitis, pain at the injection site and must be reconstituted into a solution, limiting its clinical use.

Recently, intravenous acetaminophen has been developed. Its efficacy is based on enhanced bioavailability, its capability to enter the cerebrospinal fluid within fifteen minutes following administration [30]. In a study of patients admitted to the ICU after major abdominal or pelvic surgery, patients treated with intravenous acetaminophen consumed less opioids post-operatively and had a shorter time to extubation compared to placebo [31]. Sinatra et al. demonstrated intravenous acetaminophen to be a rapid and effective analgesic in patients undergoing TJA. Additionally, they found intravenous acetaminophen to be less likely to cause local irritation and pain at the injection site compared to propacetamol [32]. Nevertheless, oral acetaminophen continues to be the most commonly prescribed route of administration.

Pregabalin and Gabapentin

Neuropathic pain is a complex phenomenon recognized in as high as 12.7% of patients following TKA [33]. Pregabalin is an anticonvulsant medication, which along with its predecessor gabapentin is used in the treatment of neuropathic pain. Both medications bind to the $\alpha_2\text{-}\delta$ (alpha₂-delta) subunit of voltage gated calcium channels in the central nervous system, decreasing the release of neurotransmitters. In a prospective, double-blind, randomized, placebo-controlled study, the combination of pregabalin and acetaminophen did not decrease post-operative morphine consumption nor pain scores for patients undergoing abdominal hysterectomy [34].

However, Buvanendran et al. as part of a multimodal pain regimen randomized patients undergoing TKA to either perioperative pregabalin versus placebo. They found that 300mg pregabalin administered before TKA and 150mg to 50mg dosed twice daily for fourteen days after surgery reduced the incidence of neuropathic pain after TKA with less opioid consumption, less sleep disturbance, faster time to meeting hospital discharge criteria, and better range of motion at thirty days post-operatively. The authors did note increased risk of early post-operative sedation and confusion [35].

Glucocorticoids

Dexamethasone and methylprednisolone are long-acting glucocorticoids, which have been shown to be effective in preventing post-operative nausea [36-38]. Additionally, dexamethasone has been shown to reduce post-operative pain and decrease opioid consumption in a meta-analysis of randomized controlled trials, perhaps by decreasing the post-operative inflammatory response [39].

These results have been demonstrated for patients undergoing TJA as well [40,41]. Kardash et al. demonstrated that a single pre-operative IV dose of 40mg dexamethasone decreased dynamic pain scores twenty-four hours after THA and decreased post-operative nausea. Additionally, they found that C-reactive

protein (CRP) levels, markers of inflammation, were significantly lower in the dexamethasone group compared to placebo. This suggests that dexamethasone has a prolonged suppressive effect on the peri-operative inflammatory response [40].

Koh et al. demonstrated similar effects in a randomized trial of 269 patients undergoing TKA treated with either dexamethasone and ramosetron, a 5-HT₃ antagonist antiemetic, or ramosetron alone. Patients in the dexamethasone and ramosetron group had a lower incidence of nausea and vomiting 72 hours post-operatively, experienced less pain and consumed less opioid medications. They found no difference in wound complications between the groups and each group had one case of periprosthetic infection. The authors concluded that dexamethasone as part of a multimodal regimen reduced post-operative emesis and pain without an increased risk of wound complications [41].

LOCAL ANESTHETIC INJECTION

Multiple studies have demonstrated the advantages of local infiltration analgesia in TJA [42-44]. Andersen et al. [42] compared patients undergoing THA treated with intra-operative analgesic infiltration around the hip joint with single-shot intra-articular injection versus patients treated with epidural infusion alone. They found that narcotic consumption was significantly reduced in the group receiving local and intra-articular anesthetic injections compared to epidural alone. Additionally, patients treated with local and intra-articular infiltration had a reduced length of stay by two days (36%).

Analgesia secondary to local infiltration has shown promising results in patients undergoing TKA as well. Essving et al. [43] in a double blind study, randomized patients to either local infiltration analgesia using ropivacaine, ketorolac and epinephrine infiltrated in the knee during the operation and bolused intra-articularly post-operatively or intrathecal morphine. The multimodal local infiltration analgesic group had lower morphine consumption, better pain relief as assessed on VAS, higher patient satisfaction, and shorter median hospital stay. They found no differences in the incidence of adverse events [43]. These results confirmed similar results from the same group in another subset of patients undergoing TKA randomized to either local infiltration analgesia or no injection [44].

REGIONAL ANESTHESIA

A meta-analysis of randomized clinical trials has shown that the addition of continuous peripheral nerve blockade decreases post-operative pain and opioid related side effects compared to opioids alone. Additionally, nausea and vomiting, sedation and pruritus were all found to be more common in patients receiving opioid analgesia alone Richman [45].

The results of a retrospective case-control study of patients undergoing TJA, similarly demonstrated the benefits of peripheral nerve blocks as part of a multimodal pain regimen. All patients in the multimodal pathway cohort were treated with a single injection sciatic nerve block and lumbar plexus perineural catheter placement. No intravenous opioids were administered during the post-operative period to this cohort. Compared to patients treated with traditional anesthetic techniques, patients treated with a multimodal regimen emphasizing peripheral

nerve blockade demonstrated lower VAS scores at rest and with activity, significantly less opioid requirements, decreased nausea and vomiting and decreased urinary retention. Additionally, post-operative milestones such as bed to chair transfer, discharge eligibility, and hospital dismissal were achieved sooner in the patients treated with a multimodal pain regimen [13].

AUTHOR'S PREFERRED METHOD FOR PRIMARY TOTAL JOINT ARTHROPLASTY

Our multimodal approach for patients scheduled for primary TJA, starts in the office. At this time, in addition to answering any and all of the patient's questions, patients are given a booklet on total joint arthroplasty compiled by the senior author, which includes both pre- and post-operative instructions. Patients are instructed to continue any pre-operative exercise routine they have been on up until their day of surgery. A pre-operative pain medication test dose of MS Contin 15mg is given to the patient and is suggested to be taken two weeks prior to surgery at home, following a meal when they are not planning on driving and are home with a family member. Patients are instructed to notify us the following day as to their tolerance of the test dose. The results of the test dose allow us to determine the patient's narcotic tolerance during a time when the patient is not under the stress of surgery. The dosing is adjusted according to the patient response and is used as the baseline long-acting narcotic dose post-operatively (e.g. patients that were not able to tolerate the MS Contin dose due to it being too strong are placed on Percocet post-operatively only with no long acting narcotic medication).

Two days prior to surgery, patients are started on senna tablets for constipation. The night before surgery, the patients are called by the operative surgeon as an opportunity to confirm their surgery as well as to answer any last minute questions; minimizing pre-operative anxiety has been shown to correlate with decreased post-operative pain [46].

The morning of surgery at home, patients are directed to place a Lidoderm patch on their lower back over the site where the spinal injection will be administered, allowing for patients to undergo a spinal injection in the face of significant lumbo-sacral arthritis with minimal discomfort. A prescription for this patch is given to the patient at the time of signing up for the procedure. At the same time, the book on total joint arthroplasty given to the patient demonstrates the proper location for placement of the patch (Figure 1).

In the pre-operative holding area, patients are given an appropriate dose of MS Contin, based on their pre-operative test dose tolerance, ranitidine, an H₂-receptor antagonist, intravenous ketorolac, metoclopramide, ondansetron, a scopolamine patch, acetaminophen, and gabapentin. Our preferred method of anesthesia is a spinal for THA and a spinal with a femoral nerve/adductor canal block for TKA. Intra-operatively, a two-thirds/one-third mixture of 0.25% lidocaine with epinephrine (60 cc) and 0.25% lidocaine without epinephrine (30 cc) is prepared, equaling a total 90 cc of the solution. A total of 80 cc of the mixture are used for injection into key locations around the hip and knee joint.

For TKA, the solution is injected into the posteromedial knee joint capsule and surrounding soft-tissues. Injection of

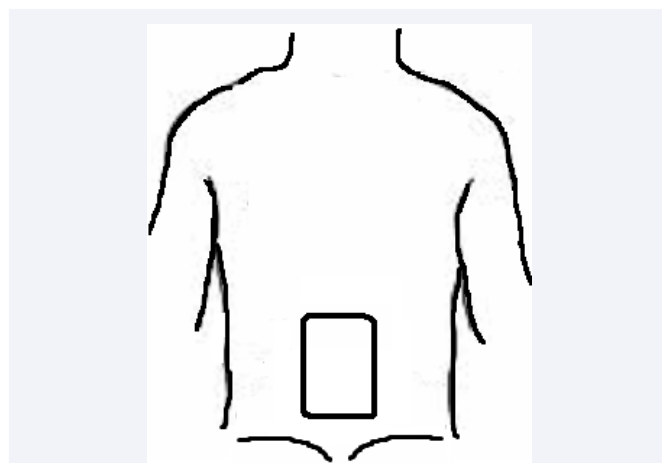


Figure 1 Cartoon illustration for location of proper pre-operative placement of the Lidoderm patch.

the mixture is avoided in the posterolateral corner to prevent inadvertent injury to the peroneal nerve. In the setting of THA, the solution is injected into the inferior joint capsule as well as the surrounding soft-tissues. The anterior division of the obturator nerve typically sends a recurrent branch to the inferior capsule with a high density of pain fibers, thus making this a key location for the injection.

Foley catheters are no longer used for primary TJA and the routine use of post-operative hemovac drains has also been discontinued. All wounds are closed with a subcuticular Biosyn closure along with an adhesive (e.g. Dermabond) for the skin, obviating the need for staple or suture removal in the office as well resulting in improved wound cosmesis. A silver impregnated adhesive dressing is placed on the incision, which remains in position until the patient's first post-operative visit. The dressing allows the patient to shower immediately upon hospital discharge. The use of a continuous passive motion machine has been abandoned following TKA which typically leads to chronic shearing of tissues, increased intra-articular bleeding within the knee and overall more pain during the immediate post-operative period, with no reported clinical benefit regarding achievement of range of motion [47]. All patients are typically placed on aspirin 325 mg po bid for 6 weeks for DVT prophylaxis, unless there are specific patient conditions that require the use of warfarin or a low molecular weight heparin.

Immediately following surgery, the operation itself and post-operative plan is discussed with family members as well as the patient. On post-operative day number one, the surgery and post-operative plan is again discussed with the patient. Thus the patient's post-operative and discharge plans are discussed four times during the perioperative period: in the office, over the phone the night prior to the procedure, and twice in the hospital. This repetition of the plan, including estimated post-operative day of discharge and discharge destination, is a beneficial tool to align the patient's expectations with the surgeon's expectations, optimizing the chance for a favorable clinical result [48].

Post-operatively in the hospital, our patients are started on a multimodal pain regimen including MS Contin, the dose of which

is correlated to the pre-operative test dose. Most commonly, the use of long-acting narcotics is discontinued ten days post-operatively at the time of the patient's first post-operative visit. Another opioid, Percocet is given as needed for breakthrough pain. The selective NSAID celecoxib is started in the hospital and taken for six weeks after surgery. Gabapentin, a neuropathic pain agent is given for two weeks after surgery. thescopalamine patch is used for the first three post-operative days as an adjunctive agent for nausea, in addition to metoclopramide and ondansetron as needed. Senna tablets are continued post-operatively while the patient is taking opioid analgesics. To help with sleep patients are started on zolpidem, a non-benzodiazepine hypnotic, as needed, after they have completed their course of long-acting narcotics.

The patient booklet includes instructions for taking the medication regimen as well as activity modification, a thorough review of what to expect after surgery in the hospital and at home, patient exercises and contact information for our office with instructions for follow-up.

SUMMARY

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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