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Does Intrathecal Morphine in Spinal Anesthesia Have a Role in Modern Multimodal Analgesia for Primary Total Joint Arthroplasty?

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ABSTRACT

Background: Intrathecal morphine (ITM) combined with bupivacaine spinal anesthesia can improve postoperative pain, but has potential side effects of postoperative nausea/vomiting (PONV) and pruritus. With the use of multimodal analgesia and regional anesthetic techniques, postoperative pain control has improved significantly to a point where ITM may be avoided in total joint arthroplasty (TJA).
Methods: We performed a retrospective study of primary TJA patients who underwent a standardized multimodal recovery pathway and received bupivacaine neuraxial anesthesia with ITM vs bupivacaine neuraxial anesthesia alone (control).
Results: In total, 598 patients were identified (131 controls, 467 ITMs) with similar demographics. On postoperative day 0 (POD 0), ITM patients had significantly lower mean visual analog scale scores (1.5 ± 1.6 vs 2.5 ± 1.9, $P < .001$) and consumed less oral morphine equivalents (10.5 ± 25.4 vs 16.8 ± 27.2, $P = .013$). ITM patients walked further compared to controls by POD 1 (133.6 ± 159.6 vs 97.3 ± 141 m, $P = .028$) and were less likely to develop PONV during their entire hospital stay (38.5% vs 48.6%, $P = .043$). No significant differences were seen for total morphine equivalents consumption, rate of discharge to care facility, length of stay, and 90-day readmission rates.
Conclusion: ITM was associated with improved POD 0 pain scores and less initial oral/intravenous opioid consumption, which likely contributes to the subsequent improved mobilization and lower rates of PONV. In the setting of a modern regional anesthesia and multimodal analgesia recovery plan for TJA, ITM can still be considered for its benefits.

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Intrathecal morphine (ITM) combined with spinal anesthesia has been shown to improve postoperative pain significantly. In a non-multimodal analgesia setting, Murphy et al [1] utilized a randomized controlled trial with varying ITM doses and found that 100 mcg of ITM achieved a balance of improved analgesia while minimizing postoperative nausea and/or vomiting (PONV) and pruritus in total hip arthroplasty (THA) patients. In both total knee arthroplasty (TKA) and THA patients, Rathmell et al [2] found improved analgesia at 100-200 mcg ITM doses and even found improved patient satisfaction with pain control when utilizing higher 200-300 mcg ITM doses.

In contrast to ITM's analgesic characteristics, it is also associated with negative side effects, such as PONV and pruritus, depending on the dose and patient population [3–5]. The Apfel simplified risk score is used to stratify the risk of PONV. It is based on 4 predictors: female gender, history of PONV and/or motion sickness, nonsmoking status, and use of postoperative opioids. The incidence of PONV with the presence of 0, 1, 2, 3, and 4 risk factors is approximately 10%, 20%, 40%, 60%, and 80%, respectively [6]. Orthopedic surgery was found to be a significant independent predictor for PONV [7]. Gehling et al [5]

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utilized a meta-analysis to find that ITM doses greater than 300 mcg had a significant risk of increased nausea, vomiting, pruritus, and respiratory depression compared to doses less than 300 mcg. Due to the risk of adverse side effects related to ITM, other investigators have avoided ITM and utilized multimodal nonopioid analgesia and regional anesthesia to achieve comparable postoperative pain control [4,8,9]. Other subspecialties of orthopedic surgery have employed multimodal perioperative analgesic pathways that utilize nonopioid analgesics in the preoperative, intraoperative, and postoperative phases of care in order to reduce opioid consumption and improve analgesia [10–17].

Although the field of anesthesia has made considerable advancements in analgesia and postoperative recovery after total joint arthroplasty (TJA), it remains to be seen whether there may still be a role for ITM in a setting that utilizes a modern multimodal recovery pathway with nonopioid analgesia and regional anesthetic techniques. To investigate this, we performed a retrospective analysis of perioperative outcomes of primary THA and TKA after spinal anesthetics with and without ITM. We hypothesize that the use of ITM would be associated with decreased per os/by mouth (PO)/intravenous (IV) opioid consumption, but with increased symptoms of PONV and pruritus that would contribute to perioperative complications such as poor mobilization and extended inpatient length of stay.

Methods

Patient Selection/Data Collection

We performed a retrospective review of an institutional clinical database from July 2012 through June 2015 and included all patients undergoing primary TKA or primary THA for degenerative joint disease. We excluded patients who underwent bilateral procedures and patients with diagnoses of acute fracture or osteonecrosis in order to avoid potential confounders related to perioperative pain and analgesia. All primary joint arthroplasty patients received a uniform antibiotic regimen for surgical prophylaxis with perioperative cefazolin and vancomycin with indications to change to an alternative antibiotic for patients with antibiotic allergies.

Patients' home medications at the time of admission for TJA were reviewed. Patients were stratified by whether or not ITM was administered with a single shot dose of spinal bupivacaine anesthetic. Subgroup analysis was performed among low (100-150 mcg), medium (151-200 mcg), and high (>201 mcg) doses of ITM. Prior to surgical procedure start, patients' spinal levels were clinically assessed to ensure adequacy for the surgical procedure. Postoperatively, in the post anesthesia care unit (PACU), all patients were recovered from anesthesia and the resolution of the spinal anesthetic was confirmed prior to transfer to the ward floor. During the intraoperative phase, the patients' oxygen saturation was maintained by providing oxygen through noninvasive methods (nasal cannula or face mask) as needed. Following the procedure, all patients were weaned off of supplemental oxygen in the PACU or on the ward floor. During the surgical procedure, the patients with spinal anesthetics received sedation with a propofol infusion as their main hypnotic agent and were hemodynamically maintained with appropriate volume and hemodynamic medications as needed (phenylephrine as the primary agent). All patients were weaned off of hypnotic medications and hemodynamic supportive agents prior to leaving the operating room or in the PACU.

Patient demographics were determined from the electronic health record (EHR) system including American Society of Anesthesiology Physical Status Classification, age, gender, smoking status, and preoperative long-acting opioid use (eg, MS contin, oxycontin, fentanyl patch). Patient body mass index was calculated from height and weight data and stratified by World Health Organization classification. Intraoperative cohort characteristics were obtained from the EHR to evaluate anesthesia time, procedure time, time of day for the procedure, intraoperative vitals, estimated blood loss, and transfusion requirement.

Although all surgeons utilized a tourniquet during the TKA procedure, the tourniquet times varied among the surgical providers. A number of surgeons utilized the tourniquet throughout their total procedure, while others utilized the tourniquet only during the component-cementing phase of the procedure. Due to the high variability of tourniquet time use among providers and in the mixed cohorts of THA and TKA, the tourniquet times were not included as a study variable.

Our standard multimodal pathway for arthroplasty patients includes a number of interventions in the preoperative, intraoperative, and postoperative phases of care. Preoperatively, patients received oral gabapentin 600 mg, acetaminophen 1000 mg, and celecoxib 400 mg. During the intraoperative phase, patients received ondansetron 4 mg and additional dexamethasone if patients have greater than 2 of the following risk factors: female gender, nonsmoker, young age <50 years, and history of PONV. During the postoperative recovery, patients received oral gabapentin 300 mg three times a day, acetaminophen 1000 mg three times a day TID, and celecoxib 200 mg twice a day. Patients received 5-10 mg of oral oxycodone as needed for moderate pain and 0.4-0.6 mg IV hydromorphone for severe breakthrough pain. During the inpatient stay, oral and IV opioid usage is titrated according to patient needs and overall opioid consumption. Patients who are on a long-acting opioid are continued on their home dose of baseline opioids during their inpatient stay.

Perioperative regional anesthesia for TKA patients included femoral nerve or adductor canal nerve blocks with catheter placement for postoperative local anesthetic infusions. Femoral nerve catheters were transitioned to adductor canal catheters in May 2014 to improve quadriceps muscle strength for improved mobilization. The initial block and catheter placement was performed with 25 mL of 0.2% ropivacaine. Peripheral nerve catheter infusions utilized 0.2% ropivacaine at 8 mL/h and were initiated immediately postoperatively and subsequently discontinued on POD 1.

Outcomes of interest were obtained from EHR data. Average opioid usage was calculated using the medication administration record and averaged by postoperative day (POD), defined as number of calendar days elapsed between the timestamp of patient finishing surgery to the timestamp of medication administered. Opioid use was converted to oral morphine equivalents (MEQ) according to the equianalgesic dose chart created by the National Pharmaceutical Council and Joint Commission on Accreditation of Healthcare Organizations [18]. Visual analog scale (VAS) scores for pain were collected preoperatively and on POD 0 through 3 time periods. The distance walked by patients on POD 1 was collected from physical therapy charts, using the longest distance walked in a single physical therapy session. Length of stay, disposition location (rehabilitation center or skilled nursing facility vs home), readmission, and complications were analyzed. The incidence of PONV was defined as patients requiring 2 or greater postoperative ondansetron doses, second-line antiemetic use (prochlorperazine, metoclopramide, or promethazine), or nursing-recorded episode of emesis during the postoperative period. The incidence of pruritus was assessed by postoperative administration of intravenous low dose naloxone (0.04 mg) or oral/intravenous diphenhydramine. Subgroup analysis was performed for patient groups that were at high risk for PONV.

Statistical Analysis

All statistical analyses were performed with R version 3.0.3 (R Foundation; www.r-project.org). Descriptive statistics were

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