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Current Review of the Use of Intrathecal Morphine for Postoperative Analgesia in Total Joint Arthroplasty

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Abstract

Purpose of Review The use of neuraxial opioids (NAO) as a method for postoperative analgesia for patients undergoing total joint arthroplasty (TJA) is growing in popularity. Intrathecal morphine (ITM) remains the most commonly used NAO. The purpose of this article is to provide readers with an overview of ITM, as well as a comprehensive review of efficacy, dosing, side effects, complications, and adjuncts of ITM when used for TJA.

Recent Findings Recent randomized control trials and meta-analyses provide comprehensive evidence on the usefulness of ITM for TJA. Many of these publications demonstrate clear favorability regarding pain outcomes for TJA patients who receive ITM in the perioperative setting. Additional publications help explain the risk for adverse events and complications associated with routine use of ITM.

Summary Intrathecal morphine is a safe and efficacious modality for providing postoperative analgesia in TJA. A universal approach to optimizing postoperative pain that includes routine use of ITM has yet to be established. Continued research is needed to more clearly define the role that ITM plays in a multi-approach pathway to postoperative analgesia in TJA.

Keywords Intrathecal morphine · Intrathecal opiates · Postoperative analgesia · Total joint arthroplasty · Total knee arthroplasty · Total hip arthroplasty · Peripheral nerve blockade · Local infiltration analgesia

Introduction

Total joint arthroplasty (TJA) is growing in popularity and has been one of the most common procedures performed in the US operating rooms over the last several decades [1]. According to the American College of Rheumatology, approximately 790K knee arthroplasties (TKA) and 450K hip arthroplasties (THA) are performed annually [2]. It is widely accepted that postoperative pain following TJA contributes significantly to perioperative morbidity, hindered physical and pulmonary mobilization after surgery, chronic postsurgical pain, and patient dissatisfaction [3, 4]. Multi-approach modalities for optimizing postoperative analgesia are therefore relevant and crucial to patient-centric care. Oral opioid medications remain the mainstay method for controlling postoperative pain; however, the desire to hinder the recent opiate epidemic has led to anesthesiologists employing alternate strategies of pain control. The use of neuraxial opioids (NAOs) has drastically increased over the last 20 years due to their proven efficacy and low risk profile. Additionally, NAOs carry little risk of technical failure and reduce the undesirable side effects of systemic opioids [5]. More specifically, intrathecal morphine (ITM) for TJA has emerged in the literature as a safe, cost-effective, and efficacious method to provide postoperative analgesia [6•, 7•].

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Table 1 Characteristics of recent and relative studies on intrathecal morphine for total joint arthroplasty

Study	Type of Study	Joint Arthroplasty	N	Primary outcome measured	Findings
Cheah et al. [6•]	Retrospective review	THA and TKA	598 patients	Efficacy of ITM	ITM improves POD 0 analgesia, reduces opioid consumption, lowers PONV, and improves POD 1 mobilization
Wang et al. [7•]	Systemic review and meta-analysis	THA and TKA	18 trials including 1040 patients	Efficacy and safety of ITM	Significantly reduced postoperative 24-h morphine consumption, but higher risk of pruritus in ITM group
Gonvers et al. [8•]	Systemic review and meta-analysis	THA and TKA	29 trials including 1814 patients	Efficacy and safety of ITM	Significantly reduced pain scores but increased risk of PONV in ITM group
AbdelQadir et al. [9•]	Systemic review and meta-analysis	TKA	6 trials	Efficacy and safety of ITM	Significantly reduced pain scores at 4 and 24 h postoperatively but higher risk of pruritus in ITM group
Vitola et al. [10•]	Single-blind, prospective, randomized, controlled trial	THA	90 patients	Postoperative pain intensity within 24 h	0.2 mg ITM had superior analgesia compared to control and 0.1 mg ITM but higher incidence of pruritus
Pathonsamit et al. [11]	Double-blind, prospective, randomized, controlled trial	TKA	102 patients	Postoperative pain scores within 24 h	0.1 mg ITM provided analgesia comparable to that of 0.2 mg ITM with lower risk of PONV
Tang et al. [12•]	Systemic review and meta-analysis	TKA	5 studies including 225 patients	Efficacy of ITM vs. Femoral nerve block for TKA	ITM is associated with improved pain outcomes in acute postoperative period but higher risk of pruritus
Sundarathiti et al. [13•]	Prospective, randomized, controlled trial	TKA	68 patients	Efficacy of continuous ACB + ITM vs. continuous ACB without ITM	Continuous ACB + ITM provided superior analgesic outcomes compared to continuous ACB alone

ACB adductor canal block, *ITM* intrathecal morphine, *POD* postoperative day, *PONV* postoperative nausea and vomiting, *THA* total hip arthroplasty, *TKA* total knee arthroplasty, *POD* postoperative day

Overview of Intrathecal Morphine

Chemical Properties of Neuraxial Opioids

When administering opioid medications, it is important to understand how their chemical properties will impact the expected analgesic effect. These key factors include duration of action, propensity for cranial spread in the cerebral spinal fluid, and the potency of the opioid selected. Hydrophilic opioids, such as morphine and hydromorphone, bind with higher affinity to the opioid receptors of the dorsal horn of the spinal cord; thus, these opioids have higher potency and longer duration of action when compared to lipophilic counterparts such as fentanyl or alfentanil [5]. Morphine remains the most commonly used NAO due to its relative low cost, hydrophilicity, and proven efficacy, but this varies by region and hospital system.

Efficacy of Intrathecal Morphine in Total Joint Arthroplasty

NAOs are becoming more commonly used for postoperative pain control following TJA. There are many studies noting the efficacy of NAOs for this purpose. Spinal anesthesia with ITM has been shown to cause a significant reduction in rest pain at 8–12 h postoperatively when compared to opiate-free spinal anesthesia for TJA [8•]. Similarly, ITM has been proven to cause significantly reduced morphine consumption and pain scores at 4 h and 24 h when compared to placebo in patients undergoing TKA [9•]. When considered comprehensively, these studies show use of ITM affords patients favorable pain outcomes. Table 1, below, provides several relevant publications on the efficacy of ITM for TJA.

Dosing of Intrathecal Morphine

Since ITM was first introduced as a modality of postoperative analgesia in 1979, a wide range of ITM doses have been used [14]. Prior to the last 10 years, dosing for ITM has gone as high as 0.5 mg or higher, but anectodal effidence as well as several studies have noted that side effect concerns increase in a dose dependent manner without increasing analgesic efficacy past 0.4 mg. Several randomized controlled trials have recently been conducted to determine the optimal dose of ITM for TJA while minimizing opiate-related side effects. Thus far, these studies offer varying results. In studies comparing 0.2 to 0.1 mg ITM, 0.2 mg has been shown to provide both superior and comparable analgesia; however, 0.2 mg did carry a significantly higher risk of PONV and pruritis [10•, 11]. When comparing the analgesic efficacy of 0.1 mg, 0.2 mg, and 0.3 mg ITM, 0.2 mg and 0.3 mg ITM provided comparable levels of analgesia and were superior to that provided by 0.1 mg ITM, and all three dosages were associated with similar opiate-related side effects including PONV, pruritus, respiratory depression, or urinary retention [15]. When comparing lower doses of 0.1 mg vs 0.15 mg ITM in patients undergoing TJA, it has been shown that 0.15 mg resulted in superior analgesia and a comparable side effect profile of the 0.1 mg [16]. These studies highlight that while 0.1–0.3 mg is potentially a safe and effective dose range for ITM, further research into this topic is needed to optimize postoperative analgesia and minimize adverse effects. Despite these studies showing varying incidence of side effects associated with different dosages, all patient should be risk stratified and counseled on the potential to experience unpleasant side effects when ITM is used.

Adverse Effects

Nausea and Vomiting

Nausea and vomiting is one of the most common adverse effects associated with opioid medications and often contributes to patient dissatisfaction and longer hospital stays following the use of NAOs. Several studies have been conducted to determine the incidence of PONV in patients undergoing TJA under spinal anesthesia with ITM. One prospective study where ITM dosing varied (0.08–0.2 mg) amongst patients undergoing TJA revealed 46% of patients experienced PONV during the first three postoperative days, regardless of PONV prophylaxis [17]. Similarly, a retrospective review of patients who received < 0.3 mg, 0.3 mg, and > 0.3 mg ITM for TJA determined the incidence of PONV to be 56%, 53%, and 53%, respectively [18]. These studies emphasize that regardless of dosing used, the risk for nausea and vomiting following administration of ITM remains high. All patients should be counseled on the risk of PONV should they receive ITM as a part of their anesthetic care. The authors of this review recommend the use of ITM should be avoided in patients who are at high risk for PONV or who have a history of PONV.

Pruritus

Although the exact mechanism of opioid-induced pruritus remains unclear, it is another well-documented adverse effect of NAO that is distressing to patients. The risk of pruritus following ITM has been shown to increase with higher doses [10•, 19]. A retrospective review to determine the side-effect profile of ITM in patients undergoing TJA showed the incidence of pruritus was 35%, 48%, and 45% with ITM dosing of < 0.3 mg, 0.3 mg, and > 0.3 mg, respectively [18]. Likewise pruritus in patients who received ITM has been found to be as high as 38.8% [7•]. Unfortunately, the prevention and treatment of opioid-induced pruritus remain a challenge.

Urinary Retention

Several studies have been conducted to determine the incidence and risk factors for postoperative urinary retention (POUR) associated with ITM. In one retrospective study, authors found that 21% of patients developed POUR, and independent predictors included age over 65 and male gender [20]. Similar studies determined the overall incidence of POUR after hip or knee arthroplasties under spinal anesthesia with ITM to be 36% and 43.3% [21, 22]. The use of spinal anesthesia with ITM should therefore be considered carefully, and caution should be utilized when administering ITM in patients who are high-risk.

Respiratory Depression

Although delayed respiratory depression is a feared problem associated with ITM, it is fortunately a rare complication compared to the aforementioned side effects. In a systematic review of the efficacy and safety of ITM in TJA, authors found that the administration of ITM does not pose an increased risk of respiratory depression or hypoxemia [8•]. Furthermore, patients with diagnosed or suspected obstructive sleep apnea who are undergoing TJA can safely be administered low dose ITM (0.1 mg) without a higher risk of postoperative pulmonary complications, such as respiratory depression [23]. Other recent studies further emphasize the insignificance of respiratory depression following administration of low dose ITM [16, 18, 24].

Other Intrathecal Opiates and Medications

Fentanyl

Fentanyl is a commonly used opioid in subarachnoid block due to its rapid onset and relative potency. The use of fentanyl to supplement and decrease local anesthetic dose requirements has been demonstrated [25]. A subsequent study on intrathecal fentanyl shows less intraoperative hypotension [26]. However, additional authors failed to demonstrate a significant difference in surgical outcomes with intrathecal fentanyl administration including postoperative opioid consumption, readmission rates, or hospital length of stay [27]. Additionally, fentanyl has proven to be inferior to ITM comparing first 24-h pain scores and subsequent analgesic usage with no significant difference in rates of PONV [28]. Fentanyl has also been shown to have inferior pain control compared to morphine in intrathecal catheter infusion-based approaches [29].

Methadone, Buprenorphine, and Nalbuphine

Nalbuphine has been examined as an intrathecal adjunct medication with one group demonstrating faster onset of analgesia in the setting of total hip arthroplasty; however, the analgesic requirements after ITM were significantly lower in the first 24 h postoperatively [30]. In comparison, buprenorphine has been shown to be superior to nalbuphine in regard to visual analog scale scores and time to rescue medication [31]. The use of intrathecal methadone has been studied as well, with one author showing comparable analgesia in the first 4 h, after which morphine was superior with significantly fewer side effects [32].

Clonidine and Dexmedetomidine

While most commonly used as an antihypertensive, several authors have explored the use of neuraxial clonidine as modality of postoperative analgesia. One study comparing the addition of 25 mcg or 75 mcg of clonidine showed decreased postoperative morphine consumption when combined with ITM versus morphine alone. The authors noted increased postoperative hypotension in both clonidine groups with subsequent authors demonstrating comparable results [33, 34]. Though it should be noted that as a single agent combined with bupivacaine, ITM was superior to intrathecal clonidine with improved postoperative pain scores and opioid consumption [35]. Dexmedetomidine, an alternate α-2 agonist, has also been studied for intrathecal use. Similar to clonidine, dexmedetomidine demonstrated inferior postoperative analgesia when added to bupivacaine compared to ITM [36]. Additionally, other authors were not able to show benefit with intrathecal dexmedetomidine and morphine combined [37].

Adjuncts and Alternatives to Intrathecal Morphine

Peripheral Nerve Blockade

Peripheral nerve blockade (PNB) techniques have long been incorporated into enhanced recovery after surgery pathways for TJA due to being associated with reduced chronic postsurgical pain, opiate requirements, pain scores, and hospital length of stay, as well as improved mobilization following surgery [38–41]. The role of ITM for use in TJA when considered against PNB remains undefined. When compared in randomized control trials for use in TKA, ITM has failed to consistently provide superior analgesia over PNB. It has, however, shown to increase opiate-related side effects, reduce patient satisfaction, and increase postoperative bleeding complications [42–45]. Meta-analyses comparing ITM

to PNB for TKA again offer mixed conclusions on analgesic benefit; however, the evidence of opiate-related side effects is once again demonstrated [12•, 46]. While PNB has shown to provide superior analgesia when used alone, several studies suggest that ITM is appropriate for use in combination with PNB [13•, 13]. ITM has showed more promising results when compared to PNB for THA. Randomized control trials have showed ITM provides superior analgesia when compared to lumbar plexus block and fascia iliaca plane block, with no difference in adverse effects or patient satisfaction [48, 49].

Local Infiltration Analgesia

Local infiltration analgesia (LIA) has been shown to be a beneficial technique for improving postoperative pain following TJA, and it has gained popularity due to requiring very little technical training, its cost effectiveness, and its ability to reduce hospital length of stay [50–52]. The literature lacks consensus on the efficacy of LIA compared to ITM for postoperative pain, and studies provide mixed conclusions on the difference in opiate-related side effects. Some authors have credited LIA with reducing postoperative morphine requirements, lowering pain scores, reducing hospital length of stay, and improving patient satisfaction when compared to ITM for TKA, while others found no difference in pain outcomes or incidence of opiate-related side effects for these patients [53–57]. Comprehensive evidence from recent meta-analyses supports the use of LIA over ITM for TJA due to improved pain scores, morphine requirements, length of hospital stay, and opiate-related side effects [58–60].

Evidence suggests LIA does not perform alone as well as it does in combination with additional techniques, so it is once more important to consider LIA and ITM as modalities within a multi-faceted approach to analgesia [61]. While acute postoperative pain is the primary outcome in most of these studies, it is important to note no significant difference has been appreciated in quality of life, functional outcomes, or chronic postsurgical pain between patients who received ITM or LIA at the time of surgery [54, 62].

Discussion and Conclusions

ITM is a safe and efficacious method for providing postoperative analgesia to patients undergoing TJA. Morphine is a low-cost medication, has favorable biochemical properties, and is associated with superior analgesic benefit compared to other intrathecally administered medications. Moving forward, the continuing trend that ITM will become increasingly incorporated into enhanced recovery after surgery pathways for total joint arthroplasty is supported, when combined with other analgesic modalities such as perphereal nerve blocks, or ITM alone. ITM is not completely benign as it does carry the risk of unpleasant side effects such as nausea, vomiting, and pruritus, as well as the rather uncommon but dangerous side effect of respiratory depression or sedation. Due to the considerations of recognizing unwanted sequala of ITM, it is recommended that post injection monitoring is in place for at least 24 h [63]. When preparing a plan for adding ITM to a post operative analgesic regimen, the biggest point of contention in recent literature continues to be dosing. While the general consensus is side effects increase in a dose dependent manner without considerable analgesic efficacy with dosing past 0.4 to 0.5 mg, there is wide variability in the risk/reward profile with doses between 0.1 and 0.3 mg. The authors of this review recommend that the comorbidities and surgical circumstances be taken into consideration for each patient before administering ITM. Future research is needed to determine and to clearly define ITM dosage and its role in a multi-approach pathway to postoperative analgesia for TJA.

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Data Availability No datasets were generated or analysed during the current study.

Declarations

Competing Interests The authors declare no competing interests.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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