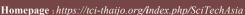
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Page: [20-26]

Efficacy and Safety of Intrathecal Morphine in Foot and Ankle Surgery Patients; a Retrospective Study

Original research article

Preeyaphan Arunakul^{1,*}, Thanachit Ruangprach¹, Prapasri Kulalert², Marut Arunakul³

¹Department of Anesthesia, Faculty of Medicine, Thammasat University, Pathum Thani 12120, Thailand ²Department of Clinical Epidemiology, Faculty of Medicine, Thammasat University, Pathum Thani 12120, Thailand ³Department of Orthopedics, Faculty of Medicine, Thammasat University, Pathum Thani 12120. Thailand

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ABSTRACT

Intrathecal morphine is an effective technique for pain control, easy to perform and simply available in all clinical settings. Studies have reported that 0.1 mg of intrathecal morphine was effective and safe in hip surgery and cesarean section. However, the efficacy of intrathecal morphine for foot and ankle surgery (FAAS) was still unknown. We aimed to evaluate the efficacy of 0.1 mg intrathecal morphine for postoperative pain control within the first 24 hours after FAAS. Data was collected from 136 patients. The numerical rating scales (NRS) taken within the first 24 hours post-operation, written in patients' medical records, were assessed. Records of time to first rescue analgesic, total rescue analgesic consumption, supplemental or multimodal analgesics, as well as incidence of nausea and vomiting, pruritus, urinary retention, and respiratory depression requiring treatment were also reviewed. The average NRS were less than 3 at 0, 6, 12, and 24 hours after intrathecal morphine administration. The number of patients who needed rescue analgesics in the first 24 hours was 25 (18.4%). Thirty-three patients (24.26 %) had nausea and vomiting, 9 patients (6.62%) had pruritus, and 16 patients (11.8 %) had urinary retention. None of the patients had respiratory depression. Therefore, it was concluded that 0.1 mg of intrathecal morphine is effective for controlling postoperative pain in FAAS, though appropriate dosage should be further studied; there are still some dose-dependent complications to be considered.

Keywords: Foot and ankle surgery (FAAS); Intrathecal morphine; Postoperative pain

^{*}Corresponding author: preeyaphan@hotmail.com

1. Introduction

Foot and ankle surgeries (FAAS) are common among orthopedic procedures and result in various degrees of postoperative pain ranging from mild to severe, depending on the type and extent of surgery.

Currently, peripheral nerve blocks, sciatic nerve blocks, with or without saphenous nerve block under ultrasoundguidance, have been widely used analgesic techniques for pain control following FAAS [1-5]. However, performing these blocks needs anesthesiologists' skill, time, and ultrasound machine access. However. ultrasound machines may not be available in all settings. The PROSPECT guidelines for Hallux valgus repair surgery [6], published in 2020, recommends ankle block or wound infiltration with local anesthetic in addition general anesthesia, which reduces postoperative opioid consumption and pain scores.

Intrathecal morphine is one of the effective analgesic techniques available for pain control after various types of surgery [7-10]. Adding morphine is simple, quick, and easily performed by anesthesiologists, especially for situations in which patients receive spinal block as an anesthetic technique. Additionally, morphine is widely available in all clinical settings. Previous studies have shown that 0.1 mg of intrathecal effective morphine is in controlling postoperative pain after hip surgery with very little or no side effects [7-9]. Basak Meco et al. also found that 0.1 mg of intrathecal morphine provides adequate postoperative analgesia for inguinal hernia repair [10]. Another study by Palmer et al. also supports the efficacy of 0.1 mg intrathecal morphine in post-cesarean analgesia [11]. However, the efficacy of intrathecal morphine for FAAS has never been studied.

The objective of our study was to report the efficacy and safety of 0.1 mg of intrathecal morphine for postoperative pain control within the first 24 hours following FAAS.

2. Materials and Methods

After approval by the Human Research Ethics Committee of Thammasat University no.1, the medical records of patients who underwent FAAS between 2013-2019 at Thammasat University Hospital were reviewed retrospectively. This study included only patients who received spinal anesthesia with bupivacaine and 0.1 mg of intrathecal morphine for FAAS.

The primary outcome was postoperative pain score using numerical rating scales (NRS) written in patients' medical records within 24 hours after intrathecal morphine was given. Secondary outcomes were: time to receive first rescue analgesic, and the number of patients who had significant nausea and vomiting, pruritus, respiratory depression, or urinary retention that required catheterization. Supplemental analgesics were also reviewed and recorded. The threshold for significant nausea, vomiting, and pruritus was defined as the patient needing rescue treatment.

We also reviewed NRS stratified by FAAS type, as well as endoscopic or MIS versus non-MIS surgery. Surgeries were also classified as being complex or non-complex. Complex surgery was defined as surgical procedures in more than one area of the foot (forefoot, midfoot, hindfoot, and ankle).

2.1 Statistical analysis

Data were analyzed using Stata version 15.1 (StataCorp, Lakeway, Texas, USA). Frequency and percentage were used to describe categorical variables. Mean and standard deviation median or interquartile range were used to describe continuous variables as appropriate. The proportion of patients free of rescue analgesic use was analyzed by Cox regression. Repeated measurement analysis was used for analyzing NRS in subgroup analysis by different types of surgery. P < 0.05 was statistically significant.

3. Results and Discussion

There were 835 patients who underwent FAAS from 2013 to 2019 at **Thammasat** University Hospital. We excluded 321 patients who received other anesthetic techniques and 377 patients who received doses of intrathecal morphine other than 0.1 mg. One additional patient was excluded due to missing postoperative pain score in the patient's chart (Fig.1).

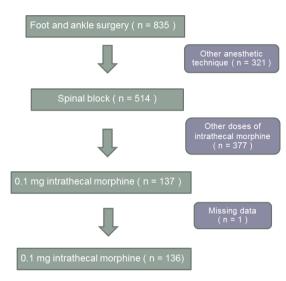


Fig.1. Study flow diagram of patients in the study.

Only 136 patients were included in our study. Demographic data are shown in Table 1. NRS were 2.29 + 1.35 at 6 hours, 2.74 + 1.22 at 12 hours, and 2.88 + 0.91 at 24 hours post-operation (Fig.2). No one had severe postoperative pain. All patients received intravenous NSAIDs intra-operatively. After surgery, all patients received oral NSAIDs and paracetamol around the clock. If patients had NRS > 4, they were given rescue analgesic (Pethidine 25 mg or Tramadol 25 mg, intravenously). Four patients (2.9 %) needed rescue analgesics within the first 6 hours, 11 patients (8%) needed rescue analgesic within the first 12 hours (Fig. 5). Twenty-five patients (18.4%) needed rescue within 24 hours after spinal anesthesia (Fig.5). Thirty-three patients had nausea and vomiting that required treatment (Table 2). Sixteen patients (11.8 %) had urinary

retention. Nine patients (6.6%) had itching (Table 2). No patients had respiratory depression. Pain scores compared between complex and non-complex FAAS at different time points were not significantly different. (Fig.3). Postoperative pain scores between endoscopic and non-endoscopic FAAS group were also not significantly different (Fig. 4).

Table 1. Demographic data.

Table 1. Demographic data (n = 136)		
Variable	n	
Mean age, years	52.3±17.7 (Min 14, Max 84)	
Male Gender	57 (41.9)	
Type of surgery		
Complex	41 (30.1)	
Non-complex	95 (69.8)	
Ankle	35 (25.7)	
Hindfoot	35 (25.7)	
Midfoot	6 (4.4)	
Forefoot	19 (13.9)	
Scope	22 (16.1)	
Insertional Achilles Tendinopathy		
Yes	24 (17.6)	
Mean operative time (minutes)	174 ± 67.8 (Min 50, Max 355)	
Operative time		
≤120 min	34 (25.0)	
Mean IV fluid (mL)	985.9 ± 445.1 (Min 150, Max 2450)	
EBL (mL)	58.9±88.2 (Min 0, Max 500)	
NSAIDs	136 (100)	

Table 2. Secondary outcomes.

Safety	n
Total side effects	58 (42.7)
N/V	33 (24.3)
Itching	9 (6.6)
Urinary retention, N=88	16 (18.2)
Respiratory depression	0 (0.0)

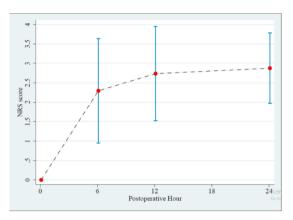


Fig.2. Postoperative pain score in 24 hours (n=136).

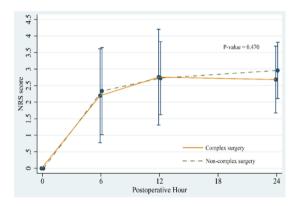


Fig.3. Comparison of postoperative pain score between Complex and Non-complex surgery.

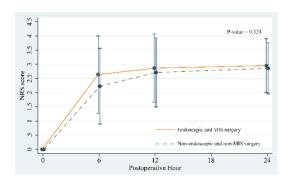


Fig.4. Comparison of postoperative pain score between Endoscopic and Non-endoscopic surgery.

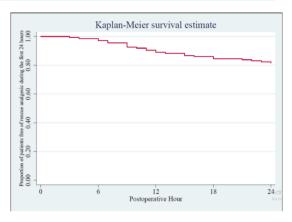


Fig.5. Proportion of patients free of rescue analgesic during the first 24 hours after spinal anesthesia. (n=136)

3.1 Discussion

In this study, we reported that adding 0.1 mg of intrathecal morphine in spinal anesthesia for FAAS showed good results for controlling postoperative pain. Patients who underwent FAAS were scheduled for early discharge within 24 hours after surgery or 48 hours in extensive or complicated procedures. Sometimes it was found that patients who received peripheral nerve blocks still had numbness in their foot after the spinal anesthesia wore off, which could have possibly made them prefer to stay in the hospital until the numbness completely resolved. Further study should be done on local anesthetic concentration and time to complete resolution. Peripheral nerve blockade is operator-dependent procedure, so different operators could possibly give different results.

To the best of our knowledge, this is the first study to provide information on the use of 0.1 mg of intrathecal morphine in FAAS. A previous study by Murphy et al showed that giving 0.1 mg of intrathecal morphine in hip surgery offers good postoperative pain control with minimal side effects [9]. According to the PROSPECT guidelines by the European Society of Regional Anesthesia and Pain Therapy, following total hip arthroplasty, 0.1 mg of intrathecal morphine could be considered if

the patient has received spinal anesthesia for the surgery [12].

In this study, an NRS of 3 or less signified acceptable post-surgery pain control. A change of more than 1 point on the NRS was considered clinically relevant [17]. Further, statistically significant differences in analgesic opioid rescue medication or in opioid induced side-effects were used as valid outcomes. In our study, NRS were less than 3 at every time point (6, 12, and 24 hours after intrathecal morphine administration). Only 18.4% of the total study population needed rescue analgesic but all were at different time points. Based on these findings, it can be concluded that 0.1 mg of morphine effective in intrathecal is controlling postoperative pain after FAAS and thus could be an alternative option when peripheral nerve blockade is not possible or not available in the hospital setting, especially in patients who are planned to receive spinal anesthesia.

Side effects of intrathecal morphine are also a concern because nausea and vomiting, urinary retention, itching, and respiratory depression can prolong both hospital-stay time and postoperative pain [10-13]. In our study, patients who received 0. 1mg of intrathecal morphine had mild postoperative pain but nausea and vomiting still occurred. In contrast, 0. 1mg of intrathecal morphine provided the best balance between analgesic efficacy and side effect profile in patients undergoing hip surgery [9].

Our study found that 18% of the patients who did not have a urinary catheter had urinary retention. First, the side effects of morphine are dose-dependent; patients could possibly have had some side effects if 0.1 mg of intrathecal morphine was insufficient for the type of operation they received [14-16]. Second, most patients after FAAS will be required to walk using gait aids, to reduce the force of weight-bearing, which can be quite hard on the first day for some patients, especially elderly and obese patients. Going

to the bathroom can also be difficult so having a urinary catheter in place might make this task easier for them. Additionally, some operations took longer than 3-4 hours, which normally requires urinary catheter insertion.

We also considered that the intrathecal morphine requirement is not equal for all types of FAAS. More side effects could occur if excess intrathecal morphine is given. As previously stated, the side effects of intrathecal morphine are dose-dependent [9-11]. Further study using different doses of intrathecal morphine, and in different types of FAAS is of interest in order to find appropriate dose levels for procedurespecific postoperative pain management. After determining the appropriate intrathecal morphine dose levels for specific types of FAAS, we could compare pain score differences, side effect profiles, and time needed for peripheral nerve blockade with more granularity.

By giving spinal anesthesia plus intrathecal morphine, drug administration only requires a single injection and gives very promising results. Compared to the combination of peripheral nerve blockade with spinal anesthesia, there would be 2-3 injections: 1 injection for spinal blockade, and another 1-2 injections for peripheral nerve blockade.

The key limitation of this study was that the data were collected retrospectively, so time to record pain scores may not have been exactly 6, 12, and 24 hours after spinal anesthesia as indicated.

As for clinical implications, 0.1mg of intrathecal morphine is effective in controlling postoperative pain after FAAS, even in complex foot surgery and deformity correction. In our study, side effects of intrathecal morphine were addressed to all patients before it was given. Since the side effects are dose-dependent, the appropriate doses for different common FAAS, such as insertional Achilles tendinopathy correction, ankle fractures, and cheilectomy, should be

further studied in detail. From our study, we found that patients who had ankle fractures may require more analgesics than patients who underwent cheilectomy, which could be explained by the extent of surgery and severity of injury to bone and tissues. In recent years, Hallux valgus repair surgery has been done using different procedures depending on the severity of injury to the hallux valgus itself. For example, Chevron osteotomy with or without Akin procedure is performed for mild severity of hallux valgus. However, treating moderate to severe hallux valgus injury is done using modified McBride and Lapidus surgery with or without Akin procedures, which are more extensive procedures and do more damage to bones and tissues.

4. Conclusion

The dose level of 0.1 mg of intrathecal morphine is effective for controlling postoperative pain in FAAS. Procedure-specific dosage should be adjusted. Side effects are dose-related and should be addressed before intrathecal morphine is given.

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