

RESEARCH

Open Access



Effect of different low doses of intrathecal morphine (0.1 and 0.2 mg) on pain and vital functions in patients undergoing total hip arthroplasty: a randomised controlled study

Eva Vitola¹, Natalija Buraka^{1,2}, Renars Erts¹, Iveta Golubovska^{1*} and Aleksejs Miscuks¹

Abstract

Background: Orthopaedic surgeries are among the most painful procedures. By adding low-dose morphine to intrathecal bupivacaine for spinal anaesthesia, the analgesic effect can be improved. The objective of the study was to compare the efficacy and safety of low-dose (0.1 mg and 0.2 mg) intrathecal morphine (ITM).

Methods: A prospective randomised study was conducted at the Hospital of Traumatology and Orthopaedics, Riga, Latvia (February 2020 to May 2021) and enrolled 90 patients undergoing primary hip arthroplasty. All subjects were randomised into three study groups, using the online tool on www.randomiser.org. Treatment groups were allocated to intrathecal morphine (0.1 mg and 0.2 mg) in addition to bupivacaine (15 to 18 mg). The primary outcome was postoperative pain intensity among the three study groups within 24 hours by NRS. The secondary outcomes: pain at rest 4 h, 7 h, 12 h, 24 h postoperatively, respiratory rate, SpO₂, morphine consumption, oxygen supply, opioid-related adverse reactions within 24 hours postoperatively. Data were analysed using R version 4.2.0, applying the Mann-Whitney test, Pearson's chi-squared test, Fisher's exact test, Friedman test, Wilcoxon test.

Results: The primary outcome in the control, ITM 0.1 mg, ITM 0.2 mg groups, respectively: 2.56, 0.87, 0.28 ($p < 0.001$). The secondary outcomes in the control, ITM 0.1 mg, ITM 0.2 mg group, respectively: pain scores 4h – 1.21, 0.48, 0.17 ($p = 0.068$); 7 h – 2.62, 1.00, 0.17 ($p < 0.001$); 12 h – 3.08, 0.65, 0.37 ($p < 0.001$); 24 h – 2.50, 1.20, 0.41 ($p < 0.001$); rescue medication requests (incidence, %): 77%, 16.7%, 13.3% ($p < 0.001$); mean respiratory rate (breath/min) – 15.2; 15.2 ($p > 0.05$); mean SpO₂ (%): 96.7%; 95.7%; 96.07%. Significant adverse effects: pruritus in ITM 0.2 mg group (23% of subjects, $p < 0.001$).

Conclusions: Adult patients undergoing THA under spinal anaesthesia with bupivacaine and 0.2 mg morphine had superior analgesia to patients who received spinal analgesia with bupivacaine or bupivacaine and 0.1 mg morphine.

Trial registration: Study ID ISRCTN37212222; 20/04/2022 (registered retrospectively)

Keywords: Spinal morphine, Hip replacement, Multimodal analgesia, Postoperative pain; Orthopaedic surgery

Background

Total hip arthroplasty (THA) is the most performed elective orthopaedic surgery in developed countries [1, 2]. THA may be associated with significant postoperative pain, which may adversely affect patient recovery and postoperative rehabilitation [3–7].

*Correspondence: ivetagolubovska@gmail.com

¹ Faculty of Medicine, University of Latvia, Riga, Latvia
Full list of author information is available at the end of the article



© The Author(s) 2022. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

The European Society of Regional Anaesthesia (ESRA) PROSPECT Guidelines 2021 recommend selective COX-2 inhibitors or classical NSAIDs (non-selective COX inhibitors) and paracetamol as first-line analgesics [6]. Numerous studies demonstrate glucocorticoids as effective co-analgesics [8, 9]. At the same time, opioids as a rescue medication for severe pain remain in high demand for the THA postoperative period despite their side effects [10].

One of the main goals of pain researchers presently is to find the optimal method of analgesia with the minimum use of opioids [11, 12]. The advantage of intrathecal morphine (ITM) is that it can be used in much lower doses, and its combination with spinal anaesthesia (SA) provides effective and safe analgesia [13]. According to the data of meta-analyses, intrathecal opioids provide most potent 24-hour intravenous morphine-sparing effects [14, 15].

Several publications suggest ITM doses from 0.1 mg to 0.25 mg [15, 16]. The ESRA PROSPECT Guidelines 2021 set out the optimal ITM dose of not more than 0.1 mg [6].

ITM still poses a risk of adverse drug reactions, such as nausea, vomiting, urinary retention, respiratory depression and pruritus [17, 18].

Although there is no shortage of studies on postoperative pain management with ITM after such procedures as caesarean section, inguinal hernia repair and intestinal and hepatic resection, studies on the possibilities of use of ITM in THA are scarce [15, 19, 20].

The objective of this study was to compare the effects of ITM doses of 0.1 and 0.2 mg on postoperative pain, respiratory function and the incidence of adverse drug reactions to morphine, and to find the optimal dose of ITM for patients undergoing THA.

Methods

This is an interventional, single-blind, prospective, randomised, controlled study.

The study was conducted at the Hospital of Traumatology and Orthopaedics (Riga, Latvia) from February 2020 to May 2021 (Protocol/serial number: 24/2020/1). Prior to that, the study was approved by the Medical Ethics Committee of that hospital. All study subjects gave informed consent for all treatments and investigations. All procedures in the study involving human participants were performed in accordance with the ethics standards of the institutional and national research committee and with the Helsinki Declaration and its later amendments or comparable ethics standards. The study was conducted and reported in accordance with the Consolidating Standards of Reporting Trials (CONSORT) 2010 statement.

This study was registered with the ISRCTN register (<https://www.isrctn.com/ISRCTN37212222>; the registration date: 20/04/2022 (retrospective registration). <https://doi.org/10.1186/ISRCTN37212222>

Participant characteristics

Subjects to be enrolled in the study were selected prior to an elective total hip arthroplasty (THA) procedure.

Subject inclusion criteria:

- An elective THA scheduled,
- The surgical procedure to be performed under spinal anaesthesia,
- Age from 18 to 80 years,
- ASA physical status classification system class I-III.

Subject exclusion criteria:

- Allergies to the medications used in the study,
- A severe respiratory disease,
- Body Mass Index (BMI) > 38 kg/m²,
- Subject's refusal to participate in the study,
- Inability to understand what the study is about,
- The subject is currently enrolled in another clinical study.

Subject distribution and interventions

On the day before the elected THA, the subjects read the Patient Information Sheet and signed the Informed Consent Form in two copies (one for the subject and the other for the researcher). Information on demographic data (age, sex), BMI and co-morbidities was acquired. Using the web tool on <https://www.randomizer.org>, the subjects were randomised to one of the three study groups. The main investigator enrolled participants, the second investigator generated the random allocation sequence and assigned the participants to interventions.

All of the study subjects were premedicated with oral etoricoxib 90 mg prior to the procedure and were given dexamethasone 8 mg IV at the operating room.

Before THA, all subjects in the operating room received spinal anaesthesia with isobaric bupivacaine at 15-18 mg doses. Each group was exposed to different doses of spinal morphine:

- control group received SA with bupivacaine 15 to 18 mg,
- ITM 0.1 mg group received SA with morphine 0.1 mg and bupivacaine 15 to 18 mg,
- ITM 0.2 mg group received SA with morphine 0.2 mg and bupivacaine 15 to 18 mg.

Participants were blinded after assignment to interventions. After surgery, all subjects were observed in the post-anaesthesia care unit (PACU) for 24 h and then transported to the patient's ward for rehabilitation. All subjects received the same standardised multimodal analgesia for the hospital stay period: oral etoricoxib 90 mg at 10 AM, acetaminophen 1 g IV every six hours on the day of surgery and continued at 500 mg orally every six hours, morphine 10 mg SC if the pain NRS score was ≥ 5 . The patients were also administered ondansetron 8 mg IV in case of vomiting and nausea. At SpO₂ falling below 92%, supplemental oxygen was given using nasal caniles or non-rebreathing masks.

Primary outcome measure

The primary outcome was the mean postoperative pain intensity within first 24 h after surgery. The result was calculated from the obtained data for each group.

Secondary outcome measure

The secondary outcomes were pain in the different time points, respiratory rate, SpO₂, oxygen supply and adverse reactions (nausea, vomiting, pruritus) within 24 hours after surgery. The rescue analgesia (morphine consumption) within the first 24 h was also measured.

At the postoperative ward, the subjects were asked about pain at rest 4 h, 7 h, 12 h and 24 h post-op. The pain was assessed using the NRS, and the data were recorded in the study protocol.

Respiratory rate (RR) and peripheral capillary blood oxygen saturation (SpO₂) were measured using a vital sign monitor at the PACU on an hourly basis. The average daily measurements were calculated from the obtained data for each group.

A nurse injected morphine 10 mg SC upon subject's request if the pain score was more than 5 points (by NRS). The nurse entered every injected dose in the narcotics inventory form, and the researcher added up the consumption over 24 h and recorded it in the study protocol.

Supplemental oxygen: the nurse noted in the patient observation form whether the subject required supplemental oxygen (yes/no), and the researcher recorded this in the study protocol.

The subjects were asked about adverse reactions, such as nausea, vomiting and pruritus. The nurse entered every adverse reaction case in the patient observation form at the postoperative ward during the first 24 hours post-op.

There were no changes made to methods after study commencement.

Statistical processing of data

Before the study started, the sample size was determined using online sample size calculator for one-way analysis of variance on the Sample size calculator (univie.ac.at), version 1.056. There was a pre-specified outcome assigned at the timepoint of 12 h after surgery for each group (mean 1 = 2.5, mean 2 = 1.1 and mean 3 = 0.9; power = 0.8 and alpha = 0.05). Comparing mean 2 (ITM 0.1 group) and mean 3 (ITM 0.2 group), we suggested the improvement of pain relief to be 20% at the timepoint of 12 h after surgery.

Data were analysed using R version 4.2.0 (R Core Team, 2022). The quantitative data were expressed as the mean (M), standard deviation (SD), minimum (min), maximum (max) and 95% confidence interval (CI) and were analysed using the Mann-Whitney test. The qualitative data were reflected as the number (N) and percentage (%) and were analysed using the Pearson's chi-squared test or Fisher's exact test.

The pain levels among the three study groups were compared using the Friedman test at different timepoints. Pain level dynamics in individual groups was analysed using the Wilcoxon test, comparing the NRS score in each group at the timepoints of 4 h and 7 h, 4 h and 12 h, 4 h and 24 h, 12 h and 24 h after surgery.

Results

Initially the study enrolled 199 subjects, of whom 87 did not meet the inclusion criteria, 11 declined to participate and five were already enrolled in another study. A total of 96 subjects were randomised and allocated, of whom six subjects were excluded – three due to changes in the anaesthesia plan, one because of lost data, one by reason of receiving the analgesics mismatching the study protocol and one due to technical issues. Consequently, the study analysed 90 subjects – 30 in each group. Recruitment started on 1 June 2020 and ended on 30 April 2021 (Fig. 1).

The subjects did not differ significantly in terms of the mean BMI, gender, and other parameters across the three studied groups (Table 1).

Primary outcome

Postoperative pain level comparison among groups

The pain intensity differed significantly among study groups within the first 24 postoperative hours (Table 2).

Secondary outcomes

Pain dynamics in each group

At the timepoint of 4 h after surgery, the mean pain level did not differ significantly among the three study groups ($p = 0.068$).

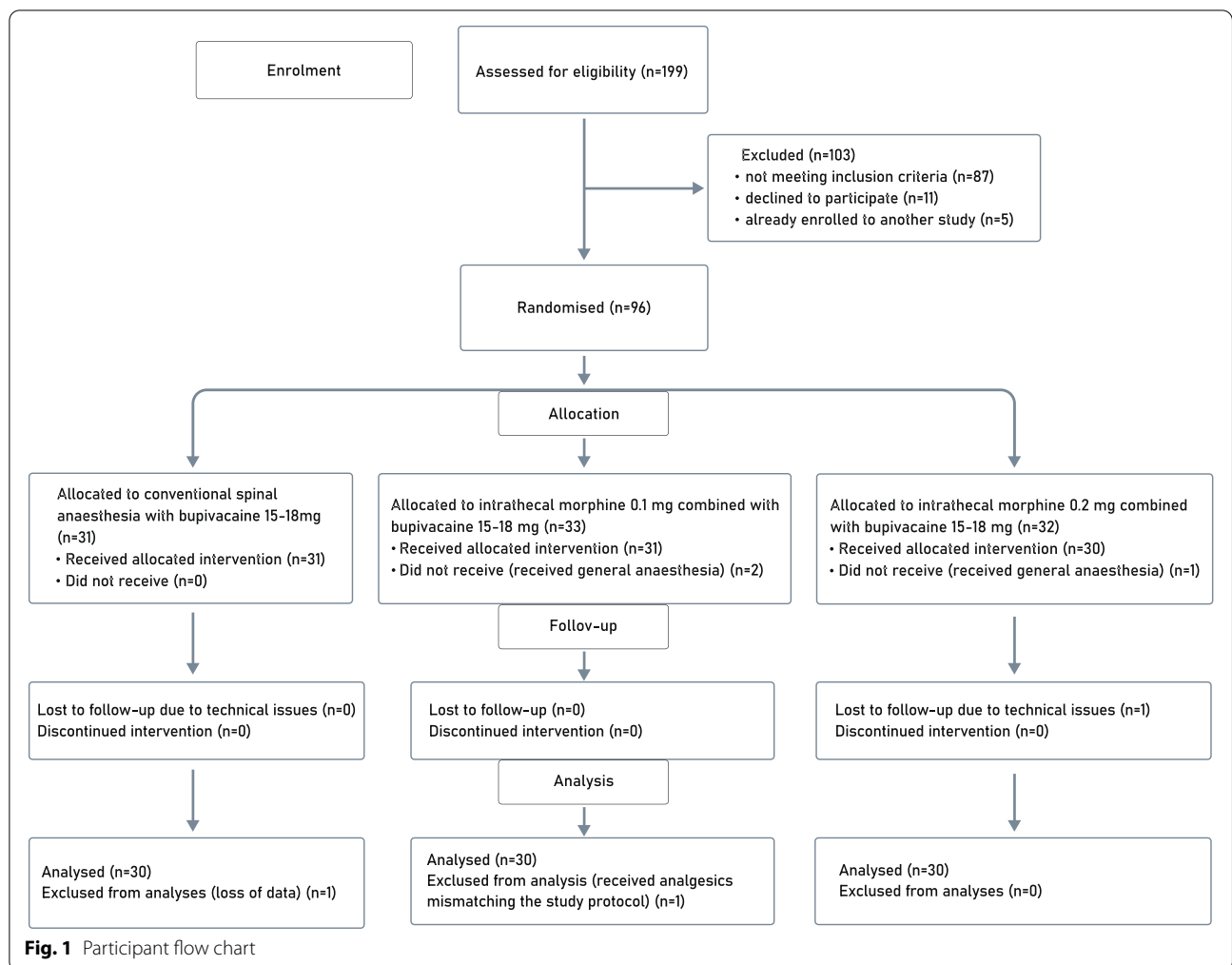


Table 1 Baseline characteristics of the study groups

	Control N=30	ITM 0.1 mg N=30	ITM 0.2 mg N=30
Gender, N (%): Female	20 (66.7 %)	18 (60.0 %)	15 (50.0 %)
Gender, N (%): Male	10 (33.3 %)	12 (40.0 %)	15 (50.0 %)
Age (years), M (SD)	69.4 (6.70)	63.6 (8.39)	57.4 (10.4)
Weight (kg), M (SD)	73.0 (7.40)	87.5 (9.10)	80.0 (9.45)
Height (cm), M (SD)	165 (9.99)	177 (9.29)	168 (8.63)
BMI, kg/m ² , M (SD)	25.7 (3.80)	28.7 (4.10)	28.6 (3.75)
Hb, g/L, M (SD)	140 (9.93)	137 (23.0)	143 (15.0)
Creat., μmol/L, M (SD)	84.5 (16.7)	77.9 (23.9)	80.7 (13.8)
Albumin, g/L, M (SD)	40.8 (3.26)	40.0 (2.16)	41.7 (3.29)
Charleston index, Md [Q1; Q3]	4.00 [3.00;5.00]	3.00 [2.00;4.00]	3.00 [1.00;4.00]
Duration of surgery, Md [Q1; Q3], min	80.0 [70.0;90.0]	80.0 [68.8;90.0]	80.0 [67.5;87.0]
Hospital stay, days, Md [Q1; Q3]	7.00 [6.00;8.00]	6.00 [4.00;7.00]	5.00 [4.00;6.50]
Blood loss, mL, M (SD)	341 (110)	366 (133)	413 (182)

Table 2 Pain intensity (NRS) within 24 hours after surgery

	Control N = 30	ITM 0.1 group N = 30	ITM 0.2 group N = 30	p
Pain, M (SD)	2.56 (2.70)	0.87 (1.91)	0.28 (1.03)	< 0.001
Pain, Md [Q1; Q3]	2.00 [0.00;5.00]	0.00 [0.00;1.00]	0.00 [0.00;0.00]	< 0.001

At the timepoints of 7h, 12 h and 24 h after surgery, the mean pain NRS scores were statistically significantly different among the three study groups. The lowest pain level manifested in the ITM 0.2 mg group (Table 3, Fig. 2).

Peripheral capillary blood oxygen saturation

The mean SpO2 measurements obtained did not differ statistically significantly among all three groups ($p = 0.294$) (Fig. 3).

Table 3 Pain level after THA at different timepoints within 24 h after surgery

Time after surgery, hours	Control group, NRS points (95% CI)	ITM 0.1 mg, NRS points (95% CI)	ITM 0.2 mg, NRS points (95% CI)	p
4 h	1.21 (0.2,2.22)	0.48 (0.03,1.00)	0.17 (0.18,0.53)	0.068
7 h	2.62 (1.57,3.63)	1.00 (0.12,1.81)	0.17 (0.12,0.46)	< 0.001
12 h	3.08 (1.92,4.24)	0.65 (0.01,1.32)	0.37 (0.07,0.83)	< 0.001
24 h	2.50 (1.35,3.65)	1.20 (0.38,2.03)	0.41 (0.07,0.9)	0.001

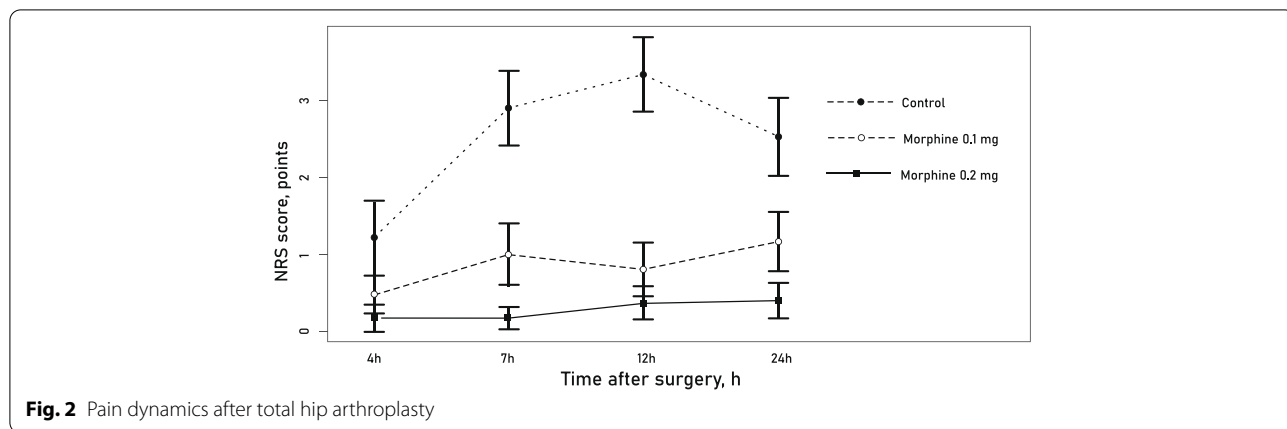


Fig. 2 Pain dynamics after total hip arthroplasty

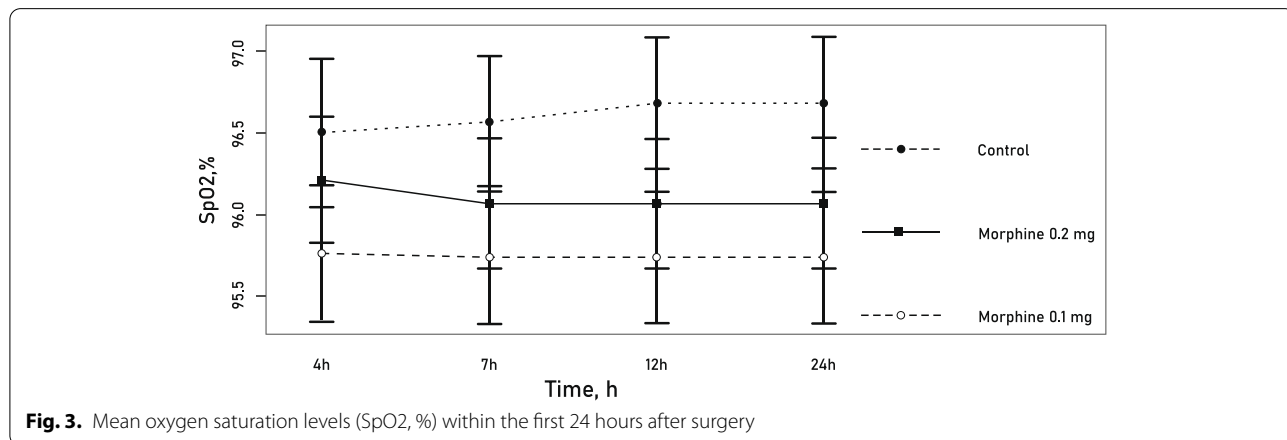
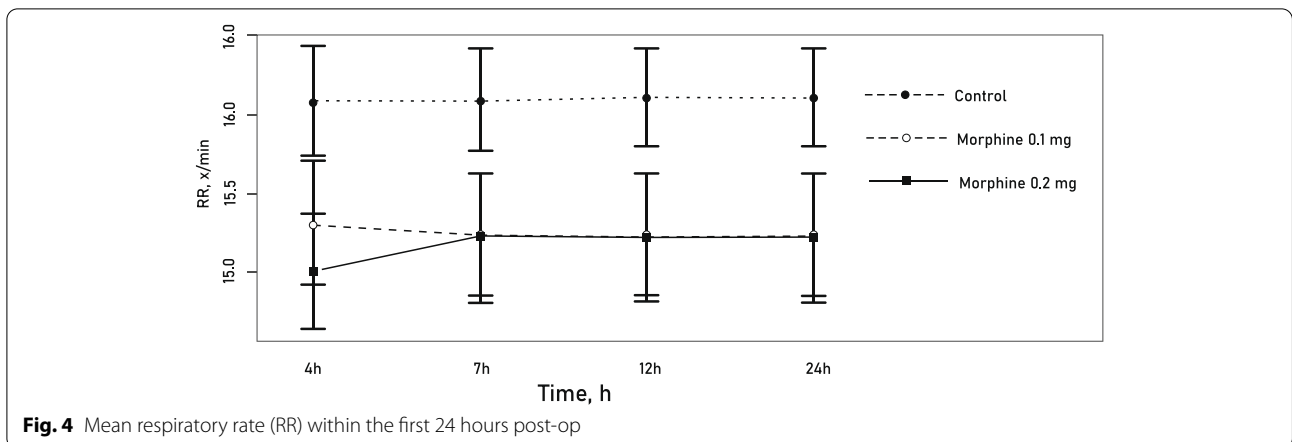


Fig. 3. Mean oxygen saturation levels (SpO2, %) within the first 24 hours after surgery



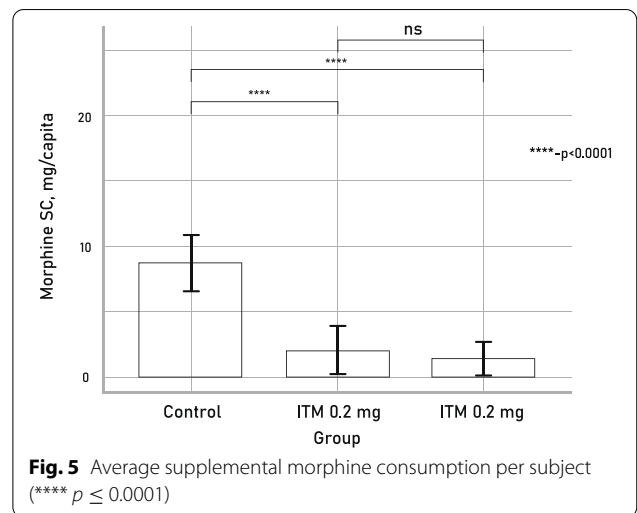
Respiratory rate

The mean respiratory rate observed within 24 hours after surgery did not differ significantly among the study groups ($p = 0.114$) (Fig. 4).

Rescue medication (morphine SC) consumption

Of the entire study population, 32 subjects or 35.6% required additional analgesia with rescue medication (morphine SC) after THA, while 58 subjects or 64.44% did not need add-on analgesia.

The average dose of additional morphine SC in the control group was 8.7 mg per capita, while in the ITM 0.1 mg group it was 2 mg per capita, and in the ITM 0.2 mg group – 1.3 mg per capita. There was a significant difference in the amount of morphine consumed post-operation between the control group and both ITM groups ($P < 0.001$) (Fig. 5).



Oxygen supplementation

No statistically significantly different data were obtained regarding the need for oxygen therapy in the postoperative period for all three study groups ($p = 0.089$).

PONV incidence

Nausea and/or vomiting after the surgical procedure were/was mostly observed in the ITM 0.1 mg group – in seven subjects or 23.3% – and, to a relatively lesser extent, in the control group and in the ITM 0.2 mg group – in three subjects or 10% in each group. The data obtained did not show statistically significant differences among the three study groups ($p = 0.279$) (Fig. 6, Table 4).

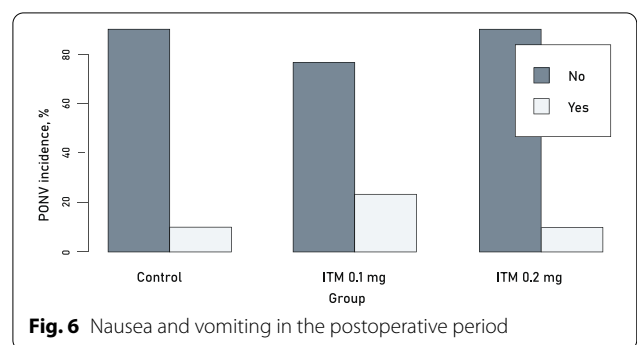


Table 4 Proportion of patients (%) receiving antiemetic therapy in the PACU within the first 24 h after surgery

PONV prophylaxis N (%):	Control	ITM 0.1	ITM 0.2
Yes	12 (35.3%)	12 (42.9%)	10 (32.3%)
No	22 (64.7%)	16 (57.1%)	21 (67.7%)

Pruritus

Pruritus in the postoperative period was observed only in the ITM 0.2 mg group – in seven subjects or 23.3%. The

obtained results were statistically significantly different among all three study groups ($p < 0.001$).

Other observed complications that are not opioid-related, such as hypotension, anaemia, bradycardia and hyperthermia, had equal incidences in all study groups.

Discussion

According to the study data, the best analgesic effect was observed in the ITM 0.2 mg group, where the mean pain level did not exceed 0.4 NRS points – a score that conventionally is defined as “no pain”. As to the postoperative pain dynamics in each group, the results of our study confirm that ITM maintained a prolonged analgesic effect – both ITM 0.1 mg and ITM 0.2 mg groups had no significant changes in pain intensity within the first 24 h after surgery. Morphine consumption in the control group was 8.7 mg per capita, which was four times more than in the ITM 0.1 mg group, where the mean morphine consumption was 2 mg per capita, while in the ITM 0.2 mg group it was only 1.3 mg per capita. The respiratory rate and SpO₂ did not present statistically significant differences among the three study groups. It is interesting to note that the control group showed a greater need in oxygen supply than both ITM groups. This could be related to a significantly higher score of subcutaneous morphine consumption. The study results show that the risk of PONV does not depend on an ITM dose.

The only statistically significant side effect associated with ITM dosage was pruritus, which presented only in the ITM 0.2 mg group, with the incidence of 23.3%. Other observed complications that are not opioid-related, such as hypotension, anaemia, bradycardia and hyperthermia, had equal incidences in all study groups.

The PROSPECT Guidelines 2021 allow the use of ITM in the optimal dose of up to 0.1 mg for diverse kinds of surgery (and a safe single ITM dose of up to 0.3 mg); however, the Guidelines also emphasise the risks and side effects associated with ITM [7]. The *Enhanced Recovery After Surgery*[®] (ERAS) Guidelines do not recommend spinal opioids for routine use due to unwanted side effects, such as respiratory depression, postoperative nausea and vomiting, and pruritus [21]. The findings of our study show that the risk of side effects does not increase by adding spinal morphine in a dose of up to 0.2 mg, except for pruritus, which occurred only in the ITM 0.2 mg group. Nevertheless, we consider that the analgesic advantage of the 0.2 mg dose of ITM is superior to the discomfort from pruritus. Both spinal morphine groups showed reduced opioid use and shorter hospital stay than the control group. This study showed that ITM at the 0.2 mg dose did not impact patient recovery after surgery and resulted in the shortest hospital stay – five

days compared to the control group, where this value was seven days.

We compared the results of our study with the study conducted by *Slappendel et al.* [22]. The latter study suggests ITM 0.1 mg as the optimal dose for reducing pain with minimal adverse effects of opioids. The study used a morphine infusion pump for additional analgesia, and its results also showed a significantly lower morphine consumption in the ITM 0.1 and 0.2 mg groups than in the control and ITM 0.5 mg groups. Similar results were obtained in the randomised study conducted by *Murphy et al.* [23], where both low-dose-morphine (ITM 0.1 mg and ITM 0.2 mg) groups reported significantly lesser pain according to the visual analogue pain scale (VAS) within the first 24 hours post-operation compared to the control group. The pain intensity according to VAS in the postoperative period, however, was equivalent in both morphine groups. The study also showed an opioid-sparing effect in the ITM 0.1 and 0.2 mg groups, where the mean morphine consumption was 3 mg and 2.5 mg per capita, respectively. Another randomised study of the use of ITM in 0.08 mg and 0.1 mg doses conducted by *Rojas et al.* led to a similar conclusion, namely, that the intensity of postoperative pain was equivalent in both morphine groups. 95.13% of patients reported a VAS score of about 0 for 48 hours postoperatively [16]. *Rathmell et al.* found the patients receiving 0.2 or 0.3 mg of ITM as more satisfied with their pain control than those receiving 0.0 or 0.1 mg after hip arthroplasty and after knee arthroplasty [24]. *Gonvers et al.* in their systematic review of the efficacy and safety of intrathecal morphine for lower extremity arthroplasty found that a dose of 0.1 mg provided the best-balanced analgesia without the prevalence of side effects. A subgroup analysis indicated no need to administer an ITM dose greater than 0.1 mg, as there were no apparent additional analgesic benefits within eight to 12 postoperative hours. The incidence (95% CI) of PONV in the intrathecal morphine and control groups was 42.4% (39.0–45.9%) and 29.9% (26.8–33.2%). The meta-analysis showed that the administration of ITM poses no increased risk of respiratory depression or hypoxaemia [25].

The study of *Albrecht et al.* did not obtain any difference in SpO₂ between the ITM and control groups, but there was a decrease in SpO₂ in the third postoperative night in the control group [26]. The incidence of nausea, vomiting and oxygen saturation of < 93% was similar in all groups [24]. The studies of *Slappendel et al.*, *Murphy et al.* and *Rojas et al.* yielded similar results – no statistically significant differences in PONV incidence were obtained [16, 22, 23]. For example, the studies of *Rojas et al.* and *Slappendel et al.* show a slightly higher incidence of PONV in the control than in the ITM groups.

In contrast, in the study of Murphy *et al.*, ITM in 0.1 mg and 0.2 mg doses exposed the subjects to the same risk of PONV. Furthermore, Moraitis *et al.* found that ITM put patients in a substantial risk of PONV. However, in the absence of intrathecal morphine, systemic opioids were given, and it was difficult to distinguish the effects of systemic and intrathecal opioids [27].

Murphy *et al.*, Rathmell *et al.*, Rojas *et al.* and Slap-pendel *et al.* obtained comparable results, with pruritus as the most frequently reported side effect associated with intrathecal opioids. Damevski *et al.* reported a significant increase in itching between the intrathecal uses of 0.05 mg and 0.1 mg of morphine [28]. Only the study by Fenten *et al.* demonstrated that, using multimodal analgesia and morphine for PCA, pain scores in THA were low, and the added analgesic value of intrathecal morphine did not outweigh the increased incidence of pruritus [29].

There were several limitations in our study. First, the sample size of the study was relatively small, and this can affect the outcome. To a certain degree, it cannot be ruled out that some side effects of ITM may be underestimated or could have another statistical distribution. Second, the study enrolled healthy patients without respiratory diseases, so the results of this study may not be applicable to patients with respiratory diseases. Third, the patients were followed for only 24 hours after surgery, so this study does not provide data of ITM effects for more than 24 hours. We used a slightly different doses of bupivacaine – from 15 to 18 mg – depending on the patient height, because taller patients need more bupivacaine to achieve the Th10 anaesthesia level.

In the future, more studies are needed to assess the effect of ITM on analgesia and side effects for patients undergoing THA.

Conclusions

The study results confirmed that adult patients undergoing elective THA under spinal anaesthesia with bupivacaine and 0.2 mg morphine had superior analgesia compared to patients who received spinal analgesia with bupivacaine or bupivacaine and 0.1 mg morphine. The ITM dose of 0.2 mg is safe for patients. While this dose may increase the incidence of pruritus, it does not expose patients to a higher risk of PONV or other systemic side effects.

Abbreviations

ASA: American Society of Anesthesiologists; BMI: Body Mass Index; COX: inhibitors of cyclooxygenase; ERAS: *Enhanced Recovery After Surgery*; ESRA: European Society of Regional Anaesthesia; IT: intrathecal; ITM: intrathecal morphine; ITM 0.1 mg: Group II; ITM 0.2 mg: Group III; IV: intravenously; NRS: numeric rating scale; NSAIDs: nonsteroidal anti-inflammatory drugs; PACU: post-anaesthesia care unit; PCA: patient-controlled analgesia; P.O.: per os; PONV: postoperative

nausea and vomiting; post-op: postoperative; PROSPECT: procedure specific postoperative pain management; R: a language and environment for statistical computing; R Foundation for Statistical Computing, Vienna, Austria); RR: respiratory rate; SA: spinal anaesthesia; SC: subcutaneously; SpO₂: peripheral capillary blood oxygen saturation; THA: total hip arthroplasty; VAS: visual analogue pain scale.

Acknowledgements

The authors gratefully thank the Departments of Anaesthesiology and Intensive Care and Orthopaedics at the Hospital of Traumatology and Orthopaedics in Riga, Latvia, and Residency Study Department of the P. Stradins Clinical University Hospital in Riga, Latvia for allowing and supporting this study.

Authors' contributions

EV and IG helped to design and conduct the study. EV and RE analysed the data and approved the final manuscript. NB and AM helped to design and conduct the study. NB and IG wrote and handed in the final manuscript. The authors read and approved the final manuscript.

Funding

No special funding.

Availability of data and materials

The datasets used and analysed in this study may be obtained from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

The study was approved by the Medical Ethics Committee at the Hospital of Traumatology and Orthopaedics (Protocol/serial number: 24/2020/1). All study subjects gave informed consent for all treatments and investigations. All procedures in the study involving human participants were performed in accordance with the ethics standards of the institutional and national research committee and with the Helsinki Declaration and its later amendments or comparable ethics standards.

Consent for publication

Declared consent for publication Not Applicable

Competing interests

The authors declare no conflicts of interest.

Author details

¹Faculty of Medicine, University of Latvia, Riga, Latvia. ²P. Stradins Clinical University Hospital, Residency Study Department, Riga, Latvia.

Received: 31 July 2022 Accepted: 21 November 2022

Published online: 05 December 2022

References

- Halpern M, Kurtz S, Lau E, Mowat F, Ong K. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *J. Bone Surg.* 2007;89:780–5.
- Deak N, Varacallo M. Hip Precautions. Treasure Island (FL): StatPearls; 2022.
- Gerbershagen HJ, Aduckathil S, van Wijck AJ, Peelen LM, Kalkman CJ, Meissner W. Pain intensity on the first day after surgery: a prospective cohort study comparing 179 surgical procedures. *Anesthesiology.* 2013;118(4):934–44.
- Belbachir A, Fuzier R, Biau D. Unexplained pain after scheduled limb surgery. *Orthop Traumatol Surg Res.* 2020;106(15):S13–S8.
- Abdallah FW, McCartney CJL. Recommendations for total hip arthroplasty pain management: what's old, what's new and what continues to be missing? *Anaesthesia.* 2021;76(8):1018–20.
- Anger M, Valovska T, Beloeil H, Lirk P, Joshi GP, Van de Velde M, et al. PROSPECT guideline for total hip arthroplasty: a systematic review and procedure-specific postoperative pain management recommendations. *Anaesthesia.* 2021;76(8):1082–97.

7. Wylde V, Sayers A, Lenguerrand E, Gooberman-Hill R, Pyke M, Beswick AD, et al. Preoperative widespread pain sensitization and chronic pain after hip and knee replacement: a cohort analysis. *Pain*. 2015;156(1):47–54.
8. Fan ZR, Ma J, Ma XL, Wang Y, Sun L, Wang Y, et al. The efficacy of dexamethasone on pain and recovery after total hip arthroplasty: A systematic review and meta-analysis of randomized controlled trials. *Medicine (Baltimore)*. 2018;97(13):e0100.
9. Lex JR, Edwards TC, Packer TW, Jones GG, Ravi B. Perioperative Systemic Dexamethasone Reduces Length of Stay in Total Joint Arthroplasty: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *J Arthroplasty*. 2021;36(3):1168–86.
10. Wang X, Tay HP, Narayan SW, Penm J, Patanwala AE. Comparison of opioid prescribing upon hospital discharge in patients receiving tapentadol versus oxycodone following orthopaedic surgery. *Int J Clin Pharm*. 2021;43(6):1602–8.
11. Coeckelenbergh S, Le Corre P, De Baerdemaeker L, Bougerol A, Wouters P, Engelman E, et al. Opioid-sparing strategies and their link to postoperative morphine and antiemetic administration: a retrospective study. *Br J Anaesth*. 2022;128(3):e242–e5.
12. McEvoy MD, Raymond BL, Krige A. Opioid-Sparing Perioperative Analgesia Within Enhanced Recovery Programs. *Anesthesiol Clin*. 2022;40(1):35–58.
13. Cummings A, Orgill BD, Fitzgerald BM. Intrathecal Morphine. StatPearls. Treasure Island 2022.
14. Højer Karlsen AP, Geisler A, Petersen PL, Mathiesen O, Dahl JB. Postoperative pain treatment after total hip arthroplasty: a systematic review. *Pain*. 2015;156(1):8–30.
15. Sato I, Iwasaki H, Luthe SK, Iida T, Kanda H. Comparison of intrathecal morphine with continuous patient-controlled epidural anesthesia versus intrathecal morphine alone for post-cesarean section analgesia: a randomized controlled trial. *BMC Anesthesiol*. 2020;20(1):138.
16. Rojas GA, Hernández PM, Vidal DP, Balkenhol NM, Opazo VM, Riquelme AM. Low dose intrathecal morphine for hip arthroplasty. *Revista Chilena de Anestesia*. 2020;49(4):548–59.
17. Koning MV, Reussien E, Vermeulen BAN, Zonneveld S, Westerman EM, de Graaff JC, et al. Serious Adverse Events after a Single Shot of Intrathecal Morphine: A Case Series and Systematic Review. *Pain Res Manag*. 2022;2022:4567192.
18. Hess SR, Lahaye LA, Waligora AC, Sima AP, Jiranek WA, Golladay GJ. Safety and side-effect profile of intrathecal morphine in a diverse patient population undergoing total knee and hip arthroplasty. *Eur J Orthop Surg Traumatol*. 2019;29(1):125–9.
19. Sultan P, Halpern SH, Pushpanathan E, Patel S, Carvalho B. The Effect of Intrathecal Morphine Dose on Outcomes After Elective Cesarean Delivery: A Meta-Analysis. *Anesth Analg*. 2016;123(1):154–64.
20. Xu Z, Tang Z, Yao J, Liang D, Jin F, Liu Y, et al. Comparison of low-dose morphine intrathecal analgesia and sufentanil PCA in elderly patients with hip fracture undergoing single spinal anesthesia - a randomized clinical trial. *BMC Anesthesiol*. 2022;22(1):124.
21. Wainwright TW, Gill M, McDonald DA, Middleton RG, Reed M, Sahota O, et al. Consensus statement for perioperative care in total hip replacement and total knee replacement surgery: Enhanced Recovery After Surgery (ERAS(R)) Society recommendations. *Acta Orthop*. 2020;91(1):3–19.
22. Slappendel R, Weber EW, Dirksen R, Gielen MJ, van Limbeek J. Optimization of the dose of intrathecal morphine in total hip surgery: a dose-finding study. *Anesth Analg*. 1999;88(4):822–6.
23. Murphy PM, Stack D, Kinirons B, Laffey JG. Optimizing the dose of intrathecal morphine in older patients undergoing hip arthroplasty. *Anesth Analg*. 2003;97(6):1709–15.
24. Rathmell JP, Pino CA, Taylor R, Patrin T, Viani BA. Intrathecal morphine for postoperative analgesia: a randomized, controlled, dose-ranging study after hip and knee arthroplasty. *Anesth Analg*. 2003;97(5):1452–7.
25. Gonvers E, El-Boghdady K, Grape S, Albrecht E. Efficacy and safety of intrathecal morphine for analgesia after lower joint arthroplasty: a systematic review and meta-analysis with meta-regression and trial sequential analysis. *Anaesthesia*. 2021;76(12):1648–58.
26. Albrecht E, Bayon V, Hirotsu C, Al Ja'bari A, Heinzer R. Intrathecal morphine and sleep apnoea severity in patients undergoing hip arthroplasty: a randomised, controlled, triple-blinded trial. *Br J Anaesth*. 2020;125(5):811–7.
27. Moraitis A, Hultin M, Walldén J. Risk of postoperative nausea and vomiting in hip and knee arthroplasty: a prospective cohort study after spinal anaesthesia including intrathecal morphine. *BMC Anesthesiol*. 2020;20(1):242.
28. Damevski V, Damevska G, Palasevska L, Nojkov O. Postoperative intrathecal analgesia for primary total hip arthroplasty—comparative clinical examination of two different small doses of morphium hydrochloride. *Bratisl Lek Listy*. 2011;112(9):497–500.
29. Fenten MG, Keijzer BA, Stienstra R. No clinically relevant advantage of intrathecal morphine in total hip arthroplasty? *Acta Anaesthesiol Belg*. 2014;65(4):161–6.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions

