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Adding intrathecal morphine to unilateral spinal anesthesia results in better pain relief following knee arthroscopy

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Abstract
Purpose. Intrathecal morphine is administered to provide profound and prolonged analgesia, and to treat acute postoperative pain. We compared the effectiveness of hyperbaric bupivacaine alone and in combination with morphine for unilateral spinal anesthesia in patients undergoing knee arthroscopy.
Methods. Sixty patients were randomly allocated to two groups to receive either 1.2 ml (6 mg) of 0.5% hyperbaric bupivacaine (group B; $n = 30$) or 1.2 ml of 0.5% hyperbaric bupivacaine containing 0.16 mg of morphine (group BM; $n = 30$). Spinal block was assessed by pinprick and a modified Bromage scale and compared between the operated and nonoperated sides. Visual analog scale (VAS) values, duration of analgesia, and total analgesic requirement of patients were recorded.
Results. Patients in group BM had significantly lower VAS values on movement at 30 min and at 2, 4, 6, and 12 h postoperatively ($P < 0.05$ and $P < 0.001$, $P < 0.001$, $P < 0.001$, and $P < 0.05$, respectively). The total analgesic requirement in the first 24 h after surgery was significantly higher in group B ($P < 0.001$). Patients in group BM had a significantly longer duration of analgesia in the first 24 h postoperatively ($P < 0.001$). Motor blockade of the operated limb in group BM was similar to that in group B ($P > 0.05$), and motor blockade of the nonoperated limb in group BM was also similar to that in group B ($P > 0.05$).
Conclusion. We conclude that unilateral spinal anesthesia with hyperbaric bupivacaine plus 0.16 mg morphine is preferable to hyperbaric bupivacaine alone with respect to analgesic requirement, duration of analgesia, and VAS values.

Key words Morphine · Intrathecal · Unilateral · Spinal anesthesia

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Introduction

Unilateral spinal anesthesia is a regional technique that is generally applied in lower-limb surgery when it is perhaps preferable to produce an anesthetic block only on the operated side. The advantages of this technique are that it is associated with a reduction of hypotension during spinal anesthesia, as well as being associated with faster recovery and increased patient satisfaction [1,2].

Inrathecal morphine (ITM) has been widely used not only for acute postoperative analgesia but also for surgical anesthesia and chronic pain treatment. The advantage of spinally administered opioids is that prolonged analgesia can be provided using a single injection at the time of surgery, without the need for cumbersome and expensive pumps in the postoperative period [3]. Pain after orthopedic surgery can be effectively controlled with ITM [3–5]. In an attempt to limit side effects, the use of low-dose spinal opioids (e.g., 0.3 mg ITM) has been advocated [4,6,7]. A single dose often suffices as the sole analgesic after orthopedic surgery [4,8]. However, the use of this technique has been limited by a high incidence of opioid-related side effects, including nausea, pruritus, and urinary retention, and the fear of respiratory depression, which may be delayed in onset [9]. The analgesia produced by ITM, in doses ranging from 0.025 to 20 mg, is adequate for pain relief after many different types of surgery [10]. In an attempt to limit major and minor opioid side effects, the use of low-dose spinal opioids has been advocated [3,5]. The optimal dose of ITM in unilateral spinal anesthesia has not been determined [11].

We hypothetized that the addition of low-dose morphine to bupivacaine would be better than bupivacaine alone for unilateral spinal anesthesia, regarding the analgesic requirement, duration of analgesia, and analgesia on movement.

The purpose of this prospective randomized study was to compare the postoperative analgesic effects of hyperbaric bupivacaine and hyperbaric bupivacaine plus 0.16 mg morphine for unilateral spinal anesthesia in patients undergoing knee arthroscopy.

Patients and methods

The study was approved by our institutional review board, and written informed consent was obtained from all subjects. Sixty-seven adult patients, American Society of Anesthesiologists (ASA) physical status I–II, scheduled to undergo knee arthroscopy under unilateral spinal anesthesia were recruited for the study. All patients were treated by partial meniscectomies under tourniquet control and all stayed at the hospital overnight. Exclusion criteria included evidence of neurological or neuromuscular disease, respiratory or cardiac disease, diabetes mellitus, or peripheral neuropathy, as well as patients receiving chronic analgesic therapy, infection at the intended site of spinal needle insertion, or hypersensitivity to amide local anesthetics or morphine.

All patients were monitored by electrocardiography, noninvasive arterial blood pressure, peripheral oxygen saturation ($S_{p_{O_2}}$), and respiratory rate (RR). Standard premedication was given, i.e., 0.03 mg·kg^{-1} midazolam IV. Baseline arterial blood pressure was recorded at the end of the infusion of 10 ml·kg^{-1} Ringer's lactate solution before inducing spinal block. Spinal anesthesia was performed with the patient in the lateral decubitus position with the operative side down, using a 27-gauge Whitacre needle at the L3–4 or L4–5 interspace (Becton-Dickinson, Franklin Lakes, NJ, USA). According to a computer-generated randomization sequence, patients were randomly allocated to two groups, to receive either 1.2 ml (6 mg) of 0.5% hyperbaric bupivacaine (group B; $n = 30$) or 1.0 ml of 0.5% hyperbaric bupivacaine plus 0.2 ml of a solution containing 2.4 ml of 0.5% hyperbaric bupivacaine plus 0.1 ml of 0.02 g·ml^{-1} morphine (group BM; $n = 30$). The total ITM dose in the BM group was 0.16 mg. Through this procedure, the local anesthetic solutions in both groups had the same density [12].

After the free flow of cerebrospinal fluid was observed, the opening of the spinal needle was turned toward the dependent side and 1.2 ml of the study solution was injected at a speed of 2 ml·min^{-1} without further aspiration maneuvers. The patients were kept in the lateral decubitus position for 15 min; afterward, the patients were turned to the supine position and transferred to the operating room, and surgery was started. Patients were judged to be ready for surgery when complete loss of pinprick sensation at T10-L2 was reported on the operative side, with concomitant complete motor block of the ipsilateral leg. An independent blinded observer evaluated the evolution of sensory and motor blocks on both sides every 30 min until complete regression of the spinal block. At the same time, cardiovascular variables were also recorded. Sensory block was assessed as a complete loss of pinprick sensation (22-gauge hypodermic needle). Motor block was assessed using a modified Bromage scale by asking the patient to flex the limb at the hip, knee, and ankle joints (0, no motor block; 1, hip blocked; 2, hip and knee blocked; 3, hip, knee, and ankle blocked). The patient, surgeon, and nursing staff in the operating theater and Day Surgery Unit were all blinded as to patient group allocation. Clinically relevant hypotension (decrease in systolic arterial blood pressure from 30% of baseline) was initially treated with a rapid infusion of 200 ml normal saline over 10 min. If this was ineffective, 5 mg ephedrine was given IV. Bradycardia (a decrease in heart rate to 45 bpm) was treated with 0.5 mg atropine IV. The time from the end of the spinal injection to readiness for surgery (onset time), the sensory level of the operated side, the sensory level of the nonoperated side, time to S2 regression (time from the completion of intrathecal administration to S2 regression), time to urination, time to ambulation, and eligibility for home discharge were also recorded. The criteria for home discharge were: stable vital signs, ability to tolerate liquids by mouth, ability to walk, spontaneously and ability to void spontaneously, the absence of nausea, and pain that was manageable with oral analgesics. The use of a visual analog scale (VAS) was described to each patient at the postoperative visit, and the effectiveness of analgesia was measured by VAS pain scores on knee flexion (a 100-mm linear scale is used and a result is demonstrated between 0 and 100 mm; with 0 mm = no pain and 100 mm = the worst pain imaginable) at 30 min and at 2, 4, 6, 12, and 24 h postoperatively. Total analgesia time was recorded as the time of first diclofenac IV dose given postoperatively. Patients received 1 mg·kg^{-1} diclofenac sodium IV whenever they felt pain greater than 40 mm on the VAS. The occurrence of adverse events, including emesis and pruritus, was also recorded.

The sample size was estimated using the data from previous studies performed at our institution for pain scores. A difference of 10 in the mean increase in the VAS pain scores between the groups and an SD of 10 were used for the calculation. Thirty patients are required to give a 96% power to demonstrate this difference at the 0.05 significance level. The data were analyzed using Student's *t*-test, and nonparametric data were analyzed using the Mann-Whitney *U*-test, χ^2 text, and Fisher's exact test, using the statistical package SPSS for Windows version 10.0 (SPSS, Chicago, IL, USA). The total analgesia times were analyzed using

Kaplan-Meier survival analysis. Unless otherwise specified, data values are given as arithmetic means and SD (mean ± SD). Differences at the level of $P < 0.05$ were considered statistically significant.

Results

Three patients in group B and 4 patients in group BM were excluded because of failure of spinal blocks. Patients' demographic data and duration of surgery are shown in Table 1. No differences were observed between the groups regarding age, weight, and sex, or duration of surgery. Patients in group BM had significantly lower VAS values on movement at 30 min and at 2, 4, 6, and 12 h postoperatively ($P < 0.05$ and $P < 0.001$, $P < 0.001$, $P < 0.001$, and $P < 0.05$, respectively), while the total analgesic requirement in the first 24 h after surgery was significantly higher in group B ($P < 0.001$; Table 2). Patients in the BM group had a significantly longer duration of analgesia in the first 24 h postoperatively (mean/SE; 22.43/0.53 h) than those in the B group (mean/SE; 7.36/0.7 h; $P < 0.001$; Fig. 1).

Motor blockade of the operated limb in the BM group (Bromage score, 0/1/2/3; 1/0/2/27) was similar to that in the B group (Bromage score, 0/1/2/3; 1/1/2/26; $P > 0.05$), and motor blockade of the nonoperated limb in the BM group (Bromage score, 0/1/2/3; 28/1/1/0) was also found to be similar to that in the B group (Bromage score, 0/1/2/3; 28/0/1/1; $P > 0.05$). A strictly unilateral sensory block (defined as no loss of pinprick sensation detectable on the nonoperative side) was observed in 26 patients from group BM (87%) and in 27 group B patients (90%; $P > 0.05$), whereas a strictly unilateral motor block (defined as no motor block detectable on the nonoperative side) was observed in 29 group BM patients (97%) and 28 group B patients (93%; $P > 0.05$). The maximum sensory level on the operated side was T11 (T10–T12) in the BM group and T10 (T9–T11) in

Table 1. Demographic data of the patients

	Group BM ($n = 30$)	Group B ($n = 30$)	P value
Age (years)	43.7 ± 12.5	39.8 ± 12.6	>0.05
Height (cm)	163.7 ± 9.0	167.5 ± 10.1	>0.05
Weight (kg)	77.5 ± 11.2	75.2 ± 13.9	>0.05
Sex (male/female)	13/17	14/16	>0.05
Duration of surgery (min)	74.7 ± 24.8	72.2 ± 32.9	>0.05

Data values are presented as means ± SD

Table 2. Values of visual analog scores (VAS; 0–100 mm) at 30 min and at 2, 4, 6, 12, and 24 h postsurgery, and total analgesic requirement (diclofenac sodium) in the first 24 h after surgery

	Group BM ($n = 30$)	Group B ($n = 30$)	P value
30 min	12 ± 9	22 ± 18	<0.05
2 h	15 ± 11	33 ± 24	<0.001
4 h	12 ± 5	33 ± 17	<0.001
6 h	11 ± 4	31 ± 17	<0.001
12 h	13 ± 6	22 ± 13	<0.05
24 h	19 ± 17	14 ± 06	>0.05
Total analgesic requirement (mg)	26.6 ± 36.7	70.1 ± 47.1	<0.001

Data values are presented as means ± SD

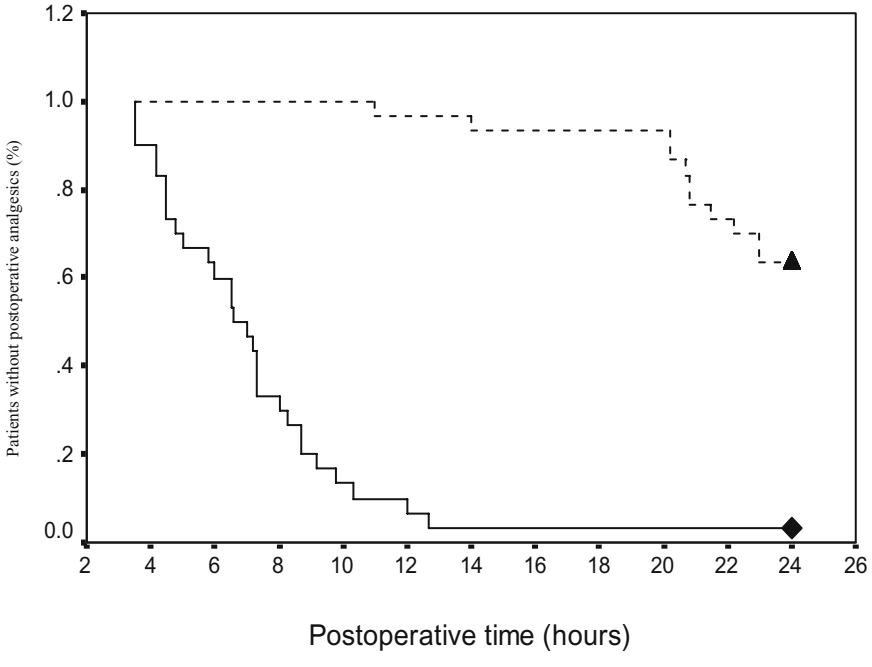

Fig. 1. Patients without additional analgesic in the postoperative period (using Kaplan-Meier survival analysis). A statistically significant difference was found between group B (bupivacaine alone; continuous *line*) and group BM (bupivacaine plus morphine; *dotted line*) according to the Kaplan-Meier analysis ($P < 0.001$)

Table 3. Comparison of sensory levels on the operated and nonoperated sides (at 15 min after intrathecal injection) and the times to regression of the sensory block to the S2 level, urination, and ambulation

	Group BM ($n = 30$)	Group B ($n = 30$)	P value
Maximum sensory level of operated side	T11 (T10–T12)	T10 (T9–T11)	>0.05
Maximum sensory level of nonoperated side	S2 (S2–L1)	S2 (S2–L2)	>0.05
Time to readiness for surgery (min)	18.2 ± 5.7	19.7 ± 4.3	>0.05
Time to S2 regression (min)	60.1 ± 13.0	65.4 ± 12.3	>0.05
Time to urination (min)	93.0 ± 20.5	98.3 ± 31.8	>0.05
Time to ambulation (min)	84.3 ± 18.1	90.9 ± 31.5	>0.05
Time to eligibility for home discharge (hours)	150 ± 31.5	142 ± 37.1	>0.05

Data values are presented as medians (ranges), or means ± SD

the B group ($P > 0.05$), while the maximum sensory level on the nonoperated side was S2 (S2-L1) in the BM group, compared with S2 (S2-L2) in the B group ($P > 0.05$). No differences were detected between the two study groups in the sensory levels on the operated and nonoperated sides or in the times to regression of the sensory block to the S2 level, urination, and ambulation (Table 3).

No differences were seen between the two groups when the systolic, diastolic, and mean blood pressure values were compared ($P > 0.05$). The heart rate, Sp_{O_2}, and RR values in the preoperative period were compared, and no differences were found between the two groups ($P > 0.05$).

No differences were observed between the BM and B groups in the postoperative period regarding the incidence of emesis (17% and 10%, respectively; $P > 0.05$) or pruritus (16% and 4%, respectively; $P > 0.05$).

Discussion

Our study shows that 0.16 mg ITM plus 6 mg 0.5% hyperbaric bupivacaine produces better postoperative analgesia in the first 24 h than bupivacaine alone in patients undergoing knee arthroscopy. This confirms earlier studies on the quality of postoperative analgesia [13–15]. The addition of morphine to an intrathecal anesthetic is an attractive therapeutic option because of its simplicity. A high dose of ITM leads to the frequent incidence of drug-related side effects. These include sedation, nausea, vomiting, pruritus, urinary retention, and delayed respiratory depression. Because side effects are dose-related, the doses necessary for postoperative analgesia in orthopedic procedures result in a side effect incidence ranging from 50% to 100% [7,16,17]. The low incidence of adverse events reported in patients with low-dose spinal opioid administration, along with the popularity of the technique, suggests that this regimen is safe [13]. In order to avoid the abovementioned adverse effects, we used a relatively low ITM dose (0.16 mg morphine), similar to that in the study of Gentili [12].

Unilateral distribution of spinal anesthesia can be achieved with the use of the lateral decubitus position, with small doses of hypobaric or hyperbaric local-anesthetic solution [18]. Intrathecal opioids have been shown to provide effective analgesia in a variety of surgical settings since the late 1970s [3]. Achieving adequate analgesia after knee arthroscopy can be a challenging task, as patients rate their pain very differently. ITM provides effective postoperative pain control for orthopedic procedures [16].

The present prospective, randomized study was designed to evaluate the early postoperative analgesic efficacy of unilateral spinal anesthesia with low-dose hyperbaric bupivacaine plus 0.16 mg morphine in patients undergoing knee arthroscopy. To our knowledge, the use of ITM in patients receiving knee arthroscopies with unilateral spinal anesthesia has not been investigated. ITM is effective for acute postoperative pain control in many different types of surgery [13–15,19]. However, the reliability of low-dose ITM was questioned by Jacobson et al. [5], who found that 0.3 mg was not as effective at providing postoperative analgesia as either 1 or 2.5 mg in patients undergoing total joint arthroplasty. Lisowska et al. [20] evaluated the analgesic efficacy and side effects of ITM in the dose range of 0.2–0.5 mg in patients undergoing elective lower-limb orthopedic operations under spinal anesthesia. They found significant differences in the duration and efficacy of the analgesia and in the incidence of morphine dose-related pruritus.

In the present study, low-dose ITM (0.16 mg) was added to hyperbaric bupivacaine in unilateral spinal anesthesia to achieve prolonged duration of postopera-

tive analgesia. Sufficient analgesia was achieved in the postoperative period in our patients who received the low-dose ITM, as shown by their lower analgesic requirement postoperatively (Table 2). It is possible that the analgesic affect of ITM varies, however, according to dose. This notion is supported by Bailey et al. [7], who found, using variable doses, that the maximal analgesic effect of ITM in volunteers occurred between hours 4 and 7. This analgesic effect then declined after 7 h towards baseline at 10–15 h. In our study, the postoperative duration of analgesia was relatively long in group BM in which ITM was used compared to that in group B (no ITM; Fig. 1). Valanne et al. [21] evaluated unilateral spinal anesthesia with 4 and 6 mg 0.5% hyperbaric bupivacaine and reported successful spinal block in 96% of patients, with readiness for home discharge after 181 and 209 min, respectively. Liu et al. [22] reported complete resolution of sensory block within 144 min after the intrathecal injection of 50 mg lidocaine, whereas Urmey et al. [23] studied 60-mg plain lidocaine 2% for knee arthroscopy and observed spontaneous micturition 170–190 min after spinal injection. In our study, no differences were found between the two study groups regarding the sensory levels on the operated and nonoperated sides or the times to regression of the sensory block to the S2 level, urination, and ambulation (Table 3). Nonetheless, a longer duration of analgesia with similar time for readiness for home discharge was achieved in patients who received ITM.

Kuusniemi et al. [24] used hypobaric and hyperbaric bupivacaine and reported that none of their patients developed postspinal headache or urinary retention, with minimal hemodynamic changes. Spinal anesthesia causes a clinically significant disturbance in bladder function due to interruption of the micturition reflex [25]. Potentially harmful urinary retention can be suspected with the presence of severe pain, bradycardia, hypotension, hypertension, heart dysrhythmias, or vomiting.

The addition of opioids to neuraxial local anesthetics improves analgesia and anesthesia quality, prolongs sensory blockade, and reduces local anesthetic requirements [3,13–15,19]. Pruritus after intrathecal opioids is an undesirable side effect of opioids that can develop with a frequency ranging from 20% to 80% [26]. In some studies it was reported that reducing the dose of intrathecal opioids reduced the incidence of pruritus, and that the pruritic effect of opioids was dose-dependent [3,13–15,19,26,27]. In the present study, we used 0.16 mg morphine intrathecally for postoperative analgesia and found no statistically significant difference between our two groups in the incidence of pruritus (16% in the BM group and 4% in the B group; $P > 0.05$).

We conclude that unilateral spinal anesthesia with hyperbaric bupivacaine plus 0.16 mg morphine is preferable for knee arthroscopy when compared to hyperbaric bupivacaine alone, with respect to analgesic requirement, duration of analgesia, and VAS values.

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