The Effect of Intrathecal Morphine Added to Continuous Femoral 3-in-1 Nerve Block for Analgesia after Total Knee Replacement

Department of Anesthesiology and Pain Medicine, College of Medicine, Eulji University; *Department of Anesthesiology and Pain Medicine, College of Medicine, Konyang University, Daejeon, Korea

Chang Kil Park, M.D., Choon Kyu Cho, M.D.*, Hyun Ho Shin, M.D., and Jung Ha Cho, M.D.

Background: Most of the patients who received a 3-in-1 nerve block for analgesia after total knee replacement (TKR) complained of pain in the back of the knee. We investigated the value of an intrathecal (IT) morphine in patients receiving continuous 3-in-1 nerve block with a PCA technique for pain control after unilateral TKR.

Methods: Group 1 (n = 20) received spinal anesthesia with IT fentanyl 10 μg. Group 2 (n = 20) received spinal anesthesia with IT morphine 0.1 mg. All patients received continuous 3-in-1 nerve block performed with 20 ml of 0.25% bupivacaine with epinephrine 1:200000, followed by a continuous infusion of 0.125% bupivacaine at the rate of 2 ml/h plus PCA boluses of 1 ml with a lockout of 10 min. The intensity of pain at rest and on movement was assessed by the patients using a visual analog scale (VAS) for the first 2 postoperative days.

Results: Patients in Group 2 reported significantly lower VAS pain scores at rest than those in Group 1 for the first 1 day (P < 0.05). Cumulative PCA bolus use of 0.125% bupivacaine in Group 2 was significantly lower than those in Group 1 for the first 2 days (P < 0.05). The incidences of pruritus in Groups 1 and 2 were 0 and 50%, respectively (P < 0.01).

Conclusions: We determined that the addition of IT morphine 0.1 mg to continuous femoral 3-in-1 nerve block improves postoperative analgesia after TKR. (Korean J Anesthesiol 2008; 54: 544 ~ 51)

Key Words: intrathecal fentanyl, intrathecal morphine, 3-in-1 block, visual analog scale.

INTRODUCTION

Total knee replacement (TKR) can result in severe postoperative pain at the surgical site, and inadequate control of postoperative pain has been associated with poor functional recovery. After TKR, postoperative pain relief can be achieved by a variety of techniques, such as IV patient-controlled analgesia (PCA), epidural analgesia, and femoral 3-in-1 nerve block. Compared with epidural analgesia, extended 3-in-1 block is associated with fewer side effects, and is, therefore, the preferred technique. However, the pain in the back of the knee after TKR was not relieved by 3-in-1 block. This suggests that both the obturator and the sciatic nerve also provide a major contribution to the innervation of the knee joint. Although speculative, intrathecal (IT) morphine use was most likely needed to provide analgesia in the sciatic nerve distribution.

Rathmell et al. demonstrated that combining small-dose (0.2 mg) IT morphine sulfate with PCA morphine provides good to excellent pain control in most patients after total hip or knee arthroplasty. However, Tarkkila et al. found that both IT morphine (0.3 mg) and continuous femoral 3-in-1 block alone were insufficient for the treatment of severe pain after major knee surgery. We hypothesized that coupling the femoral nerve block with small dose of IT morphine could be more effective than 3-in-1 block alone. The analgesic effect of spinal morphine combined with continuous femoral nerve block after TKR has not yet been established; accordingly, we arbitrarily chose 0.1 mg morphine to supplement spinal anesthesia.

In the present study, we investigated the value of an IT morphine in patients receiving continuous 3-in-1 nerve block with a PCA technique for analgesia after unilateral TKR. The postoperative analgesia and side effects were evaluated.
MATERIALS AND METHODS

After informed consent from all patients and with institutional ethics committee approval, 45 ASA physical status I or II patients scheduled for elective unilateral TKR under spinal anesthesia (SA) were enrolled. Patients were excluded if they met any of the following criteria: contraindications to regional anesthesia (e.g., local infection, sepsis, coagulation abnormality), age > 90 yr, allergy to local anesthetic and/or opioid, preexisting neurological deficit in the lower extremity, or inability to comprehend pain scales or to use a PCA device. After surgery, each patient was educated about the use of the PCA connected to the femoral catheter. There were no significant differences between the groups concerning demographic characteristics, anesthetic time, and operating time (Table 1).

We designed this prospective study to evaluate the analgesic efficacy and side effect profile of 0.1 mg of IT morphine and 10 μg of IT fentanyl when each were combined with continuous femoral 3-in-1 nerve block after TKR. Patients were randomized to receive either IT morphine or IT fentanyl added to bupivacaine. All patients received no premedication. Patients received 1 mg midazolam intravenously several minutes before SA. SA was performed, with the patient in the lateral position, at the L3−4 or 4−5 intervertebral space by using a 25 gauge Quincke needle. Free flow of clear cerebrospinal fluid before and after the injection was obtained. All patients received 8−13 mg of 0.5% hyperbaric bupivacaine with epinephrine 0.05−0.1 mg in combination with either 0.1 mg of morphine or 10 μg of fentanyl into the IT space, depending on group allocation. The doses of bupivacaine and epinephrine were chosen at the discretion of the attending anesthesiologist.

The dose of 0.1 mg morphine was prepared by extraction of 0.1 ml from the solution mixed with 0.1 ml (1 mg) of morphine and 0.9 ml saline. Further intraoperative sedation consisted of 1 mg increments of IV midazolam. All patients received supplemental oxygen via nasal cannula for the duration of the procedure. Standard monitoring, including noninvasive blood pressure, electrocardiogram, and oxygen saturations, was used in all patients for the duration of surgery. All surgeries were conducted by the same surgeon. Surgery was performed with a tourniquet applied in the thigh and inflated at 300 mmHg.

All femoral nerve blocks were performed by the same anesthesiologist before the induction of SA. Patients were placed in the supine position and the pulse of the femoral artery was identified. The needle entry site was at the level of the inguinal skin crease 1−2 cm lateral to the femoral pulse. The femoral nerve was accurately located with a peripheral nerve stimulator (Innervator®, Fisher&Paykel, New Zealand) connected to the proximal end of the metal inner needle of plastic cannula (Contiplex® set; 70 mm: B.Braun, Melsungen, Germany). With a starting output of 2.0 mA at 1-H frequency, the needle was advanced cephalad in a sagittal plane at an angle of 30°−40° to the skin until twitches of the quadriceps femoris muscle (ascension of the patella) were elicited. Its position was then judged adequate when output lower than 0.4 mA still elicited contractions of the quadriceps. The femoral nerve sheath was distended with 5 ml of saline. A 20-gauge catheter was threaded 10−15 cm into the psoas compartment from the skin and tunneled 5 cm subcutaneously. The catheter was secured in place by tying the catheter to the skin with a silk and then it was covered with a surgical drape (Ioban™ 2, 3M Health Care, USA). At the end of operation, a 20 ml bolus of 0.25% bupivacaine with epinephrine 1 : 200000 was administered into the femoral catheter after a negative aspiration test for blood. During the injection, firm pressure was manually applied just distally to the catheter entry point to encourage the cephalad spread of the local anesthetic. One hour after the bolus injection, a continuous infusion of 0.125% bupivacaine at the rate of 2 ml/h plus PCA boluses of 1 ml.

Table 1. Demographic and Perioperative Data

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n = 20)</th>
<th>Group 2 (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>65.5 ± 7.2</td>
<td>67.7 ± 6.1</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>0/20</td>
<td>1/19</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>62.4 ± 10.6</td>
<td>60.5 ± 8.2</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>150.4 ± 5.6</td>
<td>151.3 ± 9.1</td>
</tr>
<tr>
<td>Operating time (min)</td>
<td>108.8 ± 27.6</td>
<td>107.3 ± 27.4</td>
</tr>
<tr>
<td>Anesthetic time (min)</td>
<td>196.0 ± 31.7</td>
<td>180.0 ± 34.6</td>
</tr>
<tr>
<td>Total bupivacaine (mg per 2 days)</td>
<td>159.0 ± 32.2</td>
<td>147.0 ± 21.9</td>
</tr>
<tr>
<td>Bolus bupivacaine (mg per 2 days)</td>
<td>33.8 ± 26.6</td>
<td>21.8 ± 12.8</td>
</tr>
<tr>
<td>Blood loss (ml per 2 days)</td>
<td>893 ± 262</td>
<td>1002 ± 358</td>
</tr>
<tr>
<td>Number of patients transfused</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Hospital stay (day)</td>
<td>30.2 ± 16.0</td>
<td>30.9 ± 13.3</td>
</tr>
</tbody>
</table>

Values are mean ± SD except gender. Group 1: IT fentanyl, Group 2: IT morphine.
with a lockout of 10 min was begun, which was then continued into the postoperative period for 3 or 4 days. The amount of postoperative bupivacaine received by each patient in the first 2 days was noted and the femoral catheters were removed on the 3rd or 4th postoperative day (POD).

The intensity of pain at rest and with a standardized motion of the knee (30° of passive flexion) was assessed by the patients using a visual analog scale (VAS) (0 = no pain, 100 = worst possible pain), 1 hour after arrival to the PACU, at 6PM on the day of operation, and at 9AM and 6PM on POD1 and POD2, respectively. Sensory block by using a pinprick test with a blunt needle in the distributions of the femoral (anterior aspect of the thigh), the obturator (inner aspect of the knee), and the lateral femoral cutaneous nerve (outer aspect of the knee) were assessed in the middle third of the thigh twice a day by an independent observer. It was confirmed by reduced sensation involving the distribution of each nerve compared with contralateral thigh.

For postoperative analgesia, diclofenac (90 mg two times daily) was regularly administered IM to all patients on arrival to the ward and for the first two postoperative days. If the VAS was >50 or patient requested, 90 mg of diclofenac or 0.5 mg of butorphanol IM was supplemented in both groups.

The type of analgesic used was left to the treating physician. Antiemetic medications consisted of first-line treatment with 10 mg IV metoclopramide and second-line treatment consisting of 4 mg IV ondansetron on the request of patient. Treatment for pruritus consisted of 4 mg IM chlorpheniramine, and treatment in all cases was initiated on patient request. Naloxone was reserved for treatment of pruritus that was resistant to chlorpheniramine therapy. Supplemental analgesia, antiemetic and antipruritic medications, and side effects were recorded for each group at each measuring interval.

The presence and severity of nausea was assessed by using an ordinal scale (0 = no nausea; 1 = mild; 2 = moderate; 3 = severe). The presence and severity of pruritus was assessed by using an ordinal scale (0 = no itch; 1 = mild; 2 = moderate; 3 = severe).

All patients in this series were monitored for respiratory depression by assessment of respiratory rate, which is the means routinely used to monitor patients after IT morphine in our institution. Respiratory rates were assessed by the study anesthesiologist at the measurement times and also by the ward nurses every 4 h. Respiratory depression was defined as a respiratory rate < 10 breaths/min. Supplemental oxygen was not placed routinely; however, if at any time their respiratory rate was < 10 breaths/min, oxygen 3 l/min via nasal cannula was added. Intravenous naloxone in 0.1 mg increments was to be given for treatment of respiratory depression.

Sedation was scored according to the following scale: 0 = alert; 1 = drowsy; 2 = sleeping, easily aroused; and 3 = sleeping, difficult to arouse. Significant sedation was defined as a sedation score of 3. Because all patients had Foley catheters inserted prior to surgery, no attempt was made to determine the incidence of urinary retention.

At the end of the operation, a hemovac evacuator (Zimmer, USA) was placed until POD3 and applied positive pressure to the hemovac for the first 2 hours postoperatively in an attempt to reduce blood loss. Indications for blood transfusion included hemoglobin < 9 mg/dl without clinical symptoms or < 10 mg/dl associated with tachycardia, or hypotension. Postoperative blood loss and transfusions for the first 2 days were also recorded in both groups.

After surgery, all the groups started identical physical therapy regimens. Rehabilitative therapy was initiated on POD1 with an aid of a physical therapist once a day. The physiotherapist encouraged the patients to perform straight leg raise and quadriceps strength exercise. During POD3 to 7, a continuous passive motion machine was applied, and the goal was a passive knee flexion of 100° during that time. From POD8 until discharge, the patients performed active and assisted knee and hip flexion and extension exercises against gravity in the physical therapy room twice daily. Getting up from bed was encouraged as soon as possible, and ambulation with a crutch was begun after 1 week postoperatively. The surgical team, also unaware of the study group assignments, determined patients’ suitability for discharge during morning rounds. Suitability for discharge was based on knee flexion to 130°, knee extension of 0°, lower limb flexion of 90° with 0° of knee extension, adequate pain control, and absence of complications. Data on the duration of hospitalization after surgery were collected from the patient’s medical record after the patient was discharged. All data were collected by an anesthesiologist not involved in the administration of anesthesia nor in patient care in the recovery room.

Statistical analysis was performed with the SPSS software (version 12.0, USA). Data from the groups were compared by using Student’s t-test for parameters in Table 1, VAS pain scores and bupivacaine bolus use, and by using chi squared analysis for gender, number of patient transfused, postoperative
RESULTS

Out of 45 patients, 5 patients did not complete the study for the following reasons: catheter dislodgement, interruption of continuous femoral nerve infusion on patient request due to severe PONV, altered femoral infusion rate from 2 to 4 ml/h due to severe pain, excitement occurring after inadvertent administration of naloxone 0.5 mg ordered by the surgeon due to severe pruritus resisting chlorpheniramine therapy, and inadequate surgical block. When a patient was removed from the trial, the same trial was subsequently performed in another patient. The final total of 40 patients was equally distributed between the two groups.

Patients in Group 2 reported significantly lower VAS pain scores at rest than those in Group 1 at 6PM on the day of operation and POD1 9AM, respectively (P < 0.05) (Fig. 1). Although, there was no significance, VAS pain score during movement at 6PM on the day of operation in Group 2 was lower than that in Group 1 (Fig. 2). Cumulative PCA bolus use of 0.125% bupivacaine (ml) at 6PM on the day of operation, POD1 9AM and POD2 9AM in Group 2 was significantly lower than those in Group 1 (P < 0.05) (Fig. 3). There was no significant difference between the groups regarding the total consumption of 0.125% bupivacaine (mg) during the first 2 postoperative days (Table 1). Ten of the 20 patients from Group 2 complained of mild to severe pruritus versus none from Group 1 (P < 0.01) (Table 2). Five of the 10 patients received treatment for the pruritus. All 5 patients responded to chlorpheniramine therapy and did not require naloxone therapy. The incidences of PONV, the use of antiemetic medication, supplemental analgesia, and hospital stay...
Table 2. Incidence of Nausea, Vomiting, Pruritus and Rescue Medicine

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n = 20)</th>
<th>Group 2 (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>15 (75)</td>
<td>8 (40)</td>
</tr>
<tr>
<td>1</td>
<td>3 (15)</td>
<td>7 (35)</td>
</tr>
<tr>
<td>2</td>
<td>2 (10)</td>
<td>4 (20)</td>
</tr>
<tr>
<td>3</td>
<td>0 (0)</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>3 (15)</td>
<td>7 (35)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>0 (0)</td>
<td>10 (50)*</td>
</tr>
<tr>
<td>Rescue antiemetics</td>
<td>5 (25)</td>
<td>7 (35)</td>
</tr>
<tr>
<td>Rescue antipruritics</td>
<td>0 (0)</td>
<td>6 (30)*</td>
</tr>
<tr>
<td>Rescue analgesics</td>
<td>10 (50)</td>
<td>7 (35)</td>
</tr>
</tbody>
</table>

Data are number (%) of patients. Group 1: IT fentanyl, Group 2: IT morphine. *: P < 0.05 compared with Group 1.

were comparable in both groups (Table 1, 2). No patient in either group had a respiratory rate < 10 breaths/min and sedation score > 1. No significant difference was noted between the groups in the percent of patients with sensory block in each nerve for the first 2 days (Fig. 4). Success rates of complete 3-in-1 block in Groups 1 and 2 were 80 and 85%, respectively. The doses of spinal bupivacaine used were 8—13 mg (mean = 10 mg) in Group 1 and 9—12 mg (mean = 9.9 mg) in Group 2.

**DISCUSSION**

The results of our study demonstrate that IT morphine in combination with femoral 3-in-1 block provides improved analgesia, whereas IT fentanyl is not effective to any clinically significant extent. Our experience indicates that 3-in-1 block alone is insufficient to provide an ideal analgesia for pain control, and addition of IT morphine to bupivacaine produce a better analgesia, as one part of multimodal analgesia after TKR.

Tarkkila et al. found superior analgesia with 0.3 mg of IT morphine when compared with a continuous femoral 3-in-1 block. However, both IT morphine and femoral 3-in-1 block alone were insufficient for the treatment of severe pain after major knee surgery. Rathmell et al. demonstrated that patients receiving 0.2 or 0.3 mg of IT morphine were more satisfied with their pain control than those receiving 0.0 or 0.1 mg after both hip and knee arthroplasty. We assumed that the effective dose of IT morphine could be reduced to smaller one than those they speculated, if combined with 3-in-1 block. Thus, we arbitrarily chose 0.1 mg for IT morphine dose in our study. A future research project for a minimal effective dose of IT morphine when combined with 3-in-1 block could be performed.

The sensory innervation of the knee derives from the obturator, femoral, and lateral femoral cutaneous nerves as well as from the sciatic nerve. In 1973, Winnie et al. introduced the inguinal paravascular three-in-one block, which allegedly provides anesthesia of three nerves—the femoral, lateral femoral cutaneous, and obturator nerves—with a single injection. However, several investigators reported that the femoral nerve block does not consistently produce anesthesia of the obturator nerve. Therefore, difficulties were encountered in obtaining a complete 3-in-1 blockade via the anterior approaches in adults. The success rate of a complete 3-in-1 block in our study was 82.5% of patients. In the study of Marhofer et al., a complete 3-in-1 block, including a reduction of sensibility in all three nerves to less than 30% of the initial value, was observed in 85% of patients. In contrast, Capdevila et al. showed that 3-in-1 block provide sensory blockade of the three lumbar plexus nerves that supply the thigh in only 35% of procedures. In their study, however, the blockade was considered as a success when a total sensory blockade presented and a failure when partial or absent sensory blockade presented. Accordingly, we suggest that IT morphine may be a useful additive for incomplete 3-in-1...
block. Pain persisting in the back of the knee after a 3-in-1 nerve block suggests that the sciatic nerve provides a major contribution to the innervation of the knee joint. Several investigators demonstrated that in most patients, adequate analgesia after TKR cannot be achieved with continuous femoral nerve block alone and that the addition of continuous sciatic nerve block or continuous epidural analgesia with hydromorphone renders a significant improvement in analgesia. In our study, we considered that the dose of IT morphine will simultaneously provide analgesia for the sciatic nerve distribution. Our study confirmed that the analgesic duration of IT morphine is longer than that of IT fentanyl. Postoperative severe pain after TKR persists more than 2 days, therefore, IT morphine is more effective than IT fentanyl for analgesia after TKR. This is consistent with a previous study by Sibilla et al. in which they found that the quality of postoperative analgesia with 25 μg fentanyl was inferior to that with 0.1 mg morphine and not different from placebo in patients undergoing cesarean section.

The most feared complication of opioid administration is respiratory depression. No patient in either group had a respiratory rate below 10 breaths/min. The most reliable respiratory depression. No patient in either group had a depressed level of consciousness. A significant sedation in our study was also not seen in all patients; thus, we believe that no patient in either group had signs of respiratory depression. It has been shown that even a much larger dose of 25 μg intrathecal fentanyl in elderly patients did not lead to respiratory depression. Bailey et al. found that IT morphine produced dose-related respiratory depression in adult male volunteers, and respiratory depression was significant after 0.2 or 0.4 mg and profound and prolonged after 0.6 mg. In the study of Murphy et al., two patients who received 0.2 mg of IT morphine developed transient moderate hypoxemia that responded to the administration of 40% oxygen, however, no patient developed severe hypoxemia in their study. Slappendel et al. believed that 0.1 mg of IT morphine added to bupivacaine for total hip surgery provides excellent postoperative analgesia in the first 24 h, and does not cause significant respiratory depression. They further stated that after this IT morphine dose, there seems to be no need for routine intensive care-based recovery, even in elderly patients. Likewise, Glass recommended that doses of possibly 0.05—0.1 mg IT morphine may well be as effective and much safer. We also believe that 0.1 mg of IT morphine provides effective analgesia and may be relatively safer after TKR.

Although this did not reach statistical significance, PONV in our study occurred more frequently with IT morphine group compared with IT fentanyl group. The reported incidences of PONV associated with 0.1 mg IT morphine were 80% and 65% of patients. In our study, PONV incidence in IT morphine group was 60% of patients. Nevertheless it was too low to allow any meaningful comparisons, Palmer et al. found that the incidence of nausea and vomiting was low in all fentanyl groups (5 to 45 μg), and no patient requested or required treatment for these side effects. IT fentanyl has also been shown to have antiemetic effects. This is further confirmed through the fact that nausea and vomiting were more pronounced in saline group than in the other fentanyl groups (10 or 20 μg). Several authors have shown that the incidences of PONV in IT fentanyl were 20% and 13% of patients. In our study, PONV incidence in IT fentanyl group was 25% of patients. Although not confirmed, the results of these studies suggest that the incidences of PONV may be more frequent in IT morphine than those in IT fentanyl. In a previous systematic review by Dahl et al., they also found that nausea and vomiting occurred less frequently with the lipophilic opioids than with morphine.

Pruritus is another common side effect of IT opioids and at times may be quite distressing to the patient. Pruritus in our study occurred only in IT morphine group. Only one study has made direct comparisons between IT morphine and fentanyl in patients undergoing cesarean section. In that study, the incidence of pruritus was less with 25 μg fentanyl compared with 0.1 mg morphine. This result is consistent with our study. According to other authors, the incidences of pruritus with 0.1 mg IT morphine added to tetracaine and bupivacaine have been shown to be 40% and 38%, respectively. For IT fentanyl, the occurrence of pruritus has been reported to be 75% in 10 μg fentanyl only, 57% in 10 μg fentanyl plus 3 mg bupivacaine, and 27% in 10 μg fentanyl plus 7.5 mg bupivacaine. The doses of spinal bupivacaine being used in our study were 7.5—13 mg (mean 10 mg) in combination with 10 μg fentanyl, and no pruritus has been appeared. Similarly, Kim et al. also reported no pruritus in patients who received 10 μg fentanyl added to 10 mg bupivacaine spinal anesthesia. Interestingly, these data assume, but not verified, that there may be a trend toward decreasing pruritus as spinal bupivacaine dose increased. It may be that the addition of
bupivacaine to fentanyl leads to an alteration of the fentanyl dose-response relation for pruritus.\textsuperscript{31} It has been shown that spinal bupivacaine 2.5 mg reduces the incidence of pruritus of fentanyl 25 μg, and the mechanism can be either neuronal blockade or direct modulation of the opioid receptor.\textsuperscript{32,33} In our study, fentanyl was added to spinal bupivacaine in control group instead of bupivacaine alone. Fentanyl is commonly used as a IT opioid in contemporary clinical practice in our institution. Opioid and bupivacaine administered together intrathecally have a potent synergistic analgesic effect.\textsuperscript{33,34} IT fentanyl causes neither by itself nor in combination with bupivacaine any further depression of efferent sympathetic activity.\textsuperscript{34} This further confirms that sub-therapeutic doses of local anaesthetic with the addition of fentanyl could provide adequate surgical block without affecting hemodynamic stability\textsuperscript{20}; thus, supplementary fentanyl was used in control group to enhance the effect of bupivacaine and to minimize hemodynamic instability by sparing the dose of bupivacaine, especially in the elderly.

Our study has several limitations. We measured respiratory rates only intermittently and pulse oximetry has not been used for continuous assessment of arterial oxygen saturation on the orthopedic ward; thus, significant hypoxemia between observations cannot be excluded. However, with 0.1 mg IT morphine in our study, clinically significant respiratory depression should be rare. Unfortunately, the doses of bupivacaine used in our study were not standardized, but those depression should be rare. Unfortunately, the doses of morphine in our study, clinically significant respiratory observations cannot be excluded. However, with 0.1 mg IT fentanyl, 25) and in groups saline and 12.5 μg fentanyl.\textsuperscript{19} In a previous systematic review by Dahl et al.,\textsuperscript{28} they also found that 10–25 μg fentanyl does not provide meaningful postoperative analgesia; thus, we believe that 10 μg fentanyl did not affect the difference in analgesia postoperatively.

In conclusion, the addition of IT morphine 0.1 mg to continuous 3-in-1 block provides improved analgesia for the first one day after unilateral TKR. We believe that IT morphine 0.1 mg does not cause significant respiratory depression and sedation. Further study should be done on the optimal doses of IT morphine when combined with a 3-in-1 block.

REFERENCES

23. Glass PS: Respiratory depression following only 0.4 mg of intrathecal morphine. Anesthesiology 1984; 60: 256-7.