

Postoperative analgesia with minidose intrathecal morphine for bipolar hip prosthesis in extremely elderly patients

KAZUNORI YAMASHITA^{1,2}, MAKOTO FUKUSAKI¹, YUKO ANDO², TAKAHIRO TANABE¹, YOSHIAKI TERAOKA¹,
and KOJI SUMIKAWA²

¹Department of Anesthesia, Nagasaki Rosai Hospital, Sasebo, Japan

²Division of Anesthesiology, Department of Translational Medical Science, Nagasaki University School of Medicine, 1-7-1 Sakamoto, Nagasaki 852-8501, Japan

Abstract

Purpose. It is known that an optimal dose of intrathecal morphine for analgesia after total hip arthroplasty in older patients is 0.1 mg. On the other hand, minidose intrathecal morphine (0.05 mg) is useful for analgesia after the transurethral resection of the prostate in elderly patients. We evaluated the postoperative analgesic effect of minidose intrathecal morphine after bipolar hip prosthesis in seniors (age 85 years or more) undergoing spinal anesthesia.

Methods. Twenty seniors undergoing bipolar hip prosthesis under spinal anesthesia were randomly allocated to one of two groups. Group A ($n = 10$) received intrathecal injection of 0.5% isobaric bupivacaine, 2.8 ml, and group B ($n = 10$) received intrathecal injection of 0.5% isobaric bupivacaine, 2.8 ml, plus morphine, 0.05 mg. Pain, nausea, and itching were evaluated using a numerical rating scale, ranging from 0 to 10, at 0, 4, 8, 12, and 24 h after the operation.

Results. The values on the numerical rating scale for pain in group B were significantly lower than those in group A at 4, 8, and 12 h after the operation. There were no significant differences between the groups in the values on the numerical rating scale for nausea or itching throughout the time course of the study. No patient in either group showed hypoxemia or respiratory depression throughout the time course.

Conclusion. The results show that minidose intrathecal morphine provides a good analgesic effect without side effects, and it would be an effective and safe procedure for bipolar hip prosthesis in seniors.

Key words Minidose intrathecal morphine · Extremely elderly patients · Bipolar hip prosthesis

Introduction

Intrathecal morphine provides good postoperative pain relief in patients undergoing total hip arthroplasty

(THA), cesarean section, or transurethral resection of the prostate [1–4]. Murphy et al. [1] reported that 0.1 mg of intrathecal morphine provided the best balance between analgesic efficacy and side-effect profile in older patients (older than 65 years) undergoing THA.

On the other hand, Sakai et al. [3] reported the effectiveness of minidose (0.05 mg) intrathecal morphine for patients undergoing transurethral resection of the prostate. We evaluated whether minidose (0.05 mg) intrathecal morphine could provide effective postoperative analgesia in seniors (age, 85 or more) undergoing bipolar hip prosthesis under spinal anesthesia.

Patients and methods

With the approval of the Institutional Human Ethics Committee and written informed consent from each patient, we studied 20 patients aged 85 years or more, of American Society of Anesthesiologists physical status I–III, who were scheduled for bipolar hip prosthesis under spinal anesthesia. They were allocated to one of two groups according to a computer-generated table of random numbers. Excluded were patients who had cognitive dysfunction, dementia, a history of allergy to any nonsteroidal anti-inflammatory drugs (NSAIDs) or opioids, coagulopathy, renal dysfunction, or peptic ulcer disease. Spinal anesthesia was achieved at the L3–4 interspace with a 25-gauge Quincke needle, using 0.5% isobaric bupivacaine, 2.8 ml. Group A ($n = 10$) received no intrathecal morphine. Group B ($n = 10$) received intrathecal morphine 0.05 mg (preservative free) in combination with bupivacaine. An anesthesiologist prepared the drugs, and another anesthesiologist, who was blinded to the group assignment, conducted the anesthesia. Prophylactic oxygen therapy was given with a nasal cannula ($2\text{ l}\cdot\text{min}^{-1}$) in all patients throughout the study. The level of sensory block was determined by pinprick. The operation was started about 30 min after

Address correspondence to: K. Yamashita

Received: April 8, 2008 / Accepted: July 3, 2009

Table 1. Characteristics of patients in group A and group B

	Group A (<i>n</i> = 10)	Group B (<i>n</i> = 10)
Age (years)	88 ± 4	88 ± 3
Sex (M/F)	1/9	2/8
Height (cm)	145 ± 7	150 ± 10
Weight (kg)	41 ± 7	45 ± 11
Duration of surgery (min)	57 ± 9	53 ± 10
Peak level of sensory block	T4–10	T4–10

Group A, without intrathecal morphine; group B, with intrathecal morphine 0.05 mg

spinal block. Noninvasive blood pressure, percutaneous oxygen saturation (S_{pO_2}), respiratory rate, electrocardiograph, and heart rate were monitored continuously throughout the study.

All patients were instructed to express the intensity of postoperative pain at rest, and the intensity of pruritus and nausea, with a numerical rating scale (NRS) that ranged from 0 to 10 (0 being no pain, and 10 being the worst pain imaginable) at 0, 4, 8, 12, and 24 h after the operation. Pain and adverse effects were treated only when requested by patients. Postoperative pain was treated with a 25-mg diclofenac suppository. The protocols to treat patients' symptoms included metoclopramide, 10 mg i.v. for nausea, and promethazine hydrochloride, 20 mg i.m. for pruritus. The use of these additional medications was recorded. Hypotension (a greater than 25% decrease from the preoperative baseline mean blood pressure value), hypoxemia ($S_{pO_2} < 90\%$), and respiratory depression (respiratory rate < 10 breaths·min⁻¹) were also evaluated at 0, 4, 8, 12 and 24 h after the operation. The assessments and treatments were carried out by nurses blinded to the group allocation.

Data were analyzed using the Mann-Whitney *U*-test. Adverse effects and treatments were compared with the χ^2 test. Values for results were expressed as means ± SD, and $P < 0.05$ was considered significant.

Results

The demographic and intraoperative data were similar in the two groups (Table 1). There was no significant difference in the spinal anesthesia level between the two groups. No patient experienced respiratory depression or hypoxemia during the 24 h after the operation. The NRS values for pain are presented in Fig. 1. The NRS values in group B were significantly lower than those in group A at 4, 8, and 12 h after the operation ($P < 0.05$). There were no significant differences in the numbers of pain-free patients between groups A and B. The interval from the end of the operation to the first use of supplemental analgesic was significantly longer in group

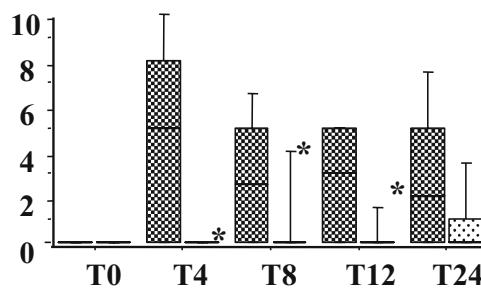


Fig. 1. Individual values on the numerical rating scale for pain are shown in the bupivacaine group (gray bars) and the bupivacaine-plus-morphine group (dotted bars). Values are expressed as medians (middle lines in the bars) with 25th–75th percentiles. Capped lines indicate 10th–90th percentiles of the data. Asterisks indicate $P < 0.05$ compared to the bupivacaine group, using the Mann-Whitney *U*-test. T0, 0 h after operation; T4, 4 h after operation; T8, 8 h after operation; T12, 12 h after operation; T24, 24 h after operation

B than in group A ($P < 0.05$), and the number of patients who required treatment of pain was significantly lower in group B than in group A ($P < 0.05$; Table 2).

There were no significant differences between the groups in values on the NRS for nausea and pruritus.

Discussion

The results of the present study show that minidose (0.05 mg) intrathecal morphine provides good postoperative analgesia without side effects in seniors undergoing bipolar hip prosthesis.

Insufficient postoperative pain relief can cause postoperative cognitive dysfunction, including delirium, especially in senile patients [5].

Murphy et al. [1] reported that the optimal dose of intrathecal morphine was not 0.05 mg but 0.1 mg in older patients (mean age, 75 years) undergoing total hip arthroplasty (THA). In the present study, 0.05 mg of intrathecal morphine was effective in seniors undergoing bipolar hip prosthesis. The reason for the effectiveness of minidose morphine in the present study can be explained as follows.

Table 2. Incidence of postoperative pain, adverse effects, and treatments in group A and group B

	Group A (n = 10)	Group B (n = 10)
Number of patients with:		
No pain	2	5
Nausea	0	1
Pruritus	1	2
Treatment of pain	8	3*
Treatment of nausea	0	0
Treatment of pruritus	0	1
Respiratory depression	0	0
Hypoxemia	0	0
Interval from the end of operation to the first use of supplemental analgesics (h)	7.9	19.6*

* $P < 0.05$ compared to group A

First, bipolar hip prosthesis is less invasive than THA. Thus, a lower dose of morphine was enough in the present study as compared to the dose used in the above study by Murphy et al.

Second, it would not be likely that older patients would require lower doses of morphine. It has been reported that the dose requirements for drugs, including morphine, decreased with increasing age [6–8]. Baillie et al. [6] reported that oral doses of morphine produced higher plasma concentrations in elderly volunteers (mean age, 74 years) than in young volunteers (mean age, 27 years), because first-pass metabolism and clearance in the elderly group had decreased. Owen et al. [7] reported that the peripheral compartment concentration of morphine was higher in older subjects than in younger subjects after intravenous administration. In the present study, although morphine was administered intrathecally, the plasma concentrations of morphine may have been similar to those in the study by Murphy et al. [1]. It has been demonstrated that a synergistic analgesic effect results from the simultaneous stimulation of spinal and supraspinal opioid receptors [9–11]; however, this effect has not been shown in humans. A supraspinal effect of an intrathecal opioid requires systemic absorption. Thus, the analgesic effect of a lower dose of intrathecal morphine in seniors may be due to the decrease in its metabolism and clearance.

Intrathecal morphine is associated with adverse effects, including respiratory depression, pruritus, and nausea [1–4,12–14]. Palmer et al. [15] reported the disadvantageous effects of an increased dose of intrathecal morphine. In the present study, we observed one case of nausea and two cases of pruritus with 0.05 mg of intrathecal morphine, and the incidence of nausea or pruritus was not significantly different between our two groups. Sp_{O_2} and respiratory rate were observed in all patients throughout the first 24 h postoperatively for

detecting delayed respiratory depression due to intrathecal morphine.

Most elderly patients have some kind of underlying disease, and so it is necessary to observe elderly patients carefully in the postoperative period. In the present study, we monitored ECG, Sp_{O_2} , and respiratory rate for all patients postoperatively to observe them carefully.

However, prophylactic oxygen therapy is controversial postoperatively, because it may blind the delayed respiratory depression caused by intrathecal morphine.

It is not known whether 0.05 mg of intrathecal morphine is the optimal dose for seniors undergoing bipolar hip prosthesis, but the dose-dependent effect would not need to be evaluated because it has been reported that 0.1 mg of intrathecal morphine showed good analgesic results after THA [3]. Although we found no disadvantageous effects, further study is needed to clarify the safety of intrathecal morphine for seniors.

We conclude that minidose intrathecal morphine (0.05 mg) provides good postoperative analgesia without side effects, and would be an effective analgesic procedure for seniors undergoing bipolar hip prosthesis.

References

1. Murphy PM, Stack D, Kinirons B, Laffey JG. Optimizing the dose of intrathecal morphine in older patients undergoing hip arthroplasty. *Anesth Analg.* 2003;97:1709–15.
2. Rathmell JP, Pino CA, Taylor R, Partin T, Viani BA. Intrathecal morphine for postoperative analgesia: a randomised, controlled, dose-ranging study after hip and knee arthroplasty. *Anesth Analg.* 2003;97:1452–7.
3. Sakai T, Use T, Shimamoto H, Fumano T, Sumikawa K. Minidose (0.05 mg) intrathecal morphine provides effective analgesia after transurethral resection of the prostate. *Can J Anaesth.* 2003; 50:1027–30.

4. Karaman S, Kocabas S, Uyar M, Hayzaran S, Firat V. The effects of sufentanil or morphine added to hyperbaric bupivacaine in spinal anaesthesia for Caesarean section. *Eur J Anesth.* 2005;23:285–91.
5. Fong HK, Sands LP, Leung JM. The role of postoperative analgesia in delirium and cognitive decline in elderly patients: a systematic review. *Anesth Analg.* 2006;102:1255–66.
6. Baillie SP, Bateman DN, Coates PE, Woodhouse KW. Age and the pharmacokinetics of morphine. *Age Ageing.* 1989;18:258–62.
7. Owen JA, Sitar DS, Berger L, Brownell L, Duke PC, Mitenko PA. Age-related morphine kinetics. *Clin Pharmacol Ther.* 1983;34:364–8.
8. Lugo RA, Kern SE. Clinical pharmacokinetics of morphine. *J Pain Palliat Care Pharmacother.* 2002;16:5–18.
9. Yeung JC, Rudy TA. Multiplicative interaction between narcotic agonisms expressed at spinal and supraspinal sites of antinociceptive action as revealed by concurrent intrathecal and intracerebroventricular injections of morphine. *J Pharmacol Exp Ther.* 1980;215:633–42.
10. Yeung JC, Rudy TA. Sites of antinociceptive action of systemically injected morphine: involvement of supraspinal loci as revealed by intracerebroventricular injection of naloxone. *J Pharmacol Exp Ther.* 1980;215:626–32.
11. Bian D, Ossipov MH, Ibrahim M, Raffa RB, Tallarida RJ, Malan TP Jr, Lai J, Porreca F. Loss of antiallodynic and antinociceptive spinal/supraspinal morphine synergy in nerve injured rats: restoration by MK-801 or dynorphine antiserum. *Brain Res.* 1999;831:55–63.
12. Rathmell JP, Lair TR, Nauman B. The role of intrathecal drugs in the treatment of acute pain. *Anesth Analg.* 2005;101:S30–S43.
13. Souron V, Delaunay L, Schiffrine P. Intrathecal morphine provides better postoperative analgesia than psoas compartment block after primary hip arthroplasty. *Can J Anaesth.* 2003;50:574–9.
14. Raffaelli W, Marconi G, Fanelli G, Taddei S, Borghi GB, Casati A. Opioid-related side-effects after intrathecal morphine: a prospective, randomised, double-blind dose-response study. *Eur J Anesth.* 2006;23:605–10.
15. Palmer CM, Emerson S, Volgoropolous D, Alves D. Dose-response relationship of intrathecal morphine for postcesarean analgesia. *Anesthesiology.* 1999;90:437–44.