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A PROSPECTIVE RANDOMIZED STUDY FOR POSTOPERATIVE PAIN RELIEF OF LOWER EXTREMITY FRACTURES: EFFICACY OF INTRATHECAL MORPHINE ADMINISTRATION

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ABSTRACT

Systemic opioids are known to be effective for controlling postoperative pain. Intrathecal morphine administration can be performed in a simple manner concurrently with spinal anesthesia. The purpose of this study was to investigate the efficacy of intrathecal morphine administration for the postoperative analgesia of lower extremity fractures. A prospective randomized study for postoperative pain relief was conducted. Fifty consecutive patients with a lower extremity fracture who underwent osteosynthesis under spinal anesthesia were enrolled. The patients were divided into two groups for comparative results. No baseline variable differences between the groups were observed. Twenty-two patients were assigned to a morphine group and were administered intrathecal bupivacaine combined with a single intrathecal injection of morphine. The other 28 patients were assigned to a control group and administered intrathecal bupivacaine alone. Pain intensity was assessed using the Visual Analog Scale (VAS). The use of supplemental analgesics, time of first request for supplemental analgesics, and side effects were investigated. During the initial 12 h after surgery, the VAS score was significantly lower in the morphine group ($p<0.05$). The use of supplemental analgesic drugs was significantly less in the morphine group ($p<0.05$). The time of first request of the control group was shorter than that of the morphine group ($p<0.001$). Side effects were seen more frequently in the morphine group though there was no significant difference. Although the use of morphine requires appropriate postoperative care, an intrathecal morphine injection can be an attractive analgesic for the postoperative pain of lower extremity fractures.

Key Words: Postoperative pain relief, Intrathecal morphine injection, Trauma surgery

INTRODUCTION

Postoperative pain is one of the problems of surgical treatment for lower extremity fractures. The best procedure for controlling postoperative pain in trauma surgery is still controversial. It is standard to use supplemental analgesics as needed for postoperative pain management. However, the effects of these methods are still not always sufficient. The utilization of opioids is widely

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accepted and effective for controlling the postoperative pain of spinal surgery.[1,2]

Some studies of preemptive analgesia have shown that the preoperative administration of systemic opioids is more effective in reducing postoperative pain than control conditions.[3-6] Intrathecal morphine is an established usage in the management of postoperative pain.[7,8] In the intrathecal administration of morphine, a single dose of a very small amount of morphine chloride is administered intrathecally together with local anesthetics such as isobaric bupivacaine at the time of spinal anesthesia. Its effectiveness is usually observed in the first 24 h after surgery. Side effects are rare if it is used at a low dose.[9]

Although the intrathecal administration of morphine is expected to be also applied to trauma surgery, to our knowledge, there are few reports that have investigated the efficacy of intrathecal morphine administration for the postoperative pain of lower extremity fractures.[10] Therefore, the purpose of a prospective randomized controlled trial was to investigate the efficacy of a single intrathecal shot of morphine for the postoperative analgesia of such lower extremity fractures. Secondary measures included pain ratings, supplemental analgesic drugs, and side effects.

SUBJECTS AND METHODS

Between June 2006 and December 2007, 205 consecutive patients with fresh lower extremity fractures underwent surgery under spinal anesthesia in our hospital. We excluded patients unable to understand the Visual Analog Scale (VAS) score, those 70 years or older, as well as those with complicating respiratory illnesses and at high risk of hypoxemia, dementia and mental disorders. A final total of fifty patients (male 25; female 25) whose mean age was 47 years (range, 16–69 years) were enrolled in this study. After Institutional Review Board approval was obtained, each patient signed a written consent form before surgery.

0.5% Isobaric bupivacaine (5mg/1ml) was used as the anesthetic for all patients. Mixing morphine chloride (3–5 μg/kg) with 0.5% bupivacaine (0.15–0.25 mg/kg), we assigned 22 patients injected intrathecally into the subarachnoid during spinal anesthesia to the morphine group, and 28 patients who received anesthesia by 0.5% bupivacaine alone to the control group. All patients were randomly divided into two groups for comparative examination—the morphine group if their identification (ID) for this hospital ended with an even number, and the control group if it ended with an odd number.

After surgery, the patients were asked to rate their pain using the VAS. Study items were the VAS (0–100:0 mm = no pain, 100 mm = worst pain imaginable) of pain from immediately after surgery (at Oh) to 1 week. VAS was recorded by questionnaires at 0, 4, 8, 12, 24, 48, 72, and 168 h (1 week) after surgery. All questionnaires were answered by self-reported patients with nurses in support. If these initial procedures failed to achieve adequate analgesia, supplemental analgesic agents were used at a patient's request.

When so desired by patients, postoperative analgesics were used according to the same prescription in both groups. The patients were first given a diclofenac sodium suppository (50 mg). If the effects of diclofenac sodium were insufficient, or there were any reasons for not using it, the patients were given 50 mg ketoprofen by intramuscular injection. The total number of times patients requested supplemental analgesics was evaluated up to 72 h after surgery. The time of each initial request for supplement analgesics was recorded. Side effects such as nausea, vomiting, respiratory depression (degree of oxygen saturation of less than 90% using a pulseoximeter), and itching were also recorded by nurses for 72 h after surgery.

Statistical analysis

All values are expressed as the mean ± standard deviation. A standard StatView (SAS Institute, Cary, NC) software package was used for the statistical analysis. A nonparametric analysis (Mann-Whitney U test) was used for analyzing differences between the groups. P values less than 0.05 were considered statistically significant.

RESULTS

Itemized results for each group are shown in Table 1. There were no significant differences between the groups as to patient gender, age, body weight, operative time and bupivacaine dose. There were also no significant differences between surgical procedures.

The mean VAS score for each data collection time was depicted in Fig. 1. It was significantly lower in the morphine group 4 h after surgery, at a mean value of 16 ± 22 mm for the morphine group and a mean value of 66 ± 38 mm for the control group ($p<0.001$). From 4 to 12 h, the VAS score in the morphine group was lower than that in the control group ($P<0.05$). There was no significant difference between the two groups after 24 h. At other collection times, the VAS score in the morphine group was always less than 40.

The number of times patients requested supplemental analgesics until 72 h after surgery was 1.6 ± 2.0 in morphine group and 2.7 ± 1.9 in the control group. Note that the number of times such requests were made was significantly lower in the morphine group ($p<0.05$). In addition, the time until the first use of supplemental analgesics was 13 ± 9.8 h of the morphine group and 3.7 ± 1.8 h of the control group. The time until the first use of supplemental analgesics was significantly shorter in the control group ($p<0.001$).

The side effects that occurred are detailed in Table 2. Although there was no significant difference, side effects were observed in 10 patients (46%) in the morphine group and 5 (18%) in the control group. There were 5 cases of respiratory depression in the morphine group, but only 1 in the control group. The patients recovered by an administration of oxygen alone. Administration

Table 1 Details of the morphine group and the control group

Item	Morphine group	Control group	p-value
Number of patients	22	28	n.s.
Gender (Male / Female)	12/10	13/15	n.s.
Mean age	47.0 years (range 16–69)	47.0 years (range 18–69)	n.s.
Mean body weight	58.0 kg (range 35–88)	55.5 kg (range 30–104)	n.s.
Mean operative time	84 minutes (range 10–170)	90 minutes (range 30–193)	n.s.
Mean bupivacaine dose	14.5 mg (range 12–16)	14.0 mg (range 12–16)	n.s.
Intramedullary nailing	6 (27%)	6 (21%)	n.s.
ORIF	14 (64%)	16 (57%)	n.s.
CHS	1 (5%)	5 (18%)	
Percutaneous pinning	1 (5%)	-	n.s.
External skeletal fixation	-	1 (4%)	

n.s.: no significant difference
ORIF: open reduction and internal fixation
CHS: compression hip screw

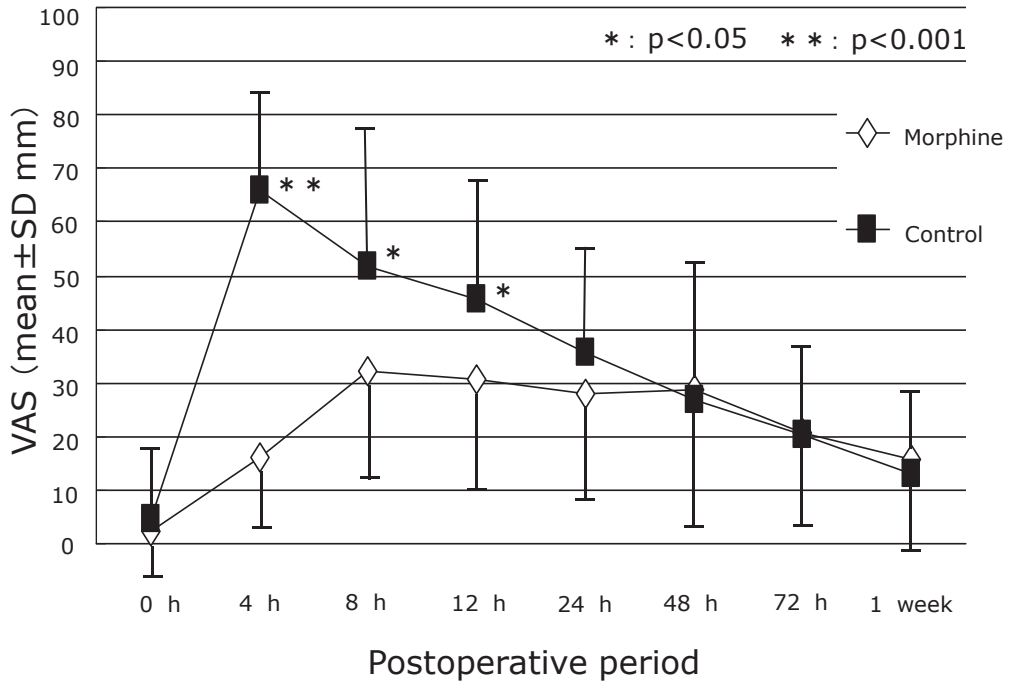

Fig. 1 Temporal change in VAS in the morphine group and control group
VAS: Visual analog scale
SD: Standard deviation
immediately after surgery (at 0 h)

Table 2 Details of side effects in the morphine group and control group

	Morphine group	Control group	p-value
Respiratory depression (SpO_2 < 90%)	5 (23%)	1 (4%)	n.s.
Nausea, vomiting	5 (23%)	3 (11%)	n.s.
Itching	2 (9%)	1 (4%)	n.s.
Total	10 (46%)	5 (18%)	n.s.

n.s.: no significant difference
SpO_2: percutaneous oxygen saturation

of the antagonistic drug (naloxone) was not necessary for only mild respiratory depression. There were no major complications such as severe respiratory depression or urinary retention.

DISCUSSION

The purpose of this study was to investigate the efficacy of a single intrathecal shot of morphine in a prospective randomized study in terms of pain VAS, supplemental analgesic drugs, and side effects. The study demonstrates that an intrathecal morphine injection adds a further

analgesic effect postoperatively. More side effects were observed in the morphine group than in the control group. However, there was no significant difference, and most of those side effects were minor complications.

The utilization of opioids is widespread and effective for controlling postoperative pain. Preemptive analgesia has been generally known and introduced for postoperative pain control. Since the discovery of morphine receptors in the brain by Pert *et al.*[11] in 1973 and the subsequent first report of clinical intrathecal administration of morphine chloride by Wang *et al.*[12] in 1979, such administrations have become one of the most common analgesia methods used worldwide.

The use of epidural morphine for postoperative analgesia has been a standard treatment in spinal surgery.[1,3,13-15] However, the procedure is sometimes made very difficult owing to degenerative change, which poses the risk of direct spinal cord injury and total spinal subarachnoid anesthesia.[16,17] Sensory or motor changes secondary to epidural analgesia can make it difficult to monitor neurologic functions in postoperative patients.[18]

Intrathecal morphine administration is simple to perform concurrently with spinal anesthesia, and is expected to be soon applied also to trauma surgery. However, to our knowledge, there are few reports that have investigated the efficacy of this procedure for the postoperative pain of lower extremity fractures.

In this present study, the postoperative VAS score was lower in the morphine group, while the use of supplemental analgesics was less common in the morphine group. Although side effects were more often observed in the morphine group, that was not significant. While the use of morphine requires appropriate postoperative care, intrathecal morphine was proven more effective for postoperative pain relief in lower extremity fractures.

Typical complications of morphine include respiratory depression, nausea, and rashes. In this procedure, respiratory depression is a clinically dangerous adverse reaction.[19] The risk of respiratory depression is reportedly low if care is taken to avoid overdosage.[20-22] No major complications were observed in either group, but a more watchful monitoring of respiratory status is required after this procedure.[23]

There were several limitations in this study. Admittedly, our study used a limited number of the same cases for lower extremities fractures, and the postoperative ambulation and rehabilitation were not investigated. The evaluation of results in this study was not blind. In addition, although a high-quality randomized double blind study would have been ideal for clinical trials, it is very difficult to perform.[24]

In conclusion, we investigated the efficacy of intrathecal morphine administration for postoperative analgesia of lower extremity fractures. Postoperative VAS was significantly lower, and analgesics were used less frequently in the morphine group. Although the use of morphine requires appropriate postoperative care, intrathecal morphine injection can be an attractive analgesia for the postoperative pain of lower extremity fractures.

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