

# Intrathecal morphine for post-operative analgesia in patients with fractured hips

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This prospective, randomised, double blind study examined the efficacy of intrathecal morphine for post-operative analgesia in Chinese patients undergoing surgery to repair fractured hips. There were a total of 40 American Society of Anesthesiologists physical status grade I to IV patients scheduled for surgery following a fractured neck of the femur. Patients were randomised to a control group in which they received subarachnoid plain 0.5% bupivacaine, 2.2 mL, and normal saline, 0.4 mL, giving a total volume of 2.6 mL, or to a study group in which they received plain 0.5% bupivacaine, 2.2 mL, and preservative-free morphine, 0.2 mg, diluted with normal saline to a total volume of 2.6 mL. Patients were monitored for up to 24 hours by staff blinded to group allocation. The level of pain was assessed by a visual analogue pain score and the time of first request for analgesia was noted. The results show the median pain-free period in the control group was nine hours (range, 2-24 hours), while it was 24 hours (range, 16-24 hours) in the morphine group, a significant difference ( $P < 0.05$ ). No major complications were reported. Intrathecal morphine is a useful technique for giving post-operative pain relief, especially in the elderly, in whom many other techniques cannot be safely used.

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## Introduction

The use of intrathecal morphine for post-operative analgesia was first documented more than 10 years ago.<sup>1</sup> It is an effective and simple method for post-operative pain management in a variety of operative procedures including caesarean section, transabdominal hysterectomy, cholecystectomy, hip surgery, aortic aneurysm surgery, and thoracotomy.<sup>2-7</sup> Intrathecal morphine in the elderly patient in whom systemic opioid side-effects are more pronounced, provides an attractive alternative. It also gives the added possible advantage of reduced metabolic response to surgery and anaesthesia, both of which increase morbidity and mortality.<sup>8</sup> The purpose of this prospective, randomised, double-blind study was to

examine the efficacy of intrathecal morphine for post-operative analgesia in patients with fractured hips in a district hospital setting.

## Methods

Approval was obtained for the study from the Ethics Committee of the Prince of Wales Hospital, and informed written consent was obtained from all patients. From July 1995 through December 1995, a total of 40 patients, American Society of Anesthesiologists (ASA) physical status I to IV, who were scheduled for emergency surgery for a fractured hip, including Austin Moore arthrodesis or compression hip screw, were prospectively randomised to one of the two study groups. Patients who had contraindications to regional anaesthesia, or an allergy to the study drugs (bupivacaine, morphine) were excluded from the study.

Each of the two study groups consisted of 20 patients. The patients in Group 1 (the control group) received plain 0.5% bupivacaine, 2.2 mL, and normal saline, 0.4 mL, making a total volume of 2.6 mL; the patients in Group 2 (the morphine group) received plain

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0.5% bupivacaine, 2.2 mL, and preservative-free morphine, 0.2 mg, diluted to a total volume of 2.6 mL with normal saline. To maintain the double-blind design, another investigator mixed the anaesthetic solution for the anaesthetist who was performing the block.

No patients were pre-medicated and all patients fasted for at least six hours pre-operatively. Intravenous fluid pre-loading with balanced salt solution (10 mL/kg) was given before the subarachnoid anaesthesia using plain 0.5% bupivacaine, with or without morphine, through a 23G Quincke spinal needle (B Braun, Melsungen, Germany) at the L2/3 or L3/4 level. The operation was allowed to proceed once the level of loss of cold (ice) discrimination had reached L1. No sedation was given to patients so that frequent communication and reassurance could be given.

All patients were monitored intra-operatively for heart rate (ECG lead II), non-invasive blood pressure and pulse oximetry. Oxygen was administered to all patients via a Hudson mask at a rate of 4 L/min regardless of their SpO<sub>2</sub> readings. Systolic blood pressure was maintained within 20% of the baseline reading (taken before subarachnoid anaesthesia was established) by replacing blood loss and further fluid load (10 mL/kg) with balanced salt solution. Boluses of ephedrine (3 mg per 5 minutes) were used intravenously if hypotension was not corrected by fluid alone.

After the operation, all patients were kept in the recovery area of the operating suite until their vital signs were stable (average, 20 minutes) before transferring back to the orthopaedic ward. During the first 24-hour post-operative period, all patients were given supplementary oxygen (4 L/min via a Hudson mask) and monitored continuously with pulse oximetry. Intravenous fluid therapy was discontinued if a patient could resume oral feeding but intravenous cannulae were kept patent by flushing with heparinised saline, 5 mL, every 4 hours, for 24 hours.

An assessment of pain level using the visual analogue pain score (VAPS: 0 = no pain, 100 = worst pain) was conducted by an investigator who was unaware of the constituents of the subarachnoid injection given. Scores were given 15 minutes before the subarachnoid anaesthesia and then at 2, 4, 8, 12, 16, 20, and 24 hours after the subarachnoid injection. The assessment was terminated if a patient requested rescue analgesia (dextro-propoxyphene, 50 mg, given intramuscularly every 4 hours, as required) and the study was considered completed for the patient. The time of first request for rescue analgesia was noted. The duration

of analgesia was determined from the time of subarachnoid injection to the patient's first request for analgesia.

Respiratory rate, sedation score (0 = awake, 1 = asleep/drowsy but easily roused, 2 = rousable only to pain, 3 = not rousable), nausea and vomiting score (0 = no nausea, 1 = nausea but no vomiting, 2 = vomited once in the last hour, 3 = vomited more than once in the last hour), blood pressure, heart rate, and complications (e.g. itchiness, urinary retention in those without Foley catheters), if present, were recorded every two hours by nursing staff on purpose-designed charts. Patients were monitored continuously with pulse oximetry for 24 hours from the time of subarachnoid injection and readings were recorded every two hours. Episodes of desaturation (SpO<sub>2</sub> <90% for 5 minutes or more) were also recorded and treatment initiated. Instructions for the treatment of complications (Table 1) were attached to patient observation charts to enable a prompt response, should complications occur.

Statistical analysis of the results was performed using Fisher's exact test, Student's *t* test and the Mann-Whitney U test, where appropriate. Differences were considered to be statistically significant if the probability of their arising by chance was less than 0.05 (P<0.05).

## Results

Four patients were excluded from the study: two because interpreters (relatives of patients) left before the 24-hour observation period elapsed, one withdrew

**Table 1. Instructions for the treatment of post-operative complications**

1. All patients are monitored with pulse oximetry continuously for 24 hours after administration of intrathecal morphine. Set oximeter to alarm if saturation falls below 90%. Inform the on-call anaesthetist if SpO<sub>2</sub> falls below 90%, administer 100% oxygen and apply basic airway manoeuvres meanwhile.
2. Inform the on-call anaesthetist if respiratory rate ≤ 10/min or sedation scores are 2 or 3. Administer 100% oxygen and apply basic airway manoeuvres meanwhile. Draw up naloxone 0.4 mg ready in a 2 mL syringe.
3. Report to the on-call anaesthetist if systolic BP is < 100 mmHg or heart rate is < 50/minute.

**Table 2. Demographic data of patients enrolled in the study**

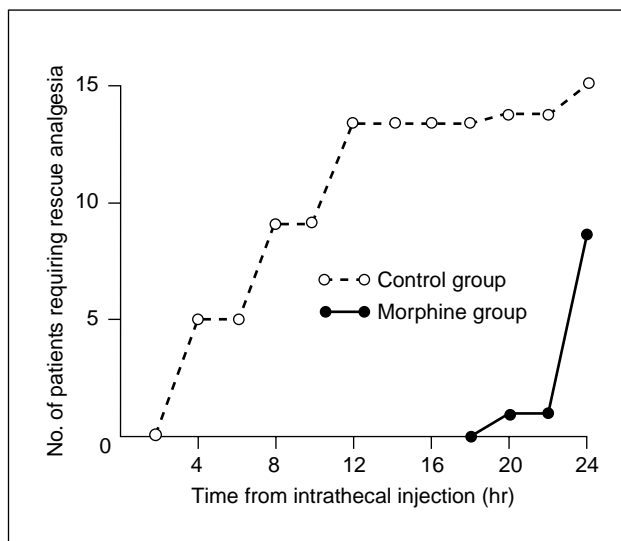
	<b>Morphine group n=18, mean (SD)</b>	<b>Control group n=18, mean (SD)</b>
Age (y)	79.2 (8.2)	79.8 (9.3)
Sex (M/F)	3/15	3/15

No significant difference between the two groups (Student's *t* test,  $P < 0.05$ )

from the study, and in another, VAPS was not recorded because of 'breakdown' of the VAPS ruler during the night. Of the remaining 36 patients, 18 belonged to each group. There were no differences in age and sex distribution between the two groups (Table 2). The VAPS values at 15 minutes before the subarachnoid injection and before rescue analgesia are shown in Table 3, which revealed no significant difference between the two groups ( $P > 0.05$ ).

There was a statistically significant difference (Mann-Whitney U test,  $P < 0.05$ ) in the duration of effective post-operative analgesia between the two groups. The median pain-free period in the control group was nine hours (range, 2-24 hours) compared with 24 hours (range, 16-24 hours) in the morphine group. The number of patients who required rescue analgesia during the first 24 hours after surgery is shown in Figure 1.

The incidence of side-effects is shown in Table 4. Four patients had nausea/vomiting; three of the four vomited three times and the other vomited once. In all patients, the nausea or vomiting settled without treatment. Two patients complained of mild itchiness that did not require treatment. One patient in the morphine group had a brief period (one hour) of confusion for which no cause could be found—there was no change in blood pressure and pulse rate, SpO<sub>2</sub> readings were consistently over 95%, and no changes were detected in 12-lead ECG and chest X-ray results. Blood tests revealed normal serum electrolyte levels



**Fig 1. Number of patients requiring rescue analgesia within the first 24 hours of surgery for hip fracture**

and the patient had no anaemia or raised white cell count. Arterial blood gas analysis was performed and the results were normal for the patient's age. The patient recovered spontaneously.

All patients were followed up until discharge and there were no reports of postdural puncture headache during their hospital stay. There were no reports of urinary retention in the non-catheterised patients but 60% of all patients were catheterised prior to being given regional anaesthesia because of incontinence. Hypopnoea (respiratory rate  $< 12$  breaths per minute) or episodes of desaturation (SpO<sub>2</sub>  $< 90\%$ ) were not observed and no patient had haemodynamic disturbance (defined as a decrease of systolic blood pressure by more than 20% of the baseline).

**Discussion**

There are a number of methods available for achieving post-operative analgesia. However, some of the

**Table 3. Mean visual analogue pain score at 15 minutes before the intrathecal injection and before the administration of rescue analgesia**

	<b>Morphine group n=18, mean (SD)</b>	<b>Control group n=18, mean (SD)</b>	<b>P value</b>
VAPS* 15 minutes before intrathecal injection given	46.8 (21.4)	54.0 (27.6)	ns
VAPS before rescue analgesia given	7.4 (9.3)	11.0 (14.5)	ns

No significant difference between the two groups (Student's *t* test,  $P < 0.05$ )

\* VAPS visual analogue pain score; ns not significant

**Table 4. The incidence of side-effects**

	Morphine group n=18, mean (SD)	Control group n=18, mean (SD)	P value
Pruritus	1 (6)	1 (6)	ns
Vomiting*	4 (22)	0 (0)	P<0.0001
Respiratory depression	0 (0)	0 (0)	ns
Other complications	0 (0)	0 (0)	ns

\*Statistically significant difference (Fisher's exact test, P<0.05)

ns not significant

commonly used means may not be the best choice for elderly patients. When intramuscular opioids are given on an as needed basis, fluctuating plasma levels result in overdosing at some times and underdosing at others.<sup>9</sup> Continuous intravenous infusions of opioids may overcome this problem, but several other problems are associated with this technique, most importantly, the potential for overdose and respiratory depression. This is especially so when the initial assessment has not taken into account the slow rate of onset of some drugs.<sup>10</sup> Hence, patients need to be monitored in a high-dependency nursing area. Recently, it has been shown that satisfactory pain relief can be obtained if a fixed dosing regimen for intramuscular morphine is calculated from a patient's initial requirements in the recovery room.<sup>11</sup> This method is not suitable for patients who have regional anaesthesia, however, because they remain pain-free for the time that they spend in the recovery area.

Patients who use patient-controlled analgesia (PCA) must understand the concept of PCA and also be physically able to depress the control button, which is designed to avoid accidental dosing. As some elderly patients are confused and some have muscle weakness, PCA is unsuitable for these groups. Giving intramuscular non-steroidal anti-inflammatory drugs (NSAIDs) has been shown to reduce post-operative opioid consumption and can be used as an alternative or complementary analgesia method.<sup>12</sup> Most elderly patients, however, have multiple medical conditions such as renal insufficiency, peptic ulcers, and reactive airways disease, which make the use of NSAIDs unsafe.<sup>13</sup> Epidural opioids are currently a well accepted method of post-operative pain management.<sup>14</sup> Some of the advantages of using epidural opioids include the following: the opioid dose can be titrated to the analgesia requirement of the patient; the patient can receive a lipophilic opioid, which has a shorter duration of action (decreased incidence of respiratory depression); and the duration of analgesia can be

prolonged by maintaining a continuous infusion or by giving repeat boluses via the indwelling epidural catheter. In a busy district hospital, however, it may not be possible to do this very much because of budgetary constraints. Moreover, some elderly patients have distorted spinal columns, making the insertion of an epidural catheter difficult.

The ability of morphine to provide analgesia when injected into the subarachnoid space has been well demonstrated.<sup>15</sup> The reported optimal analgesic dose appears to lie between 0.3 mg and 1.0 mg,<sup>16</sup> while significant respiratory depression occurs with doses of 0.8 mg to 1.0 mg.<sup>17</sup> Prior to this study being conducted, there were no data on the optimal intrathecal morphine dose for elderly Chinese patients. We chose 0.2 mg rather than 0.3 mg because Chinese patients in Hong Kong have a smaller build and appear to be more sensitive to pethidine than Caucasians.<sup>18</sup>

The intrathecal administration of narcotics in combination with local anaesthetic has been reported to be effective in non-orthopaedic operations.<sup>19</sup> The simultaneous subarachnoid administration of opioids when spinal anaesthetic is given to patients who are undergoing a total joint arthroplasty of the lower extremity, enables them to remain awake, alert, and comfortable, with a minimum of pain, during the first 24 hours after the operation.<sup>7</sup>

In this study, we examined the efficacy of a small dose of intrathecal morphine, administered simultaneously with local anaesthetic, to avoid an additional invasive lumbar procedure. The local anaesthetic provided complete pain relief during the ensuing two to four hours of the operation and covered the 30- to 60-minute time lag needed for the opioid to bind with receptors in the spinal cord to reach maximum levels for post-operative analgesia.<sup>7</sup> Although weakness of the lower limbs usually wears off two to four hours after the

subarachnoid administration of plain 0.5% bupivacaine, the median analgesic duration in the control group in whom only plain 0.5% bupivacaine was given reached nine hours. The longer median analgesic duration in the morphine group (24 hours) obviously demonstrates its efficacy in extending analgesia into the post-operative period.

Our incidence of side-effects compares favourably with figures from other studies on subarachnoid opioids.<sup>20</sup> Four of the 18 patients in the morphine group had only mild side-effects, which were amenable to conservative treatment. One patient from each group complained of pruritus. The patient in the morphine group could have been given a small dose of naloxone for relief without compromising the analgesic effect.<sup>21</sup> Intrathecal morphine-induced pruritus can also be effectively treated with propofol, 10 mg, given intravenously.<sup>22</sup>

We had no reported instances of hypopnoea (respiratory rate <12 breaths per minute) or episodes of desaturation ( $SpO_2$  <90% for 5 minutes or more), and none of the patients had sedation scores of two or above. Respiratory depression was not detected in our study based on the respiratory rate,  $SpO_2$ , and sedation scores, which can detect one of the early manifestations of respiration depression—sedation. However, we only had 18 patients in each group and such a small sample size would not be sufficient to detect this uncommon yet serious complication. Before a similar, but much larger, study is repeated, we recommend that all elderly patients who are given opioids either epidurally or intrathecally, be monitored in an area in which the nursing staff to patient ratio is adequate and that pulse oximetry be constantly monitored.

## Conclusion

We have demonstrated that 0.2 mg morphine, when administered simultaneously with local anaesthetic intrathecally, can provide up to 24 hours of adequate post-operative analgesia. This covers the most painful post-operative period for fractured hip patients who have had an Austin Moore arthroplasty or compression hip screw inserted. After the first 24 hours, oral analgesic medications can provide adequate pain relief, especially when patients are resting. Analgesic requirements will naturally increase when patients commence mobilisation, but will decline once the healing process starts.

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