

Original Research Article**Spinal Anaesthesia with Bupivacaine and Intrathecal Morphine Versus Combined Spinal-Epidural Anaesthesia using Bupivacaine and Epidural Infusion of Bupivacaine Plus Fentanyl for Postoperative Analgesia after Hip and Knee Arthroplasty**Mohd Azizan G¹, Karis M² (✉), Noordin Y³¹Department of Anaesthesiology and Intensive Care, Hospital Tengku Ampuan Rahimah, 41200 Klang, Selangor, Malaysia.²Department of Anaesthesiology and Intensive Care, Faculty of Medicine, Universiti Teknologi MARA, 47000 Sg Buloh, Selangor, Malaysia.³Department of Anaesthesiology and Intensive Care, Mahkota Medical Centre, 75000 Malacca, Malaysia.**Abstract**

This randomised single-blinded study was conducted to evaluate if there was any difference between spinal anaesthesia with hyperbaric bupivacaine 0.5% and intrathecal morphine 0.2mg and combined-spinal epidural using hyperbaric bupivacaine 0.5% with epidural infusion of bupivacaine 0.1% plus fentanyl 2.0µg/ml for 24 hours, postoperative analgesia following hip and knee arthroplasty, in terms of pain score and side effects (nausea, vomiting, pruritus and respiratory depression). Eighty patients ASA I or ASA II, aged between 18 to 75 years who underwent knee and hip arthroplasty of approximately 3-4 hours, duration were recruited. They were randomly allocated to one of two groups by using computer generated randomised numbers. The pain score during the postoperative period was evaluated using Visual Analogue Score (VAS pain score) and the side effects were documented and treated accordingly. Results showed that patients in Group 1 and Group 2 were comparable in terms of age, gender, height, weight and race. There was no statistical difference in VAS pain score between the two groups at all times intervals. However, patients in Group 1 had a higher incidence of nausea and pruritus than patients in Group 2. None of the patients in either group, experienced respiratory depression. Thus, it was concluded that both intrathecal morphine 0.2mg and epidural infusion of bupivacaine 0.1% plus fentanyl 2.0µg/ml were comparable in providing postoperative analgesia up to 24 hours following hip and knee arthroplasty. Nevertheless, the use of spinal morphine led to a higher incidence of side effects namely nausea and pruritus.

Keywords: Intrathecal morphine, epidural infusion of bupivacaine, postoperative analgesia, hip and knee arthroplasty

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Introduction

It is absolutely imperative that patients are not only adequately anaesthetized intraoperatively but should also receive adequate analgesia intraoperatively and postoperatively. Patients who receive adequate pain

relief after surgery will recover and start mobilizing early, hence minimizing the risk of prolonged immobilization and hospital stay. Literature supports the relationship between the quality of the postoperative analgesia and the immediate functional outcome following major hip and knee surgery (1).

Similar to many modes of anaesthesia and analgesia intraoperatively, there are also numerous methods of providing analgesia postoperatively. Some of the commonly used methods include intrathecal or spinal anaesthesia, combined spinal-epidural (CSE), epidural analgesia, patient controlled analgesia (PCA), peripheral nerve blocks, subcutaneous and/or intramuscular opioids such as morphine or pethidine as well as oral, parenteral and suppository analgesia. As there are different techniques available, the choice of postoperative analgesia in each patient depends on many factors. For instance, patients subjected to lower limb surgery could be offered CSE. Combined spinal-epidural anaesthesia is a combination of two anaesthetic procedures i.e. spinal and epidural anaesthesia which are performed together. It has been used increasingly over the last decade for anaesthesia as well as for postoperative analgesia (2). Another example is patients undergoing intra-abdominal surgery in which epidural analgesia can be administered. In both cases, these are methods of providing analgesia intraoperatively as well as postoperatively. Most commonly drugs used in epidural analgesia are pethidine (2.0mg/ml)-as a bolus and epidural infusion which consists of a combination of bupivacaine 0.1-0.2% plus fentanyl 2.0 µg/ml. Possible side effects include numbness of the lower limbs, pruritus, nausea, vomiting and a significant period of immobility which could lead to deleterious consequences such as deep venous thrombosis (3).

Besides CSE and epidural infusion, intrathecal or spinal morphine has also been used to provide intraoperative and postoperative analgesia (4). Intrathecal morphine has been shown to offer effective analgesia in many surgical settings since the introduction of this technique into clinical practice in 1979 (5). Several studies showed that intrathecal morphine can produce adequate analgesia in major orthopaedic and gynaecological procedures (3, 5,6,7,8).

Nevertheless, just as with other methods of postoperative analgesia, the use of intrathecal morphine is not without side effects, which limited its use in the earlier studies. Few of the common side effects include nausea and vomiting, pruritus, urinary retention and most importantly respiratory depression (3,9,10,11,12). One interesting point is that these earlier studies used intrathecal morphine doses as large as 2.5mg, which may have contributed to these side effects (6,13,14). The use of low dose intrathecal morphine (0.1 to 0.2mg) however produces no or minimal side effects, and at the same time offers effective analgesia to patients (10,15,16,17,18,19,20).

This at the end leads to a high degree of patients' satisfaction (9).

Materials and Methods

This was a randomised single blinded prospective study carried out on 80 patients after obtaining institutional approval. The sample size was calculated based on the anticipated success rate of 0.9 with the difference up to 0.2. In this calculation at least 40 patients were required in each group to obtain a study power of 0.80 with the level of significance was 0.05 ($p < 0.05$).

The subjects included ASA physical status I or II patients, aged 18 to 75 years old undergoing elective knee and hip arthroplasty, which were expected to last less than three hours. Exclusion criteria included any contraindication to central neuroaxial block and allergies to morphine and bupivacaine. In the operation theatres, they were randomly allocated to one of the groups (a single shot spinal anaesthesia or CSE) by using computer generated randomised numbers.

Prior to the operation, all eligible patients were met in the ward a day earlier. They were informed thoroughly about the anaesthetic technique that would be administered to them, including the possible side effects. Explanation on the pain score was also given. At the end of the consultation, verbal as well as written consent were obtained from them. Patients were given oral midazolam 7.5mg as premedication.

An 18 G branula was inserted at the patients' hand and 500ml of Hartman's solution was given intravenously just prior to the induction of anaesthesia. Standard monitoring which included non-invasive blood pressure (NIBP), electrocardiogram (ECG) and pulse oximeter were applied to the patients. Intra-operatively, the patients were prepared for spinal or CSE. The two anaesthetic techniques were done under aseptic technique at level of L3/L4. A single shot spinal anaesthesia was performed in Group 1 patients and they received 3.0 ml hyperbaric bupivacaine 0.5% plus 0.2mg morphine with 0.3 ml of normal saline (total volume 3.5 ml), administered intrathecally. Combined spinal-epidural anaesthesia was performed in Group 2 patients and they received 3.0 ml hyperbaric bupivacaine 0.5% with 0.5 ml of normal saline (total of 3.5 ml) given intrathecally and epidural infusion of bupivacaine 0.1% plus fentanyl 2.0µg/ml via epidural catheter (as part of a CSE technique).

Hypotension (defined as a systolic blood pressure of less than 80 mmHg) if any, was treated with fluids

(500ml of Hartmann’s solution) or vasopressor drug i.e. intravenous ephedrine in 3.0 mg increments until the blood pressure returned to normal. In the event where surgery unexpectedly lasted more than three hours, patients in Group1 were converted to general anaesthesia and thereby dropped from the study.

Postoperatively, the patients were sent to the recovery bay and further monitoring was done before they were sent to their ward 30 minutes later. Epidural infusion of bupivacaine 0.1% plus fentanyl 2.0µg/ml at 6.0ml/hour was started in Group 2 patients, on arrival at the recovery room and continued in the ward. In the ward, NIBP, HR and respiratory rate (RR) were monitored and observations were noted in the observation chart for every 8 hours during the 24 hours study period. The presence or absence of side effects i.e. nausea, vomiting, pruritus and respiratory depression (which is defined as patients taking eight breaths or less per minute) was also monitored every 8hours interval during the 24 hours. Standard medications to treat side effects were administered when necessary. These included intravenous metoclopramide (maxolon) 10mg to treat vomiting, intravenous chlorpheniramine (piriton) 10 mg for pruritus and intravenous naloxone 0.1mg for respiratory depression.

Pain scores during the postoperative period was evaluated using the VAS pain scores, where the degree of pain was numbered from 0 (no pain at all) to 10 (highest pain). A VAS pain score of 3 or less will be interpreted as patients not having any significant postoperative pain at rest.

In the event where the patients’ score was four or more, patients were treated accordingly. Patients in Group 1 were given an additional intravenous tramadol (tramal) 50mg to overcome the pain while patients in Group 2 were given a bolus of epidural lignocaine 2% 5.0ml and at the same time the epidural infusion rate increased by 2.0ml/hour.

Data was analysed by using the SPSS statistic package (version 12). As the sample size was not normally distributed, Mann-Whitney and chi-squared test were used for non-parametric data. A value of p<0.05 was regarded as statistically significant.

Results

There was no marked difference between the two groups in term of age, gender, height, weight and race (Table 1).

Table 1: Patients demographic data. Values expressed as median (minimum-maximum) unless stated otherwise.

	Group 1 (n=40)	Group 2 (n=40)
Age (years)	50 (16-70)	42 (16-75)
Gender*		
Male	29 (72.5)	16 (40)
Female	11 (27.5)	24 (60)
Height (cm)	170 (155-180)	165 (148-180)
Weight (kg)	65 (40-88)	60 (38-89)
Race*		
Malay	26 (65)	23 (57.5)
Chinese	13 (32.5)	12 (30)
Indian	1 (2.5)	5 (12)

*denotes total number + percentage in bracket for that category

Table 2: VAS pain score. Values expressed as numbers (n)

Time interval	VAS pain score*	Group 1 (n=40)	Group 2 (n=40)	‘p’ value
8 hours	4-10	1	2	1.000
	0-3	39	38	
16 hours	4-10	1	2	1.000
	0-3	39	38	
24 hours	4-10	0	2	0.494
	0-3	40	38	

*VAS pain score: 0-3 (no pain), 4-10 (pain)

In this analysis, those scored between 0 and 3 were categorized as having no pain while those of 4 and 10 were categorized as having pain. There was no statistical difference in VAS pain score between the two groups at all intervals with p>0.05 in all categories (Table 2).

Pruritus was present only in Group 1 and though occurring at all intervals, was only statistically significant at 8 and 16 hours. Nausea was present in Group 1 at 8 and 16 hours postoperatively, none in Group 2 and the difference was statistically significant between the two groups. None of the patients required treatment. Three patients in Group 1 had vomiting at 8 hours interval which did not require treatment and the difference between the two groups were not significant. None of the patients in Group 2 developed pruritus, nausea or vomiting. None of the patients in

Table 3: Number of patients with pruritus, nausea and vomiting. Values expressed as numbers (n) and percentage in bracket.

Side Effects	Time Interval (hours)	Group 1 (n=40)	Group 2 (n=40)	'p' value
Pruritus	8	30 (75)	0	0.000
	16	13 (32.5)	0	0.000
	24	3 (7.5)	0	0.239
Nausea	8	15 (37.5)	0	0.000
	16	10 (25)	0	0.000
Vomiting	24	0	0	
	8	3 (7.5)	0	0.239
	16	0	0	
	24	0	0	

both groups developed respiratory depression (Table 3). There was no hypotension and no patients required intravenous tramadol or boluses of epidural lignocaine.

Discussion

One of the challenging tasks for anaesthetists is to offer adequate analgesia to patients as a mean of providing early ambulatory to hasten their rehabilitation. Capdevila et al. reported that regional techniques (epidural or spinal anaesthesia) improved early rehabilitation after major hip and knee surgery (1).

Spinal anaesthesia using local anaesthetic and morphine was introduced 29 years ago. However, its use was limited due to its side effects such as nausea, vomiting, pruritus and respiratory depression (8). When an opioid is administered intrathecally, it simultaneously travels cephalad within the cerebrospinal fluid (CSF) and then enters the spinal cord and binds to nonspecific sites within the white matter or specific opioid receptors within the dorsal horn to give its effect (analgesia). It can also transverse the dura mater and enter the epidural space where it binds to epidural fat, and then enters the plasma compartment through vascular uptake and cause side effects (11).

Anaesthesia for total hip and knee arthroplasty should provide adequate intraoperative and postoperative analgesia with minimum side effects. Spinal anaesthesia, epidural anaesthesia and CSE using bupivacaine with or without opioid offer more benefits as they provide adequate and prolonged postoperative analgesia. However, these techniques are commonly

associated with unwanted side effects such as nausea, vomiting, pruritus and respiratory depression (3,21)

Not many studies compared spinal anaesthesia with heavy bupivacaine 0.5% and intrathecal morphine 0.2mg was superior to CSE using bupivacaine 0.5% combined with epidural infusion of bupivacaine 0.1% plus fentanyl 2.0µg/ml for postoperative analgesia after hip and knee arthroplasty. However, studies related to the use of intrathecal morphine, epidural infusion of bupivacaine with or without fentanyl, epidural morphine and epidural pethidine for postoperative pain relief following major surgical procedures other than hip and knee arthroplasty had been highlighted by few investigators.

In this study, we performed spinal anaesthesia and intrathecal morphine (0.2mg) was used for postoperative analgesia for hip and knee arthroplasty. Earlier studies did show that low doses of intrathecal morphine provided good analgesia after major arthroplasty. This included a study by Murphy et al. compared various doses of intrathecal morphine (0.05, 0.1 and 0.2mg) in 60 patients aged above 65 years undergoing elective hip arthroplasty. He concluded that 0.1mg intrathecal morphine provided the best balance between analgesia and side effect profiles (10).

Jacobson et al. also studied various intrathecal morphine doses (0.3, 1.0, 2.5mg) for postoperative analgesia in 33 who patients underwent total hip and knee replacement surgery and concluded that doses between 0.1 and 0.3mg offered good analgesia with minimal side effects (15). Rathmell et al. and Hassett et al. found that 0.2 and 0.3 mg morphine given intrathecally produced satisfactory pain control after knee and hip arthroplasty (7,20). Another study performed by Souron et al. also concluded that 0.1mg intrathecal morphine provided better postoperative analgesia than single short psoas compartment block after primary hip arthroplasty (14). A recent study conducted by Damevski et al. showed that intrathecal morphine 0.05 and 0.1mg provided optimal postoperative pain relief without side effects for patients undergoing total knee arthroplasty. However, this technique was supplemented by giving continuous 3-in-1 nerve block plus femoral PCA bupivacaine boluses (19). Therefore, it can be concluded that the dose between 0.1 and 0.3 provided adequate postoperative analgesia for hip and knee arthroplasty.

Besides intrathecal morphine, single shot epidural anaesthesia with bupivacaine 0.5% combined with morphine 0.1-0.2mg provided a synergistic analgesic effect and was found to be suitable for postoperative

pain relief after major orthopaedic surgery (21,22). Leclerc et al. and Stulberg et al. noted that continuous epidural anaesthesia by infusion had been considered as the techniques of choice for postoperative pain relief in patients undergoing hip and knee arthroplasty (23,24). It was shown that epidural infusion using bupivacaine 0.1% with fentanyl 2.0µg/ml (epidural infusion dose given was similar to our study) provided good pain relief, reduces intraoperative blood loss and incidence of deep vein thrombosis. However, unwanted side effects such as nausea and vomiting, pruritus, sedation urinary retention and respiratory depression had been observed (23,24).

Maheswari et al. used a local anaesthetic epidural infusion with and without patient-controlled epidural analgesia for 24 hours (25). They found many patients suffered rebound pain. They also tried combinations of epidural infusion with femoral nerve block, with or without intravenous PCA. All these techniques were associated with side effects that included respiratory depression, nausea, vomiting, ileus, urinary retention, pruritus, hypotension, bradycardia, and cognitive changes (25).

Continuous low-dose epidural infusion had been advocated as a method to control postoperative pain for hip surgery by Indelli et al. (26). This technique allowed pain relief to be more precisely titrated to the level of pain stimulus and could be discontinued if problems occur (26). Although epidural infusion provided superior analgesia but it was associated with hypotension, ileus, urinary retention and mild motor block (22,27).

There were mixed results in terms of side effects from these two techniques. Pruritus and nausea were statistically significant in Group 1 at 8 and 16 hours interval, respectively. However, the incidence of vomiting and respiratory depression at all intervals were not statistically significant in this study.

Pruritus is one of the unwanted effects of intrathecal morphine (3,7,12,15,16). The incidence of pruritus after intrathecal administration of opioids varies from 30% to 100%, nevertheless the exact mechanism of neuroaxial opioid-induced pruritus remains unclear (16). Postulated hypotheses included the presence of an 'itch centre' in the central nervous system, medullary dorsal horn activation, antagonism of inhibitory transmitters, modulation of serotonergic pathway and involvement of prostaglandins (11).

Rathmell et al. (7) and Murphy et al. (10) in their studies showed that pruritus was more frequent with intrathecal morphine 0.2 mg. A study by Slappender et

al. showed that pruritus occurred even at low dose of intrathecal morphine (12). Pietri et al. used intrathecal morphine 0.2 mg as a method of postoperative analgesia for patients undergoing liver resection and found the incidence of pruritus was around 16% (28). In this study 75% of patients in the intrathecal morphine group experienced pruritus at the 8th hour interval as compared to 0% in the combine spinal-epidural group.

Apart from pruritus, nausea and vomiting are also side effects of intrathecal morphine. It maybe a systemic effect versus cephalad migration in CSF and interaction with opioid receptors in the area postrema (11). Gwitz et al. noted 25% incidence of nausea and vomiting with intrathecal morphine doses ranging from 0.2 to 0.8mg (8). Pietri et al. reported the overall incidence of nausea (16%) and vomiting (4%) when using intrathecal morphine 0.2 mg (28). In our study we used a similar dose but the results were slightly different (37.5% and 7.5% of patients in Group 1 experienced nausea and vomiting respectively at 8th hour interval). However, Weber et al. carried out a study using 0.2 mg of intrathecal morphine and showed no relationship between the use of intrathecal morphine and the high incidence of nausea and vomiting (16).

The most feared side effect of intrathecal morphine is respiratory depression (4,11,20). This occurs when a hydrophilic opioid like morphine transverses slowly from the CSF to the spinal cord and epidural space slowly hence respiratory depression can persist for 18-24 hours (11). The true incidence of clinically significant respiratory depression however remains unknown. Rathmell et al. mentioned the risk of respiratory depression after intrathecal morphine was less than 1% (11). Gwitz et al. revealed a 3% incidence using 0.2 to 0.8 mg of intrathecal morphine, however this number represented only 'a potential risk' rather than the true respiratory depression (8). Sarkowska et al. found that out of 79 patients received intrathecal morphine, only one patient (1.2%) developed respiratory depression (29). A study done by Duale et al. showed that intrathecal morphine 0.075 mg given in pregnant women was effective in providing postoperative analgesia after caesarean section without causing respiratory depression (30). Hassett et al. used 0.1 and 0.2 mg intrathecal morphine for total knee arthroplasty and found that there were no differences between patients with regard to nausea, vomiting, pruritus and respiratory depression (20). In this study none of the patients in Group 1 developed respiratory depression. This could be attributed to low dose morphine used (0.2 mg).

Alternative anaesthetic techniques should be sought to avoid spinal morphine-induced pruritus and vomiting. Spinal anaesthesia with a peripheral nerve block has been used for postoperative analgesia post hip and knee arthroplasty. Study done by Barrington et al. (31) on patients underwent knee arthroplasty under spinal anaesthesia and received either a femoral infusion of bupivacaine 0.2% or an epidural infusion of ropivacaine 0.2% with fentanyl 4.0 µg/ml. Results showed that an equivalent pain relief between the two groups but there was significantly less nausea, vomiting and pruritus in the femoral infusion group (31). Spinal anaesthesia using hyperbaric bupivacaine 0.5% with a femoral, lumbosacral plexus or fascia iliaca block using hyperbaric bupivacaine or ropivacaine 0.75% had been shown to provide good quality of analgesia without pruritus. In these cases, the peripheral nerve to be blocked was located accurately by using ultrasound-guided device (32,33,34). The other technique was local infiltration analgesia using ropivacaine 0.75% plus adrenaline. The drugs were infiltrated in the knee during operation and two bolus injections of same mixture were given via an intraarticular catheter postoperatively (35,36). Therefore, the use of intrathecal morphine should be avoided to reduce side effects and improve patient safety.

Conclusion

This study showed that intrathecal morphine 0.2 mg and epidural infusion of bupivacaine 0.1% plus fentanyl 2.0 µg/ml were equally effective in providing postoperative analgesia for up to 24 hours for hip and knee arthroplasty.

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