Comparison of Morphine with Fentanyl Added to Intrathecal 0.5% Hyperbaric Bupivacaine for Analgesia After Caesarean Section

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SUMMARY

This was a prospective randomised, controlled, single-blind study done to determine the effect of intrathecal morphine 0.1 mg as compared with intrathecal fentanyl 25 µg in terms of analgesia and duration for postoperative pain relief after Caesarean section. Sixty ASA I or II parturients were randomised into two groups. Group 1 (n=33) received 1.8ml of 0.5% hyperbaric bupivacaine combined with 0.1mg morphine while Group 2 (n=27) received 1.8ml of 0.5% hyperbaric bupivacaine combined with 25µg fentanyl for spinal anaesthesia. Postoperatively, all patients were provided with patient controlled analgesia (PCA) morphine. Pain was assessed using visual analogue score (VAS) at 6, 12, 18 and 24 hours. Time to first demand of PCA morphine, cumulative PCA morphine requirement and opioid side effects were documented. The VAS for pain and the cumulative PCA morphine requirement were both significantly lower in Group 1 ($p<0.05$) during the 24 hours study period. The time to first demand was also significantly longer in Group 1 ($p<0.05$). Overall, there were no significant difference between the two groups in side effects, except for a high incidence of nausea and vomiting requiring treatment in Group B in the first six hours. In conclusion the addition of 0.1mg morphine for spinal anaesthesia provided superior and longer postoperative analgesia after Caesarean section.

KEY WORDS:
Intrathecal morphine, Intrathecal fentanyl, Caesarean section, Postoperative analgesia

INTRODUCTION

The use of regional anaesthesia for Caesarean section has become increasingly popular as data indicate that maternal mortality is more often associated with general anaesthesia. Postoperative analgesia after Caesarean section can now be conveniently given via the intrathecal or epidural route. With the advent of combined spinal-epidural anaesthesia both routes of administration for neural blocks have become possible. However, there is no clear evidence to indication superiority of one over the other.

With the introduction of fine, pencil-point needles, spinal anaesthesia has become a better choice over epidural block since it takes less time to perform, has faster onset and provides a more consistent and reliable block[1,2,3]. The use of a smaller amount of local anaesthetic drug in spinal anaesthesia also increases safety. As Caesarean section involves significant traction of peritoneum and intra-peritoneal structures, giving rise to visceral pain, addition of an opioid is useful to enhance analgesia. As a result of synergistic effect, it makes it possible to achieve satisfactory spinal anaesthesia using an even lower dose of local anaesthetic agent than before[4].

After Caesarean section, it is important to provide optimal pain relief in order to allow early ambulation, so that the mother is able to nurse her baby. Addition of an opioid to the local anaesthetic solution improves the quality of sensory blockade and provides better postoperative pain relief. Morphine and fentanyl are the opioids commonly used for this purpose[5].

Addition of intrathecal fentanyl to local anaesthetic solution to enhance subarachnoid block is a widely encountered practice. However, its analgesic effect lasts about 30 minutes due to its short elimination half-life of 1.5 – 6 hours[5]. The effect on analgesia with intrathecal fentanyl when used alone has become inferior compared to intrathecal morphine[6].

Opioid related side-effects such as respiratory depression, pruritus, nausea, vomiting and urinary retention may occur with intrathecal administration in a dose-related manner. The most feared side effect of intrathecal morphine is delayed respiratory depression since this may be a life-threatening event. Respiratory depression caused by morphine is more prolonged and may occur much later, up to 12 hours. These are generally due to an effect of stimulation at the mu (µ) receptor[7,8,9,10].

The aim of this study was to compare the efficacy and duration of analgesia of intrathecal morphine with intrathecal fentanyl after Caesarean section.

MATERIALS AND METHODS

This prospective, randomised, single-blind study was approved by the Dissertation Committee, Department of Anaesthesiology and Intensive Care, Faculty of Medicine, Universiti Kebangsaan Malaysia. After obtaining written informed consent, sixty parturients at term, ASA I or II scheduled for elective Caesarean section under spinal anaesthesia were selected. Exclusion criteria were contraindication for spinal anaesthesia, body mass index

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(BMI) more than 35kg/m^2, history of chronic drug abuse and known allergies to the study drugs.

Patients were randomly divided into two groups. Patients in Group 1 received 1.8ml 0.5% hyperbaric bupivacaine with 0.1mg preservative-free morphine (diluted in 0.5ml normal saline) and patients in Group 2 received 1.8ml 0.5% hyperbaric bupivacaine with 25µg fentanyl. Both groups received a total of 2.3ml local anaesthetic solution for each patient. Each patient was fasted for at least six hours and oral cimetidine 200mg was given the night before surgery and on morning of surgery. On arrival at the operation theatre, the patient was given 30ml of 0.3 M sodium citrate, as acid aspiration prophylaxis. Standard monitoring included non-invasive blood pressure, pulse oximetry and electrocardiography. A fluid preload with 500ml of Hartmann's solution was carried out over 15 minutes prior to the procedure. Spinal anaesthesia was performed with the patient in the sitting position under aseptic technique using 27-gauge Pencan™ needle at either L_3-L_4 or L_4-L_5 interspace. Once there was back-flow of clear cerebrospinal fluid, the patient was given 1.8ml 0.5% hyperbaric bupivacaine with morphine 0.1mg (Group 1) or 1.8ml 0.5% hyperbaric bupivacaine with fentanyl 25µg (Group 2). After spinal anaesthesia, patient was placed supine position with 15º left uterine displacement and the level of sensory loss to temperature was determined. Surgery was only allowed to commence after a satisfactory blockade up to level of T_4 was achieved. Oxygen at 6 L/min flow was administered via a face mask to the patient. Blood pressure was monitored at 1-minute intervals until stable then continued every 5 minutes. Hypotension was defined as a 20% reduction from baseline systolic blood pressure. If this occurred, patient was treated with a rapid infusion of 100ml of Hartmann's solution and intravenous ephedrine 6mg boluses.

In this study, after surgery, the patient was sent to recovery room for monitoring. Intravenous patient controlled analgesia (PCA) with morphine was provided as a rescue with the following settings; dilution of 1mg/ml of morphine, 1ml bolus, 5 minute lock-out period, 12mg/h maximal dose and no background infusion. After 30 minutes of monitoring in the recovery room, if the patient was stable, patient was allowed to return to the obstetric ward for observations. The data collection was done by trained staff nurses who were blinded to the procedure. Vital signs were monitored hourly over six hours and pain was assessed 6-hourly by using visual analogue score (VAS). Time from induction to the first demand of analgesia (PCA morphine) and the total amount of morphine used in 24 hours, were recorded. Side-effects of morphine were noted. The sedation score used was as follows: (0 =awake, 1 = mild drowsiness, 2 = moderate drowsiness, easily awaken, 3 =difficult to arouse). Sedation was considered clinically relevant if the patient was not easily awakened. Respiratory depression was defined as respiratory rate of less than 8 breath/minute. For nausea and vomiting, the following scale was used: 0 = present of nausea without vomiting, 1 = mild to moderate vomiting (not requiring treatment), 2 = severe vomiting (treatment required). For pruritus the following scale was used: 0 = no pruritus, 1 = mild to moderate pruritus (not requiring treatment), 2 = severe pruritus (treatment required). Severe vomiting (more than two episodes) was treated with intravenous metoclopramide 10mg. Severe pruritus was treated with intravenous chlorpheniramine 10mg. Patients who had received treatment for nausea, vomiting and pruritus were excluded on the next assessment. In cases of unsuccessful treatment, unpleasant pruritus or occurrence of any life threatening event, an anaesthetist would be called in to deal with the problem.

Statistical analysis of data was performed using the Statistical Package for Social Sciences (SPSS) software version 12. Data were analyzed using independent t-test or Chi-square tests where appropriate. A p-value of < 0.05 was considered statistically significant.

RESULTS

A total of 60 patients were studied. Fifty-five percent (n= 33) parturients were allocated in Group 1 and the remainder 45% (n= 27) parturients were grouped in Group 2. The demographic data are shown in Table I. There was no significant difference between the two groups in terms of age, weight, height, period of gestation and ASA grouping.

Time to the first PCA morphine dose as rescue was at (297.4 ± 112.0) minutes in Group 1 and (197.7 ± 60.0) minutes in Group 2. These results showed significant difference in time to first PCA morphine ($p<0.05$).

Over the 24-hours study period, there were significantly lower VAS pain scores at 6, 12, 18 and 24 hours in Group 1 compared in Group 2 ($p<0.05$) as shown in Figure 1. As a result of lower VAS, Figure 2 shows that there was also significantly lower mean cumulative PCA morphine consumption in Group 1 as compared to Group 2 at all time intervals in the first 24 hours study period ($p<0.05$).

Figures 3 and 4, above show the incidence of side-effects of pruritus and vomiting respectively in both groups. There was no significant difference in the incidence of pruritus as well as that which required treatment. In Figure 4, the incidence of nausea and vomiting was high in both groups. However, the incidence of vomiting that required treatment was noted to be significantly higher in Group 1 as compared to Group 2 ($p=0.04$). This event occurred mostly at the first six hours. None of the patient developed sedation or respiratory depression.

Table I: Demographic data. Result are expressed as mean ± SD

	Group 1 (n=33)	Group 2 (n=27)
Age (years)	30.5 ± 5.6	30.3 ± 4.9
Weight (kg)	71.5 ±10.0	69.3 ± 8.4
Height (cm)	154.9 ± 4.8	154.8 ± 2.4
Period of gestation (weeks)	38.1 ± 0.6	37.9 ± 0.6
ASA 1:2	20 : 13	26 : 1

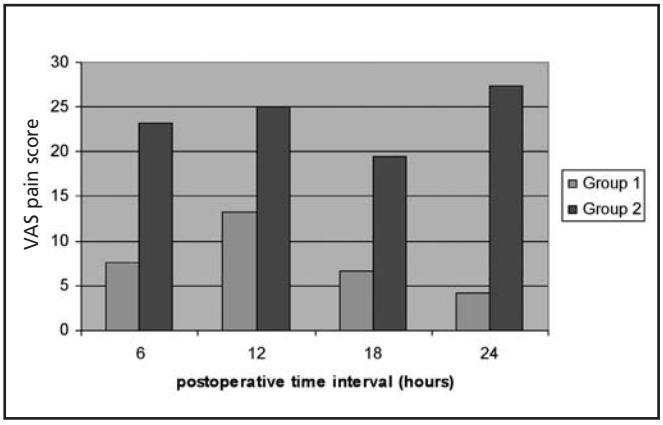

Fig. 1: Mean postoperative pain score (VAS)

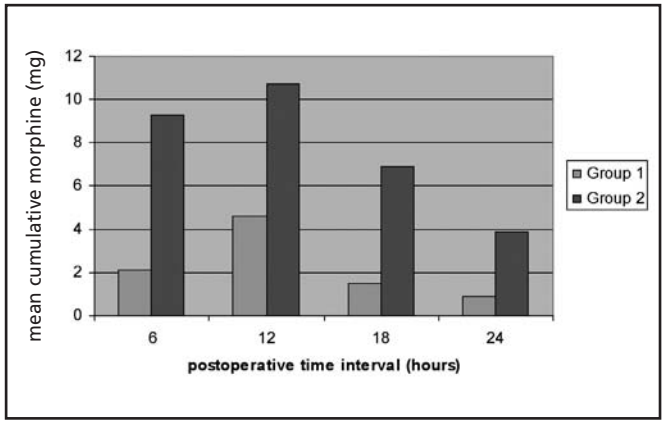

Fig. 2: Mean postoperative cumulative PCA morphine consumption

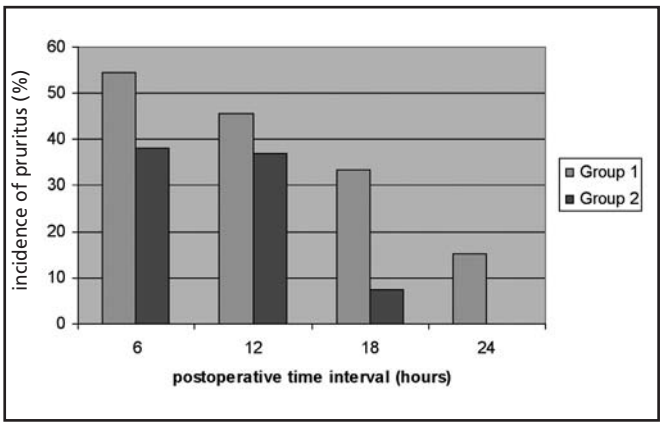

Fig. 3: Opioid side effect (pruritus) in 24 hours

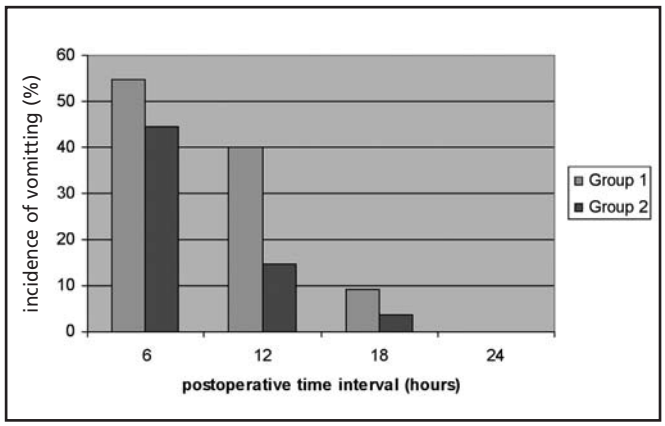

Fig. 4: Opioid side effect (nausea and vomiting) in 24 hours

DISCUSSION

In this study, the quality of post-operative analgesia with fentanyl was found to be inferior to that of morphine. This was shown by a significantly lower mean VAS for pain at 6, 12, 18 and 24 hours, and reduced cumulative PCA morphine consumption throughout the first 24 hours study period (9.2 ± 1.2 mg v/s 30.8 ± 2.3 mg). The time to first demand of PCA morphine was also longer in the intrathecal morphine group as compared with intrathecal fentanyl group (297.4 min v/s 179.7 min). A similar result was also documented by Sibilla *et al* in 1997 in their study[6].

The duration and effectiveness of the analgesia have been shown to be dose-dependent, although a ceiling effect is observed with intrathecal dose of morphine above 0.1 mg[8]. Conversely, the incidence of side effects always increases above these doses and may limit the quantity of morphine that can be given. For example, a significant incidence of respiratory depression above or at 0.2 mg IT morphine has been described of less than 1%, and can be delayed for 12 - 24 hours[1,8]. The delayed effect is due to slow transport of hydrophilic morphine by the cerebrospinal fluid circulation to the fourth ventricle, where it acts on opioid receptors adjacent to the respiratory centre. However, in this study, none of the patients encountered any clinically-detectable sedation or respiratory depression with the low dose of 0.1mg morphine used, probably because of the small sample size.

This study demonstrated a greater risk of vomiting in the IT morphine as compared to IT fentanyl. The incidence of vomiting was high in both groups for the first six hours (63.6% v/s 48.1%), with significant numbers (p=0.04) requiring treatment with intravenous metoclorpramide (54.5% v/s 14.8%). Vomiting may result either from rostral spread of the drug in CSF to the chemoreceptor trigger zone (CTZ) or the vascular uptake and delivery to the vomiting center and CTZ. Nausea and vomiting are easily treated side effects, as antiemetic treatment does not interact with analgesia. Drugs like metoclopramide, antihistamine, anticholinergic such as scopolamine and ondansetron may be used to reduce incidence of nausea and vomting[7,8,9,10].

There was no significant difference in incidence of pruritus between study groups (54.5% v/s 51.8%) with no significant difference in pruritus that required treatment with intravenous chlorpheniramine (24.4% v/s 11%). Pruritus is one of the most common side effects of intrathecal morphine, and it is more likely to be localized to the face, neck or upper thorax. Pruritus is more likely to occur in obstetric patients, perhaps due to interaction of estrogen with

opioid receptors. Usually it occurs within a few hours of injection and may precede the onset of analgesia. Paradoxically antihistamine may be effective, most likely as a secondary effect to its primary sedative effect. An opioid antagonist, naloxone 0.2mg, is effective in relieving opioid-induced pruritus. One other common side effect is urinary retention. This cannot be studied, as all patients had indwelling bladder drainage for the first 24 hours[7,9,10].

The authors would like to emphasise the importance of a multimodal approach to analgesia with the concurrent use of NSAIDs with neuraxial opioids. Although an optimal dose of IT morphine 0.1mg was used, this study had shown that no patient was completely pain free in the first 24 hours after Caesarean section and supplemental analgesia was required.

CONCLUSION

In conclusion, the result of this study showed that the addition of 0.1mg morphine to 1.8ml 0.5% hyperbaric bupivacaine in spinal anaesthesia provided satisfactory and longer duration of analgesia after Caesarean section as compared with the addition of 25µg fentanyl to 1.8ml 0.5% hyperbaric bupivacaine.

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