A COMPARATIVE STUDY OF POST OPERATIVE ANALGESIA, SIDE EFFECTS PROFILE AND PATIENT SATISFACTION USING INTRATHECAL FENTANYL WITH AND WITHOUT MORPHINE 0.1 MG IN CAESAREAN SECTION

Wirzafeldi SaWi* and Choy YC**

Abstract

Background: This was a double-blinded, prospective randomized controlled trial to compare the postoperative analgesia, side effects profile and overall satisfaction in patients who received intrathecal fentanyl with or without morphine for elective Caesarean.

Methods: Sixty ASA I and II parturients were randomized into two groups. Group I received intrathecal fentanyl with 0.1 mg morphine and Group II received intrathecal fentanyl only. Post-operatively, all patients were provided with oral analgesics. The degree of post-operative pain score was assessed by verbal pain score. The incidence of side effects was assessed every 4 hours for 24 hours, which included incidence of nausea, vomiting, pruritus, sedation and evidence of respiratory depression. Patient’s overall satisfaction was also recorded.

Results: The verbal pain score was significantly lower in morphine group up to 20 hours postoperative period. The incidence of pruritus, nausea and vomiting were statistically significant up to 12 hours postoperative. There was no incidence of severe side effects in all the patients. There was significant difference between the morphine and no morphine group in terms of overall patient satisfaction.

Conclusion: There was significant difference in terms of lower pain score, higher incidence of side effects with better patients’ overall satisfaction in morphine group.

Conflict of interest: No financial relationships between authors and commercial interests with a vested interest in the outcome of the study.

Sources of financial support: Hospital Universiti Kebangsaan Malaysia.

* MD.  
** MD, FANZCA.

Department of Anaesthesiology and Intensive Care, Hospital Universiti Kebangsaan Malaysia, Jalan Yaacob Latiff, Bandar Tun Razak, Cheras, 56000, Kuala Lumpur, Malaysia.

Corresponding author: YC Choy, Clinical Associate Professor, Department of Anaesthesiology and Intensive Care, Hospital Universiti Kebangsaan Malaysia, Jalan Yaacob Latiff, Bandar Tun Razak, Cheras, 56000, Kuala Lumpur, Malaysia. Tel: 006-03-91455783, Fax: 006-03-91456585. E-mail: choy@ppukm.ukm.edu.my/ choyynchoy@gmail.com
Introduction

Caesarean deliveries can result in moderate to severe post operative pain. Adequate pain relief will certainly improve maternal satisfaction, speed up maternal recovery and allow the parturient to adequately nurse her newborn baby. This can be eventually translated into a reduction in the cost of treatment as a result of shorter hospital stay without compromising the quality of medical care given towards patient. Spinal anaesthesia is commonly used for Caesarean section. While intrathecal fentanyl improves intraoperative analgesia, intrathecal morphine on the other hand has become widely accepted to enhance postoperative analgesia. However, there is a general concern about the side effects of intrathecal morphine, particularly pruritus, nausea, vomiting and sedation. It has also been associated with delayed respiratory depression which is the most feared complication of intrathecal morphine. These may affect overall patient satisfaction and have raised doubts about their advantages.

Intrathecal morphine in Caesarean section has been used for more than 20 years following the discovery of dorsal horn opioid receptors. published a report on the dose-response relationship between 0 and 0.5 mg of intrathecal morphine for post Caesarean section analgesia involving 108 healthy parturients. The authors concluded that a dose of 0.1 mg intrathecal morphine provides optimal analgesia. A study conducted by Milner et al (1996) also revealed the same result. However, none of the patients was completely pain free and all patients requested additional intravenous analgesia.

Pruritus is the most frequent undesirable side effects associated with intrathecal morphine. The incidence is reported to be between 43-94%. Meanwhile, incidence of nausea and vomiting were demonstrated to be 10% and 12% respectively following intrathecal morphine 0.1 mg. By using higher doses, the incidence of nausea and vomiting increased. Delayed respiratory depression on the other hand occurs between 3.5 and 12 hours after injection with a peak at 6 hours. The true incidence of respiratory depression following intrathecal morphine is unknown. Two large studies quote the incidence in obstetric population between 0.003-0.01%. The main objective of the study was to compare postoperative analgesia, side effects profile and overall satisfaction in patients scheduled for elective Caesarean section who received intrathecal fentanyl with and without morphine 0.1 mg.

Methods

This was a double blinded, prospective randomized controlled trial involving patients undergoing elective Caesarean section in maternity operation theatre, PPUKM. Approval was obtained from Dissertation Committee, Department of Anaesthesiology and Intensive Care, PPUKM and Ethics Committee, PPUKM. Following written informed consent, 60 patients were randomized into 2 groups which are morphine group and no morphine group. Random allocation was performed by shuffling sealed envelopes. Inclusion criteria were ASA physical status I and II and age between 18-45 years old. Exclusion criteria were patient refusal to participate in this study, contraindication to spinal anaesthesia and history of allergic reaction towards opioids.

Patients scheduled for elective surgery were fasted overnight and received ranitidine 150 mg orally the night before and on the morning of the operation. 30 mls of sodium citrate 0.3M was served once they were called to operation theatre. With the patient in sitting position, the subarachnoid space was identified using a 27G pencil-point spinal needle via the L3-4 or L2-3 interspace after infiltration with lignocaine 2%. On aspiration of clear cerebrospinal fluid, 1.8-2 mls of hyperbaric bupivacaine 0.5% plus 25 mcg of fentanyl were injected (no morphine group). The morphine group had morphine 0.1 mg added into spinal solution. This preparation was made by anaesthetist performing the spinal anaesthesia who took no further part in this study.

Following intrathecal injection, the patient was placed in a modified supine position with 15° of left lateral tilt. After adequate spinal anaesthesia was established, Caesarean section was allowed to proceed. Those with inadequate spinal anaesthesia requiring conversion to general anaesthesia were excluded. Hartmann’s solution was given accordingly to replace fluid deficit and for maintenance during the
case. Boluses of phenylephrine intravenously were given in order to maintain normal blood pressure at the discretion of anaesthetist.

Following surgical delivery of neonate, 5 units of slow bolus intravenous oxytocin was given upon clamping of the umbilical cord. For the supplemental analgesia, all patients received regular dose of oral NSAIDs based on obstetrician’s desire post operatively. In the events that rescue analgesia was required for breakthrough pain, co-administration of opioids were allowed with strict monitoring in acute cubicle. The observers and the patients were not aware of intrathecal drugs used.

The incidence of side effects was assessed every 4 hours for 24 hours. Patients were advised to immediately alert ward staff if any adverse event occurred and not just their present state at the particular time they were seen. Pruritus was assessed using a 4 point score: 0=no pruritus, 1=mild pruritus, 2=moderate pruritus and 3=severe pruritus. Nausea was assessed using a 4 point score: 0=no nausea, 1=mild nausea, 2=moderate nausea and 3=severe nausea. Vomiting was assessed as yes/no and number of episodes within 24 hours will be recorded. Sedation was assessed using a 4 point score: 0=alert, 1=occasionally drowsy, 2=frequently drowsy but easy to arouse and 3=drowsy and difficult to arouse.

The patient was cared for in a post natal ward following their operation. As usual, vital signs which include blood pressure, heart rate and respiratory rate were recorded every 4 hours. Respiratory depression was assessed by monitoring respiratory rate. At the same time, degree of post-operative pain score was evaluated based on verbal pain score, VPS: 0=no pain and 10=worst imaginable pain. Subsequently, the pain scores were categorized into mild (VPS ≤3), moderate (VPS 4-7) and severe pain (VPS ≥8). Overall satisfaction was assessed at 24 hours as 0=very unsatisfied, 1=unsatisfied, 2=satisfied and 3=very satisfied.

With α value determined at 0.05 and power of study at 80%, this study required 50 patients. Allowing for dropout rate of 20%, 60 patients were recruited as sample. Statistical data analysis was done using Predictive Analytics Software (PASW) Statistics. Data were analyzed using Mann-Whitney U test or Chi-square test where appropriate. A p-value of <0.05 was considered statistically significant.

**Results**

Sixty patients were enrolled in this study. None of the patients experienced intraoperative adverse surgical or anaesthesia related complications which required conversion to general anaesthesia. There were an equal number of patients in each studied group, morphine and no morphine. Table I summarised the details of socio-demographic data of the study population. There were no significant differences between the two groups with respect to age, weight, ASA grouping and gravidity.

Over the 24-hour study period, statistical analysis showed that there were significantly (p<0.05) lower VPS at 4, 8, 12, 16 and 20 hours in morphine group in

<table>
<thead>
<tr>
<th>Table 1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Socio-Demographic Data</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Morphine group (N=30)</th>
<th>Non-morphine group (N=30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)*</td>
<td>31.2 ± 4.5</td>
<td>30.17 ± 5.7</td>
<td>0.209</td>
</tr>
<tr>
<td>Weight (kg)*</td>
<td>70.383 ± 12.6</td>
<td>68.917 ± 12.6</td>
<td>1.000</td>
</tr>
<tr>
<td>Height (cm)*</td>
<td>156.5 ± 6.2</td>
<td>157.0 ± 7.2</td>
<td>0.426</td>
</tr>
<tr>
<td>ASA 1:2</td>
<td>22:8</td>
<td>26:4</td>
<td>0.333</td>
</tr>
<tr>
<td>Gravidity (primigravida: multigravida)</td>
<td>11:19</td>
<td>17:13</td>
<td>0.195</td>
</tr>
</tbody>
</table>

* Results are expressed as mean ± SD
comparison to no morphine group as shown in Figure 1. At least 86% of the patients in morphine group reported mild pain (VPS ≤3) compared to only 63% in no morphine group between 4 to 16 hours. Meanwhile at 20 and 24 hours postoperative, about 90% of the patients in morphine group and 77% of the patients in no morphine group experienced mild pain. About 40% of the patients in no morphine group experienced breakthrough pain and requested for rescue analgesia at some point of time within 24 hours postoperative period. They were served with intramuscular pethidine 75 mg stat. None of the patients in morphine group however had similar problem within the same period of time.

Figure 1
mean verbal pain score

Figure 2 showed the incidence of side effects in both groups. There was no incidence of severe pruritus, nausea or vomiting in the studied populations. However, statistical analysis showed that there was a significant difference (p<0.05) between the two groups in the incidence of pruritus at every assessment period except at 4 hours postoperative period. There was a statistically significant difference (p=0.044) between the two groups in the incidence of nausea at 8 hours postoperative. None of the patients in both groups reported nausea after 16 hours postoperative period. Patients who received morphine experienced higher incidence of vomiting and there was a statistically significant difference between the two groups at 8 hours (p=0.013) and 12 hours (p=0.011). However, none of the patients reported any vomiting after 12 hours postoperative period.

Overall patient satisfaction is good as only 13% from the morphine group and 20% from the non-morphine group were unsatisfied. It seems to be relatively clear that overall satisfaction in this study is higher in morphine group. None of the patients developed sedation or respiratory depression. In this study, both groups received multimodal analgesia in the form of oral etoricoxib 120 mg twice or naproxen 250 mg three times per day postoperatively.

Discussion

Neuraxial opioids have contributed to improved analgesia during intraoperative as well as postoperative Caesarean delivery. Two routes of administration are possible for neuraxial opioids, either intrathecal or epidural injection. There is no clear evidence to recommend one technique over the other. It is worth to note that the most important clinical question that emerges from the present reviews is whether the analgesic benefits worth the side effects induced by neuraxial opioids.

We found that in this study, the quality of postoperative analgesia with intrathecal fentanyl 25 mcg alone was inferior to that with addition of intrathecal morphine 0.1 mg. It is consistent with the study conducted by Chung et al (1997) where they added meperidine (pethidine) to intrathecal morphine and compared the quality of pain relief with either morphine or meperidine alone. The mixture was superior to either agent alone, showing the lowest pain scores, the lowest need for intravenous supplementation and higher degree of satisfaction.

Palmer et al (1999) reported that intrathecal
morphine for control of post Caesarean delivery pain is usually quite effective for the first 24 hours. However, none of the patients was completely pain free and all patients requested additional intravenous analgesia. In our study, lower VPS was demonstrated up to 24 hours in morphine group compared to no morphine group. Siti Salmah and Choy (2009) meanwhile compared the quality of postoperative analgesia between intrathecal fentanyl 25 mcg and intrathecal morphine 0.1 mg in patients undergoing Caesarean section. They found that postoperative analgesia of intrathecal fentanyl was inferior to that of intrathecal morphine.

Single epidural administration of morphine has also been used to control postoperative pain. Shymala and Choy (2008) studied the effectiveness and duration of analgesia of epidural morphine 4 mg and 5 mg for postoperative analgesia following Caesarean section. They found that epidural morphine 5 mg provided adequate and longer duration of analgesia but resulted in higher incidence of pruritus and vomiting. Sarvela et al (2002) compared intrathecal morphine 0.1 mg and 0.2 mg with epidural morphine 3 mg. They found that pain control were equally good for elective Caesarean delivery.

Pruritus is the most frequent undesirable side effects associated with neuraxial opioids. In this study, the incidence of pruritus following intrathecal morphine in patient underwent Caesarean delivery was 37%. This result was consistent to that reported by Jorgen et al (1999) which was 10% and 12% respectively. This can be attributed to an inclusion of fentanyl 25 mcg as a standard spinal solution in this study which significantly contributed to the increased incidence of nausea and vomiting in the morphine group. Majority of the patient recovered within 12 hours post-spinal administration. On the other hand, the incidence of nausea and vomiting in the no morphine group was 13% and 10% respectively, mostly resolved within 8 hours.

The aetiology of nausea and vomiting in parturients undergoing spinal anaesthesia for Caesarean delivery is complex and dependent on various factors. Maternal hypotension after induction of spinal anaesthesia is associated with increased incidence of intraoperative as well as postoperative nausea and vomiting. Hypotension leads to brainstem hypoxia, thus stimulates the vomiting centre to induce emesis. In this study, fluid infusion to replace deficit, left uterine displacement or administration of phenylephrine were performed accordingly for the prevention and early treatment of hypotension. This ensured that the incidence of nausea and vomiting can be attributed to the study drugs.

Delayed respiratory depression is the most feared side effect of intrathecal morphine. Unfortunately, there is a lack of proper definition of the term ‘respiratory depression’ in the literature. Rie Kato et al (2008) reported 6 out of 1915 patients exhibited bradypnoea as defined by respiratory rate of less than 10 breaths per minute within 24 hours following intrathecal morphine 0.15 mg. In our study, we used a combination of respiratory rate and level of sedation to monitor respiratory depression postoperatively. However, none of our patients experienced bradypnoea or had difficulty to arouse from sleep. As delayed respiratory depression is a rare event, we concluded that larger samples are required to determine its incidence.
References


