



Comparison of intrathecal morphine vs fentanyl with 0.5% Ropivacaine for Analgesia after Caesarean Section

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I. INTRODUCTION:

The responsibility of the anaesthesiologist in obstetrics is arguably greater than in any other field of Anaesthesia. Analgesia after Caesarean Section is achieved commonly by administration of opioids into the intrathecal space.

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. Due to the synergistic effect of opioids with local anaesthetics, it is possible to achieve satisfactory spinal anaesthesia using a lower dose of local anaesthetic agent than before⁴.

Optimal pain relief following Caesarean section is an important consideration that aids in early ambulation and nursing the infant. The use of opioids as an adjunct to local anaesthetics during spinal anaesthesia has shown to improve the quality of sensory blockade with minimal motor blockade and thus providing a better pain relief postoperatively with early ambulation. Morphine and fentanyl are the most commonly used adjuncts for this purpose⁵.

Fentanyl has a short elimination half life of 90 minutes to 360 minutes⁵, thus limiting its analgesic effects to about 45 minutes. The effect on analgesia with intrathecal fentanyl when used alone is inferior compared to intrathecal morphine⁶.

Intrathecal Opioids can cause side effects due to systemic absorption in a dose related manner. They include respiratory depression, pruritus, nausea, vomiting and urinary retention.

Intrathecal morphine is known to cause delayed respiratory depression. This may result in 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}.

This study compares the efficacy and duration of analgesia of intrathecal morphine vs intrathecal fentanyl along with 0.5% ropivacaine after Caesarean section.

II. MATERIALS AND METHODS:

Study design: A prospective, randomized, comparative study

Study Setting: Narayana Health Multispecialty Hospital, Bangalore

Methodology: Approval for the study was obtained from the institutional review board. After obtaining written informed consent, sixty parturients at term, ASA II scheduled for elective Caesarean section under spinal anaesthesia were selected. Exclusion criteria were contraindication for spinal anaesthesia, body mass index more than 35 kg/m², history of chronic drug abuse and known allergies to the study drugs

Patients fulfilling the above criteria were randomly allocated using computer generated randomization table into two groups:

Group 1 received 1.8mls of ropivacaine 0.5% with 100mcg preservative-free morphine (diluted in 0.5ml normal saline).

Group 2 received 1.8mls of ropivacaine 0.5% with 25 μ g fentanyl.

The two groups received a total of 2.3ml local anaesthetic solution for each patient.

All patients fasted for six hours. H₂-receptor antagonist, cimetidine 200mg was administered orally on the night before and the morning of surgery. All patients received 30ml of 0.3 M sodium citrate, as a standard prophylaxis for gastric acid aspiration.

Electrocardiography, Non-Invasive BP measurement and Pulse oximetry was the standard monitoring technique for all patients. All patients were preloaded with 500mls of Hartmann's solution over 20 minutes prior to the procedure.



Under aseptic precautions, spinal anaesthesia was performed with the patient in the sitting position using 25-gaugesprotteneedle at either L3-L4 or L4-L5 interspace. Entry into subarachnoid space was established by clear CSF flow, and the patient was given 1.8ml 0.5% ropivacaine with morphine 100mcg (Group 1) or 1.8ml 0.5% ropivacainewith fentanyl 25µg (Group 2).

Following administration of spinal anaesthesia, patient was placed in supine position with 15° left uterine displacement. The efficacy of blockade was measured by the level of sensory loss to temperature. Surgical incision was made after a satisfactory blockade up to T4 level was achieved. All patients received oxygen at 6 L/min flow via a face mask. Blood pressure was monitored at 1-minute intervals until stable then continued every 5 minutes. Hypotension was defined as a twenty percent decrease from baseline systolic blood pressure and this was treated with Ephedrine 3mg IV boluses.

The patient was sent to recovery room after an uneventful surgery, for observation. Rescue analgesia was provided with IV Morphine patient controlled analgesia (PCA) with the following setting: Bolus dose of 1mg Morphine with a Lock-out period of Five minutes, maximal dose of 12mg/hour and without a background infusion. Recovery room observation lasted for 30 minutes and the stable patient was allowed to return to obstetric ward for observations. Trained staff nurses who were blinded to the procedure, collected the data.

Vital signs were monitored hourly over six hours and pain was assessed 6-hourly by using visual analogue score (VAS). Time from spinal anaesthesia 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 awoken, 3 =difficult to arouse). Sedation was considered clinically relevant if the patient was not easily awakened. Respiratory depression was defined as respiratoryrate 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 chlorphenamine 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 software version 12. Data were analysed using independent t-test or Chi-square tests where appropriate. A p-value of < 0.05 was considered statistically significant.

III. 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.

There was no significant difference between the two groups in terms of age, weight, height and period of gestation.

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-hour study period (p<0.05).

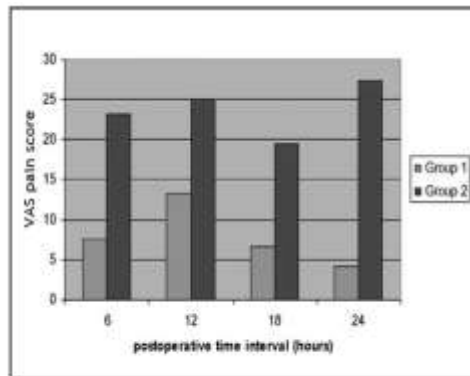


Fig. 1: Mean postoperative pain score (VAS)

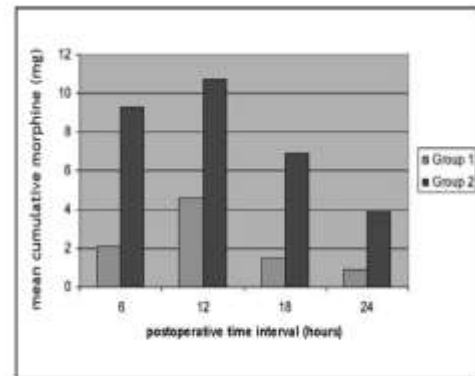


Fig. 2: Mean postoperative cumulative PCA morphine consumption

Figures 3 and 4, 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.

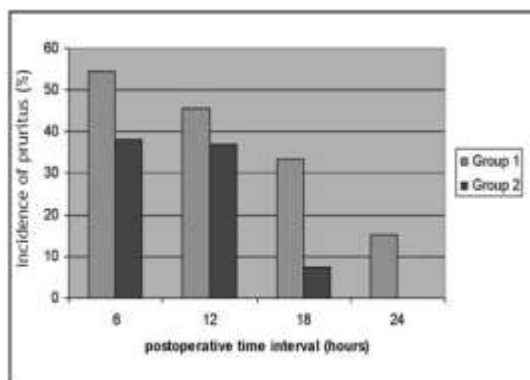


Fig. 3: Opioid side effect (pruritus) in 24 hours

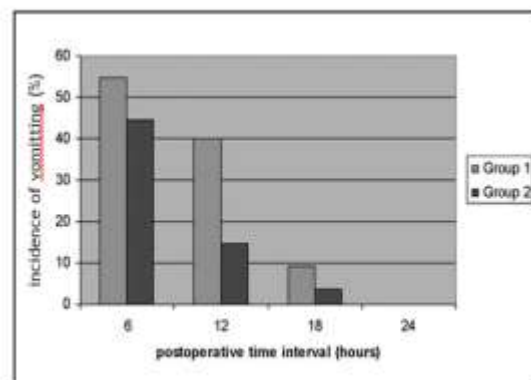


Fig. 4: Opioid side effect (nausea and vomiting) in 24 hours

IV. 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 study⁶.

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 mg⁸. 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 0.1 mg morphine used, probably because of the small sample size.

This study demonstrated a greater risk of vomiting in the IT morphine as compared to



ITafentanyl. 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 metoclopramide (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 vomiting^{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 author would like to emphasize 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.

V. CONCLUSION

In conclusion, the result of this study showed that the addition of 0.1mg morphine to 1.8ml 0.5% ropivacaine 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% ropivacaine.

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