Analgesic efficacy in caesarean section: a comparison between fentanyl and buprenorphine as an adjuvant to bupivacaine under subarachnoid block

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ABSTRACT

Background and aims: Pain is a sensory modality as well as an experience. Both general and regional anaesthesia are used during caesarean sections. Present study was undertaken to compare the analgesic efficacy of intrathecal fentanyl and intrathecal buprenorphine as an adjuvant to bupivacaine in caesarean section under subarachnoid block.

Methods: Hundred patients belonging to ASA II scheduled for caesarean section were randomly divided into two groups. Each group consisting of 50 patients, received 75 mcg of buprenorphine with 10mg of 0.5% hyperbaric bupivacaine (group BB) or 12.5 mcg of fentanyl with 10mg of 0.5% hyperbaric bupivacaine (group BF). The onset time and duration of sensory and motor block, maximum level of sensory block, duration of analgesia, two-point regression, hemodynamic changes and side effects were recorded.

Results: Bupivacaine with buprenorphine had prolonged two segment regression (105.46±14.78 mins) and duration of analgesia (488.28±156.97 mins) compared to fentanyl (100.33±12.65 mins) and (210.32±8.10 mins) respectively. Onset of sensory (1.50±0.39 mins) and maximum sensory block upto T4 (4.00±0.98 mins) was faster in fentanyl compared to buprenorphine group (2.00±0.37 mins) and (4.56±1.14 mins) respectively. Hemodynamic changes and side effects in both the groups were comparable and statistically insignificant.

Conclusion: The study thus concluded that although fentanyl produced faster sensory block, duration of analgesia was longer with buprenorphine, and both the drugs did not cause significant side effects.

Keywords: Fentanyl, buprenorphine, bupivacaine.

"Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage," according to the International Association for the Study of Pain's taxonomy work group.¹ The Greek word poine (punishment) is where the word "pain" originates.² Pain is a sensory modality as well as an experience. Surgery-related discomfort is a common occurrence that all patients experience throughout the perioperative period. Acute pain, in addition to the excruciating sensory impressions it causes, has a number of negative repercussions on physical and psychological health.²

Both general and regional anaesthesia are used during caesarean sections.³ Regional anaesthesia has several obvious benefits, such as avoiding the issue of a difficult airway, avoiding the use of multiple drugs necessary for general anaesthesia, and allowing the expectant mother to be awake to witness the delivery of her child so she can participate in and enjoy the birthing experience. The choice of which anaesthetic technique to utilize for a caesarean section should be made specifically for each patient based on the urgency and indication of the operation, maternal preference as well as coexisting medical problems and foetal risk.⁴

The use of local anaesthetics is limited by their duration of action and dose-dependent side effects on the heart and
central nervous system, despite being helpful in the management of acute and chronic pain. Because they lengthen the duration of the sensory and motor block and reduce the total amount of local anaesthetics needed, adjuvants or additives are frequently employed in conjunction with local anaesthetics. Numerous intrathecal adjuvants have been employed in the context of augmentation techniques for neuraxial blockade. Along with non-opioids like midazolam, ketamine, neostigmine, tramadol, and clonidine, this also includes opioids like morphine, fentanyl, and buprenorphine. The most researched and widely used of them have been opioids.

A Scandinavian scientist named Ekenstam created bupivacaine (1-butyl-2', 6'-pipecoloxylidide) for the first time in 1957. It was initially used in therapeutic settings in 1963. Bupivacaine, a local anaesthetic is most commonly used in spinal anaesthesia for caesarean section. It comes in two forms - an isobaric form and a denser hyperbaric form - and has a long half-life. When isobaric (or "plain") bupivacaine is combined with glucose (80 mg/ml), hyperbaric bupivacaine is created. After injection into the intrathecal space, the diffusion pattern and distribution are hypothesized to be impacted by the difference in densities between the two forms. Both types of spinal anaesthesia have been routinely utilized for caesarean sections.

The synthetic opioid fentanyl is derived from phenylpiperidine and is highly lipid-soluble. A \( \mu \) -receptor agonist, fentanyl is approximately 100 times more potent than morphine. In 1960, Dr. Paul Janssen created the first synthetic form of fentanyl.

Buprenorphine is an analogue of the alkaloid thebaine that acts centrally. A mixed agonist and antagonist drug, buprenorphine has a high affinity for both \( \mu \) and \( \kappa \) opiate receptors. The present study was undertaken to compare the analgesic efficacy of intrathecal fentanyl and intrathecal buprenorphine as an adjuvant to 0.5% hyperbaric bupivacaine in caesarean section under subarachnoid block and was conducted in the caesarean section operation theatre and its respective wards. Based on purposive sampling 100 patients of ASA grade II scheduled for caesarean section surgery the under subarachnoid block were selected for the study and divided into two groups. The protocol was explained to all the patients in detail in their language and informed and written consent was taken.

Inclusion criteria -
1. ASA II patients
2. Age: 20-40 years
3. Weight: 50-70 kgs
4. Term pregnant women planned for caesarean section
5. Living fetus
6. Intact amniotic membranes
7. No history of bleeding tendency

Exclusion criteria -
1. Patient refusal.
2. Patients having known hypersensitivity to the drugs.
3. Age: <20 or >40 years
4. ASA-I, III or more.
5. Weight: <50 kgs or >70 kgs
6. Contraindication to spinal anaesthesia (coagulopathy, significant hypovolemia, systemic or local sepsis, increased intracranial pressure, local anesthetic or bupivacaine allergy).
7. High risk pregnancies as preeclampsia, any medical disorder (DM, cardiac disease or and thyroid disease).
8. Chronic pain or daily intake of analgesic.
9. Abnormal placenta station e.g. placenta previa.

Grouping: The patients were randomly allocated into 2 groups with 50 patients in each group. Group BB received 10mg of 0.5% hyperbaric bupivacaine with 75 mcg buprenorphine making a total of 2.25 ml. Group BF received 10 mg of 0.5% hyperbaric bupivacaine with 12.5 mcg fentanyl making a total of 2.25 ml.

A routine pre-anaesthetic examination was conducted on the evening before the surgery. Parturients were taken up for the study after they met the inclusion and exclusion criteria. Parturients were asked to stay nil orally for at least 6 hours prior to the operation. All the patients were explained about the evaluation of postoperative pain with the use of VAS scores. On the day of surgery, a peripheral intravenous line with an 18-gauge cannula was secured in one of the upper limbs and infusion started with ringer’s lactate. Premedication with intravenous ranitidine 50mg and
ondansetron 4mg, 2hrs prior to the anaesthetic procedure for aspiration prophylaxis was administered. Multiparameter monitors were connected which records heart rate, non-invasive measurement of SBP, DBP, MAP, continuous ECG monitoring and oxygen saturation. All the drugs and equipments including proper sized laryngoscope, endotracheal tube, face mask, circuits, emergency resuscitation trolley and airway equipments were kept ready.

Spinal anaesthesia was performed under aseptic precautions and was performed with 25G Quincke’s spinal needle using a midline approach in the flexed lateral decubitus position at L3-L4 interspace. After clear and free flow of CSF was noted, the local anaesthetic agent that is 12.5mcg fentanyl added to 10mg of 0.5% hyperbaric bupivacaine was injected in Group BF and 75mcg buprenorphine added to 10 mg 0.5% hyperbaric bupivacaine was injected in Group BB intrathecally.

Immediately after the injection the needle was withdrawn, the parturient turned supine and wedge was given underneath the right buttock to prevent supine hypotension syndrome, and allowed to remain so until the maximum level of sensory blockade was achieved. Assessment of the sensory and the motor blockade were done at the end of each minute till the maximum level achieved. Measurements of blood pressure, heart rate, respiratory rate, and arterial oxygen saturation were continuously monitored for every 3 minutes for first 15 minutes, then every 5 min till 30 minutes, then every 10 minutes for 2 hrs, thereafter every 30 minutes till patient complains of pain. Sensory blockade was assessed by pinprick method using a blunt needle and was tested in the midclavicular line on chest, trunk and legs on either side. Analgesia was defined as loss of the sensation to pinprick and anaesthesia as loss of sensation of touch. The motor blockade was assessed using Modified Bromage Scale. Intraoperative and post operative complications like fall in blood pressure, variation in heart rate, complaints like nausea, vomiting, pruritus, hypotension were noted, treated and tabulated, if required.

At the end of the surgery, patients were shifted to recovery room. Upon arrival to recovery room, the pulse rate, respiratory rate, SPO2, blood pressure, pain score (on Visual Analogue Scale) was assessed and recorded, in the immediate postoperative period and after one hour; and later, after stabilization they were sent to their respective wards.

The following parameters were noted: 1) Induction of spinal anaesthesia: The time at which the intrathecal injection was completed. 2) Maximum sensory blockade: It is the maximum level of sensory blockade attained after the induction of spinal anaesthesia. 3) Time required for maximum sensory blockage. It is the time required to attain maximum level of sensory blockade. 4) Time required for maximum motor blockage. It is the time required to attain maximum level of motor blockade. 5) Duration of Motor blockade: Time required for recovery of complete power of lower limbs (Bromage grade 0) from the time of induction of spinal anaesthesia. 6) Duration of two segment sensory regression: is defined as the time taken from the maximum level of sensory block attained till the sensation has regressed by two segments.

After the patients were shifted to their respective wards, they were assessed on 1st, 2nd, 6th, 12th and 24th hour post operatively as per the departmental protocol. The VAS score, time for first request of analgesia and any adverse effects were noted. The data were collected as per a pre-defined proforma.

Rescue analgesic of Inj. tramadol 75mg intramuscularly was given once the VAS was 4 or more or if the patient demanded so in both groups and the timing of administration of this medication was recorded. During this period, postoperative nausea and vomiting was managed by inj. ondansetron iv.

Statistical analysis: Data from the case record proforma was entered into Microsoft Excel spreadsheet version 2021 and analyzed using IBM-SPSS version 26. Normality of the data was determined using Kolmogorov–Smirnov test. Categorical data was expressed as frequency and proportion (percentages). Numerical data was represented with mean and standard deviation for parametric data, or median and IQR in case on non-parametric data. For determining the statistical correlation in categorical data, a chi-square test or fisher exact test was applied. To calculate significant mean difference for normally distributed continuous data, a student t-test was applied, whereas, for non-normal continuous data, the non-parametric test of Mann-Whitney U was applied. P-value < 0.05 will be considered significant for all statistical comparisons.

Results

Table 1, shows the findings of the two groups with respect to age, weight, height and duration of surgery. The age, height, weight and duration of surgery showed no statistically significant difference between the study groups.

Table 2, shows the findings of the two groups with respect to onset of sensory block, onset of motor block, time
to achieve maximum sensory block upto T4 level, two segment regression time, duration of motor block and duration of analgesia. Onset of sensory (1.50±0.39 mins) and maximum sensory block upto T4 (4.00±0.98 mins) was faster in fentanyl compared to buprenorphone group (2.00±0.37 mins and 4.56±1.14 mins respectively).

Table 1: Demographic variables

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BB</td>
<td>BF</td>
<td></td>
</tr>
<tr>
<td>Age in years (years)</td>
<td>29±6</td>
<td>30±6</td>
</tr>
<tr>
<td>Weight in kg</td>
<td>58.13±5.75</td>
<td>58.10±5.39</td>
</tr>
<tr>
<td>Duration of surgery in mins</td>
<td>156±6.27</td>
<td>156±6.80</td>
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Bupivacaine with buprenorphone had prolonged two segment regression (105.46±14.78 mins) and duration of analgesia (488.28±156.97 mins) compared to fentanyl (100.33±12.65 mins and 210.32±8.10 mins respectively). The mean time for onset of motor block was 2.63±0.36 mins in group BB and 2.60 ± 0.32 mins in group BF which was statistically insignificant (p=0.4267). In our study, the mean duration of motor blockade was 157.65±12.46 mins in group BB and 153.17 ± 11.06 mins in group BF which was statistically insignificant (p=0.1246).

Table 2: Sensory and motor variables

<table>
<thead>
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<tbody>
<tr>
<td>BB</td>
<td>BF</td>
<td></td>
</tr>
<tr>
<td>Onset of sensory block in mins</td>
<td>2.00±0.37</td>
<td>1.50±0.39</td>
</tr>
<tr>
<td>Onset of motor block in mins</td>
<td>2.63±0.36</td>
<td>2.60±0.32</td>
</tr>
<tr>
<td>Maximum sensory block upto T4 in mins</td>
<td>4.56±1.14</td>
<td>4.00±0.98</td>
</tr>
<tr>
<td>Two segment regression time in mins</td>
<td>105.46±14.78</td>
<td>100.33±12.65</td>
</tr>
<tr>
<td>Duration of motor block in mins</td>
<td>157.65±12.46</td>
<td>153.17±11.06</td>
</tr>
<tr>
<td>Duration of analgesia in mins</td>
<td>488.28±156.97</td>
<td>210.32±8.10</td>
</tr>
</tbody>
</table>

Figure 1, shows the VAS which was calculated in postoperative period for post-operative analgesia. VAS was significantly lower in group BB, at 2,6,12 and 24 hours, p < 0.05.

Table 3, shows the adverse effects. Side effects in both the groups were comparable and statistically insignificant. Haemodynamic changes were comparable.

Table 3: Side effects between two groups

<table>
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<tr>
<th>Variables</th>
<th>Number</th>
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<th>Number</th>
<th>%</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BB</td>
<td>BF</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypotension</td>
<td>0</td>
<td>0%</td>
<td>2</td>
<td>4%</td>
<td>2</td>
<td>2%</td>
</tr>
<tr>
<td>Nausea</td>
<td>2</td>
<td>4%</td>
<td>5</td>
<td>10%</td>
<td>7</td>
<td>7%</td>
</tr>
<tr>
<td>Pruritus</td>
<td>1</td>
<td>2%</td>
<td>4</td>
<td>8%</td>
<td>5</td>
<td>5%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1</td>
<td>2%</td>
<td>3</td>
<td>6%</td>
<td>4</td>
<td>4%</td>
</tr>
<tr>
<td>None</td>
<td>46</td>
<td>92%</td>
<td>36</td>
<td>72%</td>
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<tr>
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<td>50</td>
<td>100%</td>
<td>50</td>
<td>100%</td>
<td>100</td>
<td>100%</td>
</tr>
</tbody>
</table>

Figure 1: Visual analogue scale (VAS) between the two groups

Discussion

The study entitled “A comparative study of analgesic efficacy of fentanyl and buprenorphine as an adjuvant to bupivacaine in caesarean section under subarachnoid block” was undertaken to evaluate the analgesic properties and duration of analgesia, hemodynamic changes and side effects if any. The age, sex, ASA category, height, weight and duration of operation showed no statistically significant difference among both the study groups.

Onset of sensory blockade is the time from the completion of the injection of the study drug till the patient does not feel the pain at T10 level. Mean time of onset of sensory block in our study group BB was 2.00± 0.37 mins and group BF was 1.50± 0.39 mins. There was significant difference in the onset of sensory blockade between the two groups. Dhawale TA et al. in their study compared intrathecal fentanyl and buprenorphine as an adjuvant to 0.5% hyperbaric bupivacaine for spinal anesthesia and found a statistically significant difference in the mean onset of sensory blockade between both the groups i.e. the earliest onset of sensory block was in the fentanyl group followed by the buprenorphine group. Alugolu M et al. conducted a comparative study of intrathecal bupivacaine 0.5% heavy...
with fentanyl versus intrathecal bupivacaine 0.5% heavy with buprenorphine in lower limb and lower abdominal surgeries and found out that the onset of sensory block was faster in buprenorphine than in fentanyl and was statistically significant.

Two segment regression time is the time interval from injection of local anaesthetic solution until the maximum level of sensory blockade has regressed by two segments. In our study, mean two segment regression time of group BB was 105.46 ± 14.78 mins while that of group BF was 100.33 ± 12.65 mins, which was statistically significant with p value 0.0012. Nithyashree N et al 13 in a comparative study of intrathecal hyperbaric bupivacaine 0.5% with fentanyl versus hyperbaric bupivacaine 0.5% with buprenorphine in lower limb and lower abdominal surgeries concluded that time for two segment regression was considerably slower in buprenorphine group than the fentanyl group and it was statistically significant.

In our study, the time taken from the time of injection till the patient complains of pain at the site of surgery i.e. the duration of analgesia was statistically significant. The duration of analgesia in group BB was 488.28 ± 156.97 min and in group BF was 210.32 ± 8.10 min and p value were 0.0000. Dhawale TA et al 14 in their study compared intrathecal fentanyl and buprenorphine as an adjuvant to 0.5% hyperbaric bupivacaine for spinal anaesthesia, maximum duration of analgesia after spinal drug administration was the highest in buprenorphine group followed by the fentanyl group and p < 0.05, which was in accordance with our study.

Since buprenorphine has a high affinity for spinal receptors and produces a high concentration at these receptors at smaller dosages, less of the drug is needed. Buprenorphine's increased lipid solubility facilitates its absorption into the spinal cord. The spinal cord's sluggish diffusion into the circulation does not reach the bulbar centers. Longer duration of effect was therefore caused by high lipid solubility, strong opiate receptor binding, and powerful and sustained activity 18. Sittaramane S et al 15 in their study compared the effect of fentanyl 25 mcg with bupivacaine 0.5% and buprenorphine 60 mcg with bupivacaine 0.5% in spinal anaesthesia for elective caesarean section and concluded that the mean duration of effective analgesia was significant statistically between the two groups.

In our study, the mean time taken for maximum sensory level upto T4 dermatome in the group BB was 4.56 ± 1.14 minutes as compared to 4.00 ± 0.98 minutes in the group BF. The time taken for maximum sensory block level in our study was statistically significant in both the groups (p=0.0362). In accordance to our study, Dhawale T A et al 11 in their study compared intrathecal fentanyl and buprenorphine as an adjuvant to 0.5% hyperbaric bupivacaine for spinal anaesthesia and found a statistically significant difference in the mean onset of maximum level of sensory block upto T4 level between the two groups. Sonya K et al 16 in their study compared two opioids, fentanyl and buprenorphine as adjuvant to spinal bupivacaine in caesarean section and concluded that maximum height of sensory block was achieved faster in fentanyl group compared to buprenorphine group. Thus, the result was in accordance with our study.

In our study, motor blockade was checked by using Modified Bromage scale and onset was taken as soon as the patient developed grade 1 motor blockade and the mean time for onset of motor block was 2.63 ± 0.36 mins in group BB and 2.60 ± 0.32 mins in group BF which was statistically insignificant (p=0.4267). Sonya K et al 16 compared two opioids, fentanyl and buprenorphine as adjuvant to spinal bupivacaine in caesarean and observed that the mean onset of motor block was comparable in both the groups taken for study. This was in accordance with our study. However, Dhawale TA et al 11 in their study compared intrathecal fentanyl and buprenorphine as an adjuvant to 0.5% hyperbaric bupivacaine for spinal anaesthesia and observed that the mean time for onset of motor block was earliest in BB group (bupivacaine with buprenorphine) as compared to BF (bupivacaine with fentanyl) and BN (bupivacaine with normal saline) group, which was statistically significant. Our findings however did not agree with Alugolu M et al 12 compared intrathecal bupivacaine 0.5% heavy with fentanyl versus intrathecal bupivacaine 0.5% heavy with buprenorphine in lower limb and lower abdominal surgeries and found that the mean time for onset of motor blockade was statistically significant and concluded that addition of buprenorphine to bupivacaine produces an earlier motor blockade onset when compared to fentanyl.

In our study the mean duration of motor blockade was 157.65 ± 12.46 mins in group BB and 153.17 ± 11.06 mins in group BF which was statistically insignificant (p=0.1246). Sonya K et al 16 and compared two opioids, fentanyl and buprenorphine as adjuvant to spinal bupivacaine in caesarean and observed that the mean duration of motor block was comparable in both the groups with p value 0.2239 and was
thus similar to our study. Sittaramane S et al in their study compared the effect of fentanyl 25 mcg with bupivacaine 0.5% and buprenorphine 60 mcg with bupivacaine 0.5% in spinal anaesthesia for elective caesarean section and observed that the mean duration of motor block in both the groups was found to be statistically insignificant. Thus, the result concurred with our study.

In accordance with our study, Muppala BM et al compared epidural injection of 0.5% bupivacaine with buprenorphine and 0.5% bupivacaine with fentanyl for lower limb surgeries and concluded that no significant haemodynamic changes were observed in both the groups.

The commonly seen adverse effects with opioid administration include nausea, vomiting, retention of urine, pruritus, respiratory depression and hypotension. Opioids produce nausea and vomiting by direct stimulation of CTZ in the area of postrema of the medulla. The effect is dose related and tolerance to it develops rapidly. The emetic effect can be treated by anticholinergics and phenothiazines, especially those which are antagonists at dopamine receptors. Pruritus, particularly facial pruritus following extradural injection of opioids is attributed variously to histamine release, an effect of opioid spreading to medulla or fourth ventricle. The patients were observed for side effects like nausea, vomiting, pruritus and hypotension in both the groups. In our study, the group receiving buprenorphine, 4% patients complained nausea and 2% complained vomiting, 2% complained of pruritus, which were mild in nature and did not require any treatment. While in the group receiving fentanyl, 4% complained of hypotension, 10% complained of nausea, 6% complained of vomiting and 8% complained of pruritus, which were mild in nature and did not require any treatment. Sittaramane S et al in their study compared the effect of fentanyl 25 mcg with bupivacaine 0.5% and buprenorphine 60 mcg with bupivacaine 0.5% in spinal anaesthesia for elective caesarean section and concluded that the incidence of nausea and vomiting was more in buprenorphine compared to fentanyl. Mild pruritus was more in fentanyl group which did not require any treatment. Patients were comfortable and composed throughout the procedure and did not require any further medication in either of the groups.

Conclusion

In this comparative study, an effort was made to study the peri-operative analgesic efficacy of inj. buprenorphine and inj. fentanyl as an adjuvant with 0.5 % bupivacaine in caesarean section. There were no significant changes in the onset of motor block, duration of motor block, haemodynamic changes and side effects in either of the groups. The difference of onset of sensory, maximum sensory block up to T4 level and two segment regression time of both the groups was statistically significant. The duration of analgesia was much longer in buprenorphine group. So, it was concluded that intrathecal buprenorphine as an adjuvant with bupivacaine was better in providing prolonged satisfactory analgesia as compared to Inj. fentanyl in subarachnoid block.

Conflict of interest: None. Disclaimer: Nil.

References


15. Sittaramane S, Dhakshinamoorthy M. A Comparative Study of the Effect of Fentanyl 25 MCG with Bupivacaine 0.5% Versus Buprenorphine 60 MCG with Bupivacaine 0.5% in Spinal Anaesthesia for Elective Caesarean Section. JMSCR. 2017; 5(11): 30301-8.


17. Muppala BM, Sindhura K, Chakravarthy K. Comparative Study of Epidural Injection of 0.5% Bupivacaine with Buprenorphine and 0.5% Bupivacaine with Fentanyl for Lower Limb Surgeries anaesthesia. JMSCR. 2020 Nov; 8(11): 566-71.


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