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Premixed Versus Sequential Administration of Intrathecal Fentanyl and Bupivacaine in Elective Caesarean Section- a Comparative Study

KEYWORDS: Intrathecal fentanyl, Bupivacaine, Premixed, Sequential use, caesarean section

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ABSTRACT Background:The literature available suggests that the sequential use of the hyperbaric bupivacaine and opioid analgesics is more beneficial in the caesarean section than the premixed use. Hence, this study was undertaken with the intention of comparison of the premixed and sequential use of the hyperbaric bupivacaine and fentanyl.

Materials and Methods: A randomized and single blinded study was conducted in the department of Anaesthesiology, Bharathi Vidyapeeth Deemed University, Pune. A total 30 patients were equally divided in to sequential group and premixed group. The hemodynamic changes, onset of sensory and motor block, side effects and regression of the motor and sensory block and duration of first rescue analgesia were studied between the sequential group and premixed group.

Results:The mean age of patients was 25.4 (± 4.1) in the study group and 25.7 (± 3.4) years in control group. There was no significant difference in the blood pressure during the intra operative period. There was significant difference between the mean systolic and diastolic blood pressures of study and control groups at 1 min, 2 min, 3 min and 4 mins after induction of anesthesia.

The mean (± SD) onset of sensory block in the study group was 2.7 (+/-0.53) mins and 5.03 (± 1.07) mins in the control group which was statistically significant. There was a statistically significant difference between the mean (± SD) time for onset of motor block in study group and control group. About 26.7% of the study group had itching as the common side effect and 23.3% of the control group had hypotension as the main side effect. The regression of the sensory block was at 173.5 (± 46.89) mins in the study group and at 116.5 (± 37.7) mins in the control group and which was statistically significant. The mean regression of the motor block was at 168.0 (± 34.9) mins in the study group and at 124.0 (± 41.5) mins in the control group which was also statistically significant. The time of rescue analgesia was at 189 (± 37.1) minutes in the study group and at 102.5 (± 32.0) minutes in the control group which was statistically significant.

Conclusion:The lower incidence of side effects, stable hemodynamic effects and earlier onset and slower regression of the sensory and motor block favours the sequential use of hyperbaric bupivacaine and fentanyl.

INTRODUCTION

Intrathecal anaesthesia in caesarean section is important in alleviating the pain. The literature suggests that a number of local anesthetics have been used in order to alleviate the pain during caesarean section. Such anaesthetics and analgesics have their own advantages and disadvantages. Hyperbaric bupivacaine is the most commonly used local anesthetic. Opioids and local anesthetics administered together intrathecally, have a potent synergistic analgesia. Intrathecal opioids like fentanyl enhance analgesia from sub therapeutic doses of local anaesthetic and make it possible to achieve successful spinal anesthesia using otherwise inadequate doses of local anaesthetic. The clinical efficacy of fentanyl has been well documented to relieve the visceral pain.[1, 2] Intrathecal opioids do not cause any further depression of efferent sympathetic activity either alone or in combination with the bupivacaine. It is possible to enhance the sensory blockage without altering the degree of sympathetic blockade with less adverse hemodynamic effects.[3]

It is a common practice to mix opioids with hyperbaric bupivacaine in a single syringe before intrathecal injection of the mixture. The mixture of these drugs may alter the density of the hyperbaric solution and thus affect the spread of local anaesthetic and opioid.[4] This spread and action of the anaesthetic solution is often influenced by a number of factors including the temperature of the solution, patient position during and after spinal injection, pH and density of the solution, volume of the drug injected and height of the patients.[5]

However, the anaesthetic effect of pre mixing of bupivacaine with fentanyl and using the two drugs has not been evaluated in a detailed manner so far. The studies are lacking to elucidate the anaesthetic effect and adverse effects of using the mixed drugs and sequential use of the drugs. Hence, this study was undertaken in order to find out if the effect of these two drugs can vary by altering their mode of administration.

MATERIALS AND METHODS

A randomized and single blinded study was conducted in the department of Anaesthesiology, Bharathi Vidyapeeth University, Pune. About 60 patients undergoing caesarean section with spinal anaesthesia were randomized in to two groups by drawing lots where the

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observer was blinded. An informed, bilingual written consent was obtained before including the participants in the study group. The approval from institutional ethical committee was also obtained before the study was started.

The patients in the age group of 18 – 35 years, Healthy Primigravida and gravid 2 patients at term, ASA Grade I and II with Body mass index of less than 30 were included in the study. Extremely short stature (height less than 4 feet), Complicated pregnancies such as multiple pregnancies, pregnancy induced hypertension and placenta previa, fetal distress, Patients with skin infections at the site of injection, patients with coagulation disorders, patients with spinal deformities, patients with history of previous spinal surgeries were excluded from the study.

A thorough preanaesthetic examination was conducted for all the patients along with necessary laboratory investigations. The patients were kept nil by mouth before the caesarean section. Group I (study group) received intrathecal fentanyl and bupivacaine in separate syringe and Group II (Control) received intrathecal fentanyl and bupivacaine in same syringe. The peripheral venous access was made using 20 G IV Canula before the procedure and the patients were preloaded with Ringer Lactate solution at the rate of 10 ml/kg/hr for 30 minutes. During the operation the crystalloid was administered to prevent hypotension. Baseline BP, heart rate, oxygen saturation was recorded and subarachnoid space accessed by using a 25 G Quincke's spinal needle through $L_3 – L_4$ or $L_4 – L_5$ in the midline.

Intra operatively, all the patients were monitored every minute minutes up to 10 minutes and every ten minutes till the end of the procedure for pulse rate, blood pressure, onset of sensory block and onset of motor block. Post operatively, the patient were evaluated every fifteen minutes for first hour, and every hourly for 4 hours after that for pulse rate, blood pressure, regression of sensory and motor block, duration of analgesia and adverse effects.

Sensory block was assessed by pin prick sensation, motor block by Extended Modified Bromage scale and pain by Visual Analogue Scale. A fall in pulse rate less than 20% of baseline rate and blood pressure less than 30% of baseline was considered as significant and necessary precautions were undertaken to restore them.

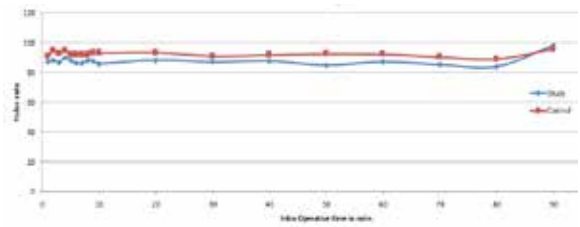
RESULTS

Table 1. Distribution of the groups according to demographic factors

Mean ± SD	Study group	Control group	T value	P value, Sig
Age in years	25.4 ± 4.1	25.7 ± 3.4	0.311	0.757, NS
Height	153.3 ± 2.9	155.5 ± 3.8	2.257	0.014, NS
Weight	60.4 ± 9.7	60.9 ± 7.6	0.207	0.837, NS
BMI	25.8 ± 4.2	25.2 ± 3.2	0.604	0.548 NS

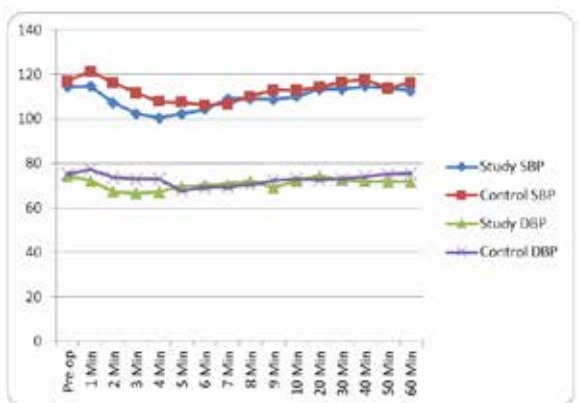
As shown in table 1, there is no statistically significant difference in the hemodynamic parameters of patients in study and control group.

Chart 1. Distribution of the study groups according to Pulse rate



The mean (± SD) pre operative pulse rate was 86.5 beats/min in the study group and 87.7 beats/min in the control group. There was no significant difference in mean pulse rate during intra operative period.

Chart 2. Distribution of the study groups according to blood pressure



The mean pre operative systolic blood pressure of the study subjects was 114.4 (5.7) mm of Hg and in the control group was 116.9 (± 6.7) mm of Hg. This difference was not statistically significant. However, there was significant difference between the mean systolic blood pressures of study and control groups at 1 min, 2 min, 3 min and 4 mins after induction of anesthesia.

The mean (± SD) diastolic blood pressure levels was 74.3 (± 4.0) mm of Hg among the study subjects and 75.1 (± 4.7) mm of Hg in control subjects during pre operative period. This difference was not statistically significant. But, there was statistically significant difference between the diastolic blood pressure of the study group and the control study subjects at 1, 2, 3 and 4 mins.

Table 2. Distribution of the study groups according to onset of sensory block

Mean ± SD	Study group	Control group	T value	P value
Onset of sensory block	2.7 ± 0.53	5.03 ± 1.07	10.714	<0.001, Sig
Onset of motor block	3.1 ± 0.3	7.23 ± 1.07	20.301	<0.001, Sig

The mean (± SD) onset of sensory block for the study group was 2.7 (+/-0.53) mins and 5.03 (± 1.07) mins among the control group which was statistically significant.

The mean (± SD) time for onset of motor block was in study group was 3.1(± 0.3) minutes in study group and 7.23 (± 1.07) minutes in control group which was also statistically significant.

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Table 3. Distribution of the groups according to type of side effects

Side effects	Study group n (%)	Control group n (%)	Total n (%)
Nil	19 (63.3)	17 (56.7)	34 (56.7)
Hypotension	2 (6.7)	7 (23.3)	9 (15.0)
Pruritis	8 (26.7)	3(10.0)	14 (23.3)
Vomiting	1 (3.3)	3 (10.0)	3 (5.0)
Total	30 (100)	30 (100)	60 (100)

About 26.7% of the study group had itching as the common side effect followed by hypotension (6.7%) and vomiting (3.3%). About 23.3% of the control group had hypotension as the side effect followed by itching in 10% and vomiting in 10% of the control group. This difference was statistically not significant.

Table 4. Distribution of the groups according to regression of the sensory block

Mean ± SD	Study group	Control group	T value	P value
Regression of sensory block	173.5 ± 46.89	116.5 ± 37.7	5.188	<0.001, Sig
Regression of motor block	168.0 ± 34.9	124.0 ± 41.5	6.759	<0.001, Sig
Time of rescue analgesia	189.0 ± 37.1	102.5 ± 32.0	9.67	<0.001, Sig

The regression of the sensory block was at 173.5 (± 46.89) mins in the study group and at 116.5 (± 37.7) mins in the control group. This difference was statistically significant. The mean regression of the motor block was at 168.0 (± 34.9) mins in the study group and at 124.0 (± 41.5) mins in the control group. This difference was statistically significant. The duration of first rescue analgesia was at 189 (± 37.1) minutes in the study group and at 102.5 (± 32.0) minutes in control group. This diference was also statistically significant.

DISCUSSION

This study was mainly undertaken to find the hemodynamic effects after administration of premixed and sequential use of Hyperbaric Bupivacaine and fentanyl. This study had shown that there was no significant change in pulse rate. However, there was a significant difference in systolic blood pressure, diastolic blood pressure within 10 minutes after induction of anesthesia. In a study of hyperbaric bupivacaine and fentanyl, Dhumal et al have observed that there was no significant difference in the heart rate. The findings of this study were in corroboration with Dhumal et al with reference to systolic and diastolic blood pressures.[6] Sachan et al had noticed a significant fall in heart rate with the lowest values after 45 min after administration of SAB in a similar study using Clonidine. Also there was an overall trend of fall in systolic blood pressure (SBP) in all the groups except during time intervals of 20 and 25 min where there was a rise unlike this study.[5]

The onset of sensory and motor block was delayed in the control group compared to the study group. Dhumal et al, in a similar study of hyperbaric bupivacaine and fentanyl observed that, the sensory analgesia was faster in the combined hyperbaric bupivacaine group than the plain bupivacaine group. The onset of motor block was faster the plain hyperbaric bupivacaine group compared to the combined bupivacaine and fentanyl group.[6] In a similar study by Sharma et al, the onset of sensory and motor block was faster in mixture group compared to the sequential group.[7] Sachan et al, in a similar study by using clonidine reported that, the onset of sensory and motor block was faster in the clonidine followed by hyperbaric bupivacaine group compared to the control group.[5]

The side effects were fewer in the study group compared to the control group in this study. A randomized trial had reported the pruritis as the main side effect in only one patient.[2] Dhumal et al reported nausea, vomiting, hypotension, shivering and pruritis were observed as the side effects significantly less in Bupivacaine with Fentanyl group.[6] Sachan et al reported hypotension as common side effect in mixture group, hyperbaric bupivacaine followed by clonidine and clonidine followed by hyperbaric bupivacaine groups.[5]

The mean time regression of the sensory and motor block was faster in the control group than the study group. In a similar study by using Clonidine, the regression of the sensory and motor block was slower in the mixture group compared administration of Hyperbaric bupivacaine and clonidine in spate syringe groups.[2] Another study by Sachan also reported similar findings.[5] Sharma et al also noticed that the regression of sensory and motor block was slower in the sequentially administered group than the premixed group.[7] The time of rescue analgesia was more prolonged in the study group than control group in this study. In a study by Desai et al[8] patients given HB and fentanyl sequentially had lower post op pain scores than premixed group. The time of rescue analgesia was 153.83 mins in control group, 235 min in HB followed by clonidine group and 240.67 mins in clonidine followed by HB in a study by Sachan et al.[9] In a study of comparison of premixed and sequentially administered hyperbaric bupivacaine and clonidine, by Sharma et al, the time of rescue analgesia was 148.6 min in the premixed group and 242.4 mins in the sequentially administered group.[7] In this study, the hemodynamic effects and side effects were fewer, earlier onset of sensory and motor block and slower regression of the blocks was observed in the sequentially administered group than the pre mixed group.

CONCLUSION

This study has shown no significant change in the pulse rate but significant difference was found in the blood pressures between the two groups. The onset of sensory and motor blocks was earlier in the study group than the controls. The regression of the sensory and motor blocks was slower in the study group. Hence, this study strongly recommends the sequential use of hyperbaric bupivacaine and fentanyl than a mixture.

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