

COMPARATIVE STUDY OF INTRATHECAL LEVOBUPIVACAINE-FENTANYL AND LEVOBUPIVACAINE IN CAESAREAN DELIVERIES

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ABSTRACT

BACKGROUND

The aim of the study is to compare the effects of intrathecal levobupivacaine-fentanyl and levobupivacaine on quality of intrathecal/subarachnoid block and haemodynamic variations in caesarean deliveries.

MATERIALS AND METHODS

The study was designed as a prospective randomised double-blind study enrolling a total of 60 female patients (age group- 20-40 years) belonging to ASA grade I and II. The patients were randomly allocated into two groups of 30 patients in each group. The Group-LF received levobupivacaine 10 mg (2 mL) + fentanyl 20 mcg (0.4 mL) and Group-LN received levobupivacaine 10 mg (2 mL) + normal saline (0.4 mL). Characteristics of spinal block, Apgar score, vital parameter variations and complications were recorded.

RESULTS

In Group LF, onset of action was faster in relation to sensory and motor blockade as compared to Group LN. Two segment regression of sensory block and duration of motor block were prolonged with addition of fentanyl to levobupivacaine. Addition of fentanyl to intrathecal levobupivacaine, prolonged duration of sensory and motor block with faster onset of sensory and motor block with better quality as compared to levobupivacaine. Statistically, no significant difference was observed in mean Apgar score at 1 and 5 minutes. There was no much difference between the groups in relation to haemodynamic variations and complications.

CONCLUSION

Intrathecal levobupivacaine with fentanyl was found to improve the quality and prolonged duration of intrathecal block. It reduced the need for rescue analgesia/supplementary analgesics for postoperative pain relief without any significant side effects. The levobupivacaine with or without fentanyl maybe used safely for spinal anaesthesia in elective caesarean deliveries.

KEYWORDS

Intrathecal Levobupivacaine, Fentanyl, Spinal Anaesthesia, Sensory and Motor Block, Haemodynamic Variations, Caesarean.

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BACKGROUND

Intrathecal anaesthesia in caesarean sections has become an established technique. The various local anaesthetics and opioids have been used, either alone or in combination. Smaller doses of opioids with local anaesthetics supplemented by intrathecal route have been recommended for spinal anaesthesia in parturients undergoing caesarean section delivery.^{1,2} Spinal anaesthesia is preferred over epidural anaesthesia due to its rapid onset, the greater degree of muscle relaxation and lower dose requirement of

local anaesthetics in caesarean cases. It also ensures reliable and good quality of block for both the mother and the newborn.³

In spinal anaesthesia, for pregnant women, the duration of motor block with bupivacaine is more as compared to levobupivacaine, which slows down venous circulation in lower limb and increases the risk of Deep Vein Thrombosis (DVT). In pregnant women, the PIH/preeclampsia are a hypercoagulable state. The bupivacaine may increase further risk of DVT.⁴ Levobupivacaine is preferred in labour analgesia because of less duration of sensory block and grade, duration of motor block is also less with levobupivacaine. Toxicity is also less as compared to bupivacaine.⁵ Hence, levobupivacaine was selected for the study. Levobupivacaine is known to produce localised anaesthesia by blocking the transmission of action potential in sensory, motor and sympathetic nerve fibers by inhibiting the passage of sodium through voltage sensitive ion channels in the neuronal membrane.⁶ The current

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pharmacodynamic evidence from animal and human studies suggests that levobupivacaine has a potentially greater margin of safety than the racemic bupivacaine.^{7,8}

In caesarean section, surgeries performed under spinal anaesthesia, it has been reported that the administration of local anaesthetics alone has a short duration of effect. Also, it is insufficient for preventing visceral pain and nausea especially during uterus manipulation and peritoneum closure. This leads to postoperative analgesic requirement at an earlier stage.⁹⁻¹¹ A number of adjuvants have been studied to prolong the effect of spinal anaesthesia. The most frequently used agent among intrathecal opioids is fentanyl, which was demonstrated to be effective for 180 to 240 minutes when administered at doses of 10 to 25 µg.¹² The number of studies on the effects of combination of intrathecal levobupivacaine-fentanyl¹³ is limited and the data on appropriate dosages for caesarean sections are inadequate. Inspired by the above findings, we selected 10 mg dose of levobupivacaine and compared it with 10 mg levobupivacaine (10 mg) with 20 µg fentanyl given intrathecally for spinal anaesthesia block in caesarean deliveries.

MATERIALS AND METHODS

After obtaining institutional ethical committee approval and written informed consent from the patients, this prospective, randomised double-blinded study was conducted in 60 pregnant women of ASA grade I and II, aged between 20-40 years, scheduled for elective caesarean section. Parturients at term of ASA I and II were included in the study. Exclusion criteria included was patient refusal to participate in the study, contraindication to spinal anaesthesia, bad obstetric history and obstetric complications in present pregnancy, evidence of foetal compromise and anomalies, patients with valvular heart disease, nephritis, renal failure and patients with psychiatric diseases.

A detailed preanaesthetic evaluation and all relevant investigations were done. In operation theatre, the standard monitoring devices SpO₂, ECG, noninvasive blood pressure, temperature probe were attached to the patient and baseline parameters pulse rate, blood pressure, respiratory rate and SpO₂ were recorded. Intravenous access was setup with a wide bore 18G intravenous cannula over forearm. Each patient was preloaded with 10 mL/kg Ringer lactated solution over a period of 20 minutes prior to spinal anaesthesia. All patients were premedicated intravenously with Inj. Ranitidine 50 mg and Inj. Ondansetron 4 mg. The patients under study were divided into two groups with 30 subjects in each group. Random selection was done for the drug to be used for the study by using computer selection.

The Group LF received levobupivacaine 10 mg (2 mL) and fentanyl 20 mcg (0.4 mL). The Group LN received levobupivacaine 10 mg (2 mL) plus normal saline (0.4 mL). Under all aseptic precautions, through midline approach, the lumbar puncture was done at L2-L3 or L3-L4 intervertebral space with 23G disposable Quincke's spinal needle. After

free flow and clear flow of CSF fluid, the study drug was injected intrathecally.

The time of injection of spinal drug was recorded as '0' minutes. Patients were placed in supine position slowly and wedge with 15-degree elevation was placed just below the right buttock for left uterine displacement to prevent supine hypotension syndrome due to IVC or aorta compression by gravid uterus. Surgery was commenced after loss of sensation to prick at T6 level. Oxygen was supplemented to each patient at a rate of 5 lit./min. via oxygen mask. The person performing the spinal block and the person who was noting down the results/observations of the study were unaware of the study drug administered to patient.

The spinal block characteristics were assessed with parameters- Sensory onset time, time to achieve complete sensory blockade and time to achieve maximum sensory level up to T6, two segment regression time, regression time to T12 for the sensory block and time of rescue analgesia.

The motor blockade was assessed using modified Bromage scale. Onset of motor block (Bromage Score-1), time to achieve maximum motor block (Bromage Score-3) and total duration of motor block were recorded. Heart rate, blood pressure, respiratory rate and oxygen saturation were monitored immediately after subarachnoid injection of drug and when patient is made supine. These observations were also noted at interval of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, 30, 45 minutes and at the end of surgery. The anaesthesia record was maintained and changes in heart rate and blood pressure were noted.

Statistical Analysis

All the observations were recorded and Student's 't' test was applied to test statistical significance between the means of the groups under study. The Chi-square test was used to find out dependencies between the two groups. A value of P<0.05 was considered to be statistically significant.

OBSERVATIONS AND RESULTS

Demographic profiles of patients in both the groups were comparable with respect to age, weight, height, Body Mass Index (BMI) and duration of surgery and were found to be statistically insignificant (Table 1).

Demography Characteristics	Group LF	Group LN	P-Value
Age (Yrs.)	26.16 ± 5.25	25.05 ± 4.61	>0.05
Weight (Kg)	62.52 ± 7.13	64.36 ± 6.54	
Height (cm)	158.32 ± 11.12	156.38 ± 10.36	
BMI (Kg/m²)	21.73 ± 5.18	22.84 ± 5.43	
Duration of Surgery (Min.)	42.63 ± 10.16	40.79 ± 9.51	
Table 1. Demographic Characteristics, BMI and Duration of Surgery			

Table 2- It shows the results regarding characteristics of subarachnoid blockade, i.e. sensory and motor blockade. The onset of sensory and motor block was found to be faster with the addition of fentanyl 20 mcg to levobupivacaine. Mean time to achieve complete sensory and motor blockade

was also significantly faster in LF group as compared to LN group. Two segment regression of sensory block was slightly slower in levobupivacaine-fentanyl group as compared to levobupivacaine, but the difference was found to be statistically nonsignificant. The addition of fentanyl to levobupivacaine significantly prolonged the duration of sensory and motor block and also the postoperative analgesia as compared to levobupivacaine alone. The grade-I of motor blockade at one minute was found to be in 12 (40%) and 15 (50%) patients in group LF and group LN, respectively. The difference in grade of block at one minute was statistically significant ($p < 0.05$).

Characteristics/Parameters of Subarachnoid (Spinal) Blockade	Group LF (N=30)	Group LN (N=30)	p-value
Sensory block parameters (min.)			
Mean onset time of sensory block (min.)	2.10 ± 0.15	5.83 ± 2.45	P < 0.05
Time to achieve complete sensory block	6.9 ± 2.8	9.34 ± 1.93	
Time to achieve highest level of sensory block T6	3.91 ± 0.72	4.76 ± 0.93	
Two segment regression time for sensory block	96.48 ± 24.83	93.70 ± 18.84	
Time to regress to T12 dermatome for sensory block	112.12 ± 16.31	101.56 ± 15.12	
Mean duration of effective analgesia	180.46 ± 35.13	154.72 ± 35.23	P < 0.05
Motor block parameters (min.)			
Time of onset of motor block - Grade I (min.)	3.93 ± 0.71	6.56 ± 1.13	
Time of completion of motor block	9.46 ± 2.13	12.72 ± 3.17	
Duration of motor block	145.35 ± 19.19	129.23 ± 18.73	

Table 2. Characteristics of Subarachnoid (Spinal) Blockade

The mean Apgar score at 1 minute in Group LF was 8.56 ± 0.50 and in Group LN was 8.32 ± 0.41 while mean Apgar at 5 minutes in Group LF was 9.61 ± 0.53 and in Group LN was 9.50 ± 0.43 with no statistical significance, ($P > 0.05$). The mean intraoperative heart rate, blood pressure systolic, diastolic and mean blood pressure, respiratory rate and SpO_2 of patients in both groups were comparable with no statistical significance ($P > 0.05$).

In Group LF, nausea was the major complication (30%) followed by hypotension (20%). In Group LN, nausea was the major complication (26.67%) followed by vomiting (13.33%). The incidences of complications were almost comparable in both the groups except pruritus and were found to be statistically insignificant (Table 3).

Side Effects/Complications	Group LF (n=30) (%)	Group LN (n=30) (%)	P-value
Headache	2 (6.67)	3 (10)	P > 0.05
Hypotension	6 (20)	2 (6.67)	P > 0.05
Bradycardia	3 (10)	3 (10)	P > 0.05
Nausea	9 (30)	8 (26.67)	P > 0.05

Vomiting	5 (16.7)	4 (13.33)	P > 0.05
Pruritus	6 (20)	1 (3.33)	P < 0.05*
Any other shivering	1 (3.33)	2 (6.67)	P > 0.05

Table 3. Side Effects/Complications

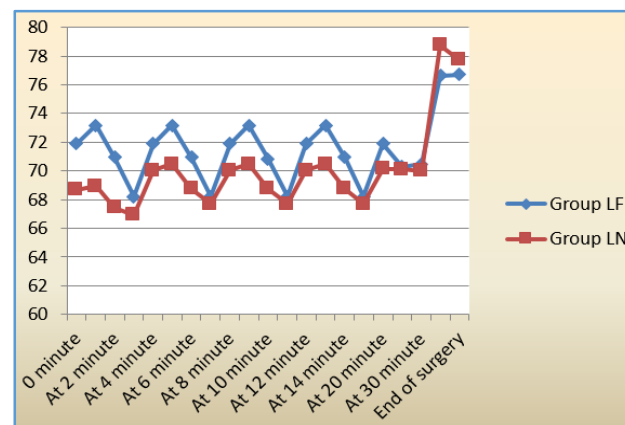


Figure 1. Intraoperative Changes in Mean Heart Rate at Various Time Interval

The mean intraoperative systolic blood pressure of patients from Group LN was more stable as compared to Group LF at different time intervals with no statistical significance ($P > 0.05$).

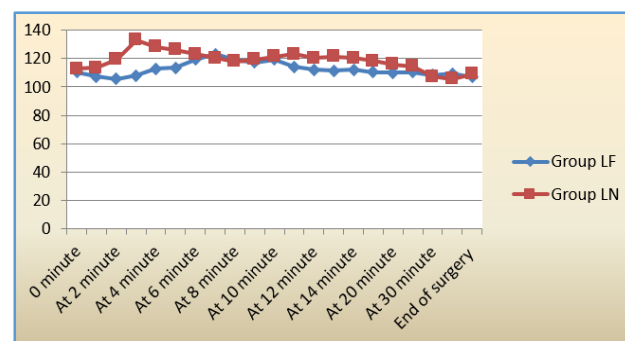


Figure 2. Intraoperative Changes in Systolic Blood Pressure at Various Time Intervals

The mean intraoperative diastolic blood pressure of patients from Group LN was more stable as compared to Group LF at different time intervals with no statistical significance ($P > 0.05$).

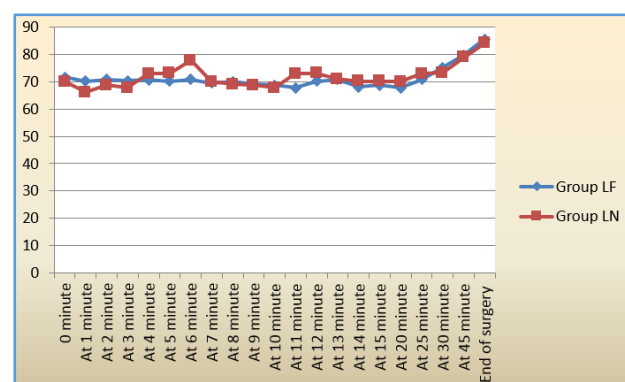


Figure 3. Intraoperative Changes in Diastolic Blood Pressure at Various Time Intervals

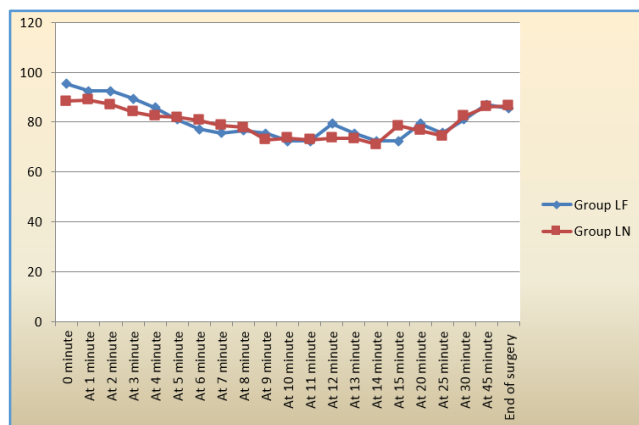


Figure 4. Intraoperative Changes in Mean Arterial Pressure at Various Time Intervals

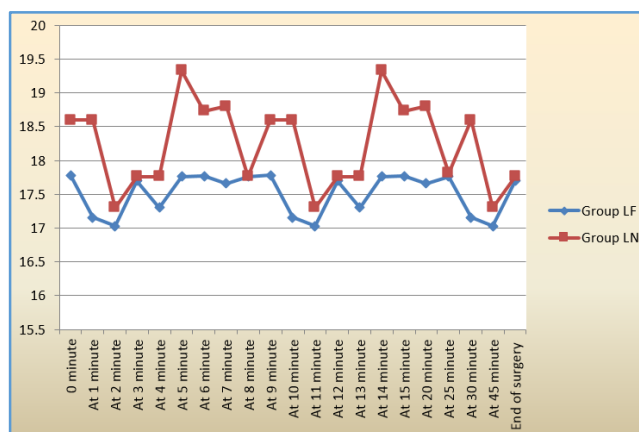


Figure 5. Respiratory Rate Changes at Different Time Interval

DISCUSSION

In the present study, mean age and weight was 26.16 ± 5.25 and 62.52 ± 7.13 in group LF, while in group LN, it was 25.05 ± 4.61 and 64.36 ± 6.54 . The age, weight, height and BMI in both the groups were comparable. The demographic profile had no influence on the study outcome.

The present study demonstrated that addition of fentanyl to intrathecal levobupivacaine during caesarean section surgery was more effective for intrathecal block than of levobupivacaine alone. The addition of fentanyl to levobupivacaine had rapid onset of sensory and motor block. It also prolonged the duration of sensory block, motor block and postoperative analgesia and also decreases postoperative analgesic requirement. Time to achieve complete sensory and motor block was faster with levobupivacaine-fentanyl group than levobupivacaine alone.

The demographic data such as age, weight and height being comparable and seems that it has no influence on outcome of the study. The sensory block in present study was tested using the loss of sensation to pinprick as used in other studies. The choice of this method instead of others was based on Hocking G study, which proved reliability and easy application of the pinprick method.¹⁴ The onset of sensory block was faster in Group LF as compared to Group LN. The cause of this earlier onset could be due to direct action on the mu receptors in the substantia gelatinosa of the spinal cord. It leads to early onset when used as

adjuvant with local anaesthetic.¹⁵ The time of completion of sensory block was significantly faster in LF group than LN group. The highest sensory level achieved in both the groups was T6.

Gautier et al¹⁶ reported that the mean time to achieve highest level of sensory block was 17 minutes. In our study, this mean time was found as 3.91 ± 0.72 min. with levobupivacaine-fentanyl combination and 4.76 ± 0.93 min. with levobupivacaine alone. The shorter times in our study might be associated with the dose and volume of levobupivacaine (10 mg). The group LF had earlier highest level T6 of sensory blockade as compared to group LN and the difference was statistically significant, ($P < 0.05$). The cause of earlier spread and earlier highest sensory blockade could be because of affinity of opioid and alpha agonist to dorsal horn.

Complete sensory block was achieved faster in group LF as compared to group LN. In our study, time to achieve complete sensory block was 6.9 ± 2.8 min. in group LF and 9.34 ± 1.93 min. in group LN. Addition of fentanyl to intrathecal levobupivacaine produced faster onset and complete sensory block. The mean time of regression by two dermatomes of the sensory block was found to be 96.48 ± 24.83 minutes in group LF, while 93.70 ± 18.84 minutes in group LN. This difference was though statistically significant ($P < 0.05$), but was clinically insignificant. The addition of fentanyl was found to prolong the mean regression time to T12 of the sensory block; this prolonged time duration might be due to addition of fentanyl intrathecally. The regression of sensory block was slightly slower in levobupivacaine-fentanyl and difference was found to be clinically insignificant though statistically significant.

Our study showed prolonged duration of sensory block with the addition of fentanyl with levobupivacaine as compared to levobupivacaine alone. The results of our study in term of sensory characteristics have supported the findings of previous studies.¹⁷⁻²² But, considering the duration of surgery in both the groups, levobupivacaine alone would be adequate for intrathecal block for elective caesarean deliveries.

In studies where intrathecal levobupivacaine was used alone, motor block onset time was reported as 10.0 minutes²³ and as 15 minutes by Burke et al.²⁴ In our study, the onset time of motor block was 3.93 ± 0.71 min. in Group LF and 6.56 ± 1.13 min. in group LN. The addition of fentanyl 20 mcg to levobupivacaine decreased onset time of motor block. The onset of grade I motor blockade was earlier in group LF than in group LN and difference was statistically significant ($P < 0.05$). The reason behind the early onset could be due to synergism between local anaesthetic and the adjuvant. In a study comparing the effects of fentanyl (10, 15 or 25 μ g) to intrathecal levobupivacaine (5, 7.5 or 10 mg) on sensory and motor blocks, the time to achieve maximum motor block was reported as being shorter in the 10 mg levobupivacaine + fentanyl group.²⁵ Similarly, in our study, onset of motor and sensory block was produced more rapidly in Group LF compared to the Group LN; this effect was probably associated with the lipophilic characters of

fentanyl. Although, the mean time to achieve complete motor blockade was significantly faster in LF group, the duration of motor block was significantly prolonged in Group LF as compared to Group LN. Our findings are comparable with different studies.^{13,17,18,24,26,27} Considering the duration of surgery in both the groups, prolongation of duration and enhancement in quality and grade of motor block was probably not required for caesarean section deliveries and thus levobupivacaine alone would be adequate for such surgeries.

The addition of intrathecal fentanyl or other opioids to local anaesthetic administration during caesarean sections did not affect the Apgar scores and new born blood gas values.^{25,28,29} In present study, there were no statistical significance differences in mean Apgar score at 1 minute and at 5 minutes. There was no direct relationship between the likelihood of hypotension and Apgar scores. No differences were observed between the Apgar scores and foetal acidosis in any of the groups. Similar findings were seen in a study done by Misirlioglu K et al.³⁰

In the present study, mean intraoperative heart rate, blood pressure (SBP, DBP and MAP), respiratory rate and SpO₂ in Group LN were comparable with Group LF at different time intervals; there were no statistical significant difference ($P > 0.05$).

Lee et al¹³ compared 2.6 mL levobupivacaine vs. 2.3 mL levobupivacaine with 15 µg fentanyl (2.6 mL) in spinal anaesthesia for TURP. There were no significant differences between the two groups regarding haemodynamic changes. They concluded that further studies might be directed to find the optimal combination of levobupivacaine with an opioid maintaining maximal haemodynamic stability.

Erdil et al³¹ noted that in spinal anaesthesia better haemodynamic stability was associated with low-dose levobupivacaine-fentanyl when compared with low-dose bupivacaine-fentanyl. In a study done by Padma T et al,³² there was statistically significant difference in haemodynamic parameters like heart rate, mean, systolic and diastolic BP, but clinically these parameters were within normal limits and did not require any intervention. The findings of the present study are similar with the findings of study of the above authors.

Visual analogue scale score was used to assess the patients for postoperative pain. VAS was 0 at 90 min. of the study period, then it started increasing in both the groups. VAS was on higher side in Group LN as compared to group LF till 180 min. ($P > 0.05$). Patients demanded first dose of rescue analgesia at 180 min. After this interval, VAS was on significantly on higher side in Group LF and patient demanded first dose of rescue analgesia at 5th hour of the study period. Hence, the total duration of analgesia was longer in Group LF as compared to Group LN. This difference was found to be statistically significant ($p > 0.05$) amongst the study groups. Prolonged duration of analgesia is probably due to more binding of the adjuvant to mu receptors and alpha-2 receptors and thus directs intense action on dorsal horn of spinal cord. Thus, the administration of intrathecal fentanyl with levobupivacaine in spinal

anaesthesia significantly prolonged the duration of surgical and postoperative analgesia and decreases the intensity of the pain at the time of analgesia request. These findings are comparable with different studies.^{21,33}

The P value > 0.05 shows that there were no statistical significant differences in the incidence of side effects such as headache, hypotension, bradycardia, nausea and vomiting, but significant difference was observed in pruritus amongst two groups. In both the groups, nausea was the major complication/side effect. Pruritus is the most frequent side effect observed with the use of intrathecal opioids. Incidence of pruritus among pregnant women with various opioids (especially lipophilic opioids) administered intrathecally was reported between 30% and 95%, although the pruritus was generally transient and mild.³⁴⁻³⁶ In our study, pruritus was observed in 6 (20%) patients in LF group during the postoperative period, whereas only 1 (3.33%) patient had pruritus in LN group. Other complications shivering- 1 (3.33%) and 2 (6.67%) was observed in patients of Group LF and Group LN, respectively. Similar findings were observed in the study done by Ayesha Goyal et al.¹⁷

CONCLUSION

On clinical comparative study of intrathecal levobupivacaine-fentanyl vs. levobupivacaine in caesarean deliveries, following conclusions are drawn-

- Intrathecal levobupivacaine-fentanyl had faster onset of sensory and motor blockade as compared to intrathecal levobupivacaine alone.
- Fentanyl added intrathecally to levobupivacaine decreases the time to achieve complete sensory and motor block.
- Addition of fentanyl to levobupivacaine had significantly prolonged the duration of sensory and motor block and grade of motor block was better as compared to plain levobupivacaine.
- Levobupivacaine-fentanyl reduced the need for rescue/supplementary analgesics in the postoperative period.
- Levobupivacaine intrathecally alone produces adequate duration of sensory and motor block with almost equal quality of the block with levobupivacaine-fentanyl.

Considering the duration of surgery in both the groups, levobupivacaine alone would be adequate for caesarean deliveries.

Limitations of Study

- Sample size of present study was very small.
- Findings of present study need to be confirmed by similar studies on large sample size.

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