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ORIGINAL RESEARCH

Comparison of Intrathecal Dexmedetomidinevs Fentanyl as Adjuvants to Hyperbaric Levobupivacaine in Infraumbilical Surgeries Under Spinal Anaesthesia

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ABSTRACT

Background: Various adjuvants have been reported to significantly enhance the quality of spinal anaesthesia. **Aim & objective:** To evaluate the effectiveness of Dexmedetomidine and Fentanyl as adjuvants to Hyperbaric Levobupivacaine 0.5% in enhancing the quality of spinal anaesthesia. **Material & Methods:** A total of 60 patients aged 18-65 were randomised into two groups ie. Group LD and Group LF, received 10 µg Dexmedetomidine and 25 µg Fentanyl respectively as adjuvants to 3 ml of 0.5% hyperbaric levobupivacaine. Time to achieve sensory and motor block, total duration of blocks, post-operative pain scores (VAS) and time to first rescue analgesia were recorded. **Results:** Time taken for onset of sensory and motor blocks was significantly longer in Group LF (3.02±0.55 min and 3.86±0.85 min, respectively) as compared to the Group LD(2.43±0.57 min and 3.35±0.56 min, respectively). However, the duration of sensory and motor block was significantly longer in Group LD (343.00±52.66 min and 338.00±52.22 min) compared to the LF group (213.00±33.75 min and 199.00±29.98 min, respectively). Duration of analgesia was also significantly prolonged in Group LD (366.90±52.02 min) compared to Group LF (232.77±33.77 min). Group LF had significantly higher mean pain scores as compared to that in Group LD at 4 hours and from 8 hours to 24 hr ($p<0.05$). **Conclusion:** Dexmedetomidine outperformed fentanyl to block quality but carried an increased risk of bradycardia.

Key words: Infraumbilical surgeries, spinal anesthesia, dexmedetomidine, fentanyl, postoperative pain.

INTRODUCTION

Spinal anaesthesia, a well-established technique, has been utilized for surgeries below the level of umbilicus for many years. Spinal anaesthesia offers reversible sensory analgesia, motor blockade, and sympathetic blockade, the extent of which depends on the dosage, concentration, and volume of the local anaesthetic administered. It requires a small amount of drug, has minimal systemic pharmacological effects, and has demonstrated exceptional safety with proper management. [1] Bupivacaine is the most commonly used long-acting local anaesthetic. Levobupivacaine, an enantiomer of racemic bupivacaine, has gained attention for its lower cardiotoxicity and neurotoxicity. The levorotatory isomers have been found to have a more favorable pharmacological profile, with reduced cardiac and neurotoxic adverse effects. [2] The addition of opioids like morphine, fentanyl, and sufentanil has been noted to enhance the quality of spinal anaesthesia. [3] Other agents such as dexmedetomidine, clonidine, magnesium sulfate, neostigmine, ketamine, and

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midazolam have also been reported to contribute positively. [4, 5, 6]

Understanding that every pain-relieving medication has potential side effects is essential. Dexmedetomidine, a targeted α-2 receptor agonist, displays sedative, analgesic, sympatholytic, and anxiolytic properties that effectively reduce numerous cardiovascular reactions during the perioperative phase.[7] Intrathecal fentanyl as an adjuvant has been found to enhance the quality of intraoperative and early postoperative central neuraxial block. However, the addition of opioids to a local anaesthetic solution has drawbacks, such as pruritus and respiratory depression. [8]

Considering the emerging evidence that supports Dexmedetomidine as a safer and potentially effective adjuvant to local anaesthetics, our study was planned to compare the efficacy of Dexmedetomidine (10 µg) and Fentanyl (25 µg) as an adjuvant to Hyperbaric Levobupivacaine 0.5% (3 ml) for infra umbilical surgeries under spinal anaesthesia. The primary objective was to compare the block characteristics regarding the onset and duration of sensory and motor blockade. Secondary objectives were to compare the time of rescue analgesia, quality of analgesia using VAS, total analgesic consumption, and hemodynamic changes.

MATERIAL AND METHOD

This prospective randomised, double-blind comparative study was conducted over one year at a tertiary teaching institute from April 2023 to March 2024. After the Institutional Ethical Committee (ICE/HIMSA Ref. No- IHEC-HIMSA/MD-MS-21/RD-09/03-23) approval and written informed consent, participants were screened for their eligibility for the study. To ensure ethical standards were upheld, the study adhered to the Declaration of Helsinki (2013) regarding medical research involving human subjects. Additionally, the study meticulously followed the Consolidated Standards of Reporting Trials (CONSORT) guidelines while preparing the manuscript.

A total of 60 patients, aged 18 to 60 years and of either gender, belonging to ASA grades I and II, posted for elective infraumbilical surgeries, were enrolled in the study. Exclusion criteria encompassed pregnant women, individuals with a BMI greater than 30 kg/m², those with any contraindications to spinal anaesthesia (such as local site infection, coagulopathies, or hemodynamic instability), patients who had previously undergone spine surgery, individuals with allergies to the study drug, those on α2 adrenergic blockers (like Prazosin), and patients with liver or renal diseases.

Patients were randomised into either of the two groups: Group LF and Group LD. A computer-generated random number table was utilized to assign patients to the various groups, ensuring fair allocation. Allocation concealment was achieved through the use of sealed opaque envelopes. Group LF received 3 ml of Hyperbaric 0.5% levobupivacaine + 0.5 ml fentanyl (25 µ gm) and Group LD received 3 ml of Hyperbaric 0.5% levobupivacaine + 0.2 ml Dexmedetomidine (10 µgm) + 0.3 ml normal saline.

Eligible patients were provided with a comprehensive explanation of the study protocol one day before the scheduled surgery. Additionally, a thorough pre-anaesthetic assessment was conducted. Appropriate fasting guidelines were followed.

On the day of the surgery, an 18-gauge cannula was introduced in the preoperative room to secure the intravenous (IV) line. The patients were be preloaded with Ringer Lactate/ normal saline 500ml over 15- 20 minutes. Premedication was done with an injection of Ondansetron 4.0mg IV, an injection of Pantoprazole 40 mg IV and an injection of Ceftriaxone 1gm IV after performing a sensitivity test. A local anaesthetic sensitivity test was also done. In Operation Theatre, baseline blood pressure (BP), heart rate (HR), respiratory rate (RR) and Oxygen saturation (SpO2) were checked. Heart rate (HR), SpO2, ECG, and non-invasive blood pressure (NIBP) were monitored continuously during the procedure. Spinal anaesthesia was administered, following all aseptic precautions at the L3-L4 or L2-L3 interspace in the sitting position, using a 25-gauge Quincke needle through the midline approach. Following the procedure, patients were promptly transitioned to a supine position, and supplemental oxygen was initiated at a rate of 4 litres per minute.

Sensory blockade was evaluated using a pinprick test using a 22G hypodermic needle. Sensory block was measured on a 3-point scale: 0 for sharp pain, 1 for dull pain (analgesia), and 2 for no pain (anaesthesia). This assessment was performed every minute after administering spinal anaesthesia. The onset time of the sensory block was determined as the period from the end of spinal anesthesia to the point when a score of 2 on the 3-point scale was reached. The duration of the sensory block was calculated from the conclusion of spinal anesthesia delivery until the total return of sensation, marked by a score of 0 on the 3-point scale. The onset of complete motor block was noted as an absence of voluntary movement in the feet, ankles, knees, and hips, corresponding to a score of 3 on the Modified Bromage scale.The duration of motor block was measured as the interval from the conclusion of spinal anesthesia administration to the restoration of full motor function in the feet, ankles, knees, and hips, as indicated by a score of 0 on the Modified Bromage scale.

Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), heart rate, and SpO2 were recorded every 3 minutes during the initial 15 minutes, then every 5 minutes until 60 minutes of the surgery, followed by monitoring every 10 minutes up to 120 minutes, and subsequently every hour for the next 12 hours.

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All Patients were monitored for complications like hypotension, bradycardia and treated accordingly and the same were noted.

Patients were made aware of visual analog scale (VAS) and perception of pain were assessed by using VAS score (0 – 10) to determine the level of analgesia postoperatively, where 0 was no pain and 10 was worst possible pain. Rescue analgesia injection paracetamol 1gm IV was given if VAS score > 4. The duration of rescue analgesia was recorded from when the subarachnoid block was given to when the patient first asked for analgesia. Postoperatively, the VAS score was recorded every 2 hours for up to 24 hours.

Sample size and Statistical Analysis: Gupta R et al. [9] reported a mean difference of 82.74 minutes in the duration of rescue analgesia, our study aimed to target a similar difference between the two groups. Formula $n=2\times(Z_{\alpha/2}+Z_{\beta})^2 \times \sigma^2/d^2$ was used for sample size calculation. A minimum of 23 patients per group was required to achieve a 95% confidence interval (CI) and 80% power. However, the study was conducted with 60 participants, randomly allocated into two groups of 30 patients each. SPSS-25 software for Windows was used for statistical analysis. Categorical (discrete) data were presented as proportions and percentages, while continuous (quantitative) data were presented as mean ± SD. The Chi-square test or unpaired Student's t-test was applied where appropriate. The p-value of <0.05 was considered statistically significant.

RESULTS

A total 76 patients aged 18-60 years were screened for eligibility for this study. A total of 65 patients fulfilled the inclusion criteria. During intervention and follow-up, a total of 5 patients (Group LF: 3, Group LD: 2) were excluded from the study due to failure of intrathecal block. So at the end of the study, data total of 60 (30 in each group) patients were available for final statistical analysis. (Table/Fig-1)

Patients characteristics like age, height, weight and BMI were comparable. Most of our patients were male and belong to ASA I grade. Also, both groups were comparable in terms of duration of surgery. (Table/Fig-2)

Time taken for onset of sensory and motor blockade were significantly longer in LF (3.02±0.55 min and 3.86±0.85 min respectively) as compared to that in LD group (2.43±0.57 min and 3.35±0.56 min respectively). However, duration of sensory and motor block was significantly longer in LD group (343.00±52.66 min and 338.00±52.22 min) compared to the LF group (213.00±33.75 min and 199.00±29.98 min respectively). Duration of analgesia was also significantly longer in LD group (366.90±52.02 min) compared to the LF group (232.77±33.77 min). (Table/Fig-3)

None of the patients experienced pain in Group LD till 4 hr follow-up whereas in Group LF none of the patients experienced pain till 2 hr follow-up interval only. Mean pain VAS scores were significantly higher in Group LF as compared to Group LD at 4 hour and from 8 hour till 24 hr ($p<0.05$). (Table/Fig-4) Number of patients requiring three or more dosages of rescue analgesic was significantly higher in LF as compared to that in LD group ($p<0.001$). (Table/Fig-5)

Mean systolic blood pressure remained insignificant ($p>0.05$) at all intervals. (Table/Fig-6) The mean diastolic blood pressure levels between the two groups at any of the follow-up intervals were comparable ($p>0.05$). (Table/Fig-7) However a statistically significant difference in mean arterial pressure between the two groups was observed at 30 min, 3 hours, 4 hours, 6 hours, 7 hours and 8 hours follow-up intervals. At all these time points , mean arterial pressure values were significantly lower in Group LF in comparison to Group LD ($p<0.05$). (Table/Fig-8) The heart rate was comparable between the two groups at any of the time intervals except at 25 min where mean heart rate value was significantly lower in LD as compared to that in LF group ($p=0.047$). (Table/Fig-9)

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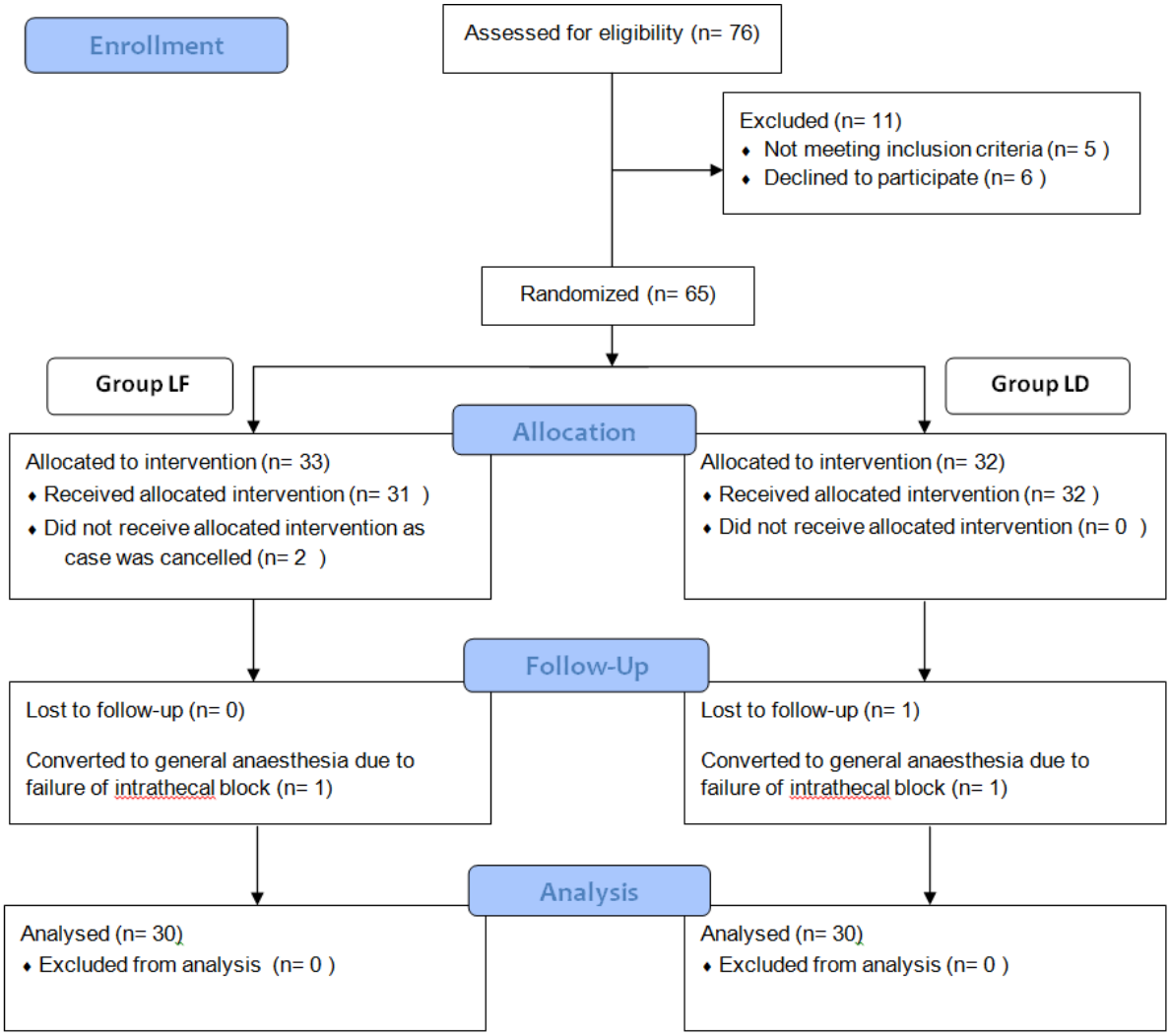

Table/Fig-1: CONSORT flowchart.

Table/Fig-2: Demographic variables

SN	Characteristic	Group LF (n=30)		Group LD (n=30)		Statistical significance	
		Mean	SD	Mean	SD	't'	'p'
1.	Age	43.60	10.77	38.73	11.97		
	Age Range	22-60		18-60		1.656	0.103
2.	Gender						
	Male	18 (60%)		19 (63.3%)			
	Female	12 (40%)		11 (36.7%)		χ^2=0.071; p=0.791	
3.	Height (m)	1.61	0.07	1.64	0.08	-1.351	0.182
4.	Weight (kg)	60.50	6.48	60.63	8.26	-0.070	0.945
5.	BMI (kg/m²)	23.38	1.94	22.60	2.08	1.501	0.139
6.	ASA						
	I	24 (80%)		18 (60.0%)			
	II	6 (20%)		12 (40.0%)		χ^2=2.857; p=0.091	
7.	Mean duration of surgery (min)	68.0	28.7	79.8	34.2	-1.453	0.152

Table/Fig-3: Comparison of two groups for block characteristics

SN	Characteristic	Group LF (n=30)		Group LD (n=30)		Statistical significance	
		Mean	SD	Mean	SD	't'	'p'
1.	Onset duration of sensory block	3.02	0.55	2.43	0.57	4.043	<0.001
2.	Onset duration of	3.86	0.85	3.35	0.56	2.741	0.008

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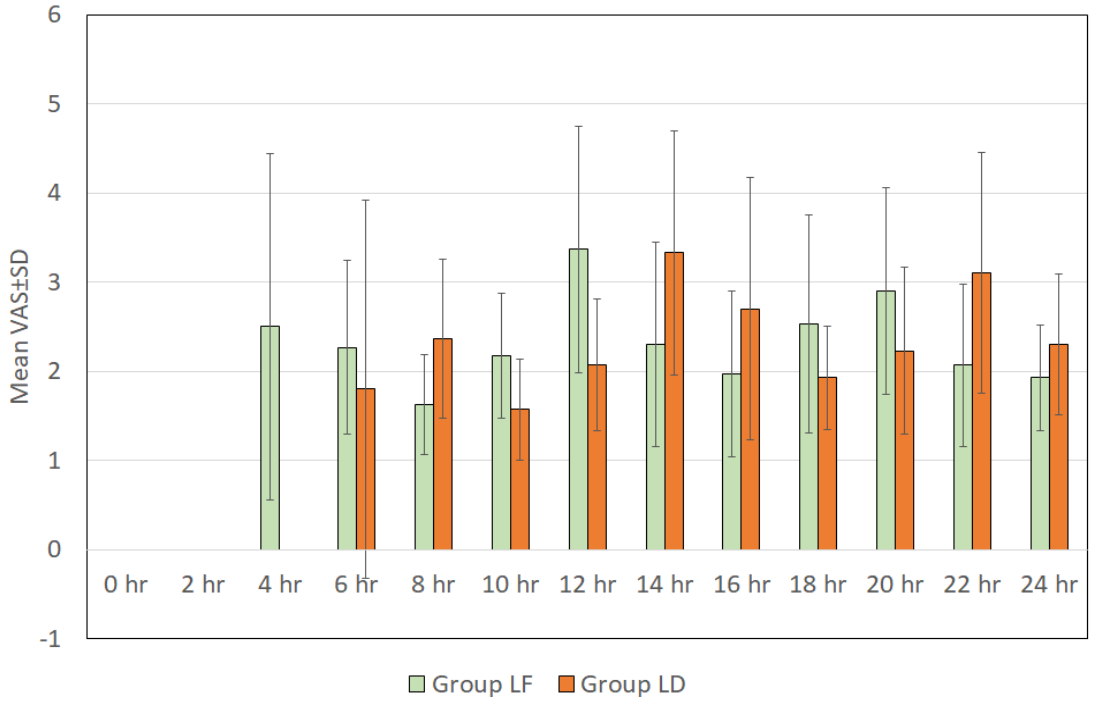
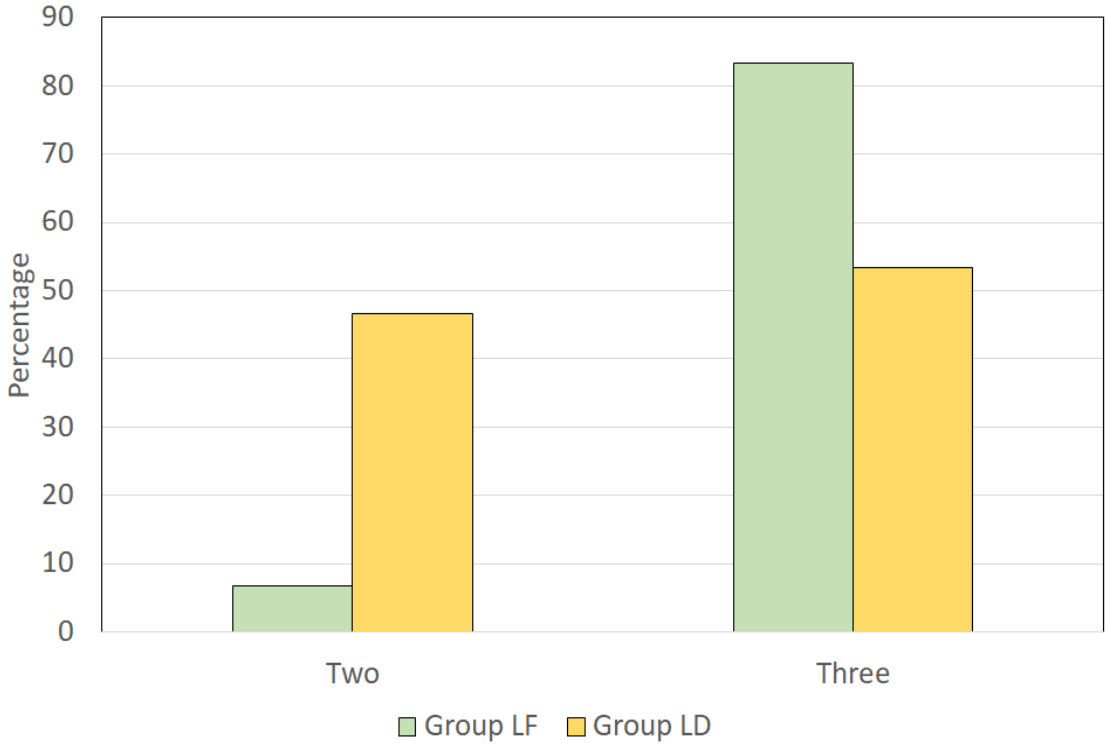
	motor block						
3.	Duration of Sensory Block (min)	213.00	33.75	343.00	52.66	-11.384	<0.001
4.	Duration of Motor Block (min)	199.00	29.98	328.00	52.22	-11.734	<0.001
5.	Time to first rescue analgesic need (min)	232.77	33.77	366.90	52.02	-11.846	<0.001



Table/Fig-4: Comparison of Mean VAS scores for pain at different post-operative follow-up intervals



Table/Fig-5: Comparison of Number of rescue analgesic dosages used during first 24 hr follow-up

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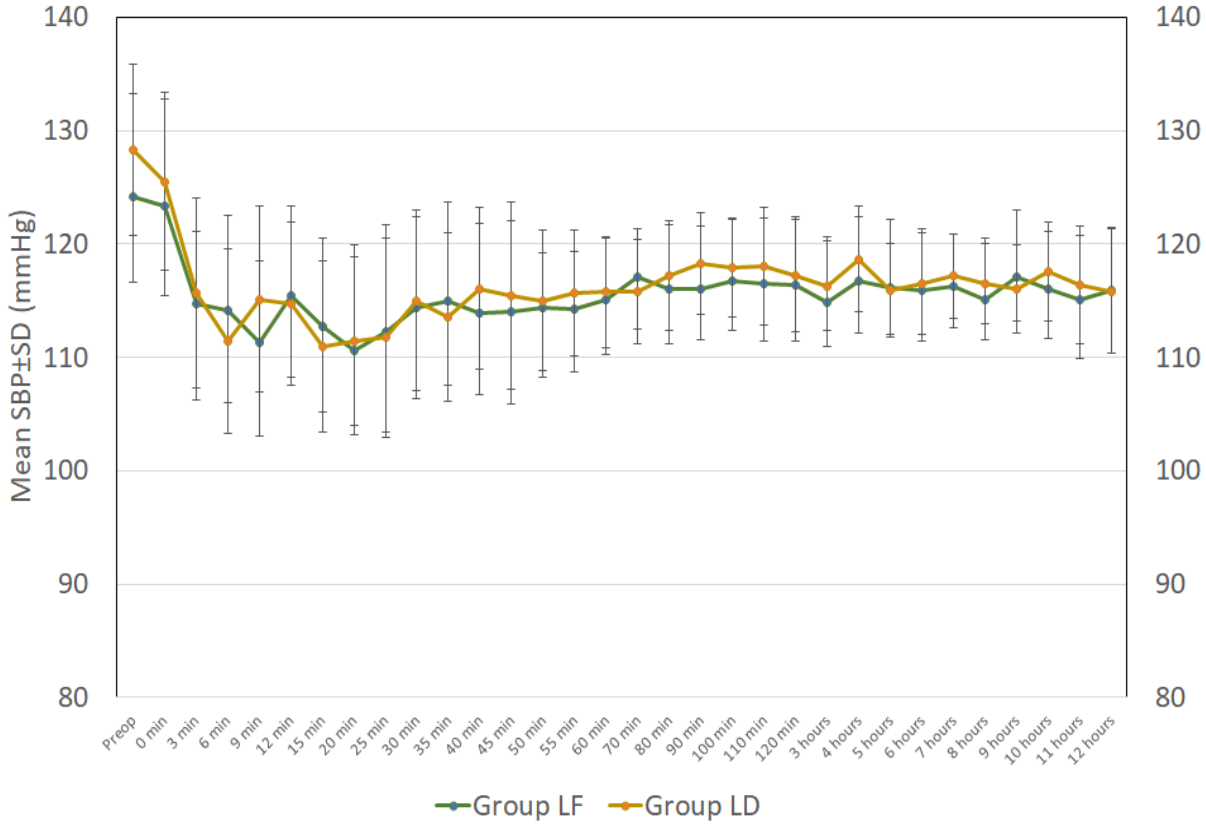

Table/Fig-6: Comparison of Systolic Blood pressure at different intraoperative and post-operative follow-up intervals

Table/Fig-7: Comparison of Diastolic Blood pressure at different intraoperative and post-operative follow-up intervals

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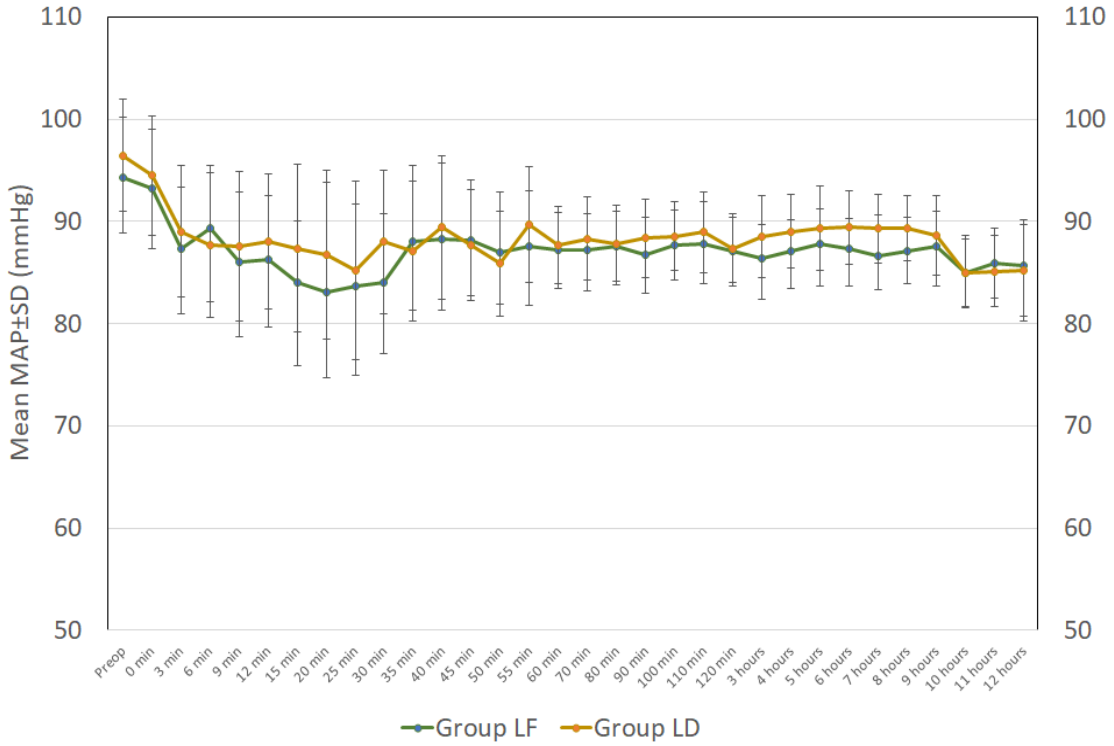

Table/Fig-8: Comparison of Mean arterial pressure at different intraoperative and post-operative follow-up intervals

Table/Fig-9: Comparison of Heart rate at different intraoperative and post-operative follow-up intervals

DISCUSSION

Nowadays, general anesthesia is increasingly being replaced by regional anesthesia due to its safety, effectiveness, and targeted anesthetic effect. Additionally, regional anesthesia offers better recovery characteristics. However, post-operative pain remains a challenge, particularly after the regional blocks wear off. Since low doses of anesthetics are used, enhancing the post-operative analgesic effect often requires adjuvants. These adjuvants not only improve the characteristics of the block but also extend their analgesic effects, leading to a better overall patient experience.

This double blind randomized-controlled study compared the efficacy of Dexmedetomidine (10 µg) and Fentanyl (25 µg) as an adjuvant to 0.5%

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hyperbaric Levobupivacaine (3 ml) for patients undergoing infraumbilical surgeries under spinal anaesthesia. There are a number of workers that used hyperbaric [10-15] forms at 0.5% concentration using 2.5 to 3 ml dosages. A number of studies had compared these two drugs at the same dosages for their adjuvant effect with levobupivacaine, ropivacaine or bupivacaine. [10, 15, 16] Though some studies used a relatively lower dose of dexmedetomidine (5 µg) and compared it with 25 µg fentanyl with levobupivacaine or bupivacaine. [11-14, 17, 18]

In current study, onset of sensory and motor blockade was significantly faster in dexmedetomidine as compared to fentanyl group, while duration of sensory and motor blockade was longer in dexmedetomidine in comparison to fentanyl group.

Contrary to the our study, Chandra *et al.*[16] found onset of sensory blockade to be faster in fentanyl as compared to dexmedetomidine group, however, they did not find a significant difference in onset time of motor blockade, achievement of sensory blockade upto level T10 and motor blockade Bromage score 3 between the two groups. Moreover, similar to the findings of our study, their study also showed duration of sensory and motor blockade to be longer in dexmedetomidine in comparison to fentanyl group. However, another study, contrary to the our study findings, showed the onset of blockade to be faster in fentanyl as compared to dexmedetomidine group , however block durations were found to be longer in dexmedetomidine in comparison to fentanyl group. [18] A number of other studies had found that dexmedetomidine definitely enhances the sensory and motor block duration more efficiently than fentanyl. [19-23]

In the present study, mean time for 1st rescue analgesic dose was below 4 hours in the fentanyl while it was six hours in the dexmedetomidinegroup. Mean VAS score more than 2 were achieved more frequently and earlier in the fentanyl group as compared to dexmedetomidine group. These findings show that dexmedetomidine was more effective to inhibit post-operative pain as compared to fentanyl. Similar to the present study, Rahimzadeh*et al.* [11] too observed an increment of rescue analgesia free time to be >1.5 times higher in dexmedetomidine in comparison to fentanyl group.

Observations to similar effect showing a longer post-operative effect, lower pain intensity and fewer rescue analgesic dose requirements in dexmedetomidine in comparison to to fentanyl were also seen by other workers like Soori*et al.* [12], Khosarvi*et al.*[24],and numbers of other workers too. [19 -23] However, Sachdeva*et al* [13] in one exceptional study found no significant difference in analgesic effect of 5µg dexmedetomidine and 25 µg fentanyl as an adjuvant to bupivacaine.

In the present study, the two groups had a comparable haemodynamic profile at various perioperative time point except for some minor but statistically significant differences between the two groups for mean arterial pressure which were significantly lower in fentanyl group as compared to dexmedetomidine group at 30 min, 3 hours, 4 hours, 6 hours, 7 hours and 8 hours follow-up intervals and significantly lower mean heart rate in dexmedetomidine as compared to fentanyl group at 25 min interval. As compared to preoperative levels, these hemodynamic parameters showed lesser variability in dexmedetomidine as compared to fentanyl group. Thus, in general dexmedetomidine had a more favourable hemodynamic profile as compared to fentanyl. As far hemodynamics is concerned, both the drugs have been reported to be safe and comparable hemodynamically. Similar to this study, Rastogi*et al.* [18] and Khosarvi*et al.* [24]did not observe any significant difference in hemodynamic changes between the two groups. Our study results are similar to study findings by Kalbande*et al.* [19], who also found that dexmedetomidine was associated with minimum intraoperative hemodynamic variations.

Limitations

This study is one of the few contemporary studies that have compared 10 µg dexmedetomidine with 25 µg fentanyl as an adjuvant with levobupivacaine for subarachnoid block, so absence of literature on exact drug-dose combinations was one of the limitations of the study as it did not permit comparison of results of study with studies using exact similar drug-dose combinations. Further studies on a larger sample size in patients with varied profiles are recommended.

CONCLUSION

The study's findings demonstrated that the dexmedetomidine as an adjuvant with hyperbaric levobupivacaine not only accelerated the onset of sensory and motor blockade but also surpassed fentanyl in terms of sensory and motor blockade duration, analgesia duration, and the reduced need for rescue analgesia. Dexmedetomidine also remained safer than fentanyl with respect to lesser haemodynamic changes.

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