Original Article

DOI: 10.7860/JCDR/2024/63889.19075

Anaesthesia Section

Combination of Dexmedetomidine with Bupivacaine versus Fentanyl with Bupivacaine Intrathecally for Prolongation of Postoperative Analgesia in Lower Limb Surgeries: A Randomised Clinical Study

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ABSTRACT

Introduction: Intrathecal adjuvants can be added to extend the duration of analgesia. To achieve this, several adjuvants, such as the combination of dexmedetomidine with bupivacaine versus fentanyl with bupivacaine, have been used with local anaesthesia during lower limb surgeries.

Aim: To compare the combination of dexmedetomidine versus fentanyl with bupivacaine administered intrathecally for the onset and duration of sensory and motor block, as well as their side-effects and the prolongation of postoperative analgesia in lower limb surgeries.

Materials and Methods: A randomised clinical study was conducted on 120 American Society of Anaesthesiologists (ASA) grade I or II patients, aged between 18 and 65 years, who were admitted to the Department of Orthopaedics and General Surgery, Aarupadai Veedu Medical College and Hospital, Puducherry, India for lower limb surgeries under spinal anaesthesia. The patients were randomly assigned to two groups using a computer-generated technique. Group BD received 0.5% bupivacaine (2.5 mL)+10 mcg dexmedetomidine (0.5 mL), while Group BF received 0.5% bupivacaine (2.5 mL)+25 mcg fentanyl (0.5 mL). The onset and duration of sensory and motor blockade, haemodynamic parameters, sedation, and side-effects of the drugs were analysed. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 2.0 after collecting all the data.

Results: There were no statistically significant differences in the subjects' demographics or duration of surgery. However, the duration of sensory block and motor block was significantly prolonged in Group BD compared to Group BF, with values of 720±32 and 640±32, respectively. The mean Heart Rates (HR) differed significantly between of the two groups (p-value=0.03). There was no significant difference in sedation scores between the two groups. Group BD showed a higher incidence of bradycardia (n=35) and hypertension (n=32).

Conclusion: The combination of dexmedetomidine with bupivacaine, when used intrathecally for lower limb surgeries, demonstrated superior effectiveness in terms of prolonging sensory and motor block duration and providing extended postoperative analgesia, compared to the combination of bupivacaine and fentanyl. However, it is important to note that patients receiving the dexmedetomidine-bupivacaine combination had a higher incidence of bradycardia and hypertension. Therefore, careful monitoring and management of haemodynamic parameters are necessary when using this combination.

Keywords: Anaesthesia, Drug combinations, Lower limb, Postoperative pain

INTRODUCTION

Surgeries of the lower limb and abdomen are performed under spinal anaesthesia in Orthopaedics, General Surgery, and Obstetrics and Gynaecology. In the modern era, to enhance the duration of action of spinal anaesthesia, improve haemodynamics, and ultimately enhance patient satisfaction, newer local anaesthetic agents and adjuvants are being utilised to provide better postoperative outcomes. The properties of spinal block include reduced risk of infection, deep block, and cost-effectiveness. However, postoperative pain remains a significant issue due to the limited duration of drug effects, necessitating the need for postoperative analgesic administration [1].

The combination of analgesics with local anaesthetics has been observed to enhance the duration of anaesthetic effects and reduce side-effects. Various spinal adjuvants have been used to improve the quality of spinal anaesthesia and extend postsurgical analgesia. These adjuvants include opioids (morphine, fentanyl, and sufentanil), α2 adrenergic agonists (clonidine), magnesium sulfate, neostigmine, ketamine, and midazolam. Among them, opioids are the most commonly used intrathecal adjuvant [2].

Dexmedetomidine and clonidine, which are α2 adrenergic receptor agonists, have garnered significant interest due to their sedative, analgesic, sympatholytic, and haemodynamic stabilising properties [3]. Dexmedetomidine, a highly selective α2 receptor agonist (α2/α1 1600:1), has gained attention as a neuraxial adjuvant. It offers stable haemodynamic conditions, high-quality intraoperative analgesia, extended postoperative analgesia, and minimal side-effects [4,5]. It is widely used for various analgesic purposes, as it is effective against anxiety and has neuroprotective effects. It is often used in combination with other drugs, particularly in caudal, epidural, and subarachnoid blocks, to prolong analgesic duration [6].

The phenylpiperidine category of synthetic opioids includes fentanyl, which is also known as Actiq, Duragesic, and Sublimaze. It is a pure receptor agonist and has approximately 100 times the analgesic potency of morphine. Fentanyl is commonly administered in this form. It is used as an intrathecal local anaesthetic to enhance anaesthesia and analgesia. However, it can also be administered intravenously and intrathecally as adjuvants [7].

Despite significant advancements in pharmacotherapy for postoperative discomfort, managing postoperative pain remains a challenge for anaesthesiologists in day-to-day practice. After conducting a literature search, the authors found trials that examined the effects of various anaesthetic procedures and adjuvant medications on the prevalence of postoperative phantom pain and sensation. However, an ideal, safe, and effective adjuvant does not currently exist [8]. Dexmedetomidine and Fentanyl are widely accepted drugs and are used as adjuvants to local anaesthetics for various types of surgeries. This is because they provide longer analgesia and a greater extent of the block [9]. Therefore, the purpose of the present study was to compare the effectiveness of combinations such as bupivacaine and dexmedetomidine and bupivacaine and fentanyl in lower limb surgeries.

MATERIALS AND METHODS

This randomised clinical study was conducted at the Department of Orthopaedics and General Surgery, Aarupadai Veedu Medical College and Hospital, Puducherry, India from 2021 to 2022. Ethical approval was obtained from the institutional ethical committee (AV/IEC/2020/123), and CTRI approval (CTRI/2021/03/032274). Informed consent was obtained from the patients undergoing lower limb surgeries. The study included 120 ASA Grade-I or II patients undergoing elective lower limb surgeries under spinal anaesthesia.

A total of 120 patients between the ages of 18 and 65 years, who presented to the hospital for lower limb surgeries within a one-year period, were included in the study.

Sample size calculation: The sample size for the study was calculated using the formula:

$$n=(S12+S22)\ (z1-\alpha/2+z1-\beta)2(x1-x2)2$$

Where:

S=standard deviation

z=Standard Deviation (SD) from the mean

α=Type I error

β=Type II error

Considering a mean difference in the time of spinal anaesthesia between the two groups, with 95% confidence limits, 70% power, and 10% error, the sample size was determined to be 59 in each group. The number was rounded up to 60 (n=60).

Inclusion and Exclusion criteria: The study included postsurgery patients with a surgical duration of 1-2 hours. Patients with hypersensitivity to any of the drugs (bupivacaine, fentanyl, or dexmedetomidine), uncontrolled diabetes mellitus or hypertension, renal and liver failure, cardiac dysrhythmias, and coagulopathies were excluded from the study.

Study Procedure

All patients included in the present study received the following drugs in the following proportions:

1. Bupivacaine (0.5%): 2.5 mL.
2. Dexmedetomidine: 0.5 mL (25 mcg).
3. Fentanyl: 0.5 mL (25 mcg).

Using randomisation, patients were enrolled into two groups using a computer-generated technique. The patients were randomly allocated to Group BD and Group BF.

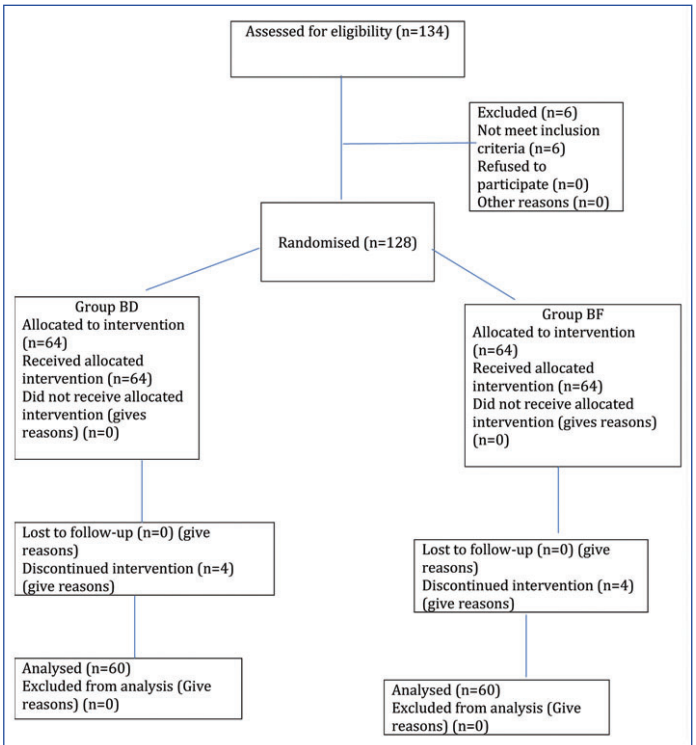
Group BD: Bupivacaine heavy (0.5%) 2.5 mL+Dexmedetomidine: 0.5 mL (25 mcg) [10].

Group BF: Bupivacaine heavy (0.5%) 2.5 mL+Fentanyl: 0.5 mL (25 mcg) [11].

The group allocation was blinded from the patients and the doctors who were assessing the treatment outcomes. After obtaining informed and written consent, the patient's histories were taken, including age, sex, detailed family history, clinical assessment, and laboratory diagnosis. The spinal needle was used to administer spinal anaesthetic at the level of the L4-L5 interface while the patient was seated in an aseptic environment. Motor and sensory status were assessed prior to spinal injection to assess the anaesthetic effect.

Following surgery, evaluations were performed every ten minutes until two sensory levels had regressed, and then every twenty minutes until both the dermatome and the motor scale using the Bromage scale had regressed. The patients were asked to assess their level of discomfort, and any adverse effects were noted. The Visual Analog Scale (VAS) scores were compared between Group BD and Group BF at different time points.

In accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines, the flow of participants through each stage of the randomised trial is illustrated in [Table/Fig-1]. Initially, 134 participants were assessed for eligibility. After exclusions based on predefined criteria, a total of 128 participants were randomised into two groups: Group BD (n=64) and Group BF (n=64). The intervention allocation and intervention receipt were consistent across both groups, with no instances of allocated intervention non reciept. There were no losses to follow-up, and only a small number of participants discontinued the intervention (n=4) due to specified reasons. Ultimately, a total of 60 participants from both groups were included in the final analysis after accounting for exclusions as detailed in the table.



[Table/Fig-1]: Revised template of the CONSORT diagram showing the flow of participants through each stage of randomised trial.

STATISTICAL ANALYSIS

Data analysis was conducted using a proforma, and statistical analysis was performed using SPSS version 2.0. The outcomes are presented as means with standard deviations or as percentages. Analysis of variance was used to compare continuous variables. Fisher's-exact test or the Chi-square test, if appropriate, was used for comparisons. Statistical significance was defined as a p-value less than 0.05.

RESULTS

In the present study, it was found that the majority of patients, i.e., 35% (n=21) and 38.33% (n=23) out of 120 patients, were in the age group of 41-50. Males had a higher preponderance than females in both the BD and BF groups (65% and 71.67%, respectively).

There was no statistical difference in patients' demographics or duration of surgery [Table/Fig-2]. In the present study, the duration of sensory block and motor block was significantly prolonged in group BD compared to Group BF, i.e., 640±32 and 430±15, respectively. Group BF had a statistically significant shorter duration of sensory block and motor block, i.e., 320±12 and 430±15, respectively [Table/Fig-3].

Variables	BD n (%)	BF n (%)	p-value
10-20	2 (3.33)	1 (1.66)	
21-30	4 (6.66)	6 (10)	
31-40	17 (28.33)	19 (31.66)	
41-50	21 (35)	23 (38.33)	
51-60	9 (15)	5 (8.33)	
61-70	5 (8.33)	4 (6.66)	
71-80	1 (1.66)	1 (1.66)	
81-90	1 (1.66)	1 (1.66)	
Total	60	60	
Gender			
Male	39 (65%)	43 (71.66%)	0.43
Female	21 (35%)	17 (28.34%)	
ASA Grade-I	41 (68.33%)	40 (66.67%)	0.31
ASA Grade-II	19 (31.67%)	20 (33.33%)	
Weight	65.3±8.15	64.9±9.19	0.80
Range	18-65 years	18-65 years	
Duration of surgery (in Minutes)	75	78	
Mean age±SD	49±9.9	48.8±9.8	0.60

[Table/Fig-2]: Proportion of age group according to the drug administration.
ASA: American society of anaesthesiologist

Block	Variables	Group BD Mean±SD	Group BF Mean±SD	p-value
Sensory	Onset (min)	11.5±2.1	14±2.5	0.18
	Duration (min)	720±32	320±12	0.0001*
Motor	Onset (min)	16.5±2.1	10.7±1.2	0.12
	Duration (min)	640±32	430±15	<0.001*

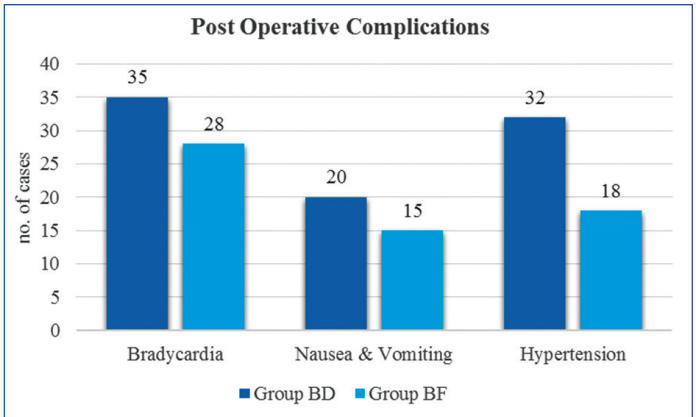
[Table/Fig-3]: Comparison of sensory and motor block onset and duration between the groups.
*=Statistically significant

The mean values of Blood Pressure (BP) and Heart Rate (HR) were highly significant between the two groups throughout the intraoperative and postoperative periods. The difference between the mean HR of the two groups was found to be significant (p-value=0.03). No significant difference was observed in the sedation scores among patients in the two groups [Table/Fig-4].

Parameters	Group BD Mean	Group BF Mean	p-value
Mean BP (mmHg)	63.5	78.7	<0.05*
Mean HR (bpm)	68.9	76.8	0.03*
Mean sedation	2.54	1.87	0.31

[Table/Fig-4]: Comparison of Mean Blood Pressure (BP) and Heart Rate (HR) between the groups.
*=Statistically significant

Bradycardia, nausea, vomiting, and hypertension were among the discomforts experienced by the subjects included in the study. Subjects receiving BD were observed to have the highest preponderance of bradycardia (n=35) with a p-value of 0.20, and hypertension (n=32) with p=0.31. On the other hand, subjects receiving BF were observed to have the highest preponderance of the same, i.e., 28 and 18 subjects, respectively. It shows a statistically significant difference (p=0.009) [Table/Fig-5].



[Table/Fig-5]: Postoperative complications between the groups.

The VAS score in the treated patients with dexmedetomidine was found to have significantly lower values than the fentanyl group at the first hour and was relatively lower in the 6-hour postoperative period [Table/Fig-6].

Time	Variables	Group BD	Group BF	p-value
First hour	VAS rest	0	0.7	<0.05*
	VAS movement	0.32-1.4	1.5-1.6	<0.05*
Sixth hour	VAS rest	0.5-2.2	1.9-3.4	<0.05*
	VAS movement	1.8-3.1	2.2-3.9	<0.05*

[Table/Fig-6]: Comparison of VAS score between the Group BD and Group BF.
*=Statistically significant

DISCUSSION

In order to prolong the duration of analgesia and reduce postoperative discomfort, the intrathecal administration of dexmedetomidine during spinal anaesthesia has recently gained attention. In the present study, the intrathecal administration of dexmedetomidine and fentanyl combined with bupivacaine was compared in patients undergoing lower limb surgeries. The results revealed that the combination of dexmedetomidine and bupivacaine showed a better effect compared to fentanyl.

In the study conducted by Laxmikanth J et al., included taken 126 patients who were divided into three groups. Group B received 0.5% bupivacaine+5 mcg dexmedetomidine+0.4 mL normal saline solution. They found that Group B exhibited a shorter time to reach sensory and motor blocks (T10 and M1, respectively) compared to Group A and Group C (p<0.001). The duration of sensory block and motor block in Group B was also longer compared to Group A and Group C (450.12±22.295 min and 390.12±22.551 min, respectively). Additionally, Group B took a longer time to require the initial rescue analgesic compared to Group A and Group C (p<0.001). The results of the present study were consistent with the present study, where the duration of sensory block and motor block was significantly prolonged in Group BD compared to Group BF, i.e., 720±32 and 640±32, respectively [12].

In the present study, bradycardia, nausea, vomiting, and hypertension were among the discomforts experienced by the patients. The minimum sedation scores were recorded, and there was no significant difference between the groups. Similar findings were reported by Ismail EF et al., in their study, where sedation scores were found to be minimum and not statistically significant [8].

The comparison of VAS scores between Group BD and Group BF showed that patients treated with dexmedetomidine exhibited significantly lower values than the fentanyl group at the first hour and relatively lower values in the 6-hour postoperative period. This result was similar to the research study conducted by Mahajan N et al., where they reported the lowest median VAS score recorded

at two hours when patients received intrathecal dexmedetomidine. This pattern persisted for four hours as well [13].

In the study conducted by Taher-Baneh N et al., the addition of both fentanyl and dexmedetomidine to bupivacaine in unilateral spinal anaesthesia increased the duration of motor block in the dependent limb. This lengthening was significantly greater in the fentanyl group compared to the dexmedetomidine group. In the present study, dexmedetomidine was found to be more effective than fentanyl when added to bupivacaine [14].

In the study by Rahimzadeh P et al., the effectiveness of bupivacaine alone or in combination with dexmedetomidine or fentanyl in lower limb surgery was assessed. The beginning of Bromage 3 and the duration of the entire motor block did not differ significantly between the groups, but the BD group took less time than the BF group to achieve the highest sensory level. There was no statistically significant difference between the BD group and BN group [6]. These results were consistent with the present study, where the BD group took less time than the BF group, and there was no significant difference between them [9].

Another recent observation by Kim DH et al., suggested that an increased dosage of dexamethasone with bupivacaine prolonged the duration of motor blockade for shoulder surgery. This observation was in line with the results of the present study, where bupivacaine in combination with dexmedetomidine showed effective outcomes [15].

In the present study, the combination of dexmedetomidine and bupivacaine demonstrated more significant findings than the combination of fentanyl and bupivacaine, which was considered a positive outcome. These observations in the present study were also consistent with other meta-analysis that used dexamethasone as an adjunct to other epidural local anaesthetics [16].

Another study by Agarwal S et al., observed that the combination of bupivacaine and dexmedetomidine provided a prolonged motor block in the treatment group compared to the control group [17]. Similarly, a study by Chavan SG et al., showed that the combination of fentanyl and bupivacaine led to an increase in the duration of sensory block [18]. However, the results of these studies were not consistent with the observations in the present study. Additionally, the present study demonstrated that dexmedetomidine provided optimal sedation levels compared to fentanyl in the treated groups.

The recent advancement in the use of local anaesthetics, such as tonicaine and n butyl-tetracaine, has gained significant popularity. However, before the routine clinical use of local anaesthetics, multiple human trials were conducted [19].

In the present study, the efficacy and safety of different combinations, specifically bupivacaine with dexmedetomidine and bupivacaine with fentanyl, were assessed for lower limb surgeries. The results indicated that the combination of bupivacaine with dexmedetomidine demonstrated superior effectiveness in prolonging both sensory and motor block duration compared to the combination of bupivacaine with fentanyl. Additionally, it was observed that postoperative analgesia was more satisfactory when using dexmedetomidine in combination with bupivacaine compared to the combination of fentanyl with dexmedetomidine. Overall, the study's observations showed that the postoperative time and the duration of analgesia were more efficient in the dexmedetomidine group compared to the fentanyl group.

Limitation(s)

The present study study was conducted at a single centre and included a limited number of patients from the Department of Orthopaedics and General Surgery. The assessment of analgesia was done using VAS, which is a subjective tool. It is important to note that the use of a subjective tool like VAS could have influenced the measurement results.

CONCLUSION(S)

In conclusion, the combination of dexmedetomidine with bupivacaine proved to be more effective in terms of sensory and motor block duration and the extent of analgesia, compared to the combination of bupivacaine and fentanyl. This advantageous combination outperformed the other in terms of both the duration and sustainability of sensory and motor blockade, as well as the broader range of analgesic effects. These findings highlight the potential of dexmedetomidine as a crucial adjunct in regional anaesthesia techniques. However, it is important to acknowledge the need for further research, particularly in elderly patients who may have multiple underlying health conditions. Additional research efforts are therefore necessary to fully understand the implications and benefits of incorporating dexmedetomidine in this context, ultimately contributing to a more comprehensive understanding of its clinical usefulness.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Mar 13, 2023
- Manual Googling: Aug 09, 2023
- iThenticate Software: Oct 18, 2023 (15%)

ETYMOLOGY: Author Origin

EMENDATIONS: 9

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Mar 04, 2023**
Date of Peer Review: **Apr 15, 2023**
Date of Acceptance: **Oct 23, 2023**
Date of Publishing: **Feb 01, 2024**