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Optimizing Subarachnoid Block; A Randomized Trial of Intrathecal Fentanyl, Dexmedetomidine and Clonidine As Adjuvants with Hyperbaric Bupivacaine in Adults Patients

[1]Syed Kamran Habib, Department of Anaesthesiology, Jawaharlal Nehru Medical College, Aligarh- 202001, Uttar Pradesh, India

[1]Umar Sherwani, Department of Anaesthesiology, Jawaharlal Nehru Medical College, Aligarh- 202001, Uttar Pradesh, India

[1]Mukesh Kumar, Department of Anaesthesiology, Jawaharlal Nehru Medical College, Aligarh- 202001, Uttar Pradesh, India

Corresponding Author: Umar Sherwani, Department of Anaesthesiology, Jawaharlal Nehru Medical College, Aligarh-202001, Uttar Pradesh, India.

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Abstract

Introduction: Effective pain management of lower limb surgeries is critical for ensuring patient comfort, optimising surgical outcomes and reducing postoperative complications. A randomised control was carried out to compare intrathecal fentanyl, dexmedetomidine and clonidine as adjuvants for pain management in patients undergoing lower limb surgery.

Materials and methods: Following approval by the institutional ethical committee, a prospective randomized controlled study was conducted on 90 adult patients aged between 18 and 50 undergoing elective lower limb surgery under sub-arachnoid block during the year 2022-2024. Group BF received intrathecally 12.5mg (2.5ml) 0.5% bupivacaine with fentanyl 25mcg(0.5ml), group BD with Intrathecally 12.5mg (2.5ml) 0.5% bupivacaine with pre-diluted Dexmedetomidine 5mcg (0.5ml and group BC with Intrathecally 12.5mg (2.5ml) 0.5% bupivacaine with clonidine 30mcg(0.2ml) +preservative free normal saline (0.3ml).

Results: The onset of sensory and motor block (mins) was similar in all three groups with Group BD (5.51 ± 0.91, 6.18 ± 0.782) and Group BC (5.61 ± 0.87, 6.21 ± 0.816) and Group BF having a mean onset time of (5.70 ± 1.14, 6.25 ± 1.15). The total sensory and motor duration was prolonged in Group BD (322.83 ± 11.49, 277.33 ± 14.06) compared to Group BC (275.16 ± 16.94,

214.70 ± 10.42) and Group BF (247.00 ± 11.64, 194.66 ± 10.41). The duration of the spinal block was significantly longer in Group BD (303.66 ± 10.83) compared to Groups BF (230.50 ± 10.53) and BC (248.66 ± 7.76). The time to two-segment regression was also significantly longer in Group BD (147.46 ± 9.16) compared to Groups BF (80.10 ± 3.42) and BC (100.63 ± 4.90). At 3 hours postoperative, Group BF had a higher VAS score (3.01) compared to Group BD (2.52) and Group BC (2.98)

Conclusion: All three studied drugs (fentanyl, dexmedetomidine, clonidine) were found to have clinically acceptable sedation levels and minimal complications therefore rendering them a viable choice as intrathecal adjuvants to hyperbaric bupivacaine for subarachnoid block in adult patients. Group BD (Dexmedetomidine) exhibited a significantly longer duration of motor and sensory block, and duration of spinal anaesthesia, with a delayed two-segment regression compared to the other two study groups (Group BC and Group BF) and suggesting a more prolonged effect of the subarachnoid block in this study group. However, larger randomized controlled trials might further elucidate our findings.

Keywords: Bupivacaine, Dexmedetomidine Levobupivacaine, Morbidity

Introduction

Effective pain management during and after lower limb surgeries is essential for patient comfort, recovery and decreased morbidity. Poorly managed postoperative pain can lead to various complications such as delayed recovery, risk of venous thromboembolism, inadequate sleep, chronic pain and prolonged hospital stays[1]. Regional anaesthesia, particularly spinal anaesthesia, has become a preferred technique for lower limb procedures due to its benefits of maintained consciousness, minimal systemic effects, and comfortable recovery[2]. It was first successfully administered by August Bier in 1898 using cocaine as the anaesthetic agent[3]. Spinal anaesthesia is one of the most clinically utilised regional anaesthesia procedures due to its unique benefits such as patients retaining consciousness during surgery (unlike general anaesthesia), maintaining spontaneous breathing, and experiencing minimal changes in body chemistry which translates to a more comfortable recovery process[4].

Over the years, advancements in pharmacology and technology have refined the technique and made it safer and more effective. Several local anaesthetics are used intrathecally with specific characteristics like Bupivacaine, Lidocaine, Ropivacaine and Levobupivacaine. The mechanism of local anaesthetics is still not entirely clear however it primarily targets voltage-gated sodium channels located on nerve fibres which open and allow sodium ions to flow into the nerve cell resulting in nerve impulse transmission[5]. This action effectively produces reversible loss of sensation and motor function, enabling a broad range of surgical procedures with minimal patient discomfort. By understanding the intricate mechanisms and pharmacological properties of these agents, anaesthesia providers can optimize patient outcomes and enhance the safety and effectiveness of spinal anaesthesia. Yet, the need for prolonged postoperative analgesia has led to the use of different adjuvants in the late 20th and early 21st century to prolong the duration of the block, reduce the potential dose of local anaesthetics, better success rate, patient satisfaction, decrease resource utilisation and faster recovery.

The addition of intrathecal adjuvants, such as fentanyl, dexmedetomidine, and clonidine, has further improved

the quality and duration of intraoperative and postoperative analgesia and anaesthesia[6]. Fentanyl, a lipid-soluble opioid, offers rapid onset and prolonged postoperative pain relief. The effects of opioids within CSF are complex because of a combination of direct spinal cord dorsal horn opioid receptor activation, cerebral opioid receptor activation after CSF transport and central systematic effects after vascular uptake. The addition of fentanyl to intrathecal local anaesthetic solution increases the duration of postoperative pain relief and reduces anaesthetic drug-related side effects including pruritis, nausea and vomiting[7].

Alpha-adrenergic agonists have been demonstrated to have sedative, analgesic, perioperative sympatholytic, anaesthetic-sparing and hemodynamic–stabilising properties[8]. Dexmedetomidine, a potent alpha-2 agonist, provides analgesia, sedation, and hemodynamic stability without respiratory depression. Intrathecal dexmedetomidine is found to have an antinociceptive action for both somatic and visceral pain. Low-dose dexmedetomidine has anxiolytic and hypnotic properties and added advantages of hemodynamic stability without respiratory depression. Its mechanism is to bind to α2 receptors in the locus coeruleus which causes sedation and anxiolysis. At the same time, action at laminae VII and VIII of the ventral horn of the spinal cord produces analgesia[9].

Clonidine, the first clinically used alpha-2 agonist, enhances sensory and motor block duration but requires careful dosing to avoid side effects. , clonidine provides a dose-dependent increase in the duration of sensory and block besides having antinociceptive properties. However, its use requires careful dosing and monitoring to mitigate potential side effects such as hypotension, bradycardia and sedation[10]. Various clinical trials have found that administration of fentanyl, dexmedetomidine and clonidine as adjuvants intrathecally with local anaesthetics prolonged the duration of sensory and motor blockade[11]. This study compares the effects of intrathecal fentanyl, dexmedetomidine, and clonidine as adjuvants to hyperbaric bupivacaine in terms of block characteristics, sedation, pain scores, and hemodynamic stability in adult patients undergoing elective lower limb surgeries.

Aims and objectives

Primary Objective is to compare the intrathecal fentanyl, dexmedetomidine and clonidine as adjuvants to hyperbaric bupivacaine for lower limb surgery based on duration of sensory and motor block. Secondary Objective is to compare the onset of sensory and motor block, Time to two segments regression of block, Duration of Spinal Anesthesia in each group, To compare the hemodynamic changes heart rate (HR), mean arterial pressure (MAP) among three groups, Perioperative Ramsay Sedation Score (RSS), Complications (nausea, vomiting, pruritis)

Materials and methods

This study was registered with the Clinical Trials Registry of India (CTRI/2023/04/051460) and approval by the institutional ethics committee (IECJNMC/784). After obtaining informed consent, the study was conducted in the Department of Anaesthesiology and Critical Care, Jawaharlal Nehru Medical College and Hospital in the period between 2022-24 on Ninety patients of ASA I and ASA II patients of either sex, aged between 18 to 50 years and who were scheduled for elective lower limb surgery under subarachnoid block. Patients with contraindications to regional anaesthesia, diseases like diabetes and neuropathy, history of ischaemic heart diseases, hypertension, impaired renal

functions, rheumatoid arthritis, severe liver disease, known allergy to local anaesthesia, pregnant patients, chronic alcoholics, AV Blocks, incomplete heart blocks, intake of alpha-blockers were excluded from the study.

Preanesthetic evaluations were performed by an anaesthesiologist a day before the surgery and all the patients were explained the purpose and conducting the procedure and informed consent was also obtained. After the pre-anaesthetic checkup, all the selected patients were uniformly premedicated with an Injection of Ondansetron (0.1mg/kg) and received ringer lactate infusion (15ml20ml/kg) via an 18-Guage intravenous (IV) cannula before intrathecal injection.

Patients were randomly divided into three groups using the 'Chit in the box' method: Group BF received 12.5 mg of 0.5% bupivacaine with 25 mcg of Fentanyl; Group BD received 12.5 mg of 0.5% bupivacaine with 5 mcg of Prediluted Dexmedetomidine; and Group BC received 12.5 mg of 0.5% bupivacaine with 30 mcg of Clonidine plus preservative-free normal saline. Baseline heart rate, blood pressure, oxygen saturation, sedation score, and pain level were recorded.

Under all aseptic precautions, the subarachnoid block was administered at the L2–3 or L3–4vertebral level using a 25-gauge Quincke spinal needle after infiltrating the skin with 2% Lignocaine with patients in the sitting position. A volume of 3ml of the study drug mixture of each group was administered intrathecally after confirming a free and clear flow of CSF. Patients were made supine following the block.

Sensory and motor block evaluation

The onset of sensory block was defined as the time between injection of intrathecal anaesthetic and the absence of pain at the T8 dermatome assessed by 23-G blunt tip hypodermic needle every 2 min till T8 dermatome was achieved. B. Motor block onset was defined as the time when the patient attained a modified Bromage score of 3 from the time of intrathecal injection. Modified Bromage score is categorized into four levels: Bromage 0 indicates that the patient can move the hip, knee, and ankle freely. Bromage 1 signifies that the patient is unable to move the hip but can move the knee and ankle. Bromage 2 describes a condition where the patient cannot move the hip and knee but retains the ability to move the ankle. Finally, Bromage 3 represents a complete motor block, with the patient unable to move the hip, knee, or ankle.

Hemodynamic monitoring

Vitals were recorded 5 min before intrathecal injection; Immediately after intrathecal injection and subsequently every 15 minutes till 60 minutes. IV fluids were given to maintain the blood pressure. Hypotension was defined as either a 25% reduction in systolic blood pressure from baseline or a reading below 90 mmHg. It was managed with intravenous mephentermine, administered in 6 mg increments. Bradycardia, defined as a heart rate of less than 60 beats per minute, was treated with 0.6 mg of intravenous atropine, particularly if it was accompanied by hypotension.

Ramsay sedation score

Ramsay sedation scale (levels were when the patient is 1-fully awake and anxious, 2- calm and cooperative, 3- gets arousable to verbal commands, 4- gets arousable to a mild stimulus or vigorous reaction to a painful stimulus, 5- shows slow or incomplete reaction to painful physical stimuli, 6- shows no reaction to painful stimulation) were used to assess sedation scores in all groups.

Adverse effects

Patients were monitored for adverse effects including inadequate block, hypotension, bradycardia, respiratory

distress, nausea, vomiting, pruritus, shivering, and anaphylactic reactions during the surgery.

Statistical analysis

Statistical analysis was performed using the computer program Statistical Package for Social Science (SPSS version 27.0). Qualitative and non-parametric data like Gender, ASA grade, Type of lower limb Surgery, and Complications were analyzed using Pearson's chi-square test (Descriptive Statistics). Age distribution was analyzed using ANOVA with Fischer's Exact test. Parametric data like Duration of surgery, Duration of Sensor and Motor Block, Onset of Sensory and Motor Block, Duration of spinal block, Time to two segment regression, Hemodynamic parameters, Ramsay Sedation Score, and VAS score were analyzed using ANOVA followed by unpaired t-test. The α level of analysis was set at 0.05 and p-value < 0.05 was considered statistically significant.

Results

Table 1: Comparison of spinal block characteristics

	Group BF(n=30) Mean± SD	Group BD(n=30) Mean ± SD	Group BC(n=30) Mean ± SD	P value
Sensory Block mean onset of spinal block	5.70±1.14	5.51±0. 91	5.61±0. 87	BF vs BD: 0.474 BF vs BC: 0.745 BD vs BC: 0.696
Motor Block mean the onset of spinal block	6.25±1.15	6.18±0.782	6.21±0.816	BF vs BD: 0.782 BF vs BC: 0.890 BD vs BC: 0.850
Duration of spinal block (minutes)	230.50±10.53	303.66±10.83	248.66±7.76	BF vs BD: 0. 001 BF vs BC: 0. 001 BD vs BC: 0.001
Time to two segment regression (minutes)	80.10±3.42	147.46±9.16	100.63±4.90	BF vs BD: 0. 001 BF vs BC: 0. 001 BD vs BC: 0 001

Table 2: Comparison of Hemodynamic Parameters

Time interval	Metric	Group BF (Mean±SD)	Group BD (Mean±SD)	Group BC (Mean±SD)	BF vs BD (p-value)	BF vs BC (p-value)	BD vs BC (p-value)
Baseline	Heart Rate	92.70±10.97	92.53± 10.83	93.23 ± 6.94	0.947	0.833	0.782
	MAP	92.96±10.75	90.36± 10.82	91.46 ± 9.27	0. 331	0.574	0.680
Injection	Heart Rate	104.20±10.25	106.66±8.98	105.33±9.42	0.587	0.648	0.181
	MAP	86.30±1066	86.53±12.89	85.13±15.00	0.945	0.729	0.677
15 Min	Heart Rate	84.50±11.25	82.76 ± 11.50	83.53±10.03	0.541	0.733	0.787
	MAP	80.43±8.60	80.76 ± 9.01	81.73± 8.37	0.882	0.563	0.667
30 Min	Heart Rate	81.00±11.41	78.83± 10.29	81.66± 11.33	0.449	0.815	0.322
	MAP	79.56±10.71	77.23± 11.11	78.53±10.53	0.405	0.712	0.642
45 Min	Heart Rate	79.63±6.75	76.26± 9.69	78.93±6.31	0.345	0.021	0.185
	MAP	78.83±8.11	75.56± 10.32	75.93±9.24	0.176	0.229	0.879
60 Min	Heart Rate	76.53±6.72	74.36 ± 8.67	75.13± 8.34	0.410	0.318	0.392
	MAP	78.30±8.58	74.16 ± 9.47	74.46± 9.36	0.084	0.108	0.899

Table 3: Comparison of Mean Ramsay sedation score among study groups

Time Interval	Ramsay Sedation Score (Mean ± SD)			P-Value
	Group BF(n=30)	Group BD(n=30)	Group BC(n=30)	
		Mean ± SD	Mean ± SD	
1 Hour	2.08±0.282	2.10 ± 0.305	2.06 ± 0.253	BF vs BD: 0. 769 BF vs BC: 0. 769 BD vs BC: 0.725
6 Hour	0.95±0.272	2.08 ± 0.302	2.04 ± 0.243	BF vs BD: 0. 247 BF vs BC: 0. 407 BD vs BC: 0.725
12 Hour	0.84±0.222	2.06 ± 0.301	2.02 ± 0.232	BF vs BD: 0. 754 BF vs BC: 0. 732 BD vs BC: 0.732

Table 4: Distribution of Complications among study groups

Variable	Group BF(n=30)	Group BD(n=30)	Group BC(n=30)
Nausea	2 (6.67%)	1 (3.33%)	2 (6.67%)
Vomitting	1 (3.33%)	0 (0%)	0 (0%)
Pruritis	1 (3.33%)	0 (0%)	1 (3.33%)
Urinary retention	2 (6.67%)	1 (3.33%)	2 (6.67%)

Hypotension	2 (6.67%)	3 (10%)	3 (10%)
Bradycardia	0 (0%)	2 (6.67%)	1 (3.33%)

Discussion

This study aimed to compare the effects of intrathecal Fentanyl, Dexmedetomidine, and Clonidine as adjuvants to hyperbaric bupivacaine in adult patients undergoing elective lower limb surgery. We evaluated the duration and onset of sensory and motor blocks, regression time, duration of spinal anaesthesia, sedation levels, VAS score, and hemodynamic stability. The results showed that the use of 5 µg dexmedetomidine intrathecally resulted in a comparable onset of the motor block but significantly extended its duration.

Similar findings, with the sensory block onset times averaging 8.6 minutes for Group BF, 8.3 minutes for Group BC, and 8.3 minutes for Group BD. These differences were not statistically significant (p = 0.113). Similarly, motor block onset times were 9.0 minutes for Group BF, 9.8 minutes for Group BC, and 9.7 minutes for Group BD, also showing no significant difference (p = 0.086) [11]. Our findings show similar onset times for sensory and motor blocks across groups but significantly longer block durations in Group BD. Dexmedetomidine (Group BD) notably extends the spinal block duration, benefiting longer surgeries.

The time to two-segment regression was also significantly longer in Group BD compared to Groups BF and BC. Group BD had the longest mean time to two-segment regression of 147.46 ± 9.16 minutes followed by Group BC (100.63 ± 4.90 minutes) and then Group BF (80.10 ± 3.42 minutes) as shown in Table 1. Similarly, a study observed that the time for two-segment regression from the highest sensory level varied significantly among the groups, with times of 88.90 ± 12.85 minutes in the BF group and 149.00 ± 23.17 minutes in the BD group, with a p-value of less than 0.001 [12]. In another study 100 minutes in the BF group and 113.27 minutes in the BD group, with a p-value of less than 0.031[13].

In our study, we evaluated the hemodynamic parameters of patients receiving spinal anaesthesia with fentanyl (BF), dexmedetomidine (BD), and clonidine (BC) as adjuvants. Our findings have revealed no significant differences in hemodynamic changes at specified time intervals between the three study groups as shown in Table 10 (Heart Rate) and Table 11 (Mean Arterial Pressure). Specifically, there were no statistically significant differences in Mean Arterial Pressure (MAP), or heart rate (HR) throughout the observed study period (P>0.05).

These results are consistent with several studies that have examined the hemodynamic effects of adjuvants used in spinal anaesthesia. A study found that the addition of dexmedetomidine to spinal anaesthesia did not lead to significant hemodynamic changes compared to fentanyl [14]. Similarly, a survey showed that both dexmedetomidine and fentanyl, when used as adjuvants, did not produce marked differences in hemodynamic stability in the BF group [15].

Complication rates were comparable among the groups, with minor variations (Table 16). Group BD had slightly higher rates of hypotension (10%) and bradycardia (6.67%) compared to the other groups, but differences were not statistically significant. Other studies observed similar observations. A study concluded that hypotension was observed in 54.5% of patients in Group BD and 67.3% in Group BF, but this difference was not statistically significant (P = 0.171). Bradycardia

occurred in 14.5% of Group BD patients compared to 9.1% in Group BF, with this difference also not reaching statistical significance (P = 0.376). Respiratory depression was reported equally in both groups, at 1.8%, indicating no difference between the groups (P = 1.000). Shivering was more prevalent in Group BF (16.4%) compared to Group BD (7.3%), though this difference did not achieve statistical significance (P = 0.140). Finally, nausea and vomiting were seen in 5.5% of Group BD patients and 9.1% of Group BF patients, with no significant difference between the groups (P = 0.716). Overall, the comparison shows no statistically significant differences in the rates of complications between the two groups [16].

In another study comparing the addition of dexmedetomidine and fentanyl to intrathecal bupivacaine for orthopaedic lower limb procedures, the incidence of complications varied among the groups. Nausea occurred in 3.3% of both the BF and BD groups. Vomiting was absent in the BF and BD groups. Chilling was reported in 6.7% of BF groups and 3.3% in the BD group. Pruritus was observed only in 6.7% of the BF group. Hypotension and bradycardia were more common in the BF group (10% each) compared to the BD group (3.3% each) [12].

The limitations of our study were that the subjects were healthy ASA Grade 1 and 2 patients; observations, especially the hemodynamic parameters cannot be implied for ASA Grade 3 & 4 patients. Further studies may be needed to deduce the clinical findings on ASA 3 and 4 patients. The study was done only on elective patients, undergoing lower limb surgeries. So, the results of the emergency room procedure must be considered using different study models. The study focused on adult patients aged 18-50; therefore, the observations may differ if geriatric and paediatric patient populations were included.

Conclusion

Based on our study, we conclude that along with fentanyl, both dexmedetomidine and clonidine, have emerged as alternative, safe, and clinically viable intrathecal adjuvants, demonstrating enhanced subarachnoid block characteristics. All three studied drugs (fentanyl, dexmedetomidine, clonidine) were found to have clinically acceptable sedation levels and minimal complications therefore rendering them a viable choice as intrathecal adjuvants to hyperbaric bupivacaine for subarachnoid block in adult patients. Dexmedetomidine has emerged as an agent offering enhanced duration of action compared to the other two adjuvant drugs. However, larger randomized controlled trials might further elucidate our findings.

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