ISSN: 2581 – 3633
PubMed - National Library of Medicine - ID: 101745081

*International Journal of Medical Science and Advanced Clinical Research (IJMACR)*

*Available Online at:www.ijmacr.com*

*Volume – 6, Issue – 2, April - 2023, Page No. : 17 - 26*

# A comparative study of intrathecal dexmedetomidine, clonidine and fentanyl as adjuvants to hyperbaric bupivacaine for lower limb surgery

[1]Dr Vidya ShankarraoLawand, Senior Resident, Bharatratna Dr.Babasaheb Ambedkar Hospital, Kandivali West, Mumbai 400067, India

[2]Dr Aparna Gunderao Kulkarni, Associate professor, SRTR GMC Ambajogai 431517, India

[3]Dr Devanand Bhimrao Pawar, Associate professor, Govt. Medical college, Alibag 402201, India

**Corresponding Author:** Dr Vidya ShankarraoLawand, Senior Resident, Bharatratna Dr. Babasaheb Ambedkar Hospital, Kandivali West, Mumbai 400067, India

**How to citation this article:** Vidya S. Lawand, Aparna G. Kulkarni, Devanand B. Pawar, "A comparative study of intrathecal dexmedetomidine, clonidine and fentanyl as adjuvants to hyperbaric bupivacaine for lower limb surgery", IJMACR- April - 2023, Volume – 6, Issue - 2, P. No. 17 – 26.



**Type of Publication:** Original Research Article

**Conflicts of Interest:** Nil

**Abstract**

Spinal anesthesia is most used technique in surgeries due to its success rates. However, the challenge of attaining adequate post-operative analgesia with just the local anesthesia remains. Various adjuvants like clonidine, dexmedetomidine, midazolam etc. are being used with local anesthetics for prolongation of intraoperative and postoperative analgesia. Hence, a single-center, cross-sectional study was carried out with 120 American Society of Anesthesiology (ASA) class I and II patients to know the effects of the combination of intrathecal Dexmedetomidine/ fentanyl / Clonidine to hyperbaric bupivacaine was carried out. 30 patients each were randomly allocated to 4 groups, where all the patients 12.5 mg 0.5% hyperbaric bupivacaine and other adjuncts like0.5 mL normal saline in group BS, group BF received 25 µg fentanyl, group BC received 30 µg clonidine, and group BD received 5 µg dexmedetomidine. We assessed the change in time of onset and duration of sensory and motor blockade, adverse effects associated on addition of intrathecal Dexmedetomidine/ fentanyl / Clonidine to hyperbaric bupivacaine, duration of post-operative analgesia. Other objectives were to assess the hemodynamic changes after administration of the block, complications associated intraoperatively and post-operatively. We observed that the duration of sensory and motor block was significantly prolonged in group BD (122.2 ± 3.2 and 263.3 ± 54.2 minutes respectively) as compared to other groups with the $p < 0.05$. Total duration of analgesia 287.5 ± 49.31 minutes in group BD with $p<0.05$. The study established that dexmedetomidine as an adjunct to

spinal bupivacaine in the surgical procedures, provides a horizon of beneficial effects in intraoperative and post-operative analgesia, hemodynamical stability.

**Keywords:** Modified Bromage score, Modified Ramsay sedation scale, α2-adrenoreceptor agonist, Opioids, intrathecal

**Introduction**

Spinal anesthesia is the reliable and versatile technique in lower limb surgeries due to its success rate over 90%, predictability, better patient satisfaction, lower incidence of complications and pain control than intravenous drugs[1]. Yet, postoperative analgesiaposes a hurdle to the use of spinal anesthesia when only local anesthetics are administered. This is due to its relatively shorter duration of action necessitating the early analgesic intervention in the postoperative period. Several adjuvants like clonidine and midazolam etc, have been studied to prolong the effect of spinal anesthesia.

Clonidine and Dexmedetomidine are two α2 agonists affecting via pre- and post-synaptic α2 receptors. Food and Drug Administration (FDA) has approved the usage ofDexmedetomidine in various peri-operative and critical care settings. A few hypothesis states that intrathecal 5 µg dexmedetomidine produces greater postoperative analgesic effect with hyperbaric bupivacaine in spinal anesthesia with minimum side-effects [2]. The affinity of dexmedetomidine is about eight-times greater compared to clonidine.

Synthetic opioids like Fentanylare generally used for analgesia. Combination of intrathecal fentanyl with local anesthetics offersan improved quality of intra-operative and post-operative effects [3].

Literature search revealed that a very few studies have been carried out comparing the effects of intrathecal Dexmedetomidine, Clonidine and Fentanyl as an adjuvant to Hyperbaric Bupivacaine in lower limb surgeries. Hence, we strived to explore these effects. The primary objective of the study was to determine the change in time of onset and duration of sensory and motor blockade, adverse effects associated on addition of intrathecal Dexmedetomidine/ fentanyl / Clonidine to hyperbaric bupivacaine. Also, to evaluate the duration of post-operative analgesia. The secondary objectives were to assess the hemodynamic changes after administration of the block, complications associated intraoperatively and post-operatively.

**Materials and methods**

A single-center, cross-sectional study was carried out in tertiary care hospital between July 2019- December 2021. Study was conducted after approval was sought from the Institutional Ethics Committee. 120 adult patients (18-60 years) of either sex, belonging to American Society of Anesthesiology (ASA) class-I and II who were scheduled for lower limb surgery were enrolled in this study. Patients refusing the consent or contraindicated to the spinal anesthesia were excluded. History of significant co-existing conditions like heart block/ dysrhythmia, renal/ hepatic or biliary dysfunction were not included in the study. Patients on therapy with adrenergic receptor antagonist, calcium channel blocker, and/or ACE inhibitor or on tranquilizers, hypnotics, sedatives & other Central nervous system depressant drugs were also exempted. Other exclusion criteria included the history of substance abuse, allergy to the study drugs, ASA > III.

An interview was conducted by the study team to obtain the socio-demographic details, history of addiction, clinical profile, and relevant medical history. Patients were advised fasting for 6 hours and received oral Diazepam 0.2 mg/kg as premedication. Patients were

continuously monitored using electrocardiogram (ECG), pulse oximetry, and noninvasive blood pressure. Readings at the baseline were noted.

An intravenous (IV) line was secured to preload all the patients with Ringer Lactate 20ml/kg. Under aseptic measures, 23G pencil-point spinal needles were introduced through L3–L4 interspaces in sitting position. The study participants were randomly assigned to four groups by blinding surgeon, patient, and the observing anesthesiologist to the treatment arm.

Table 1: Study groups

| Groups | Study drug |
|---|---|
| Group BD | Intrathecal 12.5mg (2.5 mL) volume of 0.5% hyperbaric bupivacaine and 5 µg (0.5 ml) dexmedetomidine in 0.5 mL of normal saline |
| Group BC | Intrathecal 12.5mg (2.5mL) volume of 0.5% hyperbaric bupivacaine with 30 µg (0.2 ml) Clonidine |
| Group BF | Intrathecal 12.5mg (2.5 mL) volume of 0.5% hyperbaric bupivacaine with 25 µg (0.5ml) fentanyl |
| Group BS | Intrathecal 12.5mg (2.5 mL) volume of 0.5% hyperbaric bupivacaine with 0.5 ml preservative free normal saline |

[BD- Bupivacaine Dexmedetomidine; BC- Bupivacaine Clonidine; BF- Bupivacaine Fentanyl; BS- Bupivacaine Saline]

After confirming the block, patients were put to supine position. The study team recorded the highest dermatome level of sensory blockade, the time to reach this level from the time of injection, time to S1 level sensory regression, time to urination, incidence of adverse effects associated with the drug administered.

Patients with the pulse oximeter reading less than 90% were administered with oxygen (5L/min) via a mask. Hypotension was defined as a decrease of systolic blood pressure by more than 30% from baseline or a fall below 90 mmHg and were treated with incremental IV doses of ephedrine 5 mg and IV fluid as required. We defined bradycardia as heart rate < 50 bpm and treated the patients with IV atropine 0.3–0.6 mg. Sensory testing was carried out using a sterile 23G needle every 2 minutes until the highest level was stabilized by the consecutive tests. Presence of loss of pinprick sensation and dermatomes levels were assessed. Surgery was allowed to commence on achieving T7 sensory blockade. Testing was then be conducted every 10 minutes until the point of two segment regression of the block was observed. Further testing was performed at 20-minutes interval until the recovery of S2 dermatome.

The motor blockade was assessed using modified Bromage score and sedation was assessed with modified Ramsay sedation scale.

Table 2: Modified Bromage Score [4]

| Grades | Description |
|---|---|
| Bromage 0 | Patient can move the hip, knee, and ankle |
| Bromage 1 | Patient is unable to move the hip |
| Bromage 2 | Patient is unable to move hip and knee, but can move the ankle |
| Bromage 3 | Patient is unable to move the hip, knee, and ankle |

Table 3: Modified Ramsay sedation scale [5]

| Score | Description |
|---|---|
| 1 | Patients awake and alert, minimal or no cognitive impairment |
| 2 | Patient is awake but tranquil, purposeful responses to verbal commands at conversation |

| | |
|---|---|
| 3 | Patient appears asleep, purposeful responses to verbal commands at conversation level |
| 4 | Patient appears asleep, purposeful responses to verbal commands but at louder than usual conversation level or requiring light glabellar tap |
| 5 | Patient is asleep, sluggish purposeful responses only to loud verbal commands or strong glabellar tap |
| 6 | Patient is asleep, sluggish purposeful responses only to painful stimuli |
| 7 | Patient is asleep, reflex withdrawal to painful stimuli only (No purposeful response) |
| 8 | Unresponsive to external stimuli, including pain |

Using a Visual analog scale (VAS) with scores between 0 and 10 (0 = no pain, 10 = most severe pain), post-operative pain was evaluated in all patients. VAS was administered every hourly in the first 2 hours, further the frequency was every two hourly for the next 8 hours and then after every fourth hourly till 24 hours. We administered Intramuscular diclofenac (rescue medication) to all the patients with a VAS >4. History of post-operative headache, pain and dysesthesia in the buttock, thighs or lower limb was noted in all patients on Day-7.

**Statistical analysis**

Statistical analyses were performed by using IBM SPSS statistics Version 21.0 (SPSS Inc., Chicago, IL, USA) and Openepi version 2.3.1. To calculate the sample size, a power analysis of = 0.05 and = 1.00 showed that 30 patients were needed per study group to detect an increase of 30 minutes difference between the median duration of spinal sensory block between the groups [2].Data was expressed as either numbers and percentage or mean and standard deviation (SD) or median and Inter-quartile range (IQR). The comparisons were made using Chi square test for qualitative data and student t test for quantitative data. p >0.05 was regarded as statistically significant.

**Results and discussion**

The study was completed with 120 patients.

I. Demographics:

The demographic details of the patients have been described in Table 4. There was a statistically significant difference observed in the demographical details of the patients, average height, and average weight of the patients. However, no significant difference was observed in other parameters among the study groups.

Table 4: Demographic details of study participants

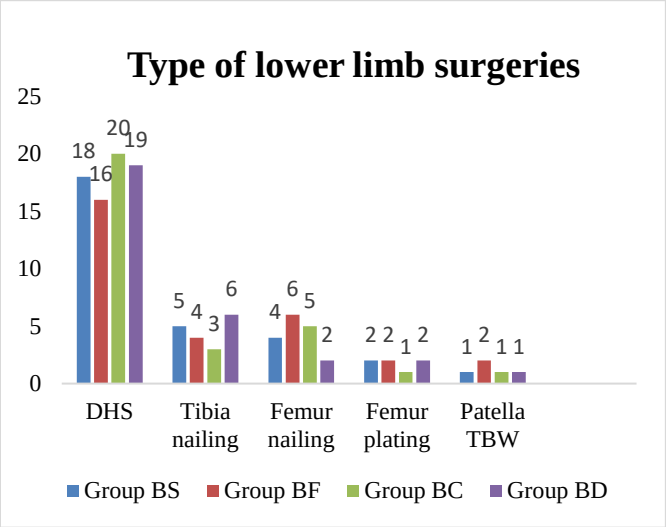
| Parameters | Group BS | Group BF | Group BC | Group BD | p-value |
|---|---|---|---|---|---|
| Median age (years) Median [IQR] | 26 [18-56] | 33 [30-45] | 44.5 [18-54] | 44.5 [18-54] | |
| Gender | | | | | |
| Male | 19 | 20 | 21 | 18 | 0.86 |
| Female | 11 | 10 | 9 | 12 | |
| Average weight (kg) | 63.2 ±6.43 | 65.4 ± 4.5 | 68.5 ± 8.3 | 66.6 ± 8.03 | 0.0001* |
| Average height (cm) | 165.4 ± 5.53 | 166.5 ± 34 | 168 ± 3.3 | 167.4 ± 3.6 | 0.0001* |
| Ratio of ASA status | 28/2 | 28/2 | 26/2 | 28/2 | 0.72 |

II. Type of lower limb surgery performed:

Majority patients included in the study underwent Dynamic hip screw (DHS) fixation. It can be observed from the table 5 that a 18/30 (60%) patients underwent DHS Among Group BS, 6/30 (20%) underwent tibial nailing from Group BD, 6/30 (20%) underwent femur nailing from Group BF, 2/30 (6.7%) femur plating each

from Group BS, Group BF and Group BD and 1/30 (3.3%) patient patella-TBW from Group BF.

Figure 1: Graphical representation depicting the type of lower-limb surgeries performed.




III. Baseline vitals

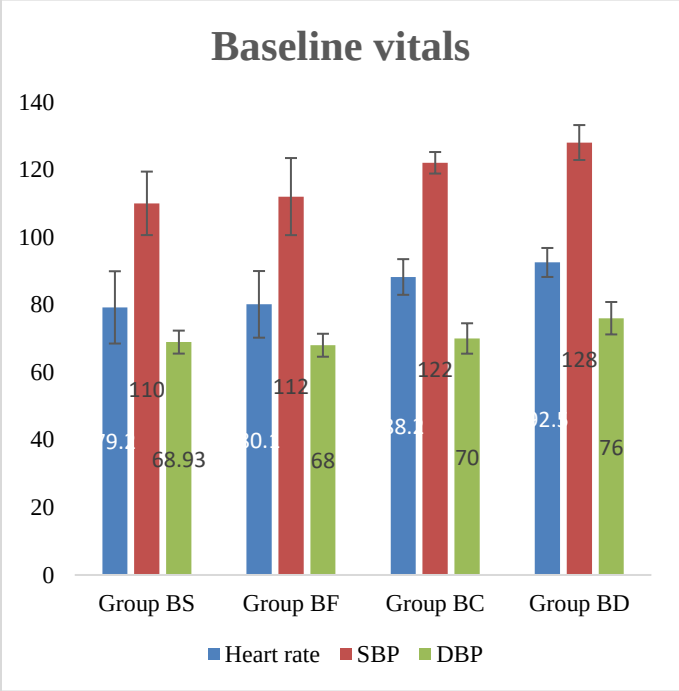
All the patients were evaluated for the baseline vitals. It was observed that Group BD had the highest baseline Heart rate of 92.5±4.29 beats/minute., SBP of 128±5.17 mmHg and DBP of 76.± 4.8 mmHg. The study showed that there was significant difference in the Heart rate among the study groups with p <0., however, the heart rate of group BC and BD were comparable.

Similarly, there was a significant difference in the systolic blood pressure among the study groups. But no significant difference was observed among the group BS and BC with p >0.05.

On analyzing the diastolic blood pressure (DBP), the results were comparable among groups BS, Group BF and BC. However, there was significant difference in the DBP in Group BD compared to the other three groups with p< 0.00001. The oxygen saturation was 97%, 96%, 98% and 99% in the groups BS, group BF, group BC and group BD respectively.

Figure 2: Baseline vital parameters

SBP= Systolic blood pressure, DBP= Diastolic blood pressure




IV. Characteristics of spinal block

With an aim to understand the characteristics of the spinal block, we evaluated various variables mentioned in the objectives. The details have been noted in the table 5. It can be observed from the above table that Bupivacaine Saline group had minimum mean onset of sensory block (7.6± 1.27 minutes) while, Group BF had the minimum mean onset motor block (9 ± 0.82 minutes).

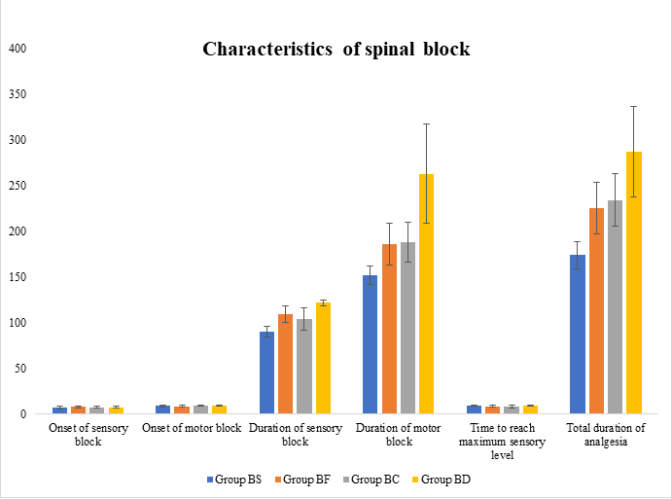
The duration of sensory and motor block was significantly prolonged in group BD as compared to other groups with the p-value <0.05. However no statistical difference was observed in the onset of motor block among the study groups with p=0.3.

Table 5: Characteristics of spinal block

| Parameters (minutes) | Group BS | Group BF | Group BC | Group BD | p-value |
|---|---|---|---|---|---|
| Onset of sensory | 7.6 ± 1.27 | 8.1 ± 0.8 | 7.9 ± 0.9 | 7.9 ± 0.9 | 0.0006* |

| | | | | | |
|---|---|---|---|---|---|
| block | | | | | |
| Onset of motor block | 9.1 ± 0.75 | 9 ± 0.82 | 9.6 ± 1 | 9.6 ± 1 | 0.3 |
| Duration of sensory block | 90.5 ± 5.64 | 109.2 ± 9.01 | 104.3 ± 12.2 | 122.2 ± 3.2 | 0.01 * |
| Time to reach maximum sensory level | 9.2 ± 0.62 | 8.9 ± 0.71 | 8.5 ± 1.1 | 9.5 ± 0.93 | 0.006 * |
| Duration of motor block | 152.3 ± 10.51 | 186.5 ± 22.6 | 188.5 ± 22.7 | 263.3 ± 54.2 | <0.00001 * |
| Total duration of analgesia | 174.2 ± 14.61 | 225.3 ± 28.32 | 234.6 ± 29 | 287.5 ± 49.31 | 0.01 * |

Figure 2: Graphical representation depicting the characteristics of spinal block

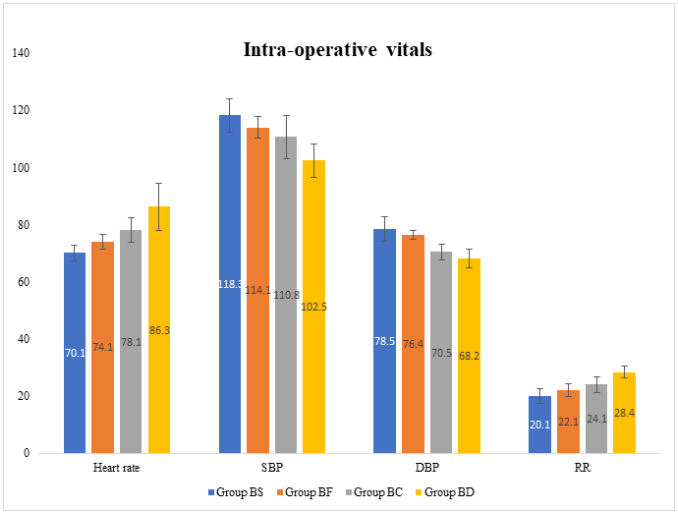



V. Intra-operative parameters:

Among group BS showed highest mean systolic BP 118.3± 5.89 mmHg and mean DBP 78.5±4.3 mmHg. However, maximum mean Heart rate and respiratory rate was shown in group BD with 86.3±8.3 beats/minute and 28.4 ± 2.08 cycles/minutes. On analyzing the heart rate and SBP, the groups BF, BC, and BD were comparable with p<0.00001. However, comparable heart rates were observed in group BF and BS, BC. The DBP was comparable between group BC and BD with p= 0..03992. While other groups showed a statistically significant difference on post-hoc analysis. There was a statistically significant difference among all the groups with respect to respiratory rate with p< .00001.

Figure 3: Intra-operative vital parameters

SBP= Systolic blood pressure, DBP= Diastolic blood pressure, RR= Respiratory rate




VI. Intra-operative complications:

Group BD showed maximum number of Intra- operative hypotension12 (40%) cases and headache in 9 (30%). Group BS and Group BF showed maximum number of 2 (6.7%) cases with nausea and vomiting score. Group BS showed maximum number of 6 cases (20%) with pain.

Table 6: Intra-operative complications

| Details | Group BS (N=30) | Group BF (N=30) | Group BC (N=30) | Group BD (N=30) |
|---|---|---|---|---|
| Hypotension | 3 (10%) | 8 (26.7%) | 9 (30%) | 12 (40%) |
| Headache | 2 (6.7%) | 1 (3.3%) | 4 (13.4%) | 9 (30%) |
| Nausea and vomiting score | 2 (6.7%) | 2 (6.7%) | 1 (3.3%) | 1 (3.3%) |
| Pain | 6 (20%) | 4 (13.4%) | 4 (13.4%) | 2 (6.7%) |

VII. Post-operative parameters:

The table 7 enlists the post-operative parameters are mentioned. It was observed that post-operative analgesia was not needed in patients of Group BD only. The Bupivacaine Dexmedetomidine group showed

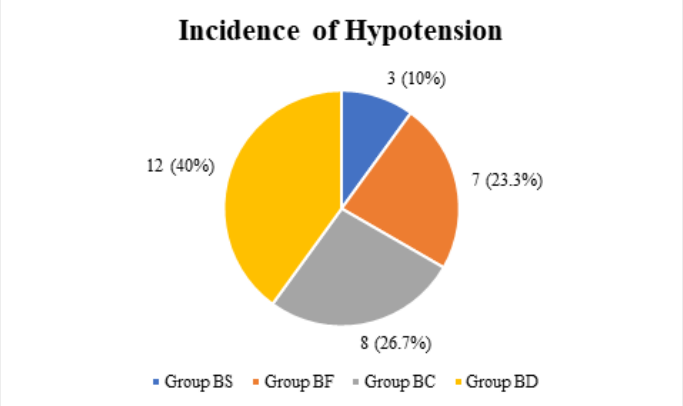
maximum duration of motor block and duration of analgesia 230.11± 46.9 minutes and 7 minutes.

Table 7:Post-operative analgesia

| Parameter | Group BS | Group BF | Group BC | Group BD |
|---|---|---|---|---|
| Duration of motor blockade (In minutes) | 170± 9.23 | 176.19 ± 7.55 | 190.19 ± 11.2 | 230.1 ±46.9 |
| Duration of rescue analgesia (In minutes) | 2 | 3 | 5 | 7 |
| Number of rescue analgesia needed | 5 | 3 | 2 | 1 |

All parameter showed statistical significance. P<0.00001

Figure 4: Representation of incidences of complication in post-operative patient 4A. Incidence of hypotension




4B. Incidence of headache

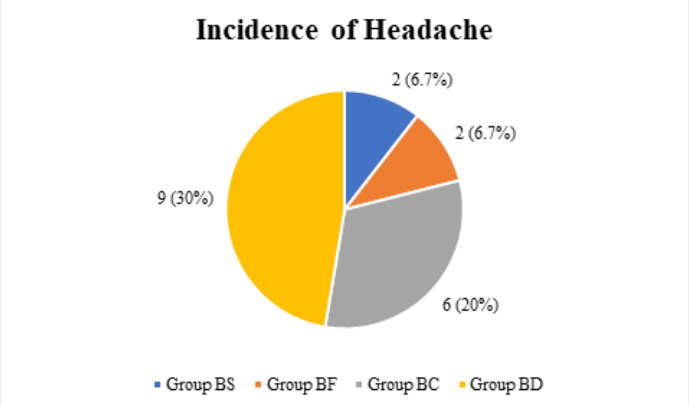
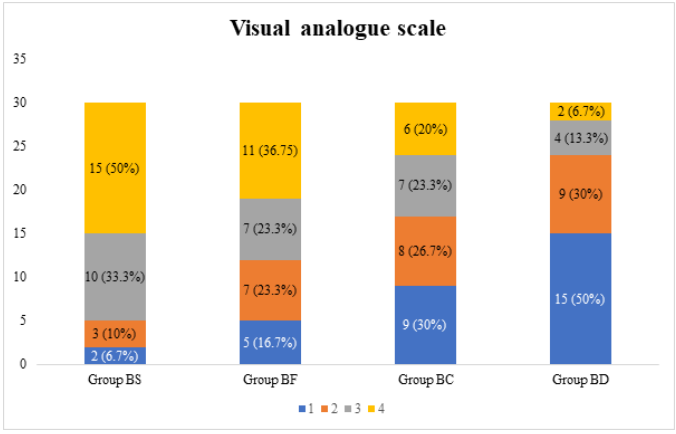



Figure 5: Visual analogue scale




## Discussion

Our study compared the change in time of onset and duration of sensory and motor blockade, adverse effects associated on addition of intrathecal Dexmedetomidine/ fentanyl / Clonidine to hyperbaric bupivacaine. The results of our study highlight that the highest median (IQR) age was 44.5 [18-54] years was noted in the group BC and BD. The study had 78 (65%) males and 42 (35%) females. Our results only signify that the duration of motor block and sensory block was significantly longer in a patient where intrathecal dexmedetomidine was added to the hyperbaric bupivacaine. Combination with dexmedetomidine has also aided in prolonging the duration of analgesia in patients post-operatively.

Studies have been carried out to assess the mechanism and advantages of addition of α2- adrenoceptors agonists with intrathecal local anesthesia. Postulated hypothesis suggests that the action of α2- adrenoceptors binding to C-fibers and postsynaptic dorsal horn neurons leads to lower release of C-fiber transmitters and hyperpolarization of postsynaptic dorsal horn neurons. This synergistic combination aids in a prolonging the motor and sensory blockade [6]. Other theory states that the location on primary afferent terminals (both at peripheral and spinal endings), on neurons in the superficial laminae of the spinal cord, and within several

brainstem nuclei implicated in analgesia aiding in analgesia at periphery, spinal and brain-stem sites [7].

A comparative study by Gupta R et al, was conducted on 60 patients with ASA I-II scheduled for lower abdominal surgeries by randomly allocated to receive 12.5 mg hyperbaric bupivacaine plus either 5 µg dexmedetomidine or 25 µg fentanyl. The results of the study were in line with our results. The patients on dexmedetomidine showed a significantly longer sensory and motor block time than patients in fentanyl group [3].

A similar study by Mahendru V et al was performed with 120 patients randomly assigned to four groups with 12.5 mg hyperbaric bupivacaine with normal saline or 25 g fentanyl or 30 g clonidine or 5 g dexmedetomidine. The patients on dexmedetomidine showed significantly longer sensory and motor block times than patients in other groups. The mean duration of sensory and motor blockade with dexmedetomidine was 146.7 ± 20.5 minutes and 273.3 ± 24.6 minutes. The results were parallel in our study where the dexmedetomidine 122.2 ± 3.2 minutes and 263.3 ± 54.2 minutes [2].

Our study showed that there existed a significant difference in the onset of sensory blockade while time to reach complete motor blockade was comparable among all the study groups. Our results conflicted a randomized trial steered by Rahimzadeh P et al, where time to sensory block was similar among patients on hyperbaric bupivacaine with dexmedetomidine or fentanyl or normal saline [8].

The adverse drug reaction with anesthetic agentsis inevitable. The study highlighted that the maximumincidence of hypotension and headache wererecorded with dexmedetomidine. The results were in concordance with the study by Gupta R et al. The study featured a higher rate of hypotension encountered by patients on dexmedetomidine, but no statistical significance was noted between the group [3].However, in several other studies no significant differences were observed in the rates of side-effects associated with the drug [9].

Use of dexmedetomidine with bupivacaine has also been studied in various other indications like cesarean section to provide a better post-operative analgesia. Study by Bi HY et al, has concluded that co-administration of 3µg dexmedetomidine offered animprovedintraoperative somato-visceral sensory block characteristics and postoperative analgesia, with the results falling in line with our study [10].

Though studies have been conducted to ascertain the role of combination of α2- adrenoceptors agonists with intrathecal local anesthesia globally, a very few studies have distinctly compared the effects of dexmedetomidine, fentanyl and clonidine in a compact study. Hence, the study caters to the advancement in the knowledge of the anesthesiologists suggesting the role of intrathecal dexmedetomidine as an adjuvant to bupivacaine as an appealing alternate to fentanyl and clonidine for long duration surgical procedures.

**Conclusions**

The study has concluded that dexmedetomidine seems to have widened the scope of its utilization as an adjunct to spinal bupivacaine in the surgical procedures by offering a better intraoperative and post-operative analgesia, hemodynamical stability.

**Ethics approval and consent to participate**

Study was conducted after approval was sought from the Institutional Ethics Committee. A written informed consent was taken from all the participants included in the study. The participants denying the consent were

excluded. Participants had the right to opt out at any time during the study.

**List of abbreviations**

1. FDA: Food and Drug Administration
2. ASA: American Society of Anesthesiology
3. ECG: Electrocardiogram
4. BD: Bupivacaine-dexmedetomidine
5. BS: Bupivacaine-saline
6. BC: Bupivacaine-clonidine
7. BF: Bupivacaine-fentanyl
8. VAS: Visual analog scale
9. SBP: systolic blood pressure
10. DBP: Diastolic blood pressure
11. RR: Respiratory rate

**Authors' contributions:** Protocol designing, Data collection and analysis

**Acknowledgements:** I thank my department for wholeheartedly supporting our team to complete the study.

**References:**

1. Hunie M, Fenta E, Kibret S, Teshome D. The current practice of spinal anesthesia in anesthetists at a comprehensive specialized Hospital: A single center observational study. Local Reg Anesth. 2021;14:51–6.
2. Mahendru V, Tewari A, Katyal S, Grewal A, Singh MR, Katyal R. A comparison of intrathecal dexmedetomidine, clonidine, and fentanyl as adjuvants to hyperbaric bupivacaine for lower limb surgery: A double blind controlled study. J Anaesthesiol Clin Pharmacol. 2013;29(4):496–502.
3. Gupta R, Verma R, Bogra J, Kohli M, Raman R, Kushwaha JK. A Comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to Bupivacaine. J Anaesthesiol Clin Pharmacol. 2011;27(3):339–43.
4. Bromage PR. A comparison of the hydrochloride and carbon dioxide salts of lidocaine and prilocaine in epidural analgesia. Acta Anaesthesiol Scand Suppl. 1965; 16:55–69.
5. Klein RH, Alvarez-Jimenez R, Sukhai RN, Oostdijk W, Bakker B, Reeser HM, et al. Pharmacokinetics and pharmacodynamics of orally administered clonidine: a model-based approach. Horm Res Paediatr. 2013;79(5):300–9.
6. Eisenach JC, De Kock M, Klimscha W. α2-Adrenergic Agonists for Regional Anesthesia: A Clinical Review of Clonidine (1984 - 1995) Anesthesiology. 1996;85:655–74.
7. Unnerstall JR, Kopajtic TA, Kuhar MJ: Distribution of alpha 2 agonist binding sites in the rat and human central nervous system: Analysis of some functional, anatomic correlates of the pharmacologic effects of clonidine and related adrenergic agents. Brain Res Rev 1984; 7:69-101.
8. Rahimzadeh P, Faiz SHR, Imani F, Derakhshan P, Amniati S. Comparative addition of dexmedetomidine and fentanyl to intrathecal bupivacaine in orthopedic procedure in lower limbs. BMC Anesthesiol. 2018;18(1).
9. Ravipati P, Isaac GA, Reddy PN, Krishna L, Supritha T. A comparative study between intrathecal isobaric Ropivacaine 0.75% plus Dexmedetomidine and isobaric Ropivacaine 0.75% plus fentanyl for lower limb surgeries. Anesth Essays Res. 2017;11(3):621–6.
10. Bi Y-H, Cui X-G, Zhang R-Q, Song C-Y, Zhang Y-Z. Low dose of dexmedetomidine as an adjuvant to bupivacaine in cesarean surgery provides better

intraoperative somato-visceral sensory block characteristics and postoperative analgesia. Oncotarget. 2017;8(38):63587–95.