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Original Research Article

A Comparative Study on Efficacy of Intrathecal Clonidine with Bupivacaine and Dexmedetomidine with Bupivacaine for Surgeries below Umbilicus

Mani Parashar[1], Ambreen Ashraf[2], Asma Shafique[3], Lokesh Kumar Gupta[4]

[1,3]Residents, Department of Anaesthesiology and Critical Care, Saraswathi Institute of Medical Sciences and Hospital, Hapur, Uttar Pradesh, India

[2]Senior Resident, Department of Anaesthesiology and Critical Care, Saraswathi Institute of Medical Sciences and Hospital, Hapur, Uttar Pradesh, India

[4]Professor, Department of Anaesthesiology and Critical Care, Saraswathi Institute of Medical Sciences and Hospital, Hapur, Uttar Pradesh, India

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Corresponding Author: Dr. Ambreen Ashraf

Conflict of interest: Nil

Abstract:

Background: Pain management is crucial in healthcare. Neuraxial anaesthesia, particularly intrathecal administration of local anaesthetics, is effective for intraoperative and postoperative pain relief. Both clonidine and dexmedetomidine, alpha-2 adrenergic agonists, show promise in prolonging sensory and motor blockade and reducing supplemental analgesia. The aim of this study is to provide evidence to guide clinical practice and improve anaesthesia for surgeries below the umbilicus.

Methods: 120 patients belonging to ASA I and II, posted for infraumbilical surgeries were divided into 3 groups of 40 each and received intrathecal drug as follows: **Group-B:** 0.5% Bupivacaine 15mg (3ml) + 0.5 ml Normal saline (NS) (Total volume 3.5ml). **Group-C:** 0.5% Bupivacaine 15mg (3ml) + 50 µg Clonidine (0.5ml) (150 µg [1ml] diluted to 1.5ml with NS and 0.5 ml was given). **Group-D:** 0.5% Bupivacaine 15mg (3ml) + 5 µg Dexmedetomidine (0.5ml) (50 µg [0.5ml] diluted to 5ml with NS and 0.5ml was given) Total Volume 3.5ml). Onset and duration of sensory and motor block, hemodynamic parameters, duration of analgesia and complications (if any) were observed.

Results: The time of onset of sensory and motor block was fastest in group C followed by group D and then group B. The mean duration of sensory, motor blockade and duration of analgesia was longest in group D followed by group C and group B. ($p < 0.05$).

Conclusions: The present study showed that supplementation of Bupivacaine in spinal block with low dose Dexmedetomidine produced a statistically significant longer duration of sensory and motor block and prolonged duration of analgesia when compared to Clonidine.

Keywords: Bupivacaine; Dexmedetomidine; Clonidine; Spinal anaesthesia; Analgesia.

Introduction

Consistent with Hippocrates' timeless wisdom, pain management is a vital aspect of healthcare. Pain's roots can be traced back to the Latin word for penalty or punishment, highlighting its significance. While intraoperative pain relief is essential, it's equally important to extend this comfort to the postoperative period.

Among the various approaches to achieve effective analgesia, neuraxial anaesthesia, particularly intrathecal administration of local anaesthetics, has gained popularity for its ability to provide targeted and profound pain relief. Pain management in perioperative settings remains a paramount concern for anaesthesiologists, surgeons, and healthcare providers, emphasizing the continuous quest for optimal techniques and pharmacological agents.

The rationale for conducting this comparative study stems from the evolving landscape of anaesthesia and the persistent need for evidence-based practices in perioperative care. Understanding the comparative efficacy of intrathecal clonidine with bupivacaine and dexmedetomidine with bupivacaine is essential for tailoring anaesthesia protocols to optimize patient outcomes. Additionally, such comparative analyses contribute valuable insights to the existing body of literature, aiding clinicians in making informed decisions regarding the choice of adjuvants for spinal anaesthesia.

Material and Methods

After approval from the institutional ethical committee (SIMS/FMT/ETHI/21/2022 dated 15/09/ 2022), a written informed consent was obtained from all patients undergoing infraumbilical surgeries under spinal anaesthesia and a comparative observational clinical study was carried out at Department of Anaesthesiology and Critical Care, Saraswathi Institute of Medical Sciences, Anwarpur, Hapur (Uttar Pradesh).

Study Duration: July 2022 to June 2024.

Sample Collection: All cases included in the study (equally divided in each group). With sample size N=120.

The sample size for the study was calculated by using formula as below:

$n=4pq/d^2$

Where n = sample size; P = prevalance (Considered as 50% from the previous study);q= 100 – p = 100 – 50 = 50%; d = standard error (10 % at 95% confidence interval).

Therefore, $n = 4 \times 50 \times 50 / (10)^2$

n = 100, the sample size of this study was 120 patients.

Patients were randomly divided on an alternative basis into 3 groups of 40 each and received intrathecal drug as follows:

- **Group-B**: 0.5% Bupivacaine 15mg (3ml) + 0.5 ml Normal saline(NS) (Total volume3.5ml)
- **Group-C**: 0.5% Bupivacaine 15mg (3Ml) + 50 µg Clonidine (0.5ml) (150 µg [1ml] diluted to 1.5ml with NS and 0.5 ml was given.)
- **Group-D**: 0.5% Bupivacaine 15mg (3ml) + 5 µg Dexmedetomidine (0.5ml) (50 µg [0.5ml] diluted to 5ml with NS and 0.5ml was given).

Statistical Analysis

The collected data was entered in MS Excel and was imported in IBM SSPS VS.25.0. The collected data was analyzed by appropriate statistical tests, techniques and tests such as mean ± SD, graphical representation of data, frequency distribution, and chi-square test. A $p<0.05$ was considered as statistically significant.

Inclusion Criteria:

- Patient posted for elective lower limb and lower abdominal surgeries under spinal anaesthesia
- All gender, Age 18- 60 year.
- Patient coming under American Society of Anaesthesiologist (ASA) I-II

Exclusion Criteria:

- Any contraindication to spinal anaesthesia.
- History of allergy to Bupivacaine, Clonidine and Dexmedetomidine.
- Pregnant patient.

One day before the operation, every patient had a thorough examination at the pre-anaesthesia clinic. After midnight, all patients were advised to maintain an overnight fast. The night before surgery, all patients were premedicated with tab alprazolam 0.5 mg orally. Patients were thoroughly explained about the procedure. All patients had a drug sensitivity test (DST) one night before surgery.

Following patient arrival in Operation Theatre (OT), an Intravenous Line (IV) was established using an 18G IV cannula, and the patient was monitored with conventional monitoring equipment such as an Electrocardiogram (ECG), Non Invasive Blood Pressure (NIBP) cuff, and a pulse oximetry probe (SPO2). Heart rate (HR) and baseline blood pressure (BP) were noted. No premedication was administered, and the preloading procedure involved using Ringer lactate solution at a dose of 15 ml/kg/body weight (BW) over a 15-minute period. The patient was explained about the procedure of the Subarachnoid Block (SAB). Injectable ephedrine (6 mg/ml) and atropine (0.6 mg/ml) syringes were loaded and stored in a ready-to-use state. Following the implementation of all aseptic measures and appropriate lumber interspace draping, L3–L4 were located in a seated posture. A 25G Quincke spinal needle was used to administer spinal anaesthesia. Once free flow of cerebrospinal fluid (CSF) occurred, research solution was then injected at a rate of 1 ml/ 5 sec while the needle's bevel was cephalad.

The patient was immediately put back into a supine position following spinal anaesthesia. The patients were assigned to one of the three groups by “slip in the box technique” by an anaesthesiologist who prepared the same drug combination according to the combination mentioned in the slip. The intrathecal study drug combination was not known to the anaesthesiologist performing the spinal anaesthesia and managing the patient.

The following variables were noted and observed:

1**. Vital Parameters**: Following the block, heart rate (HR), respiratory rate (RR), blood pressure (BP), and oxygen saturation (spo2) were tracked and recorded every three minutes for the first fifteen minutes of the intraoperative phase. Thereafter, they were recorded and monitored every 5 minutes for next 15 minutes and thereafter every thirty minutes until the surgery was completed.

2**. Evaluation of sensory blockade**: A blunt 25-gauge needle was used to measure the loss of pinprick feeling bilaterally along the midclavicular

line once every minute until the greatest level was reached. Statistical analysis was performed using the higher level when there was a difference between the left and right. Surgery was permitted once the T10 sensory blockage level was reached. The termination of intrathecal injection to the loss of T10 (pinprick sensation) was considered the onset of sensory block. The time interval from the start of the sensory blockade and the recovery of the pinprick sensation to the S1 dermatome (lateral aspect of the calcaneus) was used to measure duration of sensory block.

3. **Evaluation of motor blockage** (Bromage scale was used): The onset time of motor block was determined to be the interval from the time a drug was injected intrathecally into the subarachnoid space until the patient was unable to raise their leg straight (Bromage 3). The duration of the motor block was measured from the end of the intrathecal injection until the motor block completely disappeared, allowing the patient to raise their extended leg (Bromage 0).

4. **Evaluation of analgesia** (The VAS, or Visual Analog Score was used): The VAS is made up of a 10-centimeter line that is labelled "No pain" at one end and "Worst Pain Imaginable" or "Pain As Bad As Can be" at the other. The clinician measured the line length to mark a point scale after the patient merely marked the line to indicate the degree of pain. Every patient received instruction regarding the VAS and how to indicate their level of discomfort on a scale from 0 (no pain) to 10 (worst pain). The duration of analgesia was measured as the interval between the spinal injection and the first reported VAS >4 or when rescue analgesic was requested. Rescue analgesia was given as injection diclofenac sodium 75 mg intramuscularly, which was repeated every 8 hours if necessary. Inj diclofenac rescue dosages were noted. All durations were calculated considering the time of spinal injection as time zero. Following sensory regression, to the S1 dermatome and Bromage score 0 patients were moved from the Post Anaesthesia Care Unit (PACU). After being moved to the postoperative ward, patients were monitored until a rescue analgesic was given. Adverse effects include dry mouth, bradycardia, hypoxia (SPO2<90%), nausea and vomiting, pruritus, hypotension, and respiratory depression (RR<8/min) were noted. The incidence of bradycardia, defined as HR <60/min, was treated with atropine 0.6 mg intravenous stat, and hypotension, defined as arterial BP <20% of baseline or MAP <60mmHg, was treated with injection ephedrine 6 mg intravenous increments. IV inj. ondansetron 4 mg was used to relieve nausea and vomiting. Warm intravenous fluid and drapes were used to treat shivering.

Results

Demographic parameters such as Age, Gender, Weight, height and ASA Class were comparable among the three groups.

Table 1: Demographic profile in the three groups:

Parameter	Group B (n=40)	Group C (n=40)	Group D (n=40)	P-value
Age	39.2 ±12.3	44.9 ±10.2	40.7 ±12.4	0.053
Gender M/F	19 (47.5%)/21 (52.5%)	18 (45.0%)/22 (55.0%)	15 (37.5%)/25 (62.5%)	0.64
Weight (in kg)	66.65 ± 8.9	64.93 ± 8.7	66.77 ± 7.5	0.55
Height (in cms)	153.60 ± 4.4	154.10 ± 4.8	152.02 ± 4.9	0.13
ASA I/II	23(57.5%)/17(42.5%)	22(55.0%)/18(45.0%)	18(45.0%)/22(55.0%)	0.49

Sensory Block parameters:

Onset of sensory block: Onset of sensory block was earliest in Group C >Group D> Group B.

Duration of sensory block: Duration of sensory block was longest in Group D> Group C> Group B.

Motor Block parameters:

Onset of motor block: Onset of motor block was earliest in Group C> Group D>Group B.

Duration of motor block: Duration of motor block was longest in Group D>Group C> Group B.

Table 2: Block parameters:

Block parameter	Group B	Group C	Group D	P- value
Onset of sensory block(in mins)	6.9 ± 0.7	5.9 ± 1.2	6.6 ± 1.1	0.001*
Duration of sensory block (in mins)	200.1 ± 13.6	341 ± 11.9	405.5 ± 8.6	0.001*
Onset of motor block (in mins)	14.6 ± 1.9	9.5 ± 1.1	11.0 ± 0.9	0.001*
Duration of motor block (in mins)	173.3± 12.5	273.9 ± 41.9	363.7 ± 13.4	0.001*

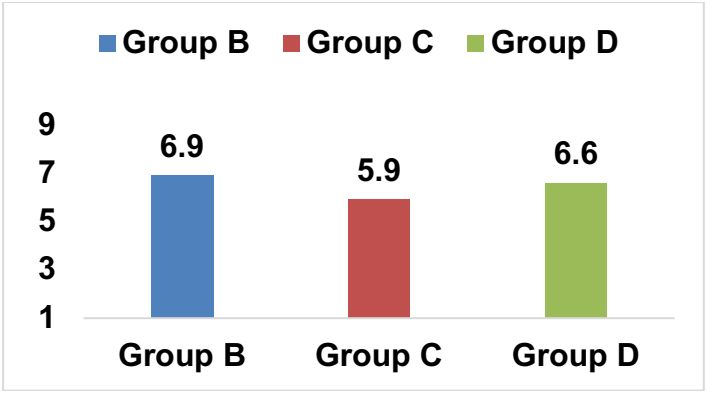

Figure 1: Comparison of onset of sensory block to T10 (min) in the 3 groups

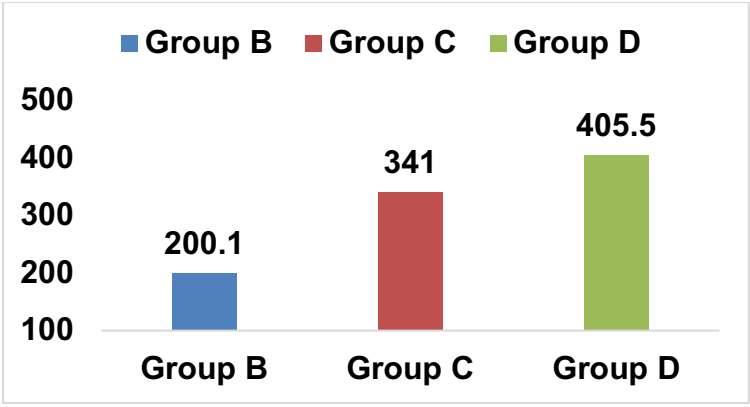

Figure 2: Comparison of duration of sensory block (min) in the 3 groups

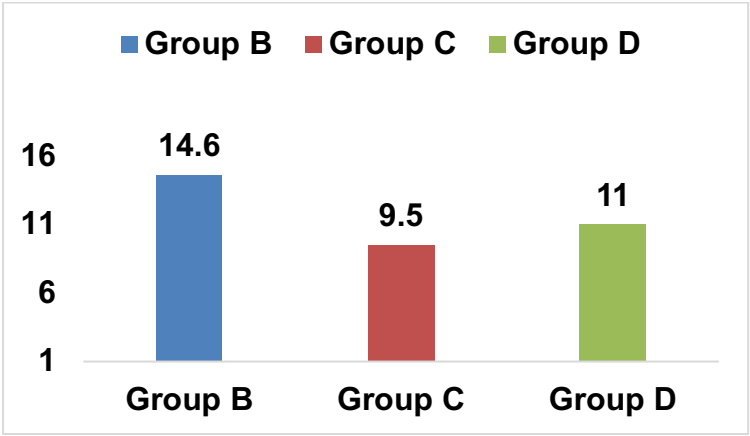

Figure 3: Comparison of onset of motor block (min) in the 3 groups

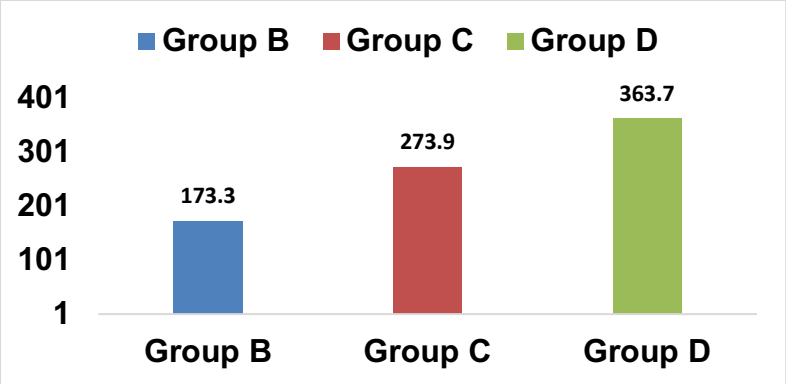

Figure 4: Comparison of duration of motor block (min) in the 3 groups

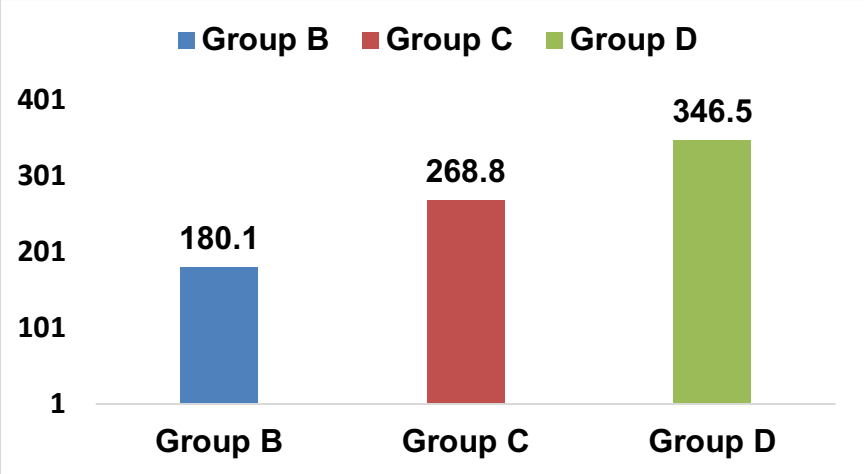

Figure 5: Duration of postoperative analgesia

Post-operative analgesia: Duration of analgesia in Group B displayed the shortest mean time at 180.1 ± 6.3minutes, followed by Group C with 268.8 ± 7.3, and Group D with the longest mean time of 346.5 ± 15.8. The data indicated a statistically significant difference among the groups (p value<0.05).

Table 3: Time to rescue analgesia in the three groups:

Parameter	Group B	Group C	Group D	p-value
Time to rescue analgesia (in mins)	180.1 ± 6.3	268.8 ± 7.3	346.5 ± 15.8	0.001*

Table 4: Adverse events:

Side effect	Group B	Group C	Group D	Total	P value
Hypotension	4(10%)	8(20%)	4(10%)	16(40%)	0.315
Bradycardia	0	0	2(5%)	2(5%)	-
Pruritis	0	0	0	0	-
Nausea/Vomiting	4(10%)	2(5%)	4(10%)	8(25%)	0.646
Respiratory depression	0	0	0	0	-
Dry mouth	0	0	0	0	-

Overall hypotension was observed in 16 participants (40%), bradycardia in 2 participants (5%), and nausea/vomiting in 8 participants (25%). However, There was no stastically significant differences in side effects between groups (p value >0.05).

Hemodynamic parameters:

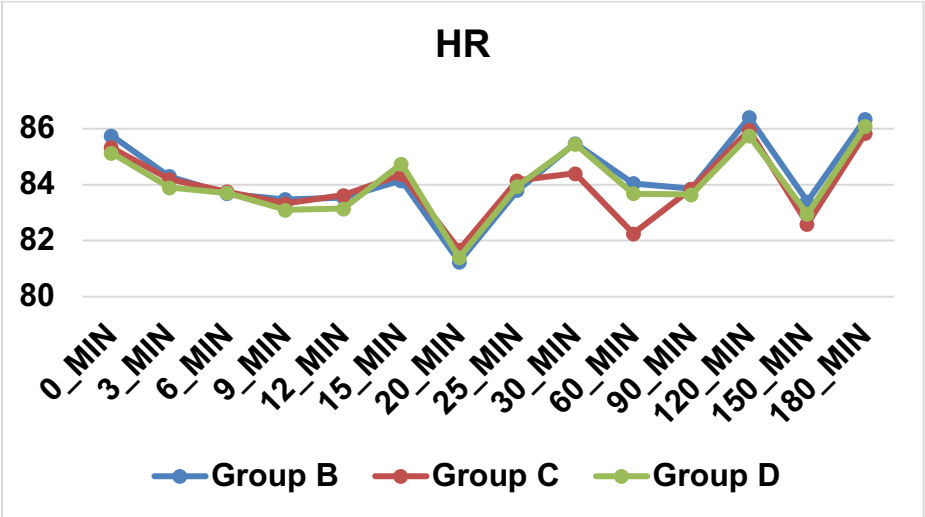

Figure 6: Intra-operative Heart rates at different time intervals

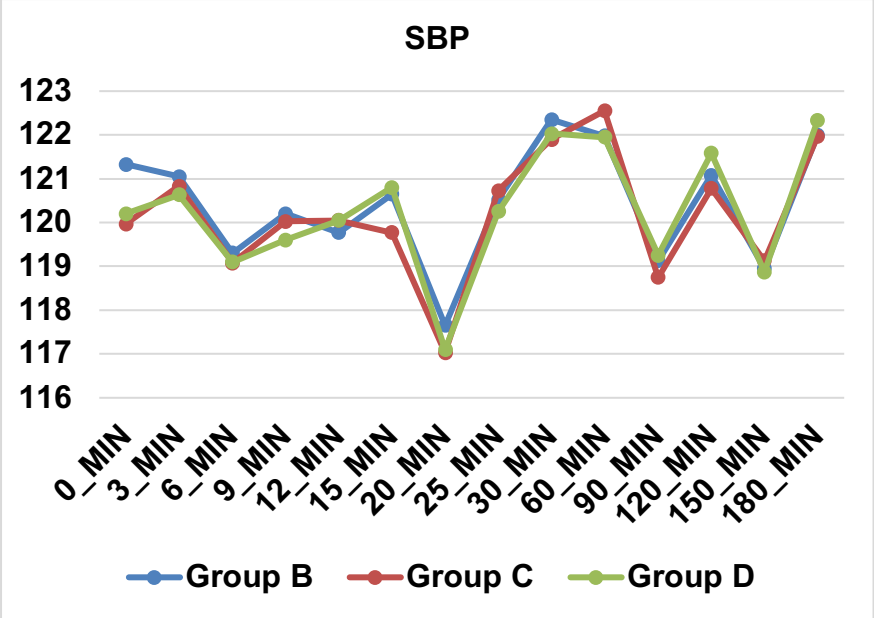

Figure 7: Intraoperative SBP at different time intervals

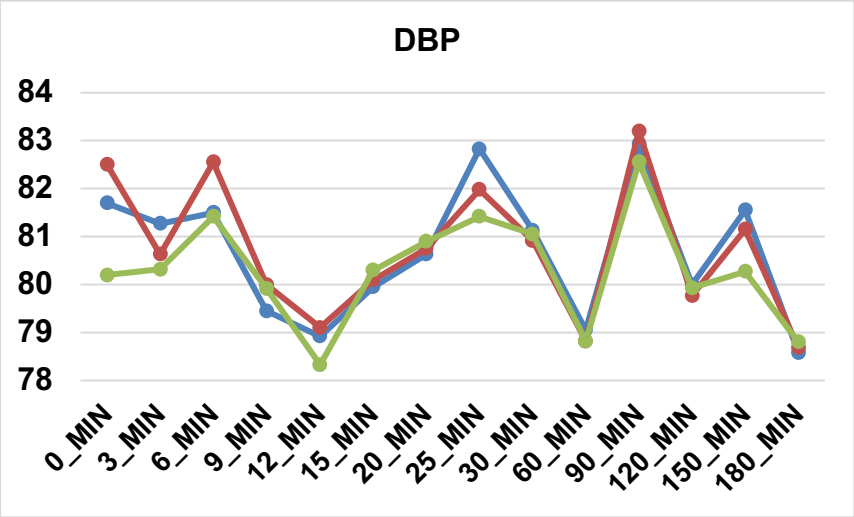

Figure 8: Intraoperative DBP at different time intervals

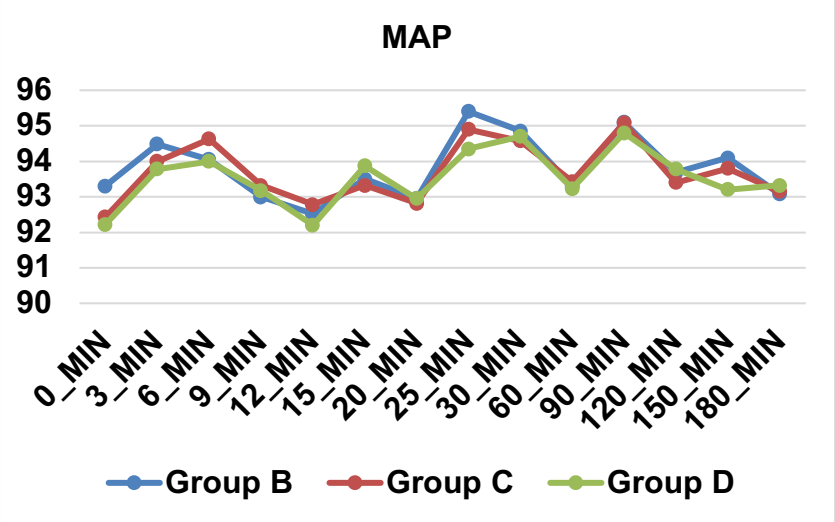

Figure 9: Intra-operative MAP at different time intervals

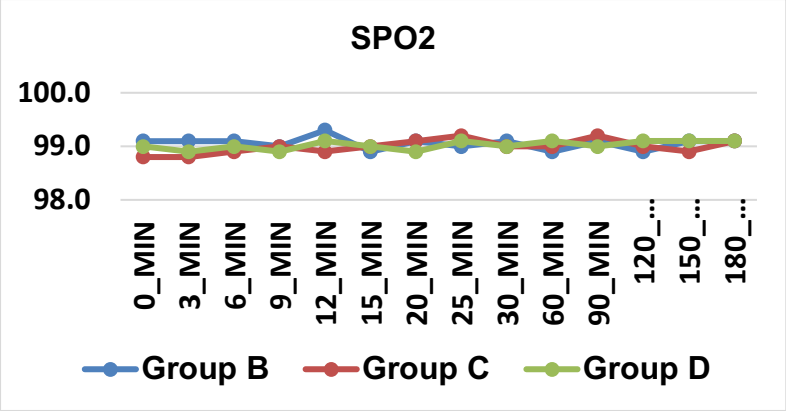

Figure 10: Intra-operative spo2 at different time intervals

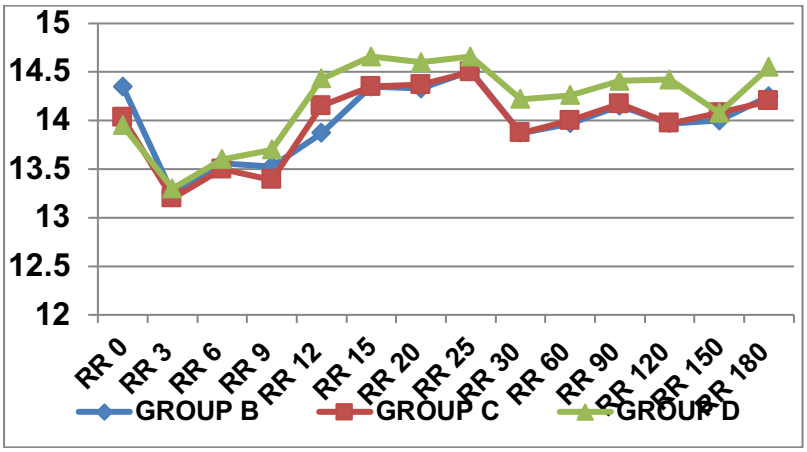

Figure 11: Intra-operative Respiratory rates at different time intervals

Discussion

Demographic profile was comparable between the groups. (p>0.05)

Onset of sensory block

The onset of sensory block was earlier in Group C> Group D> Group B. This result aligned with previous research by Sarma et al. (2015) [1] and Kanazi et al. (2006) [2], where they noted a quicker onset of sensory block in Group C (Bupivacaine with clonidine), followed by Group D (Bupivacaine with dexmedetomidine), and Group B (Bupivacaine with normal saline) exhibiting the slowest onset, mirroring the findings of present study.

Duration of sensory block

Group D experienced the longest mean time of sensory block (405.5 ± 8.6), followed by Group C (341 ± 11.9). Group B (200.1 ± 13.6) had the lowest mean durations. A statistically significant difference was indicated by a p-value of 0.001 for the duration of sensory block in all groups.

These findings differed with research by Manoharan et al.(2023)[3] and Swami et al(2012)[4], which had shown that patients receiving clonidine in addition to bupivacaine analgesia experienced a longer duration of sensory block than those receiving dexmedetomidine.

These findings were consistent with a study by Kataria et al (2018) [5], which showed that the group receiving bupivacaine experienced a shorter mean duration of sensory block than the group receiving dexmedetomidine. Between the groups, every difference was statistically significant ($p < 0.001$).

These findings align with the research of Singh et al (2014) [6], Neimi et al (1994) [7], Grandhe et al(2008)[8], and Sapate et al(2014)[9], who found that the addition of clonidine to bupivacaine prolonged the duration of sensory block ($p < 0.05$).

Onset of motor block

Onset of motor block was earlier in Group C>Group D> Group B. (p<0.05>).

This finding was in concordance with the studies conducted by Sarma et al (2015), who in their study observed that the onset of motor block was faster in Group C (Bupivacaine with clonidine) and Group D (Bupivacaine with dexmedetomidine) as compared to Group B (Bupivacaine with normal saline) as in present study. The time to reach Bromage scale 3 was fastest in Group C followed by Group D (p< 0.001).

These results were in concordance with Kanazi et al (2006) who in their study observed that the time to achieve Bromage 3 motor block was significantly shorter in clonidine group (11.7 ± 5.9 min) and dexmedetomidine group (13.2 ± 5.6 min) than in bupivacaine group (20.7 ± 10.3 min, p = 0.002), whereas p values of C versus D were not statistically different.

Duration of motor block

Based on the data analysis, it is apparent that Group D exhibited a motor block that lasts noticeably longer than that of Group B and Group C. Group B had a mean duration of motor block of 173.3± 12.5, Group C had a mean duration of 273.9 ± 41.9, and Group D had the highest mean duration at 363.7 ± 13.4. These results were in concordance with Kataria et al (2018), Eid H et al (2011)[10] studies found that the mean duration of motor block was observed to be longer in the dexmedetomidine group compared to the bupivacaine group. p < 0.001 indicated that statistically highly significant difference. These results were in concordance with the study conducted by Swami et al (2012), who in their study showed that the patients who received dexmedetomidine had a longer duration of motor block when compared to those receiving clonidine as additives to bupivacaine analgesia.

Time to rescue analgesia

The time to rescue analgesics needed in Group B was the shortest mean time of 180.1 ± 6.3 minutes, followed by Group C with 268.8 ± 7.3, and Group D with the longest mean time of 346.5 ± 15.8. The difference between three groups were statistically significant (p value<0.001) in terms of rescue analgesia demand. The individuals in Group D require a significantly longer time before needing rescue analgesics compared to those in Group B and Group C. These findings were in concordance with Manoharan et al (2023), Srinivas et al (2019)[11], Reddy et al(2013)[12], who found that patients in the dexmedetomidine group experienced a delayed need for rescue analgesia compared to those in the clonidine group and the bupivacaine group. This difference was statistically significant with a p value<0.001.

Hemodynamic parameters: Baseline as well as intra-operative hemodynamic parameters were comparable between the three groups and no statistically significant differences were noted.

Side effect profile: The results were comparable and statistically insignificant (p value>0.05) in terms of nausea/ vomiting and hypotension. Group D had 2 instances of bradycardia (5%). Across all groups, there were no reported cases of pruritis, respiratory depression, or dry mouth. (Table 17, Figure 19). The results were in concordance with Sarma et al (2015), who in their studies observed that incidence of bradycardia was higher in dexmedetomidine group.

Conclusion

The findings of present study suggested the significant advantages of supplementing bupivacaine spinal block with either dexmedetomidine or clonidine. Both dexmedetomidine and clonidine demonstrated notable benefits, including shorter onset of motor and sensory block, prolonged duration of sensory and motor block. Furthermore, when comparing the two adjuncts, dexmedetomidine exhibited superior outcomes, with prolonged sub-arachnoid block duration, effective postoperative analgesia, delayed need for rescue analgesia, and reduced subsequent analgesic requirements when compared to clonidine. These results suggested that dexmedetomidine at 5µg concentration could be considered as a preferable adjunct for enhancing the efficacy of bupivacaine spinal block. Further research and clinical trials may be warranted to validate and expand upon these findings, paving the way for optimized anaesthesia protocols in clinical practice.

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