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ORIGINAL ARTICLE

A study to compare the efficacy of intrathecal dexmedetomidine versus nalbuphine as an adjuvant to 0.5% hyperbaric bupivacaine for postoperative analgesia in lower abdominal surgeries

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Abstract

Background: The subarachnoid block is a commonly used technique for lower abdominal surgeries. Bupivacaine being a cost-effective drug gives satisfactory analgesia for 90–120 min. Adjuvants such as dexmedetomidine and nalbuphine extend the analgesia in the postoperative period. In this study, we aimed to compare the effects of intrathecal dexmedetomidine and nalbuphine as an adjuvant to hyperbaric bupivacaine regarding the duration of analgesia as the primary objective and the time of onset of sensory and motor blockade, duration of motor blockade, haemodynamics parameters like mean heart rate and mean arterial blood pressure, and side effects if any being the secondary objectives. Eighty patients, aged 18–65 years of ASA physical status I and II, were randomly allocated into two groups. Group NB (n = 40) received 0.5% Inj. hyperbaric bupivacaine 18 mg (3.6 ml) + Inj.nalbuphine 1.0 mg (0.1 ml) while group DB (n = 40) received 0.5% Inj. hyperbaric bupivacaine 18 mg (3.6 ml) + Inj.dexmedetomidine 10 μg (0.1 ml).

Results: Patients in group DB had a significantly prolonged duration of analgesia as compared to group NB. The early onset of sensory and motor blockade was noted in group DB($P < 0.05$). The duration of motor blockade was significantly prolonged in group DB ($P < 0.05$). Patients in both groups showed no significant difference in haemodynamic changes and incidence of side effects ($P > 0.05$).

Conclusions: Dexmedetomidine as an intrathecal adjuvant was found to have prolonged sensory and motor block and provide good quality of postoperative analgesia and stable haemodynamics with minimal side effects as compared to nalbuphine.

Keywords: Dexmedetomidine, Nalbuphine, Bupivacaine, Spinal anaesthesia, Lower abdominal surgeries

Background

Spinal anaesthesia defined as regional anaesthesia obtained by blocking the nerves in the subarachnoid space was introduced in clinical practice by Karl August Bier in 1898 (Brown & Spinal, 2000). This is the most commonly used technique worldwide. The advantage being patient remained awake, easy to perform, rapid onset of action, minimal drug cost, minimal stress response, relatively fewer side effects, and rapid patient turnover has made this the choice of many surgical procedures including lower abdominal surgeries (Barasch & Coller, 2006). Hyperbaric bupivacaine 0.5% is the most common local anaesthetic used for spinal anaesthesia for lower abdominal and lower limb surgeries. One disadvantage

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with using hyperbaric bupivacaine alone is a relatively shorter duration of action which means that early analgesic intervention is needed in postoperative period. Neuraxial adjuvants are used to improve or prolong analgesia and to decrease the adverse effects associated with the usual or high doses of a single local anaesthetic agent alone (Wang et al., 1979). Dexmedetomidine is a new highly selective alpha-2 adrenergic agonist that was approved by the FDA in 1999, for use in humans as a short-term medication for sedation/analgesia in the intensive care unit (Shaikh, 2014), and possesses hypnotic, sedative, anxiolytic, sympatholytic, opioid-sparing and analgesic properties without producing significant respiratory depression (Tufanogullari et al., 2008). It acts by inhibiting the release of nor-epinephrine at the locus coeruleus. Dexmedetomidine in different doses has been used with hyperbaric bupivacaine in subarachnoid block to produce early onset and prolonged duration of motor and sensory block with preserved haemodynamic stability and minimal side effects. We selected 10 mcg as the optimal intrathecal dose for lower abdominal surgeries (Abdel Hamid & El-lakany, 2013; Shagufta et al., 2016).

Nalbuphine is a mixed agonist-antagonist opioid which produces analgesia and sedation through agonism at the kappa receptor and lesser side effects through antagonism at the mu receptor (Chen et al., 1991; Pick et al., 1992; Gunion et al., 2004). Hence, intrathecal nalbuphine produces lesser adverse effects like pruritus, nausea, and vomiting when compared to intrathecal morphine (Culebras et al., 2000) and does not cause addiction and any significant haemodynamic or respiratory complications (Tiwari et al., 2013).

Based on the earlier studies (Shagufta et al., 2016; Haribhagwan & Sriram, 2018; Michael & Mehta, 2016), it was hypothesized that intrathecal 10 μg dexmedetomidine or 1.0 mg nalbuphine with hyperbaric bupivacaine would provide effective spinal anaesthesia with minimal side effects. Therefore, the study was to compare the efficacy of intrathecal dexmedetomidine versus nalbuphine hydrochloride with 0.5% hyperbaric bupivacaine for postoperative analgesia in patients undergoing various lower abdominal surgeries under spinal anaesthesia.

Methods

The randomized, double-blind study was carried out on 80 patients of either sex, aged 18–65 years, weighed 30–80 kg, ASA physical status I and II undergoing lower abdominal surgeries and general and gynaecological surgeries using subarachnoid block after obtaining written, and informed consent of patients and desired approval taken from the institutional committee. The study was registered prospectively at the Clinical Trials Registry-India. The exclusion criteria included patient's refusal; patient is undergoing caesarean section; uncooperative patients; any renal-neurologic disease; any known hypersensitivity or contraindication of bupivacaine, dexmedetomidine, and nalbuphine hydrochloride; and any known history of convulsion and bleeding disorder. The study population was randomly divided into two groups (n = 40) using computer-generated tables of random numbers. The nalbuphine-bupivacaine group (group NB) received 0.5% Inj. hyperbaric bupivacaine 18 mg (3.6 ml) + Inj.nalbuphine 1.0 mg (0.1 ml) while the dexmedetomidine-bupivacaine (group DB) received 0.5% Inj. hyperbaric bupivacaine 18 mg (3.6 ml) + Inj. dexmedetomidine 10 μg (0.1 ml). A day before the arrival of the patient in the operation theatre, a routine pre-anaesthetic examination was done in which general condition, airway assessment by mallampatti grading, nutritional status, the body weight of the patient and a detailed examination of the cardiovascular and respiratory system were assessed. It also included investigations like CBC, BT, CT, blood sugar, blood urea, serum creatinine, LFT, X-ray Chest, ECG, and urine examination for albumin sugar. All patients were kept nil per oral for a minimum period of 6 h before the surgical procedures. To ensure the double-blinded study, the drug was prepared and administered by two different anaestheologists. After the arrival of the patient in the operation theatre, an intravenous cannula 18 gauge was inserted in the upper limb, and preloading with Ringer's lactate was started. Using all aseptic conditions, spinal anaesthesia was performed in a sitting position at the level of L3–L4 through a midline approach using a 25-gauge Quincke spinal needle.

The time of intrathecal injection was noted, and monitoring of clinical parameters, VAS, and any side effects was observed. The onset of sensory block was assessed bilaterally in the midclavicular line by assessing the changes in pinprick sensation with hypodermic needle until no sensation was achieved at dermatome level T_{10} (normal sensation, grade 0; blunted sensation, grade 1; no sensation, grade 2, were taken as the onset of the sensory block). The highest dermatome level of sensory block and time taken to achieve the highest level of sensory block were noted. The time of two-segment regression was noted by the highest segment level of sensory block to regress up to two segments of spinal cord level.

The onset of motor block was assessed till complete motor block (grade 3) was achieved, according to the Bromage scale in the limbs (grade 0, no motor block grade 1, inability to raise extended legs; grade 2, inability to flex knees; grade 3, inability to flex ankle joints), and grade 3 was taken as a complete motor block. Duration of motor block was assessed by the time taken to regress from maximum Bromage motor block to scale 0.

The duration of analgesia was defined as the time from intrathecal injection to the time when VAS score

becomes > 3 or when the patient first time demands for IM/IV analgesia (rescue analgesia). Visual analogue scale for pain: pain was assessed using a standard 10 visual analogue score (VAS), with 0 corresponding to no pain and 10 designating the worst possible pain. VAS Numeric Pain Distress Scale was recorded before the start of the procedure and postoperatively until the patient demands IM/IV analgesia. Assessment of sedation was done using the Ramsay Sedation Scale.

Intra-operative non-invasive monitoring of vitals (HR, SBP, DBP, MAP, and SpO_2) was done every 2 min for the first 10 min, every 5 min for the next 20 min, every 15 min for the next 90 min, and every 30 min thereafter till the completion of the surgical procedure. Postoperative non-invasive monitoring of vitals (HR, SBP, DBP, MAP, and SpO_2) was done once hourly. Oxygen was administered at the rate of 4–5 L/min via face mask when SpO_2 falls below 90% at any stage. Side effects such as hypotension, bradycardia, nausea, vomiting, pruritus, drowsiness, respiratory depression, and urinary retention were observed, recorded, and treated accordingly.

Statistical analysis

The sample size of 80 patients was calculated using power and sample size calculator (PS version 3.0.0.34), using a 95% confidence interval and power of 80%. Standard qualitative and quantitative tests were used to compare the data (e.g. unpaired Student *t*-test, ANOVA, chi-square).

Results

A total of 80 patients were included in the study and assessed for different parameters. Our study adheres to CONSORT guidelines (Fig. 1). The outcome of this study revealed that the demographic profile of the two groups with respect to age, weight, ASA physical status, type, and duration of surgery were comparable to each other (Table 1). The duration of analgesia was 295.63 ± 88.0 min in group NB and 419.25 ± 116.75 min in group

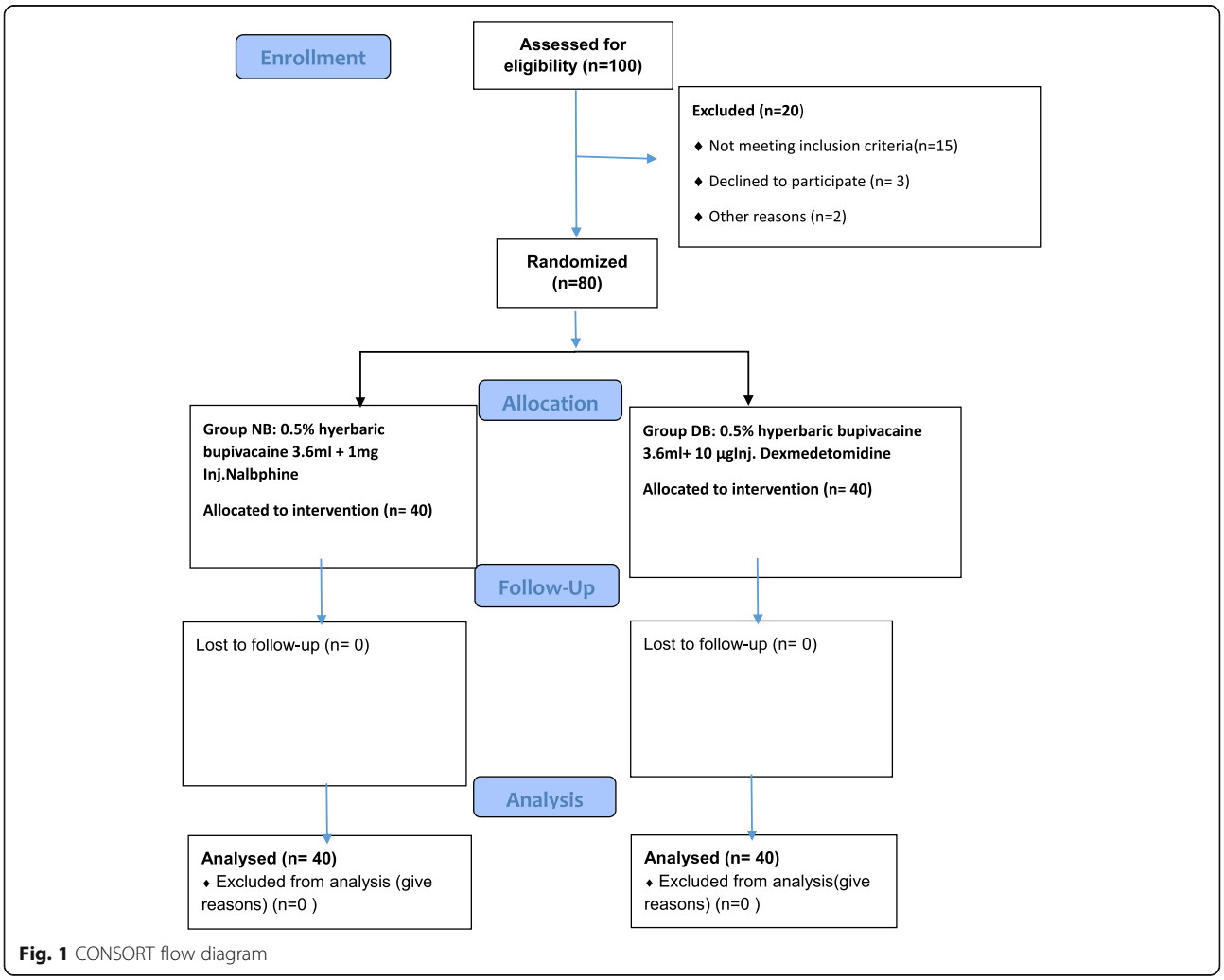

Fig. 1 CONSORT flow diagram

Table 1 Demographic profile

	Group NB, *N* = 40	Group DB, *N* = 40	*P* value
Age (years)	44.62 ± 8.11	42.95 ± 9.35	0.395 (NS)
Sex (M/F)	12/28	9/31	0.291 (NS)
Weight (kg)	59.15 ± 7.6	60.35 ± 6.9	0.463 (NS)
Duration of surgery (min)	78.75 ± 24.3	83 ± 18.8	0.386 (NS)
ASA Physical status (I/II)	34/6	35/5	
Type of surgery			
General	12	9	–
Gynaecologic	28	31	–

Values are expressed as mean ± SD and *n* (%), $P < 0.05$ (significant)
S significant, *NS* not significant

DB with a *P* value of 0.000 (S) which was statistically significant. Thus, we observed that the duration of sensory block was significantly prolonged in group DB (Table 2). The mean time of onset of sensory block was 3.07 ± 1.45 min in group NB and 2.50 ± 0.99 min in group DB with a *P* value of 0.04 (S) which was statistically significant. Thus, we observed that the onset of sensory block was significantly earlier in group DB as compared to group NB (Table 2). The highest level of sensory block was up to T4 in 7 (17.5%) patients, T5 in 2 (5%) patients, T6 in 17 (42.5%) patients, T7 in 4 (10%), and T8 in 10 (25%) patients in group NB whereas in group DB, the highest level of sensory block was up to T4 in 15 (37.5%) patients, T5 in 3 (7.5%) patients, T6 in 18 (45%) patients, and T8 in 4(10%) patients (Table 2). The mean time to achieve the highest level of sensory block was 6.77 ± 1.71 min in group NB and 5.98 ± 1.19 min in group DB with a *P* value of 0.03 (S) which was statistically significant. Thus, we observed that the mean time to achieve the highest level of sensory block was significantly shorter in group DB compared to group NB (Table 2).

The mean time for the two-segment regression was 127.25 ± 24.30 min in group NB and 151.825 ± 66.02 min in group DB with a *P* value of 0.029 (S) which was statistically significant (Table 2). The mean time of onset of motor block was 5.85 ± 1.48 min in group NB and 5.017 ± 0.811 min in group DB with a *P* value of 0.001 (S) which was statistically significant and is evidence of the earlier onset of motor block in group DB (Table 2). The mean duration of motor block was 275.63 ± 84.22 min in group NB and 331.31 ± 82.16 min in group DB with a *P* value of 0.003 (S) which was statistically significant and thus witnessed that the significantly prolonged mean duration of motor block was in group DB compared to group NB (Table 2).

In our study, the Ramsay sedation score remained 2 for the whole duration of surgery. There was no significant difference in the mean sedation score of both groups over time ($P > 0.05$) (Table 2 and Fig. 2).

VAS score remained 0 up to 150 min. in both groups NB and DB. At 180 min, 240 min, and 300 min, VAS score became 1 and 2 in groups NB, while it was 0 and 1 in group DB, and the values were significant $P < 0.05$(S). From 300 min onwards, VAS score increased up to 4 in both groups, and the values were non-significant ($P > 0.05$) (Fig. 3).

During the study, the heart rate remained the same except at 20, 25, and 30 min in both groups ($P < 0.001$); thereafter, no significant change in the mean heart rate over time was noted in both groups NB and DB (Fig. 4). There was a decrease in mean arterial blood pressure at 2 to 30 mins in both groups NB and DB which was not

Table 2 Characteristics of subarachanoid block

	Group NB, *N* = 40	Group DB, *N* = 40	*P* value
Onset of sensory block (min)	3.07 ± 1.45	2.50 ± 0.99	0.04 (S)
Distribution of the highest level of sensory block	T4–T8	T4–T8	0.05 (S)
Time to achieve the highest level of sensory block (min)	6.77 ± 1.71	5.98 ± 1.19	0.03 (S)
Time for two-segment regression (min)	127.25 ± 24.30	151.82 ± 66.02	0.029 (S)
Duration of analgesia (min)	295.5 ± 88.01	419.25 ± 116.7	0.000 (S)
Onset of motor block(min)	5.85 ± 1.48	5.01 ± 0.811	0.001 (S)
Duration of motor block (min)	275.62 ± 84.22	331.37 ± 82.16	0.03 (S)
Ramsay sedation score	2	2	0.334 (NS)

Values are expressed as mean ± SD and *n* (%). $P < 0.05$ or 0.01 (significant), $P < 0.001$ (highly significant)
S significant, *NS* not significant

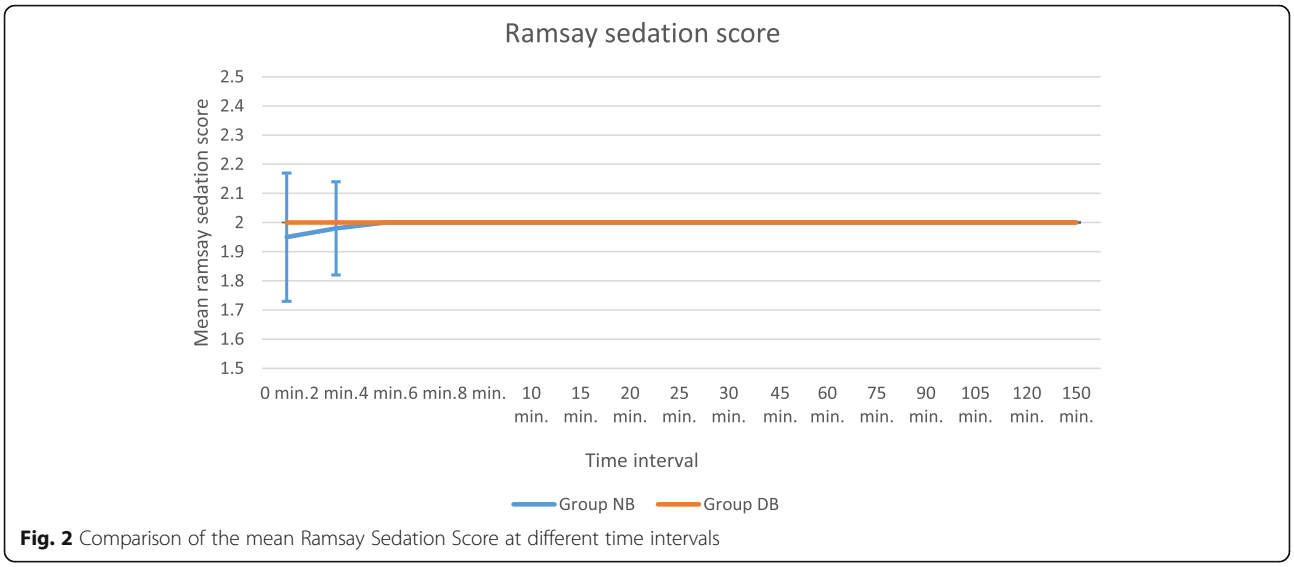

Fig. 2 Comparison of the mean Ramsay Sedation Score at different time intervals

significant ($P > 0.05$), but at 45 min, the pattern of decrease in mean blood pressure was significant ($P < 0.05$). Again, the decrease in the mean blood pressure became non-significant at 60 to 600 min ($P > 0.05$) (Fig. 5). There was no significant difference in oxygen saturation over time in both group NB and group DB (Fig. 6).

In our study, hypotension was observed in 3 (7.5%) patients in both groups. The values were statistically non-significant. ($P > 0.05$) which was treated by inj. mephenteramine 6 mg i.v. Nausea and vomiting were observed in 4 (10%) patients in group NB and 3 (3.75%) patients in group DB ($P > 0.05$) which were treated by inj. ondansetron 4 mg i.v. No patients showed bradycardia, pruritus, urinary retention, and respiratory depression.

Discussion

Lower abdominal surgeries are widely done under spinal anaesthesia due to their efficiency, speediness, and consistency and relatively less exposure to depressant drugs than other anaesthetic techniques. Adding an intrathecal adjuvant along with a local anaesthetic agent elongates the period of anaesthesia. Dexmedetomidine owns selective α2-adrenoceptor agonism, especially for the 2A subtype of the receptor, which causes it to be a much more effective analgesic agent (Bhana et al., 2000; Antilla et al., 2003), thus emerging as a promising intrathecal adjuvant and providing adequate intraoperative and postoperative analgesia stable haemodynamic and minimal side effects.

Opioid receptors in the dorsal grey matter of the spinal cord (substantia gelatinosa) are triggered by the

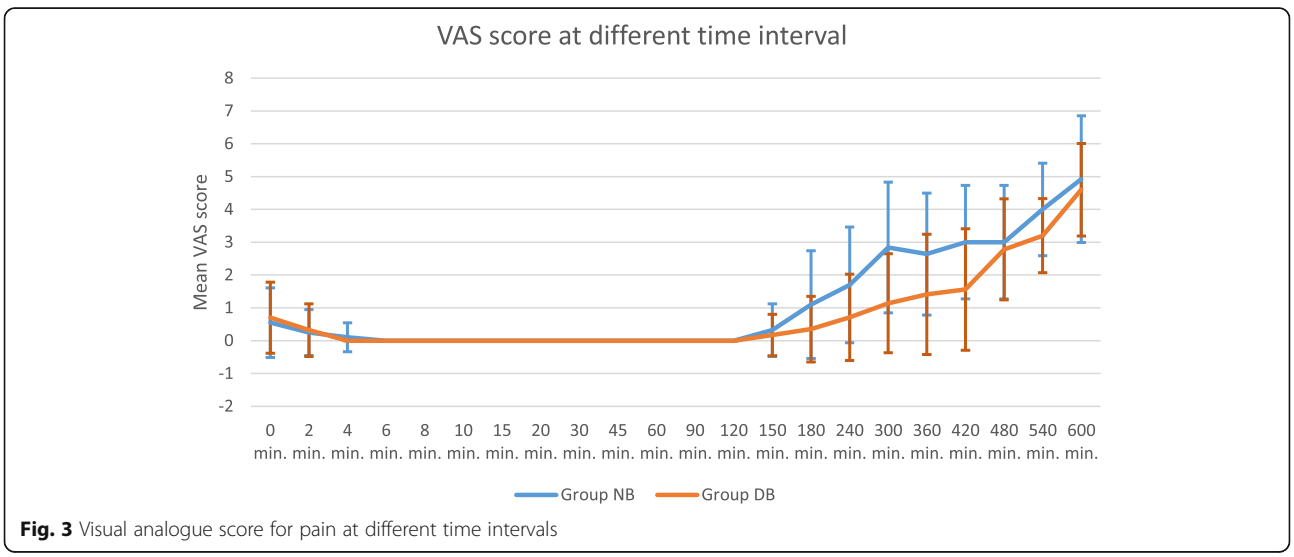

Fig. 3 Visual analogue score for pain at different time intervals

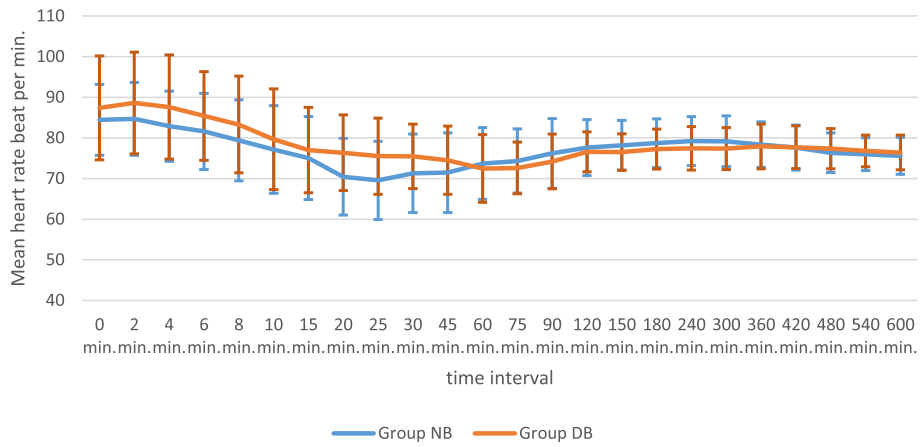

Fig. 4 Comparison of the mean heart rate at various time intervals

intrathecal nalbuphine in order to modify the function of afferent pain fibres (Gunion et al., 2004; Fields et al., 1980). Although very few studies have been carried out to compare the effect of nalbuphine and dexmedetomidine along with hyperbaric bupivacaine, therefore, the quest to explore their comparative effects this study was designed.

Our study revealed that there was no significant difference in demographic profile, i.e. both group NB and group DB were comparable to age, sex, weight, and ASA physical status I/II. There was no significant difference in the type (lower abdominal surgeries including general surgeries and gynaecologic surgeries) and duration of surgery between both groups.

In our study, the mean duration of analgesia was prolonged in group DB compared to group NB with a *P* value of 0.000 (S) which was statistically significant. Our results coincide with Michael and Mehta's (Michael & Mehta, 2016) study, in which they found that the mean duration of analgesia in group N was 86.73 ± 17.95 min compared to 110.97 ± 20.77 min in group D which was found to be statistically significantly higher (*P* value < 0.001). Kapinegowada et al. (Kapinegowda et al., 2017) in their study found a total duration of analgesia in group D5 of 322.50 ± 71.87 min, group D10 358.70 ± 73.89 min, and group D15 458.33 ± 95.21 min, which was statistically highly significant (*P* = 0.000) (group D15 > group D10 > group D5). Jain et al. (Jain et al., 2020) in their study found that the mean duration of analgesia was significantly prolonged in Group D (348.26 ± 22.35 min) than in group M (268.01 ± 11.31 min) (*P* < 0.001). Kataria et al. (Kataria et al., 2018) in their study found that the mean duration of analgesia in Groups N, K, and

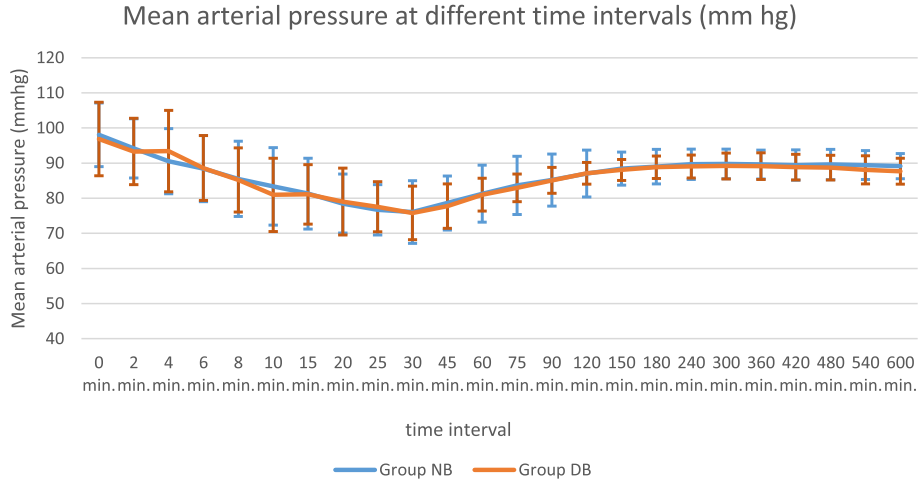

Fig. 5 Comparison of the mean arterial pressure at various time intervals

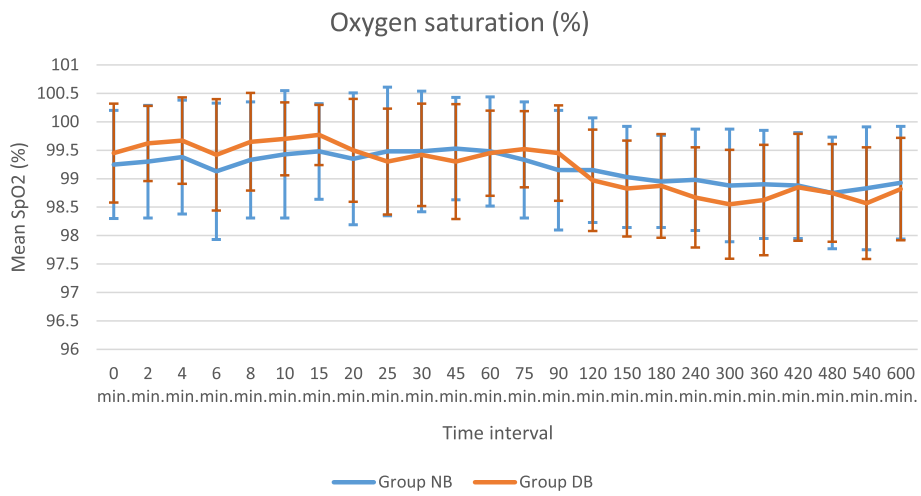

Fig. 6 Comparison of the mean oxygen saturation SpO_2 (%) at various time intervals

B was 290 ± 6.09, 220 ± 5.03, and 154 ± 6.04 min, respectively.

The mean time of onset of sensory block was earlier in group DB than in group NB with a *P* value of 0.04 (S) which was statistically significant (Table 2). Our result coincides with Michael and Mehta's (Michael & Mehta, 2016) and Haribhagwan and Sriram's (Haribhagwan & Sriram, 2018) studies in which they showed the early onset of sensory blockade was achieved with Group D which showed a highly significant difference from group N ($P < 0.001$.) In our study, the dose of hyperbaric bupivacaine was the same in both groups, so the difference in the onset of sensory block was attributed to the addition of nalbuphine or dexmedetomidine with bupivacaine. The highest level of sensory block ranged from T4 to T8 in both groups NB and DB in which the highest T6 level was noted in maximum patients (Table 2) which is coinciding with the study of Thada et al. (Thada et al., 2017) where the highest level was achieved at T6 level in both groups BD and BF. Our study revealed that the time to achieve the highest level of sensory block was early in the DB group in comparison with the NB group with a *P* value of 0.03 (S) which was statistically significant. This parameter was not observed in previous studies. The mean time for the two-segment regression was 127.25 ± 24.30 min in group NB and 151.825 ± 66.02 min in group DB with a *P* value of 0.029 (S) which was statistically significant. In our study, we observed that the mean time for the two-segment regression was significantly prolonged in group DB compared to group NB. Our result coincides with Michael and Mehta's (Michael & Mehta, 2016) study, which showed that the meantime of the two-segment regression was found to be 106.13 ± 19.475 min in group N, while it was 122.47 ± 18.627 min in group D which was significantly longer ($P < 0.001$). Kapinegowada et al. (Kapinegowda et al., 2017) in their study found the mean time taken for the two-segment sensory regression group D5 is 96.66 ± 33.67, group D10 116.80 ± 36.27, and group D15 120.96 ± 30.24 ($P = 0.014$).

In our study, the mean time of the onset of motor block was faster in group DB compared to group NB with a *P* value of 0.001 (S) (Table 2) which was statistically significant. This parameter was observed in the findings of Haribhagwan and Sriram (Haribhagwan & Sriram, 2018) where they showed that the mean time taken for the onset of motor blockade was 6.5667 ± 1.006 mins in group N (nalbuphine group) and in group D (dexmedetomidine group) was 5.0667 ± 0.868 mins. There was a statistically significant difference between group N and group D ($P = 0.000$). Similar results were obtained by Michael and Mehta (Michael & Mehta, 2016). In our study, we observed that the mean duration of motor block was significantly prolonged in group DB compared to group NB. This parameter was observed by Michael and Mehta (Michael & Mehta, 2016), where they found the mean duration of motor blockade was 184.17 ± 27.104 min in group N, while it was 247.43 ± 28.538 min in group D which was highly significantly prolonged (*P* value < 0.001).

The results of our study were corresponding to the above-mentioned studies reiterating the fact that dexmedetomidine when used as an adjuvant to Bupivacaine decreases the mean onset of sensory and motor block but prolongs the mean duration of sensory and motor block.

The sedation score remained 2 for the whole period in both groups (Fig. 1). There was no significant difference in the mean sedation score of both groups over time

($P > 0.05$). Our study coincides with Michael and Mehta's (Michael & Mehta, 2016) study, where the difference in the sedation score of both groups N and D was not significant ($P > 0.05$).

VAS score remained 0 up to 150 min in both groups NB and DB and thereafter increased gradually up to 4 and 3.2 till 540 mins in both groups, respectively, while at 600 mins, the VAS score 4.6 was noted in group DB (Sisinti Sanjeeb Patro et al. (Patro et al., 2016)). Intraoperative visual analogue score was < 3 in both groups. At the end of 3 h postoperatively, it was 0.03 and 1.03 in group II and group I, respectively. But at the end of 6 h, VAS was 2.67 and 3.7 in group I and group I where rescue medication was started for group I. Twelve hours postoperatively, the scores were 6.3 and 6.8 in group II and group I, respectively. VAS values were significantly lower up to 3 and 6 h postoperatively in group II implying patients had better pain relief in the postoperative period than in group I.

In our study, there was no significant difference in haemodynamic parameters (mean HR and mean MAP) and SpO_2 between the groups at different time intervals which are similar to other studies (Figs. 4, 5 and 6 (Haribhagwan & Sriram, 2018; Michael & Mehta, 2016; Kishore et al., 2015). Nausea and vomiting were more observed in group NB than in group DB. None of the patients had pruritus, urinary retention, or respiratory depression. Our findings are similar to Ganesh and Krishnamurthy's (Ganesh & Krishnamurthy, 2018), Micheal and Mehta's (Michael & Mehta, 2016), Hari Kishore et al.'s (Kishore et al., 2015), and Sun et al.'s (Sun et al., 2019) findings.

Limitations of our study

- Assessment of the visual analogue scale is subjective and varies with the level of understanding between the patient and the anaesthesiologist.
- Our study determines the precision of the sensory level of the block within two dermatomal levels by pinprick.

Conclusions

Dexmedetomidine as an intrathecal adjuvant was found to have prolonged sensory and motor block, provide good quality of postoperative analgesia, and stable haemodynamics with minimal side effects as compared to nalbuphine.

Abbreviations

J.L.N.: Jawahar Lal Nehru; ASA: American Society of Anaesthesiologists (classification); ECG: Electrocardiogram; *P*: *P* value; MAP: Mean arterial pressure; Inj.: Injection; IV: Intravenous; IM: Intramuscular; LFT: Liver function test; vs: Versus; NA: Not applicable; S: Significant; NS: Non-significant; SD: Standard deviation; SE: Standard error; BP: Blood pressure; CNS: Central nervous system; SBP: Systolic blood pressure; TES: Transcutaneous electrical stimulation; O_2: Oxygen; CT: Clotting time; BT: Bleeding time; S. No.: Serial number; RFT: Renal function test; LFT: Liver function test; SpO_2: Oxygen saturation; VAS: Visual analogue score; GS: General surgery; Gyn S: Gynaecological surgery; HLSB: Highest level of sensory block

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None

Authors' contributions

AK: concept, design, manuscript preparation, and guarantor. MC: literature search and review, concepts and conduction of the study work, manuscript preparation, and statistical analysis. BT: literature review and manuscript editing and review. VM: concept and design and literature review. DG: data analysis and manuscript editing. NT: manuscript editing. The authors read and approved the final manuscript.

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Availability of data and materials

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Declarations

Ethics approval and consent to participate

Institutional Ethical Committee J.L.N. Medical.
Written informed consent was obtained from the patients

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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