Randomized Trial

Effect of 3 Different Doses of Intrathecal Dexmedetomidine (2.5µg, 5µg, and 10 µg) on Subarachnoid Block Characteristics: A Prospective Randomized Double Blind Dose-Response Trial

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Background: The extended analgesic efficacy of intrathecal dexmedetomidine (ITD) has been investigated in a few clinical trials; however, there is a lack of conclusive evidence upon its ideal dosage.

Objectives: To elucidate the dose-response relationship between ITD and subarachnoid block characteristics, particularly the duration of analgesia and differential analgesia (DA: defined as time difference from the offset of motor blockade to the first analgesic requirement on numerical rating scale ≥ 4.0).

Study Design: Prospective, randomized double blind active control trial.

Setting: Medical college teaching hospital.

Methods: Ninety adult (18 – 60 years) patients undergoing elective lower abdominal and lower limb surgeries were randomized into 3 groups to receive intrathecal 0.5% bupivacaine 3 mL with 2.5 µg (group BD2.5), 5µg (group BD5), or 10 µg (group BD10) dexmedetomidine in 0.5 mL normal saline. The 2 segment sensory regression times (TSSRT), duration of motor blockade analgesia, DA, and perioperative adverse effects were assessed. The primary outcome was duration of analgesia and DA.

Statistics: ANOVA, Kruskal Wallis test, Chi-square ($\chi 2$), and Fisher's exact test, significance: $P < 0.05$.

Results: The onset of sensory block was significantly earlier in group BD10 compared with group BD5 ($P = 0.035$) and BD2.5 ($P = 0.010$) while the onset of motor block was significantly earlier in group BD10 compared with BD2.5 ($P = 0.020$). There was a significant and dose-dependent prolongation of the duration of sensory block (127.50, 149.17, and 187.50 minutes; $P < 0.001$), motor block (258.50, 331, and 365 minutes; $P < 0.001$), analgesia (306.17, 396.50, and 512 minutes; $P < 0.001$), and DA (47.67, 65.50, and147 minutes; $P < 0.001$) with escalating doses of ITD, respectively. Group BD10 required significantly fewer rescue analgesics compared with other 2 groups ($P = 0.001$). Except for mild sedation which was significantly higher in group BD10; all the groups were comparable with respect to hemodynamic and other adverse effects.

Limitations: Lack of placebo group, exclusion of higher doses (15µg) of ITD, and short duration of postoperative follow-up.

Conclusions: The addition of 10 µg compared with 2.5 µg or 5µg ITD to 0.5% hyperbaric bupivacaine is associated with significantly earlier onset of sensory and motor block as well as prolonged duration of sensory block, motor block, analgesia, and DA with a comparable adverse effect profile.

Key words: Analgesia, bupivacaine, dexmedetomidine, differential analgesia, intrathecal, pain, spinal anaesthesia

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Improved postoperative analgesia post lower abdominal and lower limb surgeries is associated with early mobilization, reduced risk of deep venous thrombosis, and improved patient comfort and perioperative outcome (1). Intrathecal (IT) adjuvants prolong the duration of spinal anesthesia and postoperative analgesia thereby reducing the requirement of postoperative supplemental analgesics (2). The incorporation of adjuvants also lowers the overall dose of local anesthetic and hence associated side effects (2). These adjuvants belong to different classes of drugs with different antinociceptive mechanisms. Dexmedetomidine is a relatively new highly selective $\alpha 2$ agonist with analgesia, sedation, anxiolysis, and sympatholysis as its useful pharmacological actions. The extended analgesic efficacy of IT dexmedetomidine (ITD) in the postoperative period has been shown in a few clinical studies (2-9). These authors have studied different doses (2 – 10 μg) of ITD and compared it with various other adjuvants like clonidine, fentanyl, midazolam, buprenorphine, etc., with varying results (2-14). The existing studies comparing different doses of ITD are few and have compared either lower (2 μg vs. 4μg) or higher doses (5 μg vs. 10 μg or 10 μg vs. 15μg) (3,4). Moreover none of these studies have stressed the dose-response relationship between different doses of ITD and differential analgesia (DA) defined as the time difference from the offset of motor blockade to the first analgesic requirement on numerical rating scale $\geq$ 4.0. Despite the huge clinical significance of DA which justifies the addition of IT adjuvants so as to harness their extended postoperative analgesic potential devoid of any unnecessary motor blockade, the existing literature is deficient in the same. Therefore we designed this prospective, randomized, and double blind trial to elucidate the dose-response relation between 3 different doses (2.5, 5, and 10 μg) of ITD as an adjuvant to hyperbaric 0.5% bupivacaine and subarachnoid block (SAB) characteristics in patients undergoing elective lower abdominal and lower limb surgeries. Our primary outcomes were duration of analgesia and DA while the secondary outcomes were duration of motor block and perioperative adverse effects. We hypothesized that there may be a dose dependent prolongation of DA with escalating doses of ITD dexmedetomidine.

Methods

Patient Recruitment and Exclusion Criteria

After obtaining approval from our institutional ethical committee and written informed consent, 90 patients 18 – 60 years of age, either gender, American Society of Anesthesiologists (ASA) physical status I/II scheduled for elective lower abdominal and lower limb surgeries under planned SAB were included in this prospective, randomized double blind trial.

We excluded patients with 1) contraindication to SAB, 2) sensitivity to the trial drugs, 3) on chronic analgesic therapy, 4) cognitive impairment, 5) not able to understand numerical rating pain scale (NRS) 6) pregnant, 7) significant comorbid conditions like uncontrolled hypertension, congestive heart failure, myocardial infarction in the past 6 months, and 8) heart block. The ethical principles for medical research involving human patients as specified in the Declaration of Helsinki were strictly adhered to while conducting this trial. Eight patients were excluded due the presence of one or more of the above (Fig. 1).

Pre- and Intra-operative Anesthesia Care

A detailed pre-anesthetic checkup was done and tablet alprazolam 0.25 mg was given as premedication the night before and on the morning of surgery to all the patients. Patients were familiarized with the 11 point NRS (0: no pain, 10: worst possible pain) and instructed to remain fasting for 8 hours prior to surgery. After taking patients to a pre-prepared operation theatre, non-invasive monitors were applied including electrocardiography, pulse oximetry (SpO2), and non-invasive blood pressure (NIBP), and baseline vitals were recorded. Following intravenous cannulation with an 18 gauge cannula and preloading with ringer lactate (RL) 15 mL/kg, an infusion of RL at 2 mL/kg/hour was started, continued intra-operatively, and adjusted according to the hemodynamics.

Randomization and Blinding

The patients were randomized into 3 groups of equal size (Table 1) using Stat Trek random number generator (www.stattrek.com). The randomization assignment was concealed in sealed opaque envelopes opened at the time of drug preparation. The preservative-free dexmedetomidine 100 μg/mL was loaded into a 40 unit insulin syringe (2.5 μg/unit) and subsequently

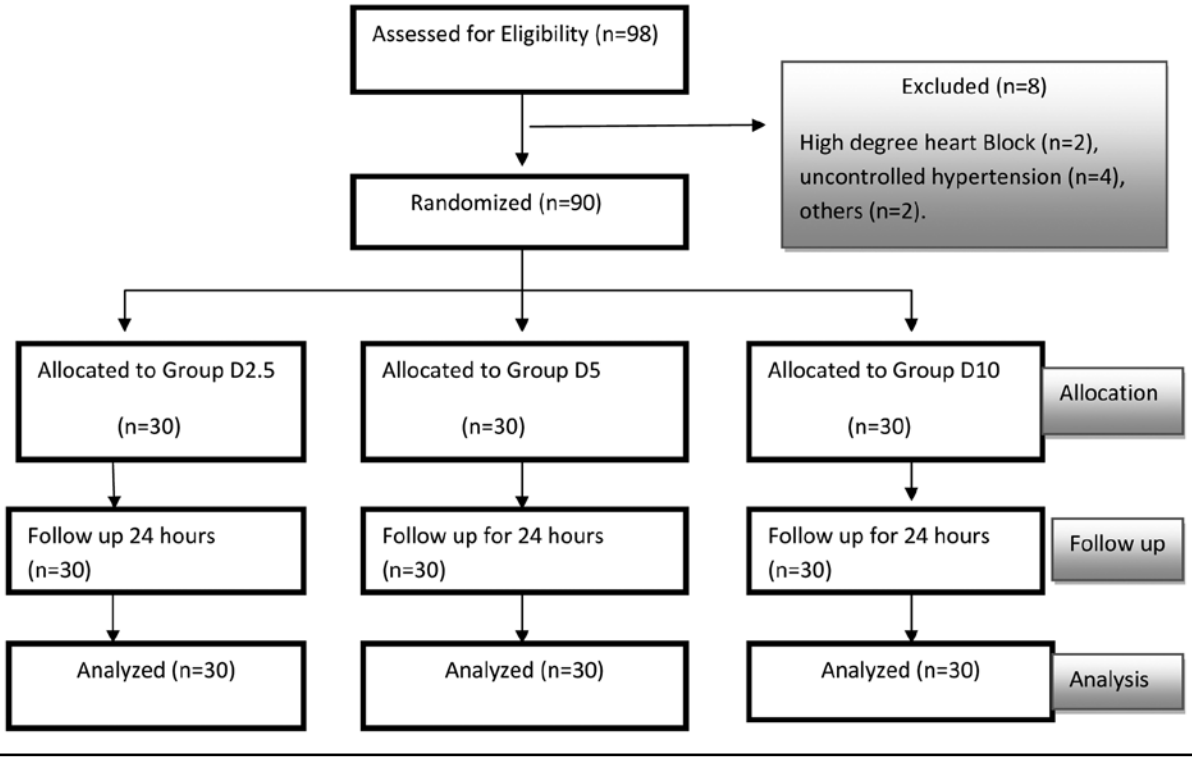


Fig. 1. *Consort flow diagram.*

Table 1. *SAB characteristics and definitions.*

SAB characteristic	Definition
Sensory block onset time	Time between completion of intrathecal injection to loss of pinprick sensation at the T10 dermatomal level.
Peak Sensory Block level	Highest sensory block level achieved on repeated testing for 3 times.
Time to attain peak sensory level	Time between completion of intrathecal injection to achieve peak sensory block level.
Two segment sensory regression time (TSSRT) / duration of sensory block	Time to 2 segment regression checked every 10 minutes after achieving peak sensory block level.
Motor block onset time	Time between completion of intrathecal injection to onset of Bromage 3 score.
Duration of motor block	Time between completion of intrathecal injection to return of Bromage 0 score.
Duration of analgesia	Time between completion of intrathecal injection to requirement of first rescue analgesic (NRS ≥ 4).
Differential analgesia	Time between onset of Bromage 0 score to requirement of first rescue analgesic.

1, 2, or 4 units were added to an identical 5 mL syringe containing 3 mL of 0.5% hyperbaric in Group BD2.5, BD5, and BD10, respectively. The total volume was 3.5 mL in all the groups by adding appropriate amount of preservative-free 0.9% saline. The trial drugs were prepared in unlabeled syringes by an independent anesthesiologist not involved further in the trial. The patients and the anesthesiologists performing the IT injection and collecting the trial data were unaware of the group allocation. The IT injection was given in the sitting position in the L3-L4 intervertebral space with a 27 gauge Quincke spinal needle through the mid-

line approach after confirming free flow and positive aspiration for CSF {sp}. The patients were immediately made supine after the injection.

Intra- and Postoperative Monitoring

The heart rate (HR), NIBP, and SpO2 were monitored (using Datex-Ohmeda, cardiocap/5, GE Healthcare, Helsinki, Finland, multichannel monitor) continuously and recorded at the baseline, one minute, and subsequently every 5 minutes for the first 15 minutes and then every 15 minutes until the end of surgery. Hypotension was defined as a fall in systolic blood pressure of > 30% below baseline or < 90 mm Hg and was treated with additional IV RL and injection of mephenteramine 6 mg, repeated if necessary. Bradycardia was defined as a fall in HR of > 30% below baseline or < 55/minute and was treated with injection of atropine 0.6 mg IV. The SAB characteristics monitored included the following (Table 1). The sensory block level was assessed by loss of pinprick sensation to 25 G hypodermic needle in the mid-clavicular line checked every minute until stabilization of highest sensory block level upon thrice repeated testing. Thereafter the pinprick test was performed every 15 minutes until 2 segment sensory regression (TSSR). The motor block was assessed using Bromage score (15): Bromage 0: no motor block, Bromage 1: unable to flex hip but able to move knee and ankle, Bromage 2: unable to flex hip and knee but able to move ankle, and Bromage 3: unable to flex hip, knee, and ankle. The pain severity was assessed using 11 point NRS hourly for the first 12 hours and then at 24 hours postoperatively. Injection of Tramadol 1.5 mg/kg slow IV was given as a rescue analgesic when the NRS was ≥ 4. The time to first rescue analgesic and the total number of rescue analgesics received by the patient over 24 hours were noted. All time durations were calculated considering time of completion of IT injection as time zero. The time of skin incision and completion of skin closure were noted and the duration of surgery was calculated in minutes. The patients were assessed for sedation using the following sedation score: Grade 1: alert/oriented, Grade 2: sedated but responding to verbal commands, Grade 3: sedated but responsive to physical stimulation, and Grade 4: sedated and unresponsive. In the postoperative period Bromage score and sensory level were assessed every fifteen minutes until recovery to Bromage 0 and TSSR, respectively. HR, NIBP, and NRS were monitored for 24 hours. Any perioperative complications inclusive of bradycardia, hypotension, nausea, vomiting, shivering, and urinary retention were recorded as and when they occurred.

Statistical Analysis

The sample size was calculated on the basis of a previous trial (3). Using (G3*Power) a 2 tailed alpha value (0.05) and power 95%, it was found that 66 patients (22 patients per group) would be sufficient to detect a significant difference in the duration of analgesia. We recruited 90 patients for the trial. Statistical analysis was performed using SPSS 17.0 for Windows (SPSS, Chicago, IL, USA). Continuous variables are presented as mean ± SD or median (range) for non-normally distributed data. Categorical variables are expressed as frequencies and percentages. The normally distributed continuous variables for the 3 groups were compared using ANOVA. Non-normal distribution continuous variables were compared using Kruskal Wallis test and further paired comparisons were done using Mann Whitney U test. Nominal categorical data between the groups were compared using Chi-squared ($\chi 2$) or Fisher's exact test as appropriate. For all statistical tests, a P value less than 0.05 and 0.001 was taken to indicate a significant and highly significant difference, respectively.

Results

A total of 90 consecutive patients meeting the inclusion criteria were enrolled and completed the trial (Fig. 1). The demographic, baseline, and surgical characteristics were comparable among the groups (Table 2).

Sensory Block Characteristics

The onset of sensory block was significantly earlier in group BD10 compared with group BD5 (P = 0.035) and BD2.5 (P = 0.010), however no statistically significant difference was observed between group BD2.5 and BD5 (P = 0.890). The peak sensory block level and the time to attain peak sensory block level were comparable among all the groups (Table 3). There was a highly significant difference with respect to 2 segment sensory regression time (TSSRT) between group BD10 vs. BD5 (P < 0.001), group BD10 vs. BD2.5 (P < 0.001), and significant difference between group BD5 vs. BD2.5 (P = 0.001) (Table 3).

Motor Block Characteristics

The onset of motor block was significantly earlier in Group BD10 compared with group BD2.5 (P = 0.020), however there was no significant difference between group BD10 vs. BD5 (P = 0.277) or group BD5 vs. BD2.5 (P = 0.450) (Table 3). Group BD10 had significantly pro-

Table 2. *Patient and surgery characteristics.*

Variable	Group BD2.5 (n = 30)	Group BD5 (n = 30)	Group BD10 (n = 30)	*P* value
Age (year)	43.40 ± 9.19	37.37 ± 10.72	41.50 ± 11.24	0.078
Male [n (%)]	25 (83.33%)	21 (70%)	25 (83.33%)	0.344
Weight (Kg)	60.03 ± 9.49	56.20 ± 7.72	57.97 ± 5.76	0.169
Height (cm)	165.40 ± 7.46	165.43 ± 8.17	164.33 ± 6.04	0.788
ASA I/II	26/4	23/7	26/4	0.487
Baseline HR	81.00 ± 13.55	84.13 ± 10.38	81.83 ± 14.63	0.627
Baseline MAP	89.30 ± 8.30	88.67 ± 1.64	91.10 ± 8.13	0.516
Type of Surgery Hernioplasty Knee Arthroscopy Appendectomy ORIF Genitourinary	 18 (60%) 6 (20%) 0 (0%) 4 (13.33%) 2 (6.67%)	 18 (60%) 4 (13.33%) 1 (3.33%) 3 (10%) 4 (13.33%)	 19 (63.33%) 3 (10%) 0 (0%) 5 (16.67%) 3 (10%)	0.831
Duration of Surgery	100 ± 33.27	99.17 ± 29.48	100.10 ± 31.42	0.975

The data are Mean ± SD.

Table 3. *Block characteristics.*

Variable	Group BD2.5 (n = 30)	Group BD5 (n = 30)	Group BD10 (n = 30)	*P* value
Peak sensory block level	T6 (T4-T8)	T6 (T4-T8)	T6 (T4-T8)	0.704
Time to attain peak sensory block level (min.)	7.97 ± 1.94	7.50 ± 1.81	7.33 ± 2.12	0.435
Sensory block onset time (min.)	4.03 ± 1.27	3.90 ± 1.03	3.17 ± 1.05	0.008*
TSSRT (min.)	127.50 ± 19.06	149.17 ± 21.66	187.50 ± 24.56	< 0.001**
Motor block onset time (min.)	5.63 ± 1.30	5.27 ± 1.08	4.80 ± 1.13	0.026*
Motor block duration (min.)	258.5 ± 23.53	331 ± 28.11	365 ± 26.52	< 0.001**
Duration of analgesia (min.)	306.17 ± 24.34	396.50 ± 35.60	512 ± 23.55	< 0.001**
Differential analgesia (min.)	47.67 ± 17.20	65.50 ± 18.26	147 ± 30.61	< 0.001**
Total 24 hour analgesic requirement (n)	2.10 ± 0.61	1.90 ± 0.48	1.53 ± 0.57	0.001*

The data are Mean ± SD. *Significant, **Highly Significant

longed duration of motor blockade than Group BD5 and BD2.5 ($P < 0.001$). The duration of motor blockade was significantly prolonged in group BD5 compared with group BD2.5 ($P < 0.001$) (Table 3).

Analgesia Characteristics

The duration of analgesia was significantly prolonged in Group BD10 compared with group BD5 and BD2.5 ($P < 0.001$). Group BD5 also had significantly prolonged duration of analgesia than group BD2.5 ($P < 0.001$) (Table 3). A highly significant difference was found with respect to duration of differential analgesia between group BD10 vs. BD5 and BD2.5 ($P < 0.001$) and group BD5 vs. BD2.5 ($P = 0.009$). Group BD10 required significantly less rescue analgesics in the first 24 hours postoperatively than group BD5 ($P = 0.033$) and BD2.5 ($P < 0.001$). There was no significant difference in the 24 hour rescue analgesic requirement between groups BD5 and BD2.5 ($P = 0.349$) (Table 3).

Perioperative Hemodynamics

Figs. 2 and 3 demonstrate perioperative mean heart rate and mean blood pressures, respectively. The incidence of bradycardia and hypotension was in following order: group BD10 > BD5 > BD2.5, however, when compared, the difference failed to reach statistical significance (Table 4).

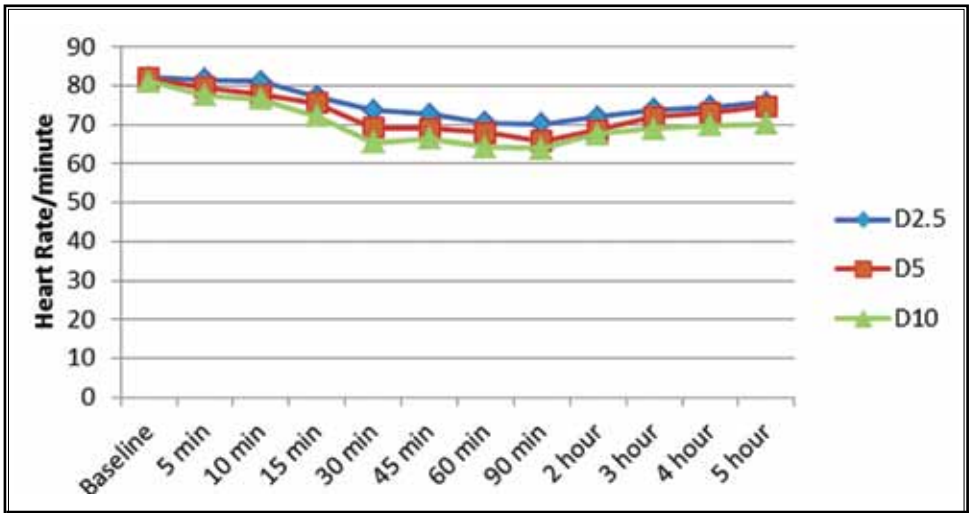


Fig. 2. *Comparison of heart rate trend over time.*

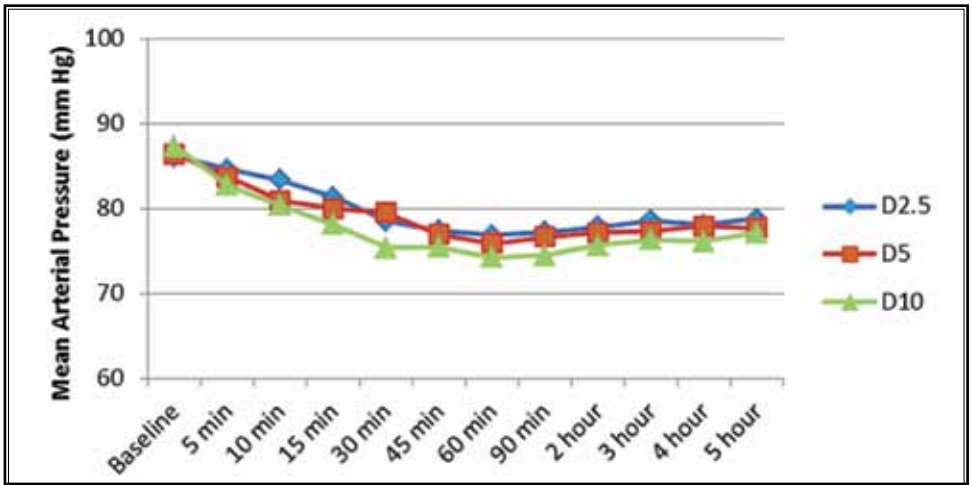


Fig. 3. *Comparison of mean arterial pressure trend over time.*

Adverse-effect Profile

Table 4 shows the incidence of perioperative complications. All the groups were comparable with respect to nausea/vomiting, urinary retention, and shivering. Group BD10 had a higher incidence of sedation score 2 i.e., sedated responding to verbal commands; however, no patient in the trial suffered from higher sedation scores i.e., 3 and 4 (Table 4). The incidence of sedation was comparable with the addition of either 2.5 µg or 5 µg ITD ($P = 0.112$).

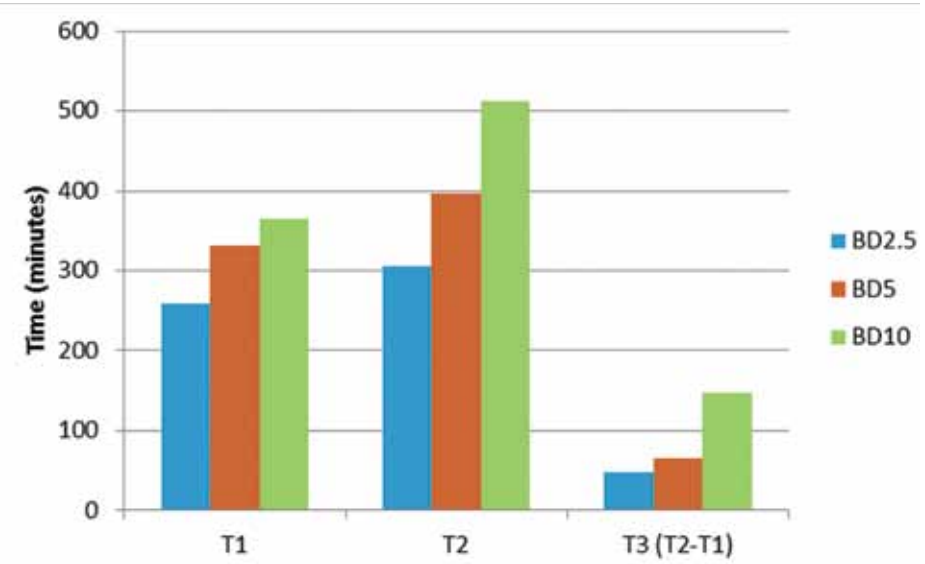
Discussion

Our trial compared 3 doses (2.5 µg, 5 µg, and 10 µg) in contrast to other authors who have compared only 2 doses of ITD. To the best of authors' knowledge this is the first trial comparing these 3 doses of ITD. Our trial showed that the TSSRT, duration of motor blockade and analgesia increased significantly and congruently with increase in the dosage of ITD with comparable hemodynamic and side-effect profile. However there was a greater increase in the duration of analgesia

Table 4. *Adverse events*.

Side effect	Group BD2.5	Group BD5	Group BD10	*P* value
Nausea/Vomiting	2	3	5	0.484
Bradycardia	1 (3.30%)	4 (13.30%)	6 (20%)	0.140
Hypotension	4 (13.30%)	7 (23.30%)	9 (30%)	0.295
Urinary Retention	3 (10%)	6 (20%)	9 (30%)	0.153
Shivering	5 (16.30%)	6 (20%)	5 (16.30%)	0.927
Sedation Score (1/2/3/4)	30/0/0/0	26/4/0/0	18/12/0/0	<0.001*

Values are frequency (%). *Significant



DA: Differential analgesia, T1: Duration of motor blockade, T2: Duration of analgesia, T3 (T2-T1): Duration of Differential analgesia.

Fig. 4. *Duration of motor block, analgesia, and DA*.

compared with the increase in duration of motor block thereby equating to a significant increase in the duration of DA ($P < 0.001$) (Fig. 4). Increasing the dosage of ITD from 2.5μg to 10 μg resulted in a 41.28% (258.5 vs. 365 minutes), 67.28% (306.17 vs. 512 minutes), and 208.37% (47.67 vs. 147 minutes) increase in the duration of motor block, analgesia, and DA, respectively. A prolongation in the duration of DA is associated with a dual advantage of minimizing the untoward sequelae of postoperative pain (delayed wound healing, depressed immune functions, prolonged hospitalization, risk of neuro-sensitization, and hence, chronic pain) as well as that of prolonged motor blockade (reduced mobilization, deep venous thrombosis, and pulmonary embolism, etc.) (16). This holds particularly true with the duration of surgery being comparable among the groups as in our trial ($P = 0.975$). Yektas et al (3), Halder et al (4), and Eid et al (5) while independently comparing 2 μg vs. 4 μg, 5 μg vs. 10 μg, and 10μg vs. 15 μg, respectively, of ITD also observed similar dose-dependent increase in the duration of sensory block, motor block, and analgesia.

ITD exhibits its facilitatory anti-nociceptive effect by a dual mechanism of inhibiting the release of neurotransmitters by acting on the presynaptic α2A receptors and by hyperpolarizing the postsynaptic neurons (17). The prolongation of motor block might be due to the inhibitory effect of α2 agonists on the motor neurons in the dorsal horn of the spinal cord (18). However the sensitivity to dexmedetomidine has been speculated to vary with the nerve fiber type with ED50 for maximum inhibition being 2.5 μg and more than 10 μg for sensory C and motor A β fibers respectively (19). This prompted us to use the dose range of

ITD between 2.5 µg and 10 µg for this trial. Although a higher dose of 15 µg of ITD has been used by Eid et al (5); the reported significant increase in sedation scores as well as the short average duration of surgeries in our trial made us preclude it from our dose-response trial design. In fact, Eid et al (5) have suggested its potential use in lengthy complex surgeries as an alternative to epidural or general anesthesia; which were outside our inclusion spectrum. ITD has been shown to be effective in nociceptive, visceral, as well as neuropathic pain, and its neurological safety has been proven for up to ten years of post anesthesia follow-up (3,20-22). In fact dexmedetomidine has been demonstrated to have a neuroprotective effect in a number of animal studies (23,24).

The median sensory block onset time was comparable among groups BD2.5 and BD5 (4 minutes), however it was significantly earlier in group BD10 (3 minutes). These findings are in agreement with those of Halder et al (4), who used the similar definition of the sensory block onset time as us and found it to be significantly earlier with 10 µg compared with 5 µg. Yektas et al (3), while comparing 2 and 4 µg of ITD reported a significant dose-dependent increase in the number of sensory segments blocked. The highest peak sensory block level observed in our trial was T4 and though groups BD5 and BD10 had higher numbers of patients achieving it (12 each vs. 9 in group D2.5); the results were clinically and statistically not significant. Our findings are supported by similar observations reported by Halder et al (4). Such a dose-independent nature of peak sensory block level might prove beneficial in mitigating the potential respiratory and cardiovascular adverse effects associated with high spinal block. Similarly we did observe a dose-dependent decrease in motor block onset time with increasing dose of ITD but this reached statistical significance only for group BD10 vs. BD2.5 and not for group BD10 vs. BD5 or BD5 vs. BD2.5. Our results contrast with those of Halder et al (4), who reported a significant earlier onset of maximum motor block onset time with 10µg compared with 5 µg ITD. However a number of other authors have also reported no significant difference in sensory or motor block onset time with the addition of ITD or other adjuvants to hyperbaric bupivacaine (6,25). An inconsistency in the onset and duration times with similar doses of dexmedetomidine exists in the literature which can be attributed to a number of variables such as demographic profile, definition of onset time (T8 vs. T10), volume of IT injectate, volume of diluent used with (0.1 mL vs. 0.5 mL) thereby affecting the concentration and baricity of bupivacaine, position (sitting vs. lateral), and last but not the least, the individual pain sensitivity.

One of the main advantages documented with the addition of ITD to hyperbaric bupivacaine spinal anesthesia is a reduction in the requirement of postoperative analgesics (3-5,7).We also observed a significant dose-dependent decrease (P = 0.001) in the 24 hour tramadol requirement with escalating doses of ITD. Eighty-six point sixty percent, 83.30%, and 50% of patients in groups BD2.5, BD5 and BD10, respectively, required ≥ 2 rescue analgesics in first 24 hours postoperatively. However on comparison, the results were significant only for groups BD10 vs. BD5 (P = 0.023) and BD10 vs. BD2.5 (P = 0.003).

The most common and clinically significant adverse effect associated with α2 agonists is hemodynamic instability, i.e., bradycardia and hypotension (17). Except for a few authors (Yektas et al) (3), the majority of the authors have not reported any significant increase in the incidence of hemodynamic side effects associated with the use or among different doses of ITD (4,6,8,14). We did observe a dose-dependent but not significant increase in the incidence of bradycardia (3.30%, 13.30%, and 20%) and hypotension (13.30%, 23.30%, and 30%) across the groups BD2.5, BD5, and BD10, respectively. The maximal sympatholysis produced by a higher volume and dose of bupivacaine used in our trial might have left little scope for any additional sympatholysis by the addition of dexmedetomidine. Our findings are supported by similar dose independent hemodynamic observations by other authors (4,5). Other side effects including nausea/vomiting, shivering, and urinary retention were comparable among the groups. Yektas et al (3) and Halder et al (4) also observed similar dose-independent side-effects.

A significant increase in the incidence of sedation was observed with 10 µg compared with 2.5 µg and 5 µg ITD (P < 0.001). The highest sedation score was grade 2 seen in 0%, 13.30%, and 40% of patients in groups BD2.5, BD5, and BD10, respectively. However, all the patients were easily arousable to verbal commands and maintained SpO_2 > 95% on room air. In fact, the mild sedation might be beneficial in the immediate postoperative period (6). The present findings are in concert with similar low sedation scores reported by other authors (8,14).

The main limitation of our trial was the absence of a control group. We excluded the control group because the primary aim of our trial was to elucidate

the change in various SAB characteristics with increasing doses of ITD. Also, the beneficial effects of adding ITD upon SAB characteristics are a well-documented and undisputed phenomenon. The second limitation of our trial was the short duration of postoperative follow-up. The effect of ITD on the development of postoperative chronic pain, e.g., post herniorrhaphy pain, is largely unknown. Future studies with a longer period of follow-up are warranted to witness any difference in the incidence of postoperative chronic pain with the addition and with different doses of ITD.

Conclusion

To conclude, 10 µg of ITD compared to lower doses as an adjuvant to hyperbaric bupivacaine significantly prolongs the duration of sensory block, motor block, and analgesia. A disproportionate increase in the duration of analgesia and motor block produces both clinically and statistically significant prolongation of the duration of differential analgesia. Addition of 10 µg of ITD is associated with fewer requirements of postoperative analgesics in patients undergoing lower abdominal and lower limb surgeries without any significant increase in the incidence of side effects.

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