Original Article

DOI: 10.7860/JCDR/2022/56621.16587

Anaesthesia Section

Effects of Intrathecal Dexmedetomidine-Bupivacaine versus Intravenous Dexmedetomidine Plus Intrathecal Bupivacaine: A Randomised Triple-blind Clinical Study

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ABSTRACT

Introduction: For administering Spinal Anesthesia (SA) 0.5% bupivacaine is employed with Dexmedetomidine (DMT) as an adjuvant. Literature review reveals that either intrathecal or low-dose intravenous DMT can enhance the characteristics of SA with bupivacaine

Aim: To evaluate the effect of a single bolus intravenous (i.v.) DMT 0.5 µg/kg given either before or after the SA in combination with intrathecal 0.5% bupivacaine compared with intrathecal bupivacaine plus DMT.

Materials and Methods: A randomised, triple-blind, single-centre and placebo-controlled study was conducted at Gayatri Vidyaparishad Institute of Health care and Medical Technology, Marikavalasa, Visakhapatnam, Andhra Pradesh, India, from April 2020 to December 2021. Eighty patients were allocated to four study groups of 20 each. Patients of group Intrathecal DMT (ITD) were given SA with 0.5% bupivacaine heavy 3.4 mL+5 µg DMT, patients of group Before Spinal DMT (BSD) were given intravenous DMT before administering the SA with bupivacaine, patients of group After Spinal DMT (ASD) were given intravenous DMT after administering the SA with bupivacaine, and the patients of group Nil DMT (ND) or control group, were given SA with 0.5% bupivacaine heavy 3.4 mL. The primary outcome variable was the difference in the duration of analgesia. The secondary outcome variables were the differences in the onset and duration of the block both motor and sensory. Differences of the parametric data were analysed using Analysis of Variance (ANOVA) and Tukey's Post Hoc test HSD Beta (Honestly significant difference). For analysis of non parametric data Chi-square test was used and a p-value of ≤0.05 was considered as statistically significant.

Results: The mean age of the study participants in group ITD, group BSD, group ASD and group ND was 61.2±9.2, 59.8±10.3, 57.9±10.2, and 60±9.4, respectively. Patients in the ITD group had a longer duration of analgesia of 280.7±5.0 min (vis-a-vis 215±9.34, 210.7±12.0 and 97.9±7.12 min in BSD, ASD and ND, respectively) with a statistically significant difference at a p-value <0.00001. They had a shorter duration of onset of motor block of 3.4±0.49 (vis-a-vis 4.6±0.53, 6.09±0.44 and 6.3±0.65 in BSD, ASD and ND groups, respectively) with a statistically significant difference at a p-value <0.00001. Duration of onset of the sensory block was 2.2±0.37 min in the patients of ITD group (vis-a-vis 3.2±4.76, 3.5±6.71 and 4±0.40 in BSD, ASD and ND groups, respectively) with a statistically significant difference at a p-value <0.00001.

Conclusion: Dexmedetomidine used as an adjuvant to intrathecal bupivacaine produces greater augmentation of duration of analgesia, earlier onset of sensory and motor block, more haemodynamic stability and fewer overall side effects compared to its intravenous bolus administration.

Keywords: Adjuvant, Analgesia, Motor block, Sensory block

INTRODUCTION

Spinal Anesthesia (SA) is the most commonly used regional anaesthetic technique for lower abdominal and lower limb surgeries with 0.5% bupivacaine employed as the local anaesthetic agent of choice because of its dense, reliable and prolonged sensory block. Though several drugs are being used as adjuvants to bupivacaine intrathecally for enhancing the block characteristics, Dexmedetomidine (DMT) has emerged as the most popular agent because of its selective action on the central and spinal alpha-2 Adrenergic Receptors (α-2AR) [1,2]. By this action it prolongs both sensory and motor block besides producing potent sympatholytic, anxiolytic, sedative and analgesic effects [3]. The DMT is an imidazoline compound and is a dextro-isomer of medetomidine and exhibits selective α-2AR agonist activity without any undesirable effects due to activation of α1 receptors. Dexmedetomidine has an additive or synergistic action on the effect of local anaesthetics and enables to decrease their clinically effective doses and does not cause respiratory depression even at high doses [4,5]. Because of its highly lipophilic nature, DMT rapidly binds to α2-AR of the spinal cord for initiating its analgesic action by suppression of the release of C fiber transmitters and hyperpolarisation of the post-synaptic neurons [6].

Studies conducted with different doses of intrathecal DMT (5 µg, 10 µg, 15 µg and 20 µg) concluded that 5 µg is the optimal dose to obtain the desired effects [7,8]. Studies have demonstrated that intrathecal as well as low-dose intravenous (i.v) DMT can prolong sensory and motor block during SA without undesirable side effects [9,10]. Different published clinical studies and meta-analyses on the effect of intravenous DMT on SA had shown that intravenous DMT given just before or after the SA improved the quality and duration of the block [11,12]. The DMT given as 1 µg/kg bolus either 20 min before or after SA with bupivacaine was reported to have produced reduced pain score and longer duration of postoperative analgesia [13]. It was observed that the prolongation of postoperative analgesia associated with the use of DMT had a plateau effect at around 0.5 µg/kg and when the loading dose was increased beyond 0.5 µg/kg excessive sedation and bradycardia were observed as the side effects [14-16].

Intravenous DMT is known to reduce the patient's anxiety level, physiological and psychological stress associated with the surgical intervention, reduces the incidence of shivering, nausea and vomiting and prolongs the duration of postoperative analgesia [17,18]. But it is not clear whether there is any difference between i.v. DMT given either before or after the administration of the SA.

In this context, to bridge the existing knowledge gap the present study was conducted to compare the effect of a single bolus i.v. DMT 0.5 µg/kg given either before or after SA in combination with intrathecal 0.5% bupivacaine heavy versus intrathecal 0.5% bupivacaine heavy +5 µg DMT. It was decided to administer a dose of 0.5 µg/kg DMT as a single bolus of slow i.v. infusion over 10 minutes, as rapid administration of DMT is known to produce bradycardia and hypotension [19]. As hypotension and bradycardia are known complications of both SA and i.v. DMT infusion, it was planned to administer the DMT either 20 minutes before or after giving SA [20].

The primary outcome variable studied was the difference in the duration of analgesia. The secondary outcome variables studied were the differences in the onset and duration of the motor and sensory blocks, differences in Pulse Rate (PR), Mean Arterial Pressure (MAP), Electrocardiogram (ECG), Respiratory Rate (RR) and peripheral oxygen saturation (SpO^2).

Total doses of rescue analgesics administered during the 1st postoperative day, Ramsay Sedation Scores (RSS), surgeon assessment scores and patient satisfaction scores.

MATERIALS AND METHODS

A randomised, triple-blind, single-centre and placebo-controlled study was conducted at Gayatri Vidyaparishad Institute of Health care and medical technology, Marikavalasa, Visakhapatnam, Andhra Pradesh, India, from April 2020 to December 2021. Institutional Ethical Committee approval was obtained (Rc No IEC/14022020, dated 14 February 2020), and the study is registered with Clinical Trial Registry of India (CTRI registration No CTRI/2020/03/023952).

Among the 100 patients attending the Institute during the study period, 80 were selected after applying inclusion and exclusion criteria and excluding those who did not agree to participate in the study, and finally 80 were enrolled for the study. All the patients were explained regarding the study protocol and the consequent risks and benefits in their mother tongue and written informed consent was obtained in the presence of two witnesses.

Sample size calculation: Sample size calculation was based on a study that reported a duration of analgesia of 243.35±56.82 (Mean±SD) and 140.75±28.52 in their two groups of patients [21].

The formula used for calculation of sample size was as given below

$N=Z^2 (SD^2)/d^2$

N=sample size in each group (25 in the study under reference 24)

Z=Normal deviate or Unit normal deviate whose value is 1.96

$Z^2=1.96*1.96=3.846$

SD^2=Pooled variance of the two groups under study which is given by the formula $SD^2=[n_1-1) (SD_1^2)+[n_2-1) (SD_2^2)/(n_1+n_{2-2})$..... Where n1 and SD1 are sample size and SD of group1; n2 and SD2 are sample size and SD of group2;

$SD^2=(25-1) (562)+(25-1) (282)/48$

=(75264+18816)/48

=94941/48

=1977.9375

d=precision or allowable error which is usually taken as less than 20% of the difference of the means of the two groups.

d=20% of the difference of two means

=(20/100) * (243.35-140.75)

=20.52

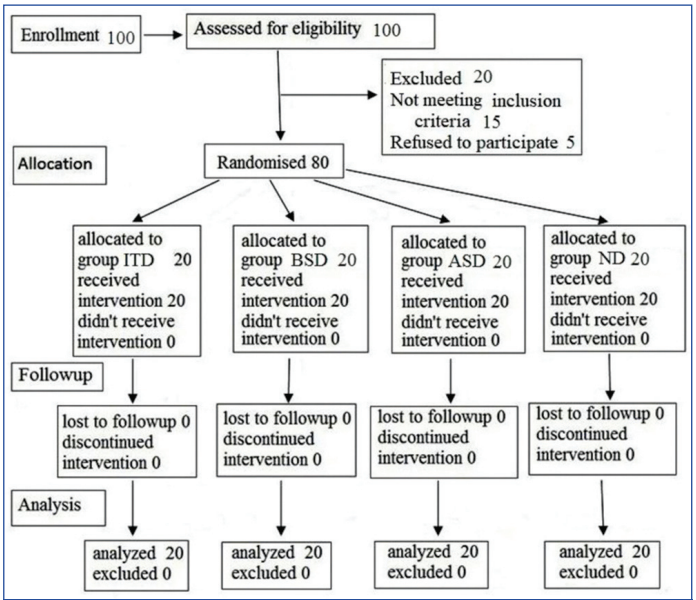
$d^2=20.52*20.52=421.0704$

Substituting the derived values in the formula $N=Z^2 (SD^2)/d^2$

N=(3.846 * 1977.9375)/421.0704=18.04

Sample size (N)=18 (rounded off to 18)

With 80% power and 5% alpha error, a sample size of 18 patients per group was required and incorporating a compensation for a non-responder's bias for an assumed attrition rate of 10%, it was calculated that a sample size of 20 patients in each group was required. The details of the patients who participated in the study are depicted in a flow diagram as per CONSORT guidelines [Table/Fig-1].



[Table/Fig-1]: Flow diagram showing patient progress through the study phases (CONSORT).

Inclusion criteria: All adult patients of age between 18 and 70 years, with body weight between 40 and 70 kg, height between 145 cm and 170 cm, Body Mass Index (BMI) (kg/m^2) between 19 and 24; and who were of American Society of Anaesthesiologists (ASA) physical status grades I and II of either gender attending our hospital for elective lower limb, lower abdominal and urological surgeries during the study period were included in the study.

Exclusion criteria: All patients with known allergy to the drugs being studied, those who are not willing for SA, those suffering from psychiatric disorders, those having coagulation or bleeding abnormalities, severe spinal deformity and those with an infection at the spinal injection site were excluded from the study.

Study Procedure

All the patients were examined in the preanaesthetic clinic by a thorough history taking and physical examination. Details of the technique of SA and methods of examination of motor and sensory block and assessment of pain on the Visual Analog Scale (VAS) from zero to 10 grading were explained to the patients. They were advised to follow the standard fasting guidelines prior to the surgery and no sedative premedication was given as it may act as a confounding variable for assessing sedation levels attained with DMT. The patients were allocated to four study groups of 20 each (n=20) utilising a computer- generated random grouping software and a sequentially numbered sealed opaque envelope method. The schedule of drugs administered to the patients in the four groups was:

- Patients of group ITD (intrathecal DMT) were given 50 mL of normal saline over 10 minute period as a placebo infusion (saline placebo) 20 minutes before administering the SA plus intrathecal 0.5% bupivacaine heavy 3.4 mL (17 mg)+5 µg DMT and a saline placebo, 20 minutes after administering the SA.
- Patients of group BSD (before spinal DMT) were given i.v. DMT 0.5 µg/kg body weight in 50 mL of normal saline as an i.v. infusion over 10 minutes (DMTinfusion), 20 minutes before administering

the SA plus intrathecal 0.5% bupivacaine heavy 3.4 mL and a saline placebo 20 minutes after administering the SA.

- Patients of group ASD (after spinal DMT) were given a saline placebo 20 minutes before administering the SA plus intrathecal 0.5% bupivacaine heavy 3.4 mL and DMT infusion 20 minutes after administering the SA and
- Patients of group ND (Nil DMT i.e. control group) were given a saline placebo 20 minutes before and 20 minutes after administering the SA plus intrathecal 0.5% bupivacaine heavy 3.4 mL.

The anaesthesiologist preparing the drugs for the study was not associated with further management and assessment of the patients. The surgeons, the patients and the data entryoperator and the statistitian were blinded to the study drugs administered to the patients as it was a triple blinded study. In the operation theater peripheral intravenous (i.v.) access was secured with an18G i.v. cannula and ringer lactate solution 10 mL/kg was infused as preloading. Pulse Rate (PR), Mean Arterial Pressure (MAP), Electrocardiogram (ECG), Respiratory Rate (RR) and peripheral oxygen saturation (SpO_2) were monitored.

The primary outcome variable studied was the difference in the duration of analgesia. The secondary outcome variables studied were the differences in the onset and duration of the motor and sensory blocks, differences in PR, MAP, RR, SpO_2, total doses of rescue analgesics administered during the 1st postoperative day, Ramsay Sedation Scores (RSS), surgeon assessment scores and patient satisfaction scores. Side effects like hypotension, bradycardia, postoperative nausea and vomiting, pruritus, shivering and dryness of the mouth,etc were also noted and treated appropriately.

Under strict aseptic precautions SA was given keeping the patient in the sitting position via a midline approach, at L2-L3 or L3-L4 intervertebral space, with a 25 gauge Quincke needle and immediately after the injection patients were placed in the supine position and were monitored with continuous ECG, non invasive blood pressure, pulse oximetry and PR. Intravenous fluids and blood were administered as required to maintain stable haemodynamic parameters.

Time to onset: Of the sensory block was assessed by the pinprick method by testing in the midclavicular line with a sterile 26 gauge needle at every one-minute intervals till the highest level of the sensory block was attained which is the dermatome where the loss of sensation was recorded on two consecutive examinations.

Recovery time: For the sensory blockade was defined as the time elapsed for two dermatome regression of sensory levels from the highest level attained. Time to onset of the motor block of Bromage grade 4 intensity was noted and the recovery of motor block was assessed using modified Bromage score at every 15-minute interval [22].

Sedation levels: They were assessed by the modified Ramsay Sedation Scores (RSS) and for statistical analysis patients attaining sedation scores 2, 3 and 4 were grouped as having satisfactory sedation levels and those with sedation scores of 1,5 and 6 were grouped as having unsatisfactory sedation levels [23].

Visual analog scale (rescue analgesia): The VAS score was serially assessed at every 15-minute interval after completion of the surgery till the patients complained of pain of VAS score 2. The duration of the effective analgesia was taken as the time elapsed from the attainment of the satisfactory sensory block to the time of administration of the first rescue analgesia when patients complained of pain of grade 2 intensity on VAS and injection diclofenac 75 mg was given intravenously as rescue analgesia.

Haemodynamic parameters: Haemodynamic parameters of PR, MAP, SpO_2, ECG, RSS and RR were recorded every 5 min for the initial 30 min of the surgery and later at every 15 min till the complete recovery of sensory and motor block.

Surgeon assessment score: The scrore was recorded by asking him to rate his satisfaction with operative conditions at the end of surgery, using a three-point verbal rating scale:

1=Not satisfactory as surgery was interrupted;

2=Satisfactory with only minor issues but not necessitating interruption of surgery;

3=Good with satisfactory operating conditions and patient having no pain.

Patients satisfaction: Patients were asked regarding their satisfaction about the anaesthetic experience on a three-point verbal rating scale:

1=Extremely dissatisfied since they had severe pain and adverse events;

2=Satisfied, had minimal pain only;

3=Extremely satisfied as there was no pain or adverse events and they were comfortable during the block and surgery.

A score of 2 or 3 was taken as acceptable satisfaction level both in the case of patients and the surgeons [24].

STATISTICAL ANALYSIS

At the end of the study, data was compiled and the parametric data were presented as mean±sd and the differences between the groups were analysed using the statistical test Analysis of Variance (ANOVA). Tukey's Post Hoc test HSD Beta was used for inter-group comparison. Non parametric data were presented as numbers and percentages and the Chi-square test was used for analysing the differences between the groups. Statistical analysis was carried out using Microsoft Windows Excel 2007 and Statistical Package for Social Sciences (SPSS) version 20.0 IBM and a p-value of ≤0.05 was considered as statistically significant.

RESULTS

The details of the patients who participated in the study are depicted in a flow diagram as per CONSORT guidelines [Table/Fig-1].

The demographic features of age, gender, weight, height, the average duration of surgery, ASA grades and the number of cases of surgeries done specialty-wise in the four groups are shown in the table and are comparable [Table/Fig-2].

Characteristics	Group ITD	Group BSD	Group ASD	Group ND	p-value
Age (years) (mean±SD)	61.2±9.2	59.8±10.3	57.9±10.2	60±9.4	0.745
Gender male/females (n)	9/11	8/12	10/10	8/12	0.905
Height (cm) (mean±SD)	151.9±7	155.2±9.2	158.6±8.5	156.3±8.5	0.093
Weight (kg) (mean±SD)	53.0±12.7	56±11.1	58.3±9.4	59±11.7	0.334
Surgery duration (min) (mean±SD)	131±21.07	131±10.98	124±9.86	130±21.17	0.473
ASA grade (numbers) gradel/grade II	14/6	15/5	13/7	12/8	0.767
Specialty-wise surgeries in each group					
Gynaecology	3	3	3	4	0.964
General surgery	5	5	5	4	0.976
Orthopaedics	10	10	12	10	0.896
Urology	2	2	0	2	0.925

[Table/Fig-2]: Demographic characteristics of the patients.
p-value <0.05 was considered significant; n=20 in all the four groups
ASA: American society of anaesthesiologists; SD: Standard deviation; Group ITD: Group intrathecal DMT, Group BSD: Group before spinal dexmedetomidine; Group ASD: Group after spinal dexmedetomidine, Group ND: Group with no dexmedetomidine

Patients in the group ITD had a longer duration of analgesia compared to the other three groups with a statistically significant difference at p-value <0.00001. Intergroup comparison showed a statistically significant difference between the groups ITD: BSD, ITD: ASD, ITD: ND, BSD: ND and ASD: ND but the comparison between the groups BSD: ASD did not reveal any statistically significant difference [Table/Fig-3].

Block characteristics	Group ITD (Mean±SD)	Group BSD (Mean±SD)	Group ASD (Mean±SD)	Group ND (Mean±SD)	p-value
Onset of sensory block (min)	2.2±0.37	3.2±4.76	3.5±6.71	4±0.40	<0.05
Two-segment sensory regression (min)	185.9 ±5.03	130.7 ±1.46	140.4±1.21	120.2±7.85	<0.05
Onset of motor block (min)	3.4±0.49	4.6±0.53	6.09±0.44	6.3±0.65	<0.05
Duration of motor block (min)	220±12.96	190.2±7.48	185.7±6.61	170.5±8.73	<0.05
Analgesic consumption 1st 24 hours (mg)	97.5±35.26	105 ±37.69	127±35.26	135±30.77	<0.05
Duration of analgesia (min)	280.7±5.0	215 ±9.34	210.7±12.0	97.9±7.12	<0.05
Pairwise comparison					
Pairwise comparison ITD: BSD	280.7±5.0	215 ±9.34	-	-	<0.05
Pairwise comparison ITD: ASD	280.7±5.0	-	210.7±12.0	-	<0.05
Pairwise comparison ITD: ND	280.7±5.0	-	-	97.9±7.12	<0.05
Pairwise comparison BSD: ASD	-	215 ±9.34	210.7±12.0	-	0.424
Pairwise comparison BSD: ND	-	215 ±9.34	-	97.9±7.12	<0.05
Pairwise comparison ASD: ND	-	-	210.7±12.0	97.9±7.12	<0.05
Pairwise comparison ITD: BSD	185.9 ±5.03	130.7 ±1.46	-	-	<0.05
Pairwise comparison ITD: ASD	185.9 ±5.03	-	140.4±1.21	-	<0.05
Pairwise comparison ITD: ND	185.9 ±5.03	-	-	120.2±7.85	<0.05
Pairwise comparison BSD: ASD	-	130.7 ±1.46	140.4±1.21	-	0.207
Pairwise comparison BSD: ND	-	130.7 ±1.46	-	120.2±7.85	<0.05
Pairwise comparison ASD: ND	-	-	140.4±1.21	120.2±7.85	<0.05

[Table/Fig-3]: Block characteristics.
p-value <0.05 was considered significant; n=20 in all the 4 groups SD: Standard deviation; Group ITD: Group intrathecal dexmedetomidine, Group BSD: Group before spinal dexmedetomidine; Group ASD: Group after spinal dexmedetomidine; Group ND: Group with no dexmedetomidine

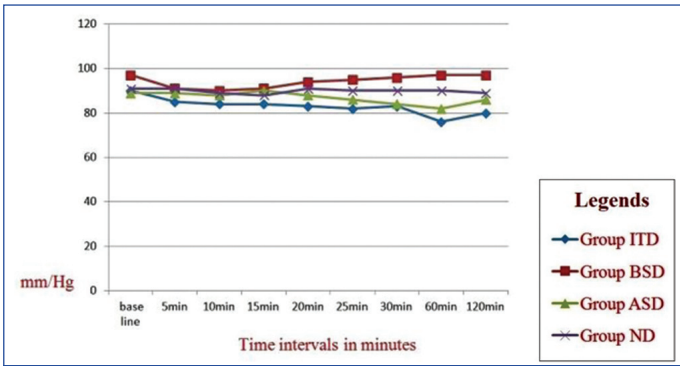
Patients in the ITD group had a shorter duration of onset of both sensory and motor blocks compared to the other three groups and this difference was statistically significant at p-value <0.00001 [Table/Fig-3].

Patients in the ITD group had a longer duration of two-segment regression of sensory blocks compared to the other three groups and this difference was statistically significant at p-value <0.00001. Inter-group comparison of two-segment regression of the sensory blocks showed a statistically significant difference between the groups ITD: BSD, ITD: ASD, ITD: ND, BSD: ND and ASD: ND but the comparison between the groups BSD: ASD did not reveal any statistically significant difference [Table/Fig-3].

Patients in the group ITD had the least amount of analgesic medicine consumed compared to the other three groups and this difference was statistically significant at p-value <0.002. Patients in the ITD group had a longer duration of motor blocks compared to the other three groups and this difference is statistically significant at p-value <0.00001 [Table/Fig-3]. The vital parameters like PR, MAP, SpO_2, RR and ECG were comparable in all the groups. The fluctuations observed in MAP and PR at the 15 minute intervals during the surgery and the postoperative periods are within the clinically acceptable limits and easily treatable with simple therapeutic interventions and are shown as line diagrams [Table/Fig-4a,b and 5a,b].

Sedation levels measured on the RSS scale at every 15 minute interval are shown in a line diagram [Table/Fig-6a,b]. Except in group ND, sedation levels observed in the other three groups were falling between RSS scores 2 and 4 (satisfactory levels). There were no instances of lower SpO_2 levels or lower RR requiring active intervention in any of the patients in the four groups. In a few cases bradycardia, hypotension, dryness of the mouth, nausea and vomiting were noted in all four groups but there was no statistically significant difference in the rates of these side effects between the groups [Table/Fig-7].

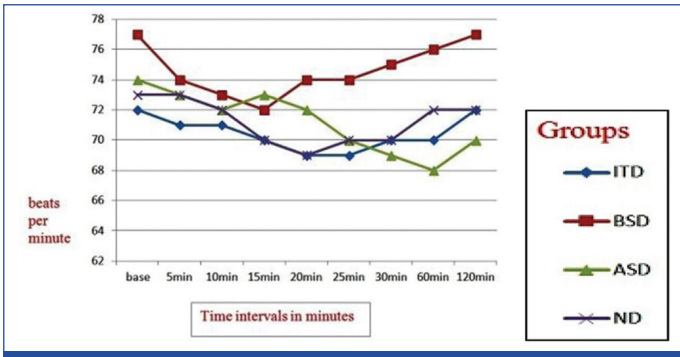
Analysis of the patient and surgeon satisfaction levels with the anaesthetic technique revealed that the patients of groups ITD, BSD and ASD and surgeons operating on the patients of these groups



[Table/Fig-4a]: Mean arterial pressure changes in millimeters of mercury (mm/Hg).

Time intervals	Group ITD	Group BSD	Group ASD	Group ND	p-value
Baseline	90	97	89	91	0.090524
5 min	85	91	89	91	0.000598
10 min	84	90	88	89	0.004675
15 min	84	91	90	88	0.001378
20 min	83	94	88	91	0.003256
25 min	82	95	86	90	0.00194
30 min	83	96	84	90	0.005541
60 min	76	97	82	90	0.022972
120 min	80	97	86	89	0.043935

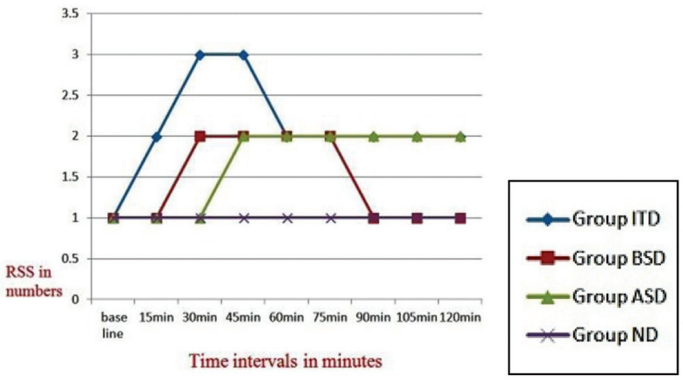
[Table/Fig-4b]: Mean arterial pressure changes in millimeters of mercury (mm/Hg).
p-value <0.05 was considered significant



[Table/Fig-5a]: Pulse rate changes in beats per minute (bpm).

Time intervals	Group ITD	Group BSD	Group ASD	Group ND	p-value
Base line	72	77	74	73	0.05541
5 min	71	74	73	73	0.059799
10 min	71	73	72	72	0.035642
15 min	70	72	73	70	0.054104
20 min	69	74	72	69	0.019219
25 min	69	74	70	70	0.03992
30 min	70	75	69	70	0.029086
60 min	70	76	68	72	0.021807
120 min	72	77	70	72	0.03622

[Table/Fig-5b]: Pulse rate changes in beats per minute (bpm).
p-value <0.05 was considered significant; n=20 in all the 4 groups



[Table/Fig-6a]: Ramsay sedation scores at various time intervals.

Time intervals	Group ITD	Group BSD	Group ASD	Group ND	p-value
Baseline	0/20	0/20	0/20	0/20	1
15 min	0/20	15/5	0/20	0/20	0.00001*
30 min	15/5	18/2	0/20	0/20	0.00001*
45 min	18/2	20/0	15/5	0/20	0.000128*
60 min	20/0	15/5	18/2	0/20	0.00001*
75 min	18/2	13/7	20/0	0/20	0.00001*
90 min	16/4	0/20	18/2	0/20	0.00001*
105 min	14/6	0/20	16/4	0/20	0.00001*
120 min	10/10	0/20	16/4	0/20	0.00001*

[Table/Fig-6b]: Sedation levels at various time intervals in numbers (satisfactory/unsatisfactory).
*p-value <0.05 was considered significant; n=20 in all the four groups
Sedation levels were assessed by the modified RSS and for statistical analysis patients attaining sedation scores 2,3 and 4 were grouped as having satisfactory sedation levels and those with sedation scores of 1,5 and 6 were grouped as having unsatisfactory sedation levels and Chi-square test was used for statistical analysis

had greater satisfaction levels in comparison with those of group ND and the differences were statistically significant at a p-value of <0.001 and p-value of <0.032 respectively [Table/Fig-7].

Parameters	ITD	BSD	ASD	ND	p-value
Bradycardia (n, %)	2 (10%)	3 (15%)	2 (10%)	1 (5%)	0.774
Hypotension (n, %)	4 (20%)	2 (10%)	3 (15%)	1 (5%)	0.515
Dryness of mouth (n, %)	2 (10%)	3 (15%)	2 (10%)	1 (5%)	0.774
Nausea and/or Vomiting (n, %)	1 (5%)	3 (15%)	2 (10%)	1 (5%)	0.632
Patients satisfied -Yes/No (n, %)	18/2	14/6	12/8	6/14	0.001*
Surgeon satisfied -Yes/No (n, %)	17/3	13/7	12/8	8/12	0.032*

[Table/Fig-7]: Comparison of side effects, patient and surgeon satisfaction scores.
*p-value <0.05 was considered significant; n=20 in all the four groups

DISCUSSION

For lower limb and lower abdominal surgeries, SA is administered with 0.5% bupivacaine with DMT as an adjuvant. It is seen from several published articles that DMT administered either intrathecally or intravenously in combination with spinal blocks prolongs the duration of sensory and motor blocks [25]. Prolongation of spinal anesthesia after intravenous DMT is believed to resultfrom its supraspinal action at locus ceruleus and dorsal raphe nucleus [26]. The DMT is a selective α2-A receptor agonist with more sedative and analgesic effects. Activation of presynaptic α2-A receptors at locus ceruleus decreases norepinephrine release and causes sedative and hypnotic effects. By modulation of descending medullospinal noradrenergic pathway DMT terminates pain signal propagation and produces analgesia. At the spinal level it decreases the transmission in nociceptive neurons of substantiagelatinosa and decreases the release of substance P thus enhancing the central analgesic effect [27]. Hence, DMT has a role in modulating pain by inhibiting the transmission and perception of pain.

The effects of DMT on the spinal block were evaluated by administration of DMT by three different methods i.e. intrathecal DMT or intravenous infusion of DMT either before or after giving SA. The above three groups of patients were compared with a control group without DMT. As higher doses of DMT are associated with bradycardia and hypotension, we administered a lower dose of DMT 0.5 μg/kg as a slow intravenous infusion over 10 min thereby reducing the incidence of bradycardia and hypotension. Thus, this study throws light on the best route and dose of DMT supplementation to be employed for SA. It was observed that the intrathecal administration of DMT had resulted in a greater enhancement of the duration of analgesia than the other two intravenous methods and the control group, besides producing shorter onset times of sensory and motor blocks, longer duration of two-segment sensory regression and motor blocks and lesser consumption of analgesic medicines in the 1st 24 hours after the surgery.

The duration of analgesia observed was longer in the present study group ITD in comparison to the other three groups with a statistically significant difference. Senapati LK and Samanta P, reported that in their patients, need for rescue analgesia was delayed and there was less analgesic consumption in the first 24 hours and these observations, in agreement with the present results [28].

It was noted that mean times for two dermatomal regressions of sensory blockade were significantly prolonged in group ITD compared with other groups with a statistical significance at p-value <0.00001. These results are in agreement with those of Kaya FN et al., who reported that two dermatomal regression of sensory blockade was 145±26 min versus 97.1±26.5 min in their groups of i.v. DMT vs the control group [29]. The regression time noted in the present study control group (120.2±7.85 min) was more than that of their study (97.1±26.5 min) and this difference could be due to the higher dose of bupivacaine used in the current study i.e, 17 mg versus 15 mg by Kaya FN et al., [29]. Further they reported that there was a decreased analgesic requirement in their patients of the DMT group compared to the control group and these findings are in agreement with the present study results.

It was noted that the duration of onset of sensory block and motor block were shorter and duration of motor block longer in the current study ITD group in comparison with the other three groups, with a statistically significant difference [Table/Fig-3].

These results are in agreement with the observations of Hamed AM and Talaat SM [30].

The patient and surgeon satisfaction levels attained were satisfactory in group ITD, BSD and ASD in comparison with the control group with a statistical significance at p-value <0.001 and p-value <0.032 respectively [Table/Fig-7]. Ramsay sedation scores were within the satisfactory levels in the DMT groups but were in the unsatisfactory levels in the control group [Table/Fig-6]. The findings are in agreement with those of Ok HG et al., who reported that adequate sedation was observed in their patients with a lower dose of DMT 0.5 mcg/kg with or without infusion [18].

Fluctuations in MAP, PR and RR observed during intraoperative and postoperative periods were comparable in all the four groups and were within the clinically acceptable normal ranges requiring only minimal interventions and the present study findings are in agreement with the observations of Tekin M et al., [31].

The total analgesic consumption in the first 24 hours of postoperative period was observed to be less in the ITD group than in the other three groups with a statistically significant difference and this clearly demonstrates that intrathecal administration of DMT as an adjuvant to bupivacaine produces better analgesia necessitating less amount of analgesic medicines than i.v. DMT with intrathecal bupivacaine. The present study findings are in agreement with those of Dinesh et al. who reported prolongation of the first analgesic request and reduction in the requirement of analgesic medicines in the 1st 24 hrs in their DMT group [32]. Though most of the studies have noted bradycardia as a prominent side effect following the use of a bolus dose of 1 µg/kg, the incidence of bradycardia in this study was low probably owing to a lower bolus dose of DMT i.e. 0.5 µg/kg used. There were a few side effects noted in a small number of cases in all the four groups like bradycardia, hypotension, dryness of the mouth, nausea and vomiting as noted in the table and the differences in the numbers of these side effects are not statistically significant [Table/Fig-7]. No cases of shivering,respiratory depression or a significant drop in the SpO_2 levels were noted in the present study and these results are in agreement with those of Affifi MH et al., [33].

Limitation(s)

Results of this study cannot be generalised to patients of American Society of Anaesthesiologists grades III and IV or older age groups.

CONCLUSION(S)

Dexmedetomidine used as an adjuvant to intrathecal bupivacaine in spinal anesthesia produces earlier onset of sensory and motor block, greater augmentation of the duration of sensory and motor block and analgesia, more haemodynamic stability and fewer overall side-effects compared to its intravenous bolus administration given 20 minutes before or after the spinal block.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Apr 04, 2022
- Manual Googling: Apr 20, 2022
- iThenticate Software: Apr 27, 2022 (9%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Mar 25, 2022**
Date of Peer Review: **Apr 23, 2022**
Date of Acceptance: **Jun 03, 2022**
Date of Publishing: **Jul 01, 2022**