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Effect of Intravenous Dexmedetomidine on Prolongation of Intrathecal Spinal Anaesthesia With 0.5% Hyberbaric Bupivacaine.

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Abstract: *Subarachnoid block (SAB) is a widely used regional anaesthetic technique, especially in lower abdomen and lower limb surgeries. α2-Agonists like clonidine and dexmedetomidine are used to prolong the duration of spinal anesthesia. The present study was designed to evaluate the effect of IV dexmedetomidine on duration of spinal anaesthesia with 0.5% of hyperbaric bupivacaine given 10 mins before and 30 mins after spinal anaesthesia. Sensory blockade was prolonged in group receiving dexmedetomidine 10 mins before intrathecal anaesthesia when compared with group receiving 30 mins after intrathecal anaesthesia . It also provided additional analgesia in group receiving before intrathecal anaesthesia.*
Keywords: *Dexmeditimidine, spinal anaesthesia,Bupivacaine,postoperative analgesia.*

I. Introduction

Subarachnoid block (SAB) is a widely used regional anaesthetic technique, especially in lower abdomen and lower limb surgeries.[1] The intrathecal local anaesthetic 0.5% bupivacaine with dextrose, is frequently used for surgeries lasting for 2-2.5 hr.[2] Adjuvants from different pharmacological classes of drugs are used to prolong the action of analgesia and enhance the efficacy of spinal anaesthesia. They also reduce the dose requirements of local anesthetic agents and their side effects.[3,4]

α2-Agonists like clonidine and dexmedetomidine are used to prolong the duration of spinal anesthesia. They provide sedation and analgesia when used as adjuvants and also decrease the sympathetic tone and the stress responses to surgery and anesthesia.[5,6]They prolong the duration of motor, sensory spinal blockade and also potentiate the effect of local anaesthetics. They also provide postoperative analgesia.[7]

Dexmedetomidine is a selective α2‑adrenoreceptor agonist; it has a α2/α1 selectivity ratio which is eight to 10 times higher than that of clonidine.[8]Prolongation of duration of action of spinal anaesthesia following IV dexmedetomidine is by its action at spinal and supra-spinal at locus ceruleus and dorsal raphe nucleus.[9] Dexmedetomidine given as a single dose before induction of anaesthesia decreased the requirement of inducing agent without any serious hemodynamic adverse effects and also provided better intubation condition.[10]

Few studies have shown the efficacy of intravenous (IV) dexmedetomidine in prolonging prilocaine/bupivacaine/ropivacaine spinal anesthesia in addition to providing good sedation and postoperative analgesia. The present study was designed to evaluate the effect of IV dexmedetomidine on spinal anesthesia with 0.5% of hyperbaric bupivacaine.

II. Objectives

To study and compare the effect of IV Dexmedetomidine on prolonging the duration of analgesia of intrathecal bupivacaine by

1. Noting two segment regression of sensory level.
2. Noting VAS score.
3. 24hour rescue analgesia required.

Side effects like dry mouth, nausea, vomiting, bradycardia, hypotension, respiratory depression, shivering, head ache will be noted.

III. Material & Methods

This study was undertaken after an institutional approval by the Committee on Human Research and Ethics, written informed consent was obtained from all patients. The study population consisted of 60 patients, who were classified as American Society of Anaesthesiologists (ASA) physical status I or II, male or female

adults between the ages of 18-65 years scheduled for various elective surgical procedures below umbilicus under intrathecal spinal anaesthesia.

3.1.Study design

This study was a prospective, randomized, and double-blinded clinical comparison study. The study participants were randomly divided into three groups by a computer generated randomization table.

Group A: Patient received IV dexmedetomidine 0.5µg/kg over 1min, 10 minutes after intralthecal spinal anaesthesia.

Group B: Patient received IV dexmedetomidine 0.5µg/kg over 1min, 30 minutes before intrathecal spinal anaesthesia.

3.2.Inclusion Criteria

Inclusion criteria for the study were ASA class I or II, age range18-65 years scheduled for various elective surgical procedures below umbilicus under spinal anesthesia.

3.3.Exclusion criteria

Exclusion criteria included Patient refusal, emergency surgeries, use of any opioid or sedative medications in the week prior to surgery, known allergy to any of the test drugs, contraindication to spinal anesthesia (as infection at puncture site, pre-existing neurological deficits in the lower extremities, coagulation defects), and cardiovascular, respiratory, neurological, psychological, hepatic, or renal disease, diabetes mellitus.

3.4.Pre Surgical Protocol

A day prior to the surgery, preoperative visit will be made and a detailed history of the patient will be taken. A thorough clinical examination will also be conducted and necessary investigations will be sent and reviewed if necessary. Airway assessment will be done using Modified Mallampatti Score on the day before the surgery. All patients will be kept nil per oral (NPO) for 8hrs prior to the surgery. They will be premedicated with Tab Ranitidine 150mg at night on the day before surgery and also at 6:00am in the morning of the surgery and Tab Alprazolam 0.5mg in the night before surgery.

3.5.Surgical Protocol

On day of surgery procedure was explained to the participants and a written informed consent was obtained from each participant. Intravenous access was secured and infusion of Ringer's lactate solution started. Patients was then shifted to the operating room after which routine non-invasive monitor was applied and vital signs are monitored. After preloading the patients with Ringer Lactate 15 ml/kg, patient was put on lateral/ sitting position and lumbar puncture was performed at L3-4 level with Quincke type point 25 gauge spinal needle and the injection bupivacaine 3ml solution will be injected intrathecally over 30 seconds. As per the group allocation injection dexmedetomidine 0.5 µg/kg in dilution of 10 ml in double-blinding was given 10mins before or 30 mins after intrathecal spinal anaesthesia over 1 min. Level of sensory loss was assessed by pin-prick test in mid axillary line. Mean arterial pressure, heart rate and oxygen saturation (SpO2) was monitored regularly and for study purpose before, after dexmedetomidine infusion at 5, 15, 45, 75, 120, and 180 minutes.

3.6.Visual Analogue Scale (VAS)

Postoperative pain was assessed by the patient using the visual analogue scale (VAS; 0=no pain; 10=worst possible pain) at 4, 8, 12, and 24 hour (hr). In addition, the overall 24-hr pain VAS was evaluated by the overall pain impression of the patient for 24 hr post operatively.[11]

3.7.Modified bromage scale

Modified Bromage Scale was used to assess motor blockade. Motor
blocked assessed every 5, 15, 45, 75, 105, 120 and 180 mins.
Bromage 0- the patient is able to move the hip, knee and ankle;
Bromage 1- the patient is unable to move the hip, but is able to move the knee and ankle;
Bromage 2- the patient is unable to move the hip and knee, but is able to move the ankle;
Bromage 3- the patient is unable to move the hip, knee and ankle.
All durations were calculated considering the time of spinal injection as time zero.[12]

3.8.Ramsay sedation scale

Ramsay Sedation Scale was used to assess level of sedation in all patients at every 5, 30, 60, 90 and 120 mins.

1-Patient is anxious and agitated or restless, or both.

2-Patient is co-operative, oriented, and tranquil.

3-Patient responds to commands only. 4-Patient exhibits brisk response to light glabellar tap or loud auditory stimulus.

5-Patient exhibits a sluggish response to light glabellar tap or loudauditory stimulus.

6- Patient exhibits no response.[13]

Duration of effective analgesia was measured from the time of intrathecal drug administration to the patient's first request for analgesia. Patients were also assessed for the side effects like nausea, vomiting, bradycardia and hypotension (systolic arterial pressure below 100 mm Hg, a decrease in the initial systolic arterial pressure of 20% from baseline, or both).[14]

IV. Results Figures And Tables

Table 1: Demographic profile of the study groups.

Variables	After Spinal (n=30)	Before Spinal (n=30)	P value
Age(yrs)	43.03±11.56	42.17±14.14	0.796
Sex(M:F)	20:10	18:12	0.592
Weight(kg)	58.13±8.40	59.33±9.64	0.609
Height(cm)	158.10±8.04	158.33±7.93	0.910
BMI (kg/m^2)	23.31±3.36	23.75±4.08	0.650

Data are presented as means ± standard deviation and ratio. There was no statistically significant difference in distribution of age, height, weight and sex in three groups (p>0.05).

Table 2 : Comparison of Heart rate (BPM) in two groups of patients studied

Heart Rate	After Spinal	Before Spinal	P value
Baseline	79.10±4.85	81.57±5.20	0.062+
5 min	83.67±4.57	85.03±4.90	0.268
10 min	87.47±4.39	89.40±4.95	0.115
15 min	83.93±3.00	84.93±3.41	0.233
45 min	83.90±5.19	86.20±4.23	0.065+
75 min	83.63±3.27	85.53±3.94	0.047*
120 min	81.10±4.03	81.97±3.96	0.404

Intra-operative heart rate was statistically significant between the Group A vs B at 75 min (p-0.047).

Table 3: Comparison of SBP (mm Hg) in two groups of patients studied

SBP (mm Hg)	After Spinal	Before Spinal	P value
Baseline	123.93±9.46	119.67±9.16	0.081+
5 min	112.70±8.87	110.73±9.25	0.404
10 min	108.17±8.12	101.80±7.89	0.003**
15 min	109.63±8.57	109.63±6.90	1.000
45 min	114.40±6.90	113.87±5.86	0.748
75 min	114.93±7.24	115.03±7.41	0.958
120 min	117.90±8.93	116.33±7.00	0.453

Intra-operative systolic blood pressure was statistically significant between the Group A and Group B at 10min (p=0.003)

Table 4: Comparison of DBP (mm Hg) in two groups of patients studied

DBP (mm Hg)	After Spinal	Before Spinal	P value
Baseline	76.77±7.70	74.40±7.04	0.219
5 min	71.37±7.17	71.77±7.31	0.831
10 min	69.67±6.00	67.57±7.78	0.247
15 min	73.03±4.47	70.53±6.54	0.089+
45 min	76.47±3.89	73.03±7.06	0.023*
75 min	77.13±4.17	73.37±5.60	0.005**
120 min	75.43±4.93	74.53±6.71	0.556

Intra-operative diastolic blood pressure was statistically significant between the Group A and Group B at 45min (p=0.023) and 75 min (p=0.005)

Table 5: Comparison of MAP (mm Hg) in two groups of patients studied

MAP (mm Hg)	After Spinal	Before Spinal	P value
Baseline	92.17±7.72	89.43±5.67	0.123
5 min	85.17±7.21	84.77±7.00	0.828
10 min	82.53±6.00	78.97±7.18	0.041*
15 min	85.17±5.00	83.57±4.75	0.209
45 min	89.03±4.30	86.70±5.57	0.075+
75 min	89.83±4.43	87.03±5.83	0.041*
120 min	89.50±5.04	88.33±6.39	0.435

Intra-operative mean arterial blood pressure was statistically significant between the Group A and Group B at 10min (p=0.04) and 75min (p=0.04).

Table 6: Comparison of study variables in two groups studied

	After Spinal	Before Spinal	P value
Onset of sensory blockade	356.23±56.43	334.17±66.23	0.170
Height of sensory blockade	T4	T4	
Time to two segment regression	139.63±5.12	151.47±8.12	<0.001**
Time for complete motor recovery	205.33±10.82	201.60±12.29	0.217
Effective duration of analgesia	184.93±7.35	203.97±12.62	<0.001**
Sensory block was higher in group A (T4- 66%) than B (T4- 50%).Time for sensory regression of two blocks was 139.63 ± 5.12min and 151.47 ± 8.12 min in group A and B respectively.Duration of motor block was similar in both the groups. The time to first request for postoperative analgesia was after 184.93 ±7.35 and 203.97 ± 12.62 min in group A and B respectively.			

Table 7: VAS Score in two groups studied

VAS Score	After Spinal	Before Spinal	Total
0	0(0%)	0(0%)	0(0%)
1-3	5(16.7%)	19(63.3%)	24(40%)
4-6	25(83.3%)	11(36.7%)	36(60%)
7-10	0(0%)	0(0%)	0(0%)
Total	30(100%)	30(100%)	60(100%)
Mean ± SD	4.43±0.94	3.37±0.49	3.90±0.92

P<0.001**, Significant, Chi-Squarest test

In VAS score of 4-6 number of patients in group receiving test drug after spinal anaesthesia were more when compared to the group where test drug was given before spinal anaesthesia.

Table 8: No of rescue analgesia given in two groups studied

No of rescue analgesia given	After Spinal	Before Spinal	Total
1	5(16.7%)	19(63.3%)	24(40%)
2	11(36.7%)	11(36.7%)	22(36.7%)
3	14(46.7%)	0(0%)	14(23.3%)
Total	30(100%)	30(100%)	60(100%)

P<0.001**, Significant, Chi-Square test

In group A patients number of rescue analgesia required were more when compared to group B patients who did not require more than 2 doses of rescue analgesia.

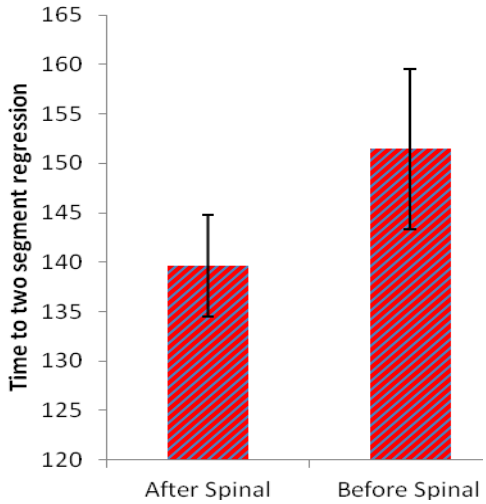

Fig 1.Showing Time to 2 segment regression of sensory block in 2 groups

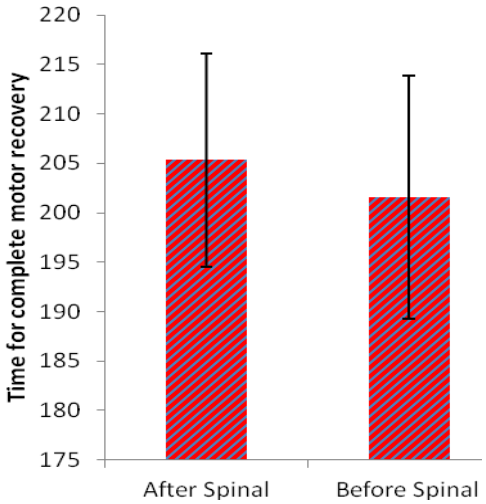

Fig 2. Showing Time to complete motor recovery in 2 groups

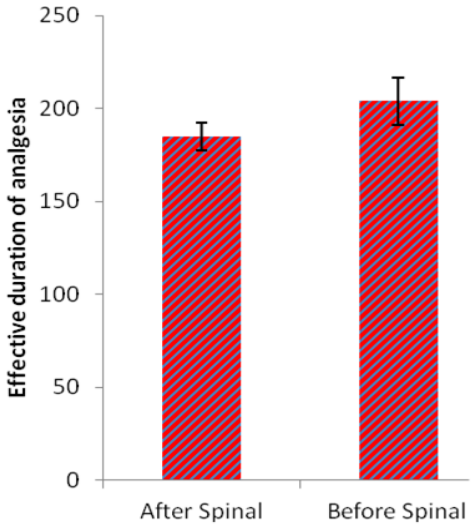

Fig 3. Showing effective duration of analgesia in 2 groups

V. Discussion

Spinal anesthesia remains one of the basic techniques in modern anesthesia despite waxing and waning of its popularity over many years since its introduction into clinical practices. Various drugs have been tried in the subarachnoid space along with local anaesthetics with the aim of improving the duration of post-operative analgesia.[15]

Recent studies have shown the efficacy of both intrathecal and IV dexmedetomidine in prolonging spinal anesthesia. Different drugs have been used as adjuvant to local anesthesia in order to prolong the duration of spinal analgesia.[9] Clonidine an α2 agonist, has been used widely in the intrathecal, oral and intravenous routes to prolong the duration of spinal analgesia.[16]

Dexmedetomidine is a more selective α2-A receptor agonist than clonidine, with α2:α1 binding ratio of 1620:1 compared to 220:1 for clonidine.[17,18] It has with more sedative and analgesic effects. Activation of presynaptic α2-A receptors at locus ceruleus decreases norepinephrine release and causes sedative and hypnotic effects, whereas its effect on descending medullo spinal noradrenergic path way results in analgesia by terminating pain signal propagation. At substantia gelatinosa of the spinal cord, it decreases firing in nociceptive neurons and release of substance P, thus producing analgesia.[9] So, dexmedetomidine has a role in modulating pain and inhibiting the transmission and perception of pain. Activation of post-synaptic α2-A receptors in CNS results in hypotension and bradycardia by decreasing the sympathetic activity. Activation of post-synaptic α2-C receptors in CNS results in anxiolysis, whereas activation of post-synaptic α2-B receptors in peripheral vasculature results in transient hypertension.[9] Side effects of dexmedetomidine, such as hypotension and bradycardia, are dose dependent.

Jorm et al. found that dexmedetomidine has an inhibitory effect on the locus ceruleus (A6 group) located at the brain stem. This supraspinal action could explain the prolongation of spinal anesthesia after intravenous administration of dexmedetomidine.[19] Dexmedetomidine has been used intravenously in doses ranging from 0.1 to 10 μg/kg/h but higher doses have been associated with a significant incidence of bradycardia and hypotension.[20,21] Aantaa et al., concluded that "The optimal dose of dexmedetomidine for single dose intravenous premedication in minor surgery appears to be in the range of 0.33 to 0.67 μg/kg.[22] Jaakolaet al., demonstrated moderate analgesia with a ceiling effect at a dose of 0.5 μgkg−1. [23]Thus we selected a dose of 0.5 μgkg‑1 as premedication in our study.

In our study in Group A the time for first request of analgesia was at 184 mins compared to Group B where the first request of analgesia was at 203 mins ($p<0.05$). The motor block in Group C was stable during the first 75 mins and started to decrease at 184 mins. In Group A and B the motor block started to decrease at 205 and 203 mins respectively ($p>0.05$). Compared with the prolongation of the sensory block, the duration of motor block was not affected by dexmedetomidine. It could be explained that conduction of sensory nerve fiber might be more inhibited than motor nerve fiber at the same concentration of dexmedetomidine, as similarly reported with clonidine.[24]

In our study, the mean time for two-dermatomal regression of sensory blockade was significantly prolonged in Group B (151.47 ± 8.12 min) compared to Group A (139.63 ± 5.12). Hong et al reported that the mean time to two-segment regression was prolonged in the dexmedetomidine group (78 min vs. 39 min for cold and 61 min vs. 41 min for pinprick for dexmedetomidine group and control group, respectively).[25]

In previous studies, it has been shown that dexmedetomidine caused minimal respiratory depression.[26] There was no respiratory depression in any of our study patients. Respiratory parameters (respiratory rate and SpO2) remained within normal limits throughout our procedure.

VI. Conclusion

Sensory blockade was prolonged in group receiving dexmedetomidine 10 mins before intrathecal anaesthesia when compared with group receiving 30 mins after intrathecal anaesthesia. It also provided additional analgesia in group receiving before intrathecal anaesthesia.

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