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Research Article

A Comparative Prospective, Randomised, Double Blind Study of the Effect of IV Dexmeditomidine on Subarachnoid Block Versus 0.9 % Normal Saline as Control

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Abstract: The objective of the study was to evaluate the effect of intravenous dexmedetomidine on the duration of subarachnoid block, hemodynamic changes and sedation in patients undergoing surgeries under spinal anaesthesia with 0.5% of hyperbaric bupivacaine. It was a prospective randomised controlled double blind trial.100 ASA physical status I/II patients undergoing elective surgeries under spinal anaesthesia were randomized into two groups of 50 each. Immediately after subarachnoid block with 3 ml of 0.5% hyperbaric bupivacaine, group D patients received a loading dose of 1 µg/kg of dexmedetomidine intravenously by infusion pump over 10 mins followed by a maintenance dose of 0.5 µg/kg/hr till the end of surgery whereas group C received an equivalent quantity of normal saline by infusion pump. Time taken for regression to Modified Bromage Scale 0, level of sensory block, two dermatomal regression of sensory blockade, duration of sensory block, intraoperative Ramsay sedation scores and time to first request for postoperative analgesic were higher in group D compared to group C (p values < 0.001). The 24 hours mean analgesic requirement is less in group D than group C (p value < 0.001). In conclusion, intravenous dexmedetomidine significantly prolongs the duration of sensory and motor block of bupivacaine spinal anaesthesia with good hemodynamic stability.
Keywords: Dexmedetomidine, Hyperbaric bupivacaine, Intrathecal, Ramsay sedation scale, Spinal anaesthesia

INTRODUCTION

Subarachnoid block is the preferred anaesthetic technique for most of lower abdominal and lower limb surgeries. Lignocaine and Bupivacaine are two commonly used drugs for subarachnoid block. Bupivacaine is three to four times more potent than lignocaine [1] and has longer duration of action. Clonidine, an α2 adrenergic agonist, has been shown to result in the prolongation of the sensory and motor blockade and the reduction in the amount or the concentration of local anaesthetic required to produce post operative analgesia [2, 3]. Dexmeditomidine is a highly selective α 2-adrenoreceptor agonist, similar to clonidine.

Locus coeruleus is among the one having highest densities of of α2 receptors which is a predominant noradrenergic nucleus in the brain and an important modulator of vigilance. Activation of α2-adrenoceptor results in hypnotic and sedative effects in this site in the CNS. The locus coeruleus site for the descending medullospinal noradrenergic pathway is an important modulator of nociceptive neurotransmission. In this site, α2-adrenergic and opioidergic systems have common effector mechanisms, which indicates, dexmedetomidine has a supraspinal site of action [4]. Thus, major sedative and antinociceptive effects of dexmedetomidine are due to its stimulation of the α2 adrenoceptors in the locus coeruleus. Moreover, studies in transgenic mice have identified that the α2A-adrenoceptor subtype is responsible for relaying the sedative and analgesic properties of dexmedetomidine [5]. Dexmedetomidine is much more effective sedative and analgesic agent than clonidine due to its improved specificity for the α2A receptor, with much less α1 effects [4].

It has been used safely as premedication or as a sedative agent in patients undergoing surgical procedures under regional anesthesia [6]. The use of dexmedetomidine as adjuvant in regional anaesthesia is still not validated [7]. Dexmedetomidine is used as an adjuvant in epidural, spinal and intravenous regional anaesthesia.

This study is done to evaluate the prolongation of spinal analgesia by the intravenous dexmedetomidine administration after the subarachnoid block, and to assess the hemodynamic changes and the level of sedation on lower abdominal and lower limb surgeries.

MATERIALS AND METHODS

This is a prospective randomised double blind study control study done on 100 patients undergoing elective surgeries. It was conducted at Mamata General Hospital, Khammam, Andhra Pradesh, during the period October 2011 to September 2013 by obtaining approval from institutional ethical committee. After a thorough clinical examination and relevant laboratory investigations of all patients, an informed, valid, written consent was obtained, both for conduct of study as well as administration of spinal anaesthesia.

All patients were kept nil by mouth from midnight before surgery and tablet diazepam 5mg was administered at bed time the day before surgery. And the patients were re-examined, assessed and weighed pre-operatively on the day of surgery. Intravenous access was established with an 18G intravenous access and preloading was done with 15 ml/kg Lactated Ringer's solution 30 minutes before procedure. Anaesthesia machine and accessories were checked and drugs, including emergency drugs like atropine were kept ready. Also monitoring equipments like pulse oximeter, non invasive blood pressure (NIBP) and electrocardiogram (ECG) monitors were checked and applied to each patient on arrival to the operating room and baseline parameters were recorded.

All the patients were randomly allocated into two groups of 50 each using computer generated random numbers by simple randomization technique.

- Group D (dexmedetomidine): This group of individuals were administered with bupivacaine and dexmedetomidine.
- Group C (Control): This group of individuals were administered with bupivacaine and saline group.

Preparation and dosage

Dexmedetomidine hydrochloride was diluted in 0.9% normal saline (1:2 ratio) prior to injection. Dexmedetomidine is generally initiated with a loading infusion of 1 μg/kg over 10 min followed by a maintenance infusion of 0.2 - 0.7 μg/kg/hour. The rate was adjusted to maintain the desired level of response.

- Under strict aseptic conditions, with the patient in the sitting position, a lumbar puncture was performed at L3-L4 intervertebral space. After ensuring free flow of CSF, subarachnoid block was performed with 3 ml of 0.5% hyperbaric bupivacaine.
- Group D patients received a loading dose of 1 μg/kg of dexmedetomidine intravenously by infusion pump over 10 mins followed by a maintenance dose of 0.5 μg/kg/hr till the end of surgery.
- Group C patients received an equivalent quantity of normal saline as loading and maintenance dose intravenously by infusion pump and served as control.

  After the various treatments, the above groups were monitored regularly for baseline reading of pulse rate, blood pressure, arterial oxygen saturation (SPO_2), respiratory rate and foetal heart sounds and following parameters were recorded.

Assessment of Sensory blockade

Sensory blockade was assessed for every 2 mins for the first 10 mins and thereafter every 15 mins during surgery and postoperatively. All the durations were calculated considering the time of spinal injection as time 0. Motor blockade was assessed by Modified Bromage Scale [8].

Table 1: Modified Bromage scale

Grade	Criteria	Degree of block
0	Able to move the hip, knee and ankle	None
1	Unable to move the hip, but is able to move the knee and ankle	Partial 33%
2	Unable to move the hip and knee, but is able to move the ankle	Partial 66%
3	Unable to move the hip, knee and ankle	Complete paralysis

The level of sedation was evaluated using Ramsay Level of Sedation Scale [9].

Table 2: Ramsay sadation score

Scale	Level of sedation
1	Patient anxious, agitated, or restless
2	Patient cooperative, oriented, and tranquil alert
3	Patient responds to commands
4	Asleep, but with brisk response to light glabellar tap or loud auditory stimulus
5	Asleep, sluggish response to light glabellar tap or loud auditory stimulus
6	Asleep, no response

The level of sedation was evaluated both intra operatively and post operatively every 15 mins using Ramsay Level of Sedation Scale till the patient is discharged from PACU. Excessive sedation was defined as score greater than 4/6.

Hypotension (systolic blood pressure less than 90 mm Hg or more than 20% fall from baseline value) bradycardia (heart rate <50/min) and post operative complications like nausea and vomiting were noted and treated appropriately. Numbers of patients requiring supplemental analgesia (1 µg/kg body weight of Fentanyl) intra operatively were noted. Time for first request for postoperative analgesic (duration of analgesia) was noted. Patients were given 20 mg/kg (maximum upto 1.2gm) IV paracetamol initially when the patient complained of pain. Diclofenac 75 mg IM was given if patient still complained of pain even after 30 mins after paracetamol infusion. Tramadol 50 mg slow IV was given if patient still complained of pain even at 30 mins after diclofenac administration.

Statistical analysis

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented as Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Chi-square / Fisher Exact test was used to find the significance of study parameters on categorical scale between two or more groups. Paired samples T test was used to find the significance of study parameters on continuous scale within the group (intra group analysis) on metric parameters. Student T test (two tailed, independent samples) was used to find the significance of study parameters on continuous scale between two groups (inter group analysis) on metric parameters. Significance is assessed at 5 % level of significance. p value <0.05 was considered significant.

RESULTS

This study was carried out on a total number of 100 patients operated under spinal anaesthesia. The total amount of dexmedetomidine given in dexmedetomidne group was 126.5±27.4mg (Bolus- 60.66±11.7 mg, Maintenance dose- 66.3±20.6 mg). Demographic data, intraoperative and postoperative hemodynamics/Respiratory rate/ oxygen saturation/ Ramsay sedation score, postoperative analgesia and side effects were compared between tested Dexmedetomidine group (Group D) and Control group (Group C).

Demographic data

Age

The mean age in the dexmedetomidine group was 35.04 ± 9.19 yrs as compared to 35.24 ± 9.14yrs in the control group and the difference was statistically not significant (p value-0.878). There was no statistically significant difference in age distribution in both groups as summarized in Table 3.

Table 3: Comparison of age distribution in both the groups

Age (yrs)	Group D		Group C		p value
	No	%	No	%	
20 to 30	19	38	19	38	0.878
30 to 40	16	32	18	36	
40 to 50	15	30	13	26	
Total	50	100	50	100	
Mean age ± S.D	35.04±9.19		35.24±9.14		

Gender

Gender distribution in both the groups is summarized in Fig. 1. There was no statistically significant difference between the two groups in gender distribution (p value- 0.663).

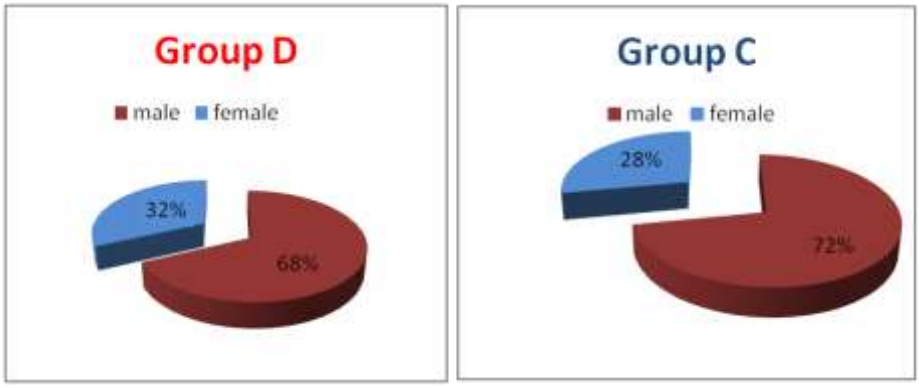

Fig. 1: Pie diagram showing gender distribution in both the groups

Weight

The mean weight in the dexmedetomidine group was 61.14 ± 7.67 kgs as compared to 59.44 ± 6.36 kgs in bupivacaine group and the difference was statistically not significant (p value- 0.517) .There was no statistically significant difference in weight distribution in both groups as summarized in Table 4.

Table 4: Weight distribution in both the groups

Weight (kgs)	Group D		Group B		p value
	No	%	No	%	
≤ 50	6	12	5	10	0.517
51-60	15	30	22	44	
61-70	24	48	20	40	
>70	5	10	3	6	
Total	50	100	50	100	
Mean+SD	61.14 ± 7.67		59.44 ± 6.36		

ASA Grade

ASA grade in both the groups is summarized in Fig. 2. There was no statistically significant difference between the two groups in ASA grade (p value- 0.663).

SURGICAL PROCEDURES:

Type of surgeries in both the groups is summarized in Table 5. There was no statistically significant difference between the two groups (p value- <0.001).

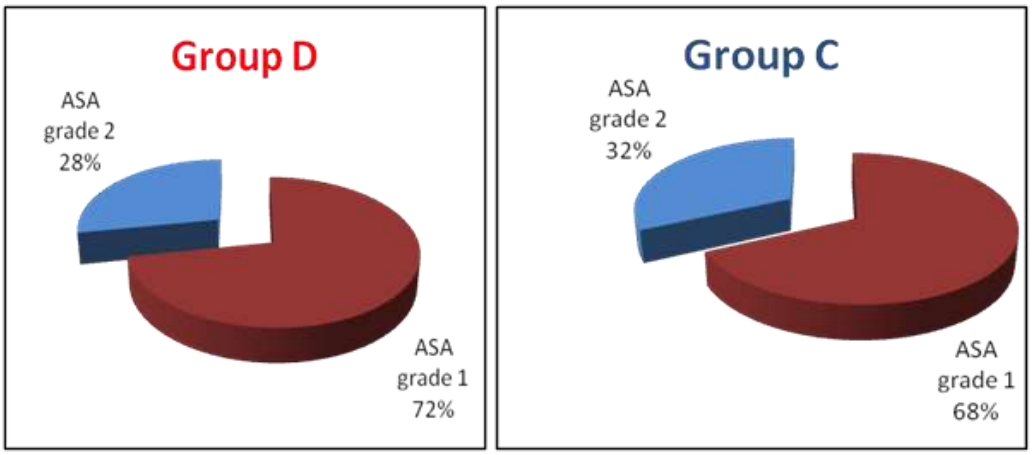

Figure 2: Pie diagram showing ASA Grade in both the groups

Table 5: Type of surgeries

Type of surgery	GROUP D		GROUP C		p -value
	No	%	No	%	
Orthopaedic	32	64	29	58	<0.001
Gynaecology	8	16	9	18	
Gen surgery	10	20	12	24	
Total	50	100	50	100	

Duration of sensory and motor blockade

The duration of sensory blockade, duration for 2 dermatomal regression of sensory blockade and the duration for motor block regression to Modified Bromage scale 0 were significantly prolonged in dexmedetomidine group as compared to control group (p value <0.001). The highest level of sensory blockade was significantly higher in dexmedetomidine group (p value <0.001). There was no difference in the time for attaining highest level of sensory blockade, time taken for motor blockade to reach Modified Bromage Scale 3 between both the groups. The motor and sensory blockade in both the groups is summarized in Table 6-8.

Table 6: Comparison of sensory and motor blockade in both groups

	Group D	Group C	p value
Highest level of sensory block [dorsal]	T 6.88±1.1	T 7.66±0.8	<0.001
Time for attaining highest level of sensory block	11.6±1.9 mins	11.9±2.1mins	0.407
Duration for 2 dermatomal regression of sensory blockade	137.4±10.9 mins	102.8±14.8 mins	<0.001
Duration of sensory blockade	269.8±20.7 mins	169.2±12.1 mins	<0.001
Duration for motor blockade to reach Modified Bromage scale 3	5.38±1.5 mins	5.04±1.9 mins	0.327
Duration for motor block regression to Modified Bromage scale 0	220.7±16.5 mins	131±10.5 mins	<0.001

Table 7: Comparison of duration for 2 dermatomal regression of sensory blockade in both the groups

Duration for 2 Dermatomal regression (minutes)	Group D		Group C		p value
	No	%	No	%	
50-75	0	0	3	6	<0.001
76-100	1	2	17	34	
101-125	7	14	29	58	
126-150	37	74	1	2	
151-175	5	10	0	0	
T0tal	50	100	50	100	

Table 8: Comparison of duration of sensory blockade in both the groups

Duration of sensory Blockade (minutes)	Group D		Group C		p value
	No	%	No	%	
140-180	0	0	43	86	<0.001
181-220	1	2	7	14	
221-260	14	28	0	0	
>260	35	70	0	0	
Total	50	100	50	100	

DISCUSSION

This study was done in 100 adult ASA grade I/II patients undergoing surgeries under bupivacaine spinal anaesthesia in Mamata General Hospital, Khammam. Patients were randomly allocated to dexmedetomidine and control groups. Immediately after subarachnoid block with 3 ml of 0.5% hyperbaric bupivacaine, patients in dexmedetomidine group (group D) received a loading dose of 1 µg/kg of dexmedetomidine intravenously by infusion pump over 10 mins followed by a maintenance dose of 0.5 µg/kg/hr till the end of surgery whereas the control group (group C) received an equivalent quantity of normal saline as loading and maintenance dose intravenously by infusion pump and served as control. The objective of the study was to compare the duration of sensory and motor block, sedation scores, intra-operative haemodynamic stability of the patients, intraoperative and postoperative analgesia and side effects between the groups

Drugs such as epinephrine, phenylephrine, adenosine, magnesium sulphate, sodium bicarbonate, neostigmine and α 2 agonists like clonidine, dexmedetomidine are used as adjuvants to local anaesthetics in order to prolong the duration of spinal anaesthesia. Among them clonindine an α 2 agonist is widely used by oral, intrathecal and intravenous routes. Efficacy of both intrathecal and intravenous dexmedetomidine prolong spinal anaesthesia. Dexmedetomdine is a more suitable adjuvant to spinal anaesthesia compared to clonidine as it has more sedative and analgesic effects due to its more selective α 2A receptor agonist activity. Systemic and intrathecal injection of dexmedetomidine produces analgesia by acting at spinal level, laminae VII and VIII of ventral horns [10]. The drug also acts at locus ceruleus and dorsal raphe nucleus to produce sedation and analgesia [11]. This supra spinal action explains the prolongation

of spinal anaesthesia after intravenous dexmedetomidine [12].

In the present study results shown that, time for attaining highest level of sensory block is comparable in dexmedetomidine and control groups. The median highest cephalad level of sensory block T 4 (T 3 – T8) was attained in 15 min in dexmedetomidine and control groups in a similar study by Whizar-Lugo *et al*. [13] The highest level of sensory block was higher in dexmedetomidine group (T 6.8 ± 1) compared to control group (T 7.66 ± 0.8) in our study. This observation is also comparable to the study done by Kaya *et al*. [14] They observed sensory block to be higher in dexmedetomidine group (T 4.6 ± 0.6) than control group (T 6.4 ±0.8).

Sensory blockade was checked with an alcohol swab in mid axillary line and the time taken for the highest level of sensory blockade, two dermatomal regression from the maximum level and regression to S1 level were noted. Motor blockade was assessed by Modified Bromage Scale. Time taken for motor blockade to reach Modified Bromage Scale 3 and regression of motor blockade to Modified Bromage Scale 0 was noted. The hemodynamic stability was assessed by heart rate, systolic, diastolic and mean arterial pressures. The level of sedation was evaluated using Ramsay Level of Sedation Scale. Analgesic requirements were compared by 24 hr analgesic consumption after surgery and the time for first demand of rescue analgesic. We noted significant prolongation in the time for 2 dermatomal regression of sensory block, duration of sensory block and time taken for regression of motor blockade to Modified Bromage scale 0.

In our study mean time for two dermatomal regression of sensory blockade was significantly prolonged in dexmedetomidine group (137.4 ± 10.9 mins) compared to control group (102.8 ± 14.8). Significant prolongation in mean time for two dermatomal regression of sensory blockade was also reported by other authors, Kaya *et al*. [14] 145 ± 26 min *vs* 97 ± 27 mins, Tekin *et al*. [15] 148.3 mins *vs* 122.8 mins in dexmedetomidine and control groups respectively. Similarly Hong *et al*. [16] reported that the mean time to two-segment regression was prolonged in dexmedetomidne group (78 mins vs 39 mins for cold, 61 mins vs 41 mins for pinprick) for dexmedetomidine group and control group respectively]. Similar results were reported by Elcıcek *et al*. [17].

The duration of sensory blockade i.e. time for regression to S1 dermatome was significantly prolonged in dexmedetomidine group (269.8 ± 20.7 min) compared to control group (169.2 ± 12.1) in our study. Significant prolongation in mean duration of sensory blockade in dexmedetomidine group was also reported by others, Al Mustafa *et al*. [18] 261.5 ± 34.8 min *vs* 165.2 ± 31.5 min, Whizar-Lugo *et al*. [13] - 208±43.5 mins vs 137±121.9 mins in dexmedetomidine and control groups respectively.

In the present study there was no significant difference in time taken for motor blockade to reach modified Bromage Scale 3 in both the groups (5.38 ± 1.5 min) in dexmedetomidine group compared to 5.04 ± 1.9 min in control group. However, the regression time to reach the modified Bromage Scale 0 was significantly prolonged in dexmedetomidine group (220.7 ± 16.5 mins) compared to control group (131.6 ± 10.5 mins). Delay in motor block regression to Bromage Scale 0 was also reported in previous studies by Al Mustafa *et al*. [18] 199 ± 42.8 min in *vs*138.4 ± 31.3 min, Whizar-Lugo *et al*. [13] 191±49.8 mins *vs* 172±36.4, Tekin *et al*. [15] 215 mins *vs* 190.8 mins for dexmedetomidine group and control group respectively. Elcıcek *et al*. [17] and Hong *et al*. [16] also found that complete resolution of motor blockade was significantly prolonged in dexmedetomidine group. But contrary to all the above studies, Kaya *et al*. [14] reported no significant prolongation in the duration of motor block in dexmedetomidine group compared to control group.

From the present study it can be concluded that, intravenous dexmedetomidine is extremely effective in prolonging the duration of motor and sensory blockade after bupivacaine spinal anaesthesia. It provides good sedation during surgery which quickly reverses after stopping the drug.

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