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Safety and Efficacy of Dexmedetomidine as an Adjuvant to Hyperbaric Bupivacaine: A Randomised Double-Blind Controlled Study

S.V. Ravikanth[1], P. Ravi Kumar[2], Anand Acharya[3]

[1]Associate Professor, Dept. of Anaesthesia, [2]Post Graduate, [3]Professor, Dept. of Pharmacology, Konaseema Institute of Medical Science, Amalapuram, Andhra Pradesh 533201, India.

Abstract

Background: Various adjuvants are co-administrated with local anaesthetic agent to improve the speed of onset of block, duration of analgesia and can decrease the dose of local anaesthetic agent. As the dose of local anaesthetic decreases, its adverse drug reaction also used to decrease specifically Bupivacaine. Present study has been designed to evaluate the, efficacy and safety of dexmedetomidine as an adjuvant to bupivacaine in spinal anaesthesia. *Method:* This is a randomised, double blind, prospective comparative study conducted in the department of anaesthesia, Based on inclusion and exclusion criteria 72 patients were enrolled for this study. These patients were randomly allocated in to two groups Group B and Group BD. Sensory parameters like, onset of sensory block; total duration of sensory block was recorded using pin prick method. Motor block was assessed with modified Bromage score. Time for onset and duration of motor block was recorded. *Result:* Mean time required for the onset of sensory block in group B was 3.24 + 1.34min and in Group B, it was 2.42 + 0.84 min. This difference is statistically significant. The P value was 0.006. The mean duration of sensory block was 181.07 + 20.8 min in group B and 263.6+38.8 min in group BD. This difference was significant statically (p=0.00001). The mean time for onset of motor block was 8.31 + 1.84 min in group B and 7.94 + 32.0 in group BD. This difference is not significant statistically. The p value was 0.1428. *Discussion and Conclusion:* From present study we conclude that 5 microgram dexmedetomidine as an adjuvant to hyperbaric bupivacaine prolong the duration of sensory and motor block. It provides good quality of analgesia, haemodynamic stability and prolongs post-operative analgesia.

Keyword: Dexmedetomidine; Adjuvant; Hyperbaric Bupivacaine; Spinal Block

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Introduction

Acute post operative pain is a normal response to surgical procedure. The pain induced reflexes brings various physiological changes that lead to surgical stress. Effective pain management is primary concern for patients and surgeon [1,2]. There are various techniques available to decrease pain in post surgical period and thereby reduces surgical stress and improve the process of recovery. Spinal anaesthesia is a commonly used regional anaesthesia technique for lower abdomen and limb surgeries. Snezana B M et al. and H. Kehlet et al. has concluded that based on endocrinal, hemodynamic

Corresponding Author: Anand Acharya, Professor, Department of Pharmacology, Konaseema Institute of Medical Science, Amalapuram, Andhra Pradesh 533201, India.

E-mail: anand_kims@yahoo.co.in

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and metabolic responses, spinal anaesthesia proved to be more effective than general in suppressing stress response in elective surgical patients [3,4] The quality of spinal anaesthesia depends upon the pharmacology of local anaesthetic used that is concentration, specific gravity, volume, speed of injection and posture of the patient. Hyperbaric bupivacaine is the most common local anaesthetic agent used for subarachnoid block [5].

Various adjuvants are co-administrated with local anaesthetic agent to improve the speed of onset of block, duration of analgesia and can decrease the dose of local anaesthetic agent. As the dose of local anaesthetic decreases, its adverse drug reaction also used to decrease specifically Bupivacaine [6]. Drugs used as adjuvant are adrenaline, α2 adrenergic agonist, neostigmine, Ketamine, midazolam, opioids, anti-inflammatory drugs and steroids.

Dexmedetomidine is a α2 adrenoreceptor agonist in view of its diverse action like, analgesic, sedative, anaesthetic sparing and cardiovascular stabilising effect, it is used as an adjuvant to various local anaesthetic agent [7,8]. It activates α2 AR in spinal cord and reduces transmission of nociceptive signals [9].

Tazim Mohamed et al. have concluded in his study that dexmedetomidine with lower doses of bupivacaine produces satisfactory anaesthesia without hemodynamic instability. SS nehtra et al has also reported that it prolong post operative analgesia, duration of motor blockade, and time ofambulation [10,11] Based on these finding present study has been designed to evaluate the, efficacy and safety of dexmedetomidine as an adjuvant to bupivacaine in spinal anaesthesia.

Materials and Methods

This is a randomised, double blind, prospective comparative study conducted in the department of anaesthesia, Konaseema institute of medical science Amalapuram A.P from 2016 to December 2018.

Selection of subject

Based on inclusion and exclusion criteria patients posted for elective surgeries below umbilical level were enrolled for study.

Inclusion criteria.	Exclusion criteria.
Age 18 to 60yrs	Contraindication for spinal block
Both sex	
ASA score I/II	Pre-existing cardiac and neurological problem
	Hypersensitivity to drug.
	Emergency surgery

Sample size: The sample size collected to be 36 as desired confidence level of 95% and an absolute precision of 4% using nMasters version 2.0 Software. So based on our exclusion and inclusion criteria 72 patients were enrolled for this study [12].

Method

Based on inclusion and exclusion criteria 72 patients were enrolled for this study. These patients were randomly allocated in to two groups Group B and Group BD. Each group have 36 patients. Computer generated randomization table was used for allocation of patients. Pre-anaesthetic evaluation was done for all patients. The procedure of sub arachnoid block was explained to all patients. Patients were explained about the use of visual analogue scale (VAS). All patients were given similar premedication after shifting into the operation theatre, intravenous access was scored with 18G I.V needle, and were preloaded with 15 ml/kg ringer's lactate 15 mins before surgery. Base line vital like SBP, DBP, HR, SP02, were recorded under all aseptic conditions lumber puncture was performed at L3-L4 space using 25G quincke spinal needle.All person involved in providing medication were blinded. Anaesthesiologist who prepared the drug was not aware about the study of drug.

Group B: Patients enrolled in group received 3 ml (0.5% hyperbaric bupivacaine + normal saline 0.5 ml).

Group BD = Received 3 ml (0.5% bupivacaine + 5ug dexmedetomidine (0.5 ml).

Intra operatively pulse rate, non invasive blood pressure, electrocardiogram, spo_2 was recorded every 2 min for first 10 min, every 5 min for next 30 min, every 10 min for next 60 min, and every 15 min till end of surgery.

Sensory parameters like, onset of sensory block, total duration of sensory block was recorded using pin prick method. Motor block was assessed with modified Bromage score (13). Time for onset and duration of motor block was recorded.

Bromage 0 -	The patient is able to more the hip, knee, and ankle.
Bromage 1 -	Unable to more the hip but is able to more the knee and ankle.
Bromage 2 -	Able to more the ankle
Bromage 3 -	Unable to move any Joint.

Modified Ramsay sedation scale was used for intra operative sedation, [14] 1= restless, 2= cooperative, 3 = respond to verbal commands, 4 = Brisk response to glabellartap, 5= sluggish response to glabellar tap, 6= No response. Hypotension was defined as 20% below base line heart rate below 50 per min was considered Bradycardia and was treated. Adverse drug effect if any was noted. Pain was assessed by visual analogue scale [15]. Scale ranges from 0 = no pain to 10 = severe pain. VAS more than 6 was given supplemental analgesia duration of analgesia was noted.

Statistical analysis: All data were analysed using SPSS version 19.0. Results were expressed as mean and percentage. The groups were compared by using unpaired t test and chi-square test. For all the tests a P value less or equal to 0.05 was considered significant

Results

In this study we have evaluated the efficacy and safety of dexmedetomidine as adjuvant to bupivacaine. Patients enrolled in this study were divided in to two groups, Group B and Group BD. Mean age of the patients in group B was 45.30 ± 7.14 years and Group BD was 44.44 ± 10.16 years. The p value was 0.3478. The sex ratio in Group B was 24/12 and group BD was 26/10. The p value was 0.6088. In group B the ASA score was I in 32 patients and II in 4 patients. In group BD ASA scare was I in 30 patients and II in 6 patients. The P value was 0.495. The Mean duration of surgery in Group B was 84.88 ± 20.18 min and 87.82 ± 22.7 min in group BD. The p value was 0.038. So both groups were comparable to each other regarding demographic profile. Table 1.

Regarding block characteristic of the patients, mean time required for the onset of sensory block in group B was 3.24 ± 1.34 min and in Group B, it was 2.42 ± 0.84 min. This difference is statistically significant. The P value was 0.006. The mean duration of sensory block was 181.07 ± 20.8 min in group B and 263.6 ± 38.8 min in group BD. This difference was significant statically (p=0.00001). The mean time for onset of motor block was 8.31 ± 1.84 min in group B and 7.94 ± 32.0 in group BD. This difference is not significant statistically. The p value was 0.1428. Table 2.

The mean duration of motor block was significantly higher in group BD then group B (292.94 ± 21.44 min VS 150.34 ± 12.3). The p value was 0.00001. The duration of analgesia was 201.4 2 ± 1.32 min in group B and 394.33 ± 28.72 min in group BD. This difference was statistically significant (p=0.00001).

Table 1: Demographic profile of patients.

Variables	Gr B (n=36) (mean + SD)	Gr BD (n=36) (mean + SD)	P value.
Age	45.30 + 7.14	44.44 + 10.16	0.3478
Sex m/f	24/12	2/10	0.6088
ASA I/II	32/4	30/6	0.495
Duration of surgery.	84.88 + 20.18	87.82 + 22.7	0.308

Table 2: Characteristics of block in two groups.

	Gr B (mean + SD)	Gr BD (mean + SD)	p value.
Onset of sensory block	3.24 + 1.34	2.42 + 0.88	0.006131
duration of sensory block	181.07 + 20.8	263.6 + 38.8	0.00001
Onset of motor block	8.31 + 1.84	7.94 + 32	0.1428
duration of motor block	156.34 + 12.73	292.94 + 21.44	0.00001
duration of analgesia	201.42 + 10.32	394.33 + 28.72	0.00001

Table 3: Hemodynamic parameters

Time interval	Heart rate		p value	Mean arterial pressure		p value
	Gr B	Gr BD		Gr B	Gr BD	
0	80.42 + 8.13	79.42 + 4.5	0.145	96.12 + 6.51	94.12 + 4.54	0.632
5	79.98 + 7.33	78.23 + 6.9	0.245	94.12 + 7.34	91.33 + 6.34	0.746
15	79.42 + 4.39	76.70 + 7.9	0.114	90.12 + 6.32	86.67 + 3.52	0.321
30	76.48 + 7.86	74.22 + 7.9	0.641	88.14 + 4.27	84.27 + 3.33	0.433
60	76.11 + 8.32	72.42 + 7.7	0.642	88.44 + 3.52	86.27 + 3.10	0.192
90	74.11 + 9.42	71.79 + 9.4	0.245	89.42 + 4.20	86.66 + 3.42	0.110

Table 4: Modified Ramsay sedation score

Time (mean)	Gr B (mean + SD)	Gr BD (mean + SD)	p value.
30 min	2.00 + 00	2.00 + 00	1
60 min	2.00 + 00	3.12 + 0.46	0.014
90 min	2.46 + 0.23	3.64 + 0.44	0.006
120 min	2.00 + 00	2.00 + 00	1

Table 5: Visual analogue score

Time (mean)	Gr B (mean + SD)	Gr BD (mean + SD)	p value.
6	2.94 + 0.46	0.00 + 00	0.0001
9	6.42 + 0.75	4.04 + 0.52	0.001
12	7.19 + 0.86	4.99 + 0.77	0.001
24 hr	6.89 + 0.12	3.04 + 0.22	0.0001

Table 6: Side effects in both groups

Side effects	Gr B	Gr BD
Vomiting	1	0
Hypertension	10	6
Bradycardia	2	0
Pruritis	0	0
Respiratory depression	0	0

As per table 3 regarding haemodynamic parameters were recorded. At 0 min the mean heart rate was 80.42 ± 8.13 per min in group B and 79.42 ± 4.5 per min in group BD. At 5 min the mean heart rate was 79.98 ± 7.33/min in group B and 78.23 ± 6.9/ min in group BD. The mean heart rate was 79.42 ± 15 min in group B and 76.70 ± 7.9/ min in group BD. After 90minmean heart rate was 74.11 ± 9.42 min in group B and 71.79 ± 9.4/ min in group BD, we have not observed any significant difference between two groups regarding haemodynamic parameter. The P value was more than 0.05. At 0 min the mean arterial pressure was 96.12 ± 6.51 mm of hg in group B and 94.12 ± 4.54 mm of hg in group BD. At 15 min the mean arterial pressure was 90.12 ± 6.32 mm of hg in group B and 86.67 ± 3.52 in group BD. At 30 min mean arterial pressure was 88.14 ± 4.27 mm of hg in group B and 84.27 ± 3.33 in group B. These finding are comparable to each other. There is no statistical significance difference between two group.

From table 4 the modified Ramsay sedation score was 2.00 in both groups at 30 min. The mean Ramsay sedation score was 2.00 ± 00 in group B and 3.12 ± 0.46 in group BD. This difference was significant statistically. After 90 min the mean modified Ramsay score was 2.46 ± 0.23 in group B and 3.64 ± 0.44 in in group BD. The p value was 0.06. The Ramsay score was 2.00 in both groups after 120 min.

As per table 5 the visual analogue scale (VAS) was significant low in group BD then group B. At 6 hr the mean VAS score in Group B was 2.94 ± 0.46 and in group BD it was 0.00. After 24hr the mean VAS score was 6.89 ± 0.12 in group BD and 3.04 ± 0.22 in group BD.

In table 6 we have observed that the hypotension and Bradycardia was more common in group B then group BD. Other side effects were equally present or absent in both groups.

Discussion

Spinal anaesthesia is most preferred anaesthesia technique for intra-umbilical surgeries. The success of spinal anaesthesia depends upon the local anaesthetic agent used. Hyperbaric bupivacaine is used most commonly for sub-arachnoid block. To shorten the onset and prolong the duration of block various adjuvants are used along with bupivacaine. Present study has been conducted to elucidate the efficacy and safety of dexmedetomidine as an adjuvant to bupivacaine.

In present study both groups were comparable to each other with regard to various demographic profiles. The value was always greater than 0.05. This finding is supported by the finding of Mohamed T et al. [16]

Regarding sensory block characteristic between two groups, the mean time for onset of sensory block

significantly reduced in dexmedetomidine adjuvant group then bupivacaine alone (2.46 ± 0.88 min VS 3.25 ± 1.34 min). The duration of sensory block was significantly prolonged in adjuvant drug group than the bupivacaine alone group. This finding corroborates with the finding of Elshalakany NA et al. [17] Routray et al has reported that time for onset of sensory block has decreased but not significant and the duration of sensory block was significantly decreased in adjuvant group. This is partially corroborating with our finding [18].

Regarding motor characteristic of block the onset of motor block was early in adjuvant group but was not significant statistically (7.94 ± 32 min vs 8.31 ± 1.84 min) (p=0.1428). But the duration of block was significantly prolonged in adjuvant group. This is supported by the finding of Xia F et al. [19]

Duration of analgesia was significantly longer in dexmedetomidine adjuvant group (394.33 ± 28.72 min vs 201.42 ± 10.32 min). So dexmedetomidine potentiate analgesia action of bupivacaine. The analgesia action of dexmedetomidine is due to depression of release C- fibre transmitters and by hyperpolarisation of post synaptic dorsal horn neurons. This is supported by the study of Rajini Gupta et al. and EisanachJc et al. [20,21].

We have observed that. There is no significant difference between hemodynamic parameter between two groups, which is supported by the work of Gupta R et al. and Mohamed T et al. [16,20]

Hemodynamic was stablein bothgroups. There is no significant difference the mean arterial pressure and heart rate between two groups. This finding is supported by the work of Elshalakany NA et al. [17]. but the number of patients developing hypotension and Bradycardia was less common in dexmedetomidine group. Ramsay sedation score was also better in dexmedetomidine group than bupivacaine alone. This finding corroborates with the finding of Safari et al. [22]. Visual analogue score was significantly low in dexmedetomidine adjuvant group then bupivacaine group. This finding corroborates with the study of Staikuc et al. [23,17]. The number of patients developing hypotension and Bradycardia was less common in dexmedetomidine group. There was no difference between other adverse drug reaction. This finding is supported by Routray SS. et al. [18]

Conclusion

From present study we conclude that 5 microgram dexmedetomidine as an adjuvant to hyperbaric bupivacaine prolong the duration of sensory and motor block. It provides good quality of analgesia, haemodynamic stability and prolongs post-operative analgesia.

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