

Original Research Article

Comparison of dexmedetomidine and clonidine with hyperbaric bupivacain in spinal anaesthesia

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Received: 18 September 2021

Revised: 16 October 2021

Accepted: 27 October 2021

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ABSTRACT

Background: Alpha-2 adrenergic agonists used as adjuvant to spinal anaesthesia produce substantial sensory and motor blockade of bupivacaine. This study was planned to compare the sensory and motor blockade characteristics of intrathecal combinations of adjuvants dexmedetomidine and clonidine with hyperbaric bupivacaine in the cases who underwent lower limb surgery under spinal anaesthesia.

Methods: This was prospective, randomized, double blind study. 90 patients of age group between 18-60 years, ASA grade I and II were allotted into 3 equal groups. Group B received 15 mg bupivacaine plain, group BD and BC received dexmedetomidine (5mcg) and clonidine (50mcg) as adjuvants to bupivacaine respectively.

Results: The duration of 2 dermatome regression time, sensory blockade and motor blockade were longest in dexmedetomidine group (129.37±4.87; 386±58.43; 353±48.87) in compared to clonidine (109.77±5.95; 296.53±57.19; 269.7±51.2) and bupivacaine group (81.03±6.83; 211.1± 30.47;181.03±20.8). Both drugs do not affect the peak level of sensory blockade, sensory block onset and motor block onset time. Dexmedetomidine and clonidine do not cause sedation in intraoperative and postoperative period.

Conclusions: We conclude that addition of dexmedetomidine and clonidine in spinal anesthesia with hyperbaric bupivacaine increase the duration of '2 dermatome regression' time, sensory and motor blockade and both are more with dexmedetomidine than with clonidine.

Keywords: Dexmedetomidine, Clonidine, Bupivacaine, SAB

INTRODUCTION

Anaesthesiologists have succeeded, to a considerable extent, in rendering the patient pain free during surgery, but once the surgery is over, the patient might face the misery of postoperative pain. Various techniques and methods of postoperative pain relief have been advocated such as analgesic agents, but The most widely used method of postoperative pain relief are pharmacological drugs, especially opioids and nonsteroidal anti-inflammatory drugs. The local anesthetic drugs used intrathecally have a limited duration of action, research was done to find various approaches and adjuvants, which could prolong sensory analgesia. Epidural and subarachnoid adjuvants have provided a means of

prolonging post-surgical pain relief and subsequent patient satisfaction.

Dexmedetomidine and clonidine, both increase the analgesic duration when used as adjuvant in intrathecal anesthesia. Dexmedetomidine is 8 to 10 times more specific for alpha-2 receptors than clonidine and inhibits the release of norepinephrine.¹⁻⁴ Activation of postsynaptic alpha-2 receptors in the CNS however, inhibits sympathetic activity and can thus decrease blood pressure and heart rate. The present randomized prospective study was undertaken to compare the prolongation in the duration of sensory and motor block when dexmedetomidine and clonidine used as adjuvant with bupivacaine 0.5% heavy in intrathecal anesthesia.

METHODS

Study design, duration and location

Current study is a prospective, randomized, controlled, double-blind study, conducted from September 2014 to October 2015, at Sri Aurobindo medical college and PG institute, Indore, Madhya Pradesh.

Inclusion criteria

Inclusion criteria for current study were; ASA grade I & II, patient aged 18-60 years of either sex, BMI less than 35 kg/m² and posted for elective lower limb surgery.

Exclusion criteria

Exclusion criteria for current study were; patients with local infection at site of SAB, septicemia and known cases of coagulopathy or other bleeding diathesis, patient with ASA grade III and above, BMI more than 35 kg/m² and patients with severe hypovolemia, increased ICP, severe stenotic valvular heart disease or ventricular outflow obstruction, uncooperative patient, pre-existing neurological deficits, demyelinating lesions, and spinal deformity were excluded from the study.

Procedure

Ninety patients were divided into three groups (n=30) each groups by computer-generated randomization. Group B; patients in this group received 3 ml (15mg) 0.5% bupivacaine heavy and 0.5 ml normal saline intrathecally. Group BD; Patients in this group received 3 ml (15mg) 0.5% bupivacaine heavy+dexmedetomidine 0.5 ml (5 mcg) intrathecally. Group BC; patients in this group received 3 ml (15 mg) 0.5% bupivacaine heavy+clonidine 0.5 ml (50 mcg) intrathecally. Patients were pre-medicated. The procedure was explained to the patients and written informed consent was obtained. In the pre-operative room concept of VAS score was introduced to the patient and baseline vital parameters were recorded.

Assessment of sensory blockade: this was done by loss of pinprick sensation. Time of onset of sensory block: defined as the time between injections of the drug to loss of pin-prick sensation at T10 level. Level of maximum sensory block: defined as the highest dermatomal level reached with loss of sensation. Time for two dermatome regression: defined as the time to regain sensation at two dermatomes lower to the initial level of highest

dermatome. Time for rescue analgesia: defined as the time at which patient complained pain at the site of surgery intraoperatively or postoperatively to be equal to VAS score > 4. At this point Inj. diclofenac 75 mg was given Intra-muscular for rescue analgesia. Assessment of motor blockade: the degree of motor block was assessed using the "modified Bromage scale". Onset time for motor block: time between injection of local anesthetic and grade III motor blockade. Duration of motor block: time from injection of drug into the subarachnoid space to return of grade zero of modified Bromage scale.

Statistical analysis

The statistical software SPSS version 16 has been used for the analysis. An alpha level of 5% has been taken, i.e. if any p value is less than 0.05 it has been considered as significant and p value of <0.001 was considered highly significant for the entire test. Continuous variables are expressed as mean±standard deviation and compared across the groups using one-way ANOVA test.

RESULTS

As shown in the (Table 1) the mean age among the groups N, D and C was 43.77, 43.13 and 44.1 respectively and the range was 23-60, 23-57 and 27-60 respectively. The difference in mean age between any two group was statistically not significant (p>0.05). As shown in the (Table 1) the distribution of mean BMI among the groups N, D and C was found to be 27.42, 26.63 and 26.7 respectively, and the range stood at 22-30, 22-33 and 22-31.

The difference in mean BMI was statistically not found to be significant (p>0.05). As shown in the (Table 2) the gender variability (female:male) among the groups N, D and C was 23:77, 20:80 and 20:80 respectively and the differences were not significant (Table 2). Sex distribution was equal between groups N, D and C, and the differences between any two group were statistically not found to be significant (p>0.05). As shown in (Table 3) the meantime to achieve T10 sensory level among the groups B, BD and BC were 5.40±1.38, 4.87±0.73 and 5.20±1.40 minutes respectively. As shown in (Table 4), the mean of peak level of sensory block achieved among the group B, BD and BC was 6.07, 5.83 and 6.13 respectively and range of peak level of sensory block achieved was T6-T10 in group B, T4-T10 in group BD and T5-T10 in group BC. As shown in (Table 5), the meantime to achieve motor block to modified Bromage scale level three among the groups B, BD and BC was 8.97±0.96, 8.33±1.56 and 8.80±1.46 min respectively.

Table 1: Age and BMI distribution.

Parameters	Group N	Group D	Group C	P value		
	Mean ±SD	Mean ±SD	Mean ±SD	N & D	N & C	D & C
Age (years)	43.77±12.32	43.13±10.01	44.1±10.27	0.828	0.91	0.713
BMI	27.42±3.01	26.63±3.07	26.7±3.02	0.322	0.361	0.933

Table 2: Sex distribution.

Parameters	Groups				P value		
	Group N N (%)	Group D N (%)	Group C N (%)	Total N (%)	N & D	N & C	D & C
Female	7 (23)	6 (20)	6 (20)	19 (21)	0.754	0.754	1.000
Male	23 (77)	24 (80)	24 (80)	71 (79)			
Total	30 (100)	30 (100)	30 (100)	90 (100)			

Table 3: Distribution of sensory block onset time.

Parameters	Group B	Group BD	Group BC	P value		
	Mean±SD	Mean±SD	Mean±SD	B & BD	B & BC	BD & BC
Onset of sensory block (min)	5.40±1.38	4.87±0.73	5.20±1.40	0.07	0.58	0.25

Table 4: Distribution of peak sensory level.

Groups	Median	Minimum	Maximum	Mean
Group B	6.00	6	10	6.07
Group BD	6.00	4	10	5.83
Group BC	6.00	5	10	6.13
Total	6.00	4	10	6.01
P value	B & BD			0.586
	B & BC			0.863
	BD & BC			0.481

Table 5: Distribution of motor block onset time.

Parameters	Group B	Group BD	Group BC	P value		
	Mean ±SD	Mean ±SD	Mean ±SD	B & BD	B & BC	BD & BC
Onset of motor block (min)	8.97±0.96	8.33±1.56	8.80±1.46	0.06	0.64	0.27

Table 6: Modified Bromage scale.

Time (min)	Modified Bromage scale	Group B	Group BD	Group BC	Total	Chi square value	P value
5	I	5	0	0	5	10.588	<0.005
	II	25	30	30	85		
	Total	30	30	30	90		
10	III	30	30	30	90	---	---
	Total	30	30	30	90		

As shown in (Table 6) the number of subjects in group BD (30 patients) and group BC (30 patients) reached grade II of modified Bromage scale in 5 min as compared to subjects of group B (25 patients). This difference between the three groups was statistically highly significant ($p < 0.005$). At 10 minutes, all the patients in the three groups attained Modified Bromage grade III. As shown in (Table 7), the meantime to achieve motor block from Bromage scale level three to Bromage scale level zero among the group B, BD and BC was 181.03 ± 20.83 , 353.37 ± 48.87 and 269.77 ± 51.95 min respectively. As shown in (Table 8) the mean duration of analgesia among

the group B, BD and BC was 211.1 ± 30.47 , 386.83 ± 58.43 and 296.53 ± 57.19 respectively. As shown in (Table 9) lowest mean VAS scores were found in patients of group BD at all-time intervals with a statistically significant difference between them ($p < 0.001$). The mean increases at 2 hours and then it decreases till 8 hours in all the groups. At all-time intervals in 8 hours' post-operative duration, the mean VAS score followed the following trend- group B > group BC > group BD reflecting the best analgesic profile post-op in group BD patients. As shown in (Table 10), the mean of Ramsey sedation score taken at baseline, was 2.13 ± 0.18 , 2.17 ± 0.38 and 2.07 ± 0.25 while maximum sedation score was 2.17 ± 0.38 , 2.27 ± 0.45 , 2.07 ± 0.25 in groups B, BD and BC respectively.

Table 7: Distribution of motor block duration.

Parameters	Group B	Group BD	Group BC	P value		
	Mean \pm SD	Mean \pm SD	Mean \pm SD	B & BD	B & BC	BD & BC
Duration of motor block (min)	181.03 \pm 20.83	353.37 \pm 48.87	269.77 \pm 51.95	<0.001	<0.001	<0.001

Table 8: Duration of sensory block.

Parameters	Group B	Group BD	Group BC	P value		
	Mean \pm SD	Mean \pm SD	Mean \pm SD	B & BD	B & BC	BD & BC
Duration of analgesia (min)	211.1 \pm 30.47	386.83 \pm 58.43	296.53 \pm 57.19	<0.001	<0.001	<0.001

Table 9: Comparison of mean VAS scores.

Time interval (hours)	Group B		Group BD		Group BC		P value
	Mean	SD	Mean	SD	Mean	SD	
End of surgery	0.66	0.63	0.13	0.33	0.31	0.46	<0.001
2	3.75	1.16	1.58	0.79	3.27	0.80	<0.001
4	3.70	0.97	1.44	0.83	2.57	0.79	<0.001
6	3.55	0.99	1.12	0.74	2.25	0.55	<0.001
8	3.14	1.01	0.81	0.58	1.87	0.61	<0.001

Table 10: Distribution of sedation score.

Parameters	Group B	Group BD	Group BC	P value		
	Mean \pm SD	Mean \pm SD	Mean \pm SD	B & BD	B & BC	BD & BC
Baseline	2.03 \pm 0.18	2.17 \pm 0.38	2.07 \pm 0.25	0.088	0.561	0.235
After 0.5 hour	2.03 \pm 0.18	2.1 \pm 0.31	2.07 \pm 0.25	0.309	0.561	0.647
After 1 hour	2.17 \pm 0.38	2.27 \pm 0.45	2.23 \pm 0.43	0.356	0.527	0.770
After 1.5 hour	2.1 \pm 0.31	2.2 \pm 0.41	2.17 \pm 0.38	0.286	0.456	0.744
After 2 hour	2.1 \pm 0.31	2.2 \pm 0.41	2.13 \pm 0.35	0.286	0.694	0.497
After 3 hour	2.07 \pm 0.25	2.17 \pm 0.38	2.1 \pm 0.31	0.235	0.647	0.456
After 4 hour	2.03 \pm 0.18	2.13 \pm 0.35	2.07 \pm 0.25	0.167	0.561	0.398
After 6 hour	2.07 \pm 0.25	2.13 \pm 0.35	2.1 \pm 0.31	0.398	0.647	0.694
After 8 hour	2.03 \pm 0.18	2.1 \pm 0.31	2.03 \pm 0.18	0.309	1.000	0.309

DISCUSSION

In our study, we compared the mean time taken to achieve sensory block. It appears that dexmedetomidine might cause faster onset of sensory block but the difference between group B and BD, B and BC, and BD and BC is statistically not significant ($P > 0.05$). So addition of low dose dexmedetomidine with bupivacaine and clonidine with bupivacaine in spinal anesthesia did not affect the onset of sensory block. On comparison of the range of peak level of sensory block, it appears that patients of dexmedetomidine group experience higher level of block than clonidine and bupivacaine group, but the difference in mean of peak level of sensory block between-groups is statistically not significant ($p > 0.05$). Our findings were in concordance with the findings of Kanazi et al in their study.⁵

On comparison of motor block onset in the study groups, it seems that dexmedetomidine causes faster onset of motor block but the difference between groups is statistically not significant ($p > 0.05$). So the addition of low doses of dexmedetomidine with bupivacaine and clonidine with bupivacaine in spinal anesthesia did not significantly affect the onset of motor block. We also observed that peak motor blockade achieved on a modified Bromage scale is the same (level 3) in all the groups. So it can be stated that the two drugs used in our study were equally efficacious. These findings of onset of motor and sensory block were in concordance with the results of Kanazii et al, Van Tuiji et al, and Al Ghanem et al.⁵⁻⁷ Al Ghanem et al observed no significant difference in the onset time in patients receiving dexmedetomidine and clonidine as adjuvants to isobaric bupivacaine. The onset times observed in the study conducted by us were relatively shorter than those observed by Al Ghanem et al, which can be attributed to

differences in patient positioning (lithotomy vs. supine) in our study.⁷ These findings of two dermatome regression time were in concordance with the results of Al Ghanem et al and Gabriel et al.^{7,8} We observed that the meantime to achieve motor block from Bromage scale level three to Bromage scale level zero (motor block duration) in between-groups was found to be highly significant statistically ($p < 0.001$). So the addition of dexmedetomidine or clonidine to bupivacaine in spinal anesthesia can be said to significantly increase the mean duration of motor blockade. It was also found that the addition of dexmedetomidine could significantly increase the duration of motor blockade in comparison of the clonidine group (group BC).

This duration of motor block, as observed in our study, was markedly prolonged when compared to the duration of motor block of 250 ± 76 min in study by Kanazi et al ($p < 0.001$) and 240 ± 64 min in study by Al Ghanem et al ($p < 0.001$), which could be attributed to higher intrathecal volume of drug (3 ml) used in our study as compared to 1.9 and 2.5 ml drug used in the respective studies.^{5,7} The comparison of the mean duration of sensory block among the groups showed a significant difference ($p > 0.05$) in our study. So addition of dexmedetomidine and clonidine to bupivacaine significantly increases the mean duration of analgesia, but dexmedetomidine is more effective.

The pain assessment through VAS scoring in three groups showed that first supplementary analgesic request was significantly prolonged in Group BD, concluding that analgesic profile of dexmedetomidine is better than other two groups. The duration of sensory block was observed in our study was markedly lengthened when compared to study by Kanazi et al and Mustafa et al ($p < 0.001$), which could be attributed to higher intrathecal volume of drug in our study (3.5 ml vs. 2.5ml).^{5,9} Our findings are also supported by similar studies done by BS Sethi et al and Dobrydnjov et al, wherein it was concluded that there was a significant prolongation of analgesia and motor blockade with intrathecal clonidine.^{10,11} Analyzing the sedation score, there was no significant sedation observed during intraoperative and postoperative period on the addition of dexmedetomidine and clonidine. This finding is consistent with the finding of studies done by Kanazi et al, Mustafa et al and Strebal S et al.^{5,9,12} Small dosages of adjuvants used in our study may be the reason for minimal or no sedation observed in any of the groups in the study. The intrathecal dose of dexmedetomidine used by Hala et al (15 μ g), showed significantly higher sedation scores.¹³ Most of the clinical experience gained in the use of intrathecal α_2 adrenoreceptor agonists has been described with clonidine.^{14,16} There is a need for more and detailed clinical studies related to intrathecal dexmedetomidine with a larger patient pool, to prove its efficacy, safety, and the suitable dose for supplementation to spinal local anaesthetics and demarcate its side effect profile.

CONCLUSION

The result of current study suggest that addition of dexmedetomidine and clonidine in doses given, to bupivacaine for subarachnoid block, prolonged sensory and motor blockade without any significant sedation.

ACKNOWLEDGEMENTS

Authors would like to thanks Sri. Aurobindo medical college and PG institute for valuable support during study.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Agrawal A, Jain S, Goyal A. Comparison of dexmedetomidine and clonidine with hyperbaric bupivacain in spinal anaesthesia. *Int Surg J* 2021;8:3563-3568.