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A Study to Compare Clonidine Versus Dexmedetomidine As An Adjuvant To 0.5% Bupivacaine For Spinal Anaesthesia

Dr. Monika Dalal Choudhary[1], Dr. Megha Singla[2], Dr. K L Garg[3], Dr. Vishakha Dhasmana[4]

[1](Junior Resident, Anaesthesiology, FMHS, SGT University, Gurugram, India)
[2](Senior Resident, Anaesthesiology, FMHS, SGT University, Gurugram, India)
[3](Professor, Anaesthesiology, FMHS, SGT University, Gurugram, India
[4](Junior Resident, Anaesthesiology, FMHS, SGT University, Gurugram, India)

Abstract
Objective:
Adjuvants enhance and prolong analgesia, lower the dose requirements and reduce the dose dependent side effects of local anaesthetics but there is limited data comparing different alpha 2 agonists as intrathecal additives. This study aims to compare clonidine and dexmedetomidine as an adjuvant to 0.5% bupivacaine for spinal anaesthesia.
Method:
A total of 60 patients undergoing infraumbilical surgery under spinal anaesthesia were included in study. Patients were randomly assigned into following two groups. Group A (n=30)- patients received 12.5 mg (2.5ml) of 0.5% bupivacaine along with 50mcg of clonidine. Group B (n=30)- patients received 12.5 mg (2.5 ml) of 0.5% bupivacaine along with 5mcg of dexmedetomidine. Time to reach T10 dermatome, onset and duration of motor block, intraoperative hemodynamic changes and time to first postoperative rescue analgesia was noted.
Result: *The two groups assessed were comparable in terms of demographic profile, baseline hemodynamics, time of onset of sensory and motor block, duration of motor block. There was fall in Heart rate (HR) more in Group B and blood pressure (both systolic SBP and diastolic DBP) more in group A after spinal anaesthesia was administered with results being statistically significant ($p< 0.05$). Also, significant difference was seen in time to first postoperative rescue analgesia that is 330 and 311 minutes in Group B and A respectively. (p value < 0.001).*
Conclusion:
Intrathecal dexmedetomidine provides longer duration of pain free period postoperatively with better hemodynamic stability than clonidine.
Key words: *Adjuvants, Clonidine, Dexmedetomidine.*

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I. Introduction

Regional anaesthesia techniques provide important advantages compared with general anaesthesia and systemic analgesia, including excellent pain control, reduced side effects and shortened stay in post-anaesthesia care unit.[1] However, these early advantages can be short-lived and limited by the relatively brief duration of action of currently available local anaesthetics (LAs), potentially resulting in block resolution before the period of worst postoperative pain.[2,3] By increasing the volume (dose) of LAs we can prolong the duration of analgesia but it also increase the risk of LA systemic toxicity.[4] So adjuvants are often added to local anaesthetic for its synergistic effect to prolong the duration of sensory and motor block.[5]

A variety of opioids from morphine, hydro morphine, fentanyl and tramadol have been used with success. However, their use has been limited by their side effects such as pruritis, nausea and respiratory depression. Other drugs like ketamine, steroids, midazolam, anti-inflammatory agents and magnesium sulphate have also been used. Alpha 2 adrenoreceptors are one of the most widely used class of LA adjuvants, which gives satisfactory effect in neuraxial as well as peripheral block.[5]

Clonidine is imidazole derivative with selective partial agonist properties, which inhibits nociceptive impulse by activation of post-junctional alpha 2 adrenoreceptor in dorsal horn of spinal cord.[1]

Dexmedetomidine a highly lipophilic, specific and selective alpha -2 adrenoreceptor agonist. It has similar mechanism of blocking hyperpolarization of activated cation channels.[6]

Different doses of clonidine and dexmedetomidine have been used in various studies with varying results. We propose this study to compare the effects of intrathecal 50 mcg of clonidine versus 5 mcg of

dexmedetomidine as an adjuvant to 0.5% bupivacaine for their efficacy, safety and postoperative analgesic profile in patients undergoing elective surgery under spinal anaesthesia. Spinal block characteristics to be perceived in relation to time of onset of sensory and motor block, total duration of motor block, effect on intra-operative hemodynamics, postoperative analgesia, and any adverse effects encountered.

II. Material and Methods

The study was done in prospective, double blind randomized manner. The study was carried out in department of anaesthesia, SGT University, Gurugram from November 2018 to November 2020. A total of sixty American Society of Anaesthesiology (ASA) class I and II patients undergoing infraumbilical surgery under spinal anaesthesia were included in study. Exclusion criteria were as follows: Patient refusal, Patients having allergy to the study drug, contraindications to spinal anaesthesia, skin/soft tissue infection at the site of needle puncture, severe hypovolemia, coagulopathy, ASA III or IV. The study was performed after taking approval from SGT University ethical committee.

All patients were examined and investigated during the pre-operative visit a day prior to surgery and were familiarized with visual analogue scale (VAS) and its use in measuring postoperative pain. Written informed consent was obtained from patients who participated in this study.

The patients were kept fasting for 8 hours prior to the scheduled time of surgery. They were premedicated with tablet alprazolam 0.25 mg orally a night before surgery. In operating room, after establishment of intravenous (IV) line all standard monitors (automated non-invasive blood pressure [NIBP], pulse oximetry [SPO2] and electrocardiogram [ECG]) were attached. IV preloading was done with 500 ml of Ringer's lactate solution over a period of 15 minutes. Heart rate and systolic/diastolic blood pressure recorded after preloading were taken to represent the basal readings of hemodynamic values. As it was a double blinded study test drugs were prepared by the fellow anaesthesiologist who was not involved in the study. Clonidine (150mcg ml^{-1}) was diluted to 1.5 ml with normal saline and 0.5 ml (50 mcg) of it was added to 2.5 ml of 0.5% bupivacaine. Dexmedetomidine (100 mcg ml^{-1}) 0.5 ml was diluted to 5ml with normal saline and 0.5 ml of this was added to 2.5 ml of 0.5% bupivacaine, keeping the total volume of the drug constant that is 3ml.

Randomization was done with computer generated random number sequence. 1:1 allocation ratio was used to randomise subjects and the allocated intervention was written on paper slips, placed in serial numbered, opaque envelops and sealed. As the eligible patients enrolled in study, the envelops were serially opened and the allocated intervention was done. Group A (n=30)- patients received 12.5 mg (2.5ml) of 0.5% bupivacaine along with 50mcg of clonidine. Group B (n=30)- patients received 12.5 mg (2.5 ml) of 0.5% bupivacaine along with 5mcg of dexmedetomidine. While patient was in sitting position, under all aseptic conditions Lumber puncture was done with 25G Quincke's needle through L3-L4 interspace and after getting free flow of clear cerebrospinal fluid (CSF), the study drug as per the group allocated was injected. Patients were placed supine and the sensory level was checked using spirit swab along the midclavicular line bilaterally at three minutes intervals for 15 minutes and then every 10 minutes after. The time to reach T10 dermatome (onset time) and time for two segment regression was recorded. The motor block was assessed according to bromage scale[7] (0-4), for onset (time to maximum level) and duration (time to bromage 0 regression).

Intraoperative monitoring of blood pressure (BP) and heart rate (HR) was done at interval of 5 minutes for 20 minutes, then after every 10 minutes interval for next 1 hour. Variations of more than 20% in HR and BP was recorded in both the groups. Bradycardia was treated with IV Atropine 0.5 mg and hypotension was treated with intravenous (IV) doses of Mephentermine 6 mg. In post anaesthesia care unit pain score was recorded using VAS, by a nursing staff who was not the part of study and time to demand of first rescue analgesia from spinal injection or score > 4 is taken as duration of effective pain relief. Injection Diclofenac 75 mg intramuscular (IM) was given as rescue analgesia.

Statistical Analysis

The statistical Package for the Social sciences vs 16.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Comparison of quantitative data between groups was done by one-way analysis of variance (ANOVA), and independent samples t-test was used for the comparisons between the two groups. Chi-square test was used for the analysis of the dichotomous data. P value of < 0.05 was considered statistically significant.

III. Results

As shown in Table 1, both the groups were comparable with respect to there demographic profile that is no significant difference was seen in age, gender, weight and ASA status. There was no statistically significant difference seen in baseline, hemodynamic of patients in both the groups. There was a fall in HR, SBP and DBP in both the groups after the respective drug was injected however fall in HR was seen more in Group B and fall in SBP as well as DBP was more in Group A with the result being statistically significant (Table 2 and

3). Onset time of sensory block (to reach T10 level, 3.48±0.42 and 3.37 ± 0.45) and onset time for motor block (to achieve bromage scale 4, 6.42 ±1.2 and 6.56± 1.5) was similar in both the groups. Statistically significant difference (p value < 0.05) was seen between the groups in time for two segment regression (118.3±9.1 and 125.7±16.2), duration of motor block (to achieve bromage scale 0, 214.1±10.9 and 224.3±22.4) and time to first rescue analgesia demanded by patient that is 311± 9.56 in Group A and 330± 22.50 in group B (Table 5). Two patients in Group A had hypotension, which was managed by single shot of 6 mg Mephentermine and none of the patients in either group experienced bradycardia.

IV. Discussion

There is enough literature regarding the benefits of intrathecal use of clonidine but studies regarding use of dexmedetomidine is limited[8,9]. In our study, baseline hemodynamic parameters were comparable in both the groups but in intraoperative and postoperative period, statistically significant difference was found. Fall in HR was observed more with dexmedetomidine and fall in SBP as well as DBP was more with clonidine. Study conducted by Sarma et al also showed the significant difference in intraoperative and postoperative HR and Mean arterial pressure with the use of these two drugs. It is seen that addition of α2 adrenoceptor agonist supplements spinal anaesthesia as they act by binding to pre-synaptic C fibers and post synaptic dorsal horn neurons whereas local anaesthetics act by blocking sodium channels. In our study we found that 50 ug of clonidine and 5 ug of dexmedetomidine when used as adjuvant to sub arachnoid block showed similar time of onset of sensory (to reach T10) and motor (to achieve bromage scale 4) block. Matching results were seen in studies done by Kanazi et al[10] and Al Ghanem et al[11]. Also, it was observed that dexmedetomidine prolongs the duration of sensory and motor block when compared to clonidine. Studies done by Mahendru et al[12] and Sarma et al[13] showed alike results. It was seen in our study that addition of dexmedetomidine prolongs the pain free duration in postoperative period. This may be explained by the decrease in release of C fiber transmitters and hyperpolarization of post synaptic dorsal horn neurons by α2 agonists[10]. Similar prolongation in time to first rescue analgesia was seen in study done by Suthor et al[14]. Hypotension and bradycardia are important side effects of α2 agonists but the incidence was very low in our study which might be due to low doses of the drugs used. Though our study adds on to prevalent knowledge about dexmedetomidine but it has its own short comings. The sample size was small and all types of infraumbilical surgeries were included in this study due to which duration of surgery was not uniform. Also, only healthy young individuals who are free from any disease which otherwise could have exaggerated the cardiovascular side effects of α2 agonists were included in study. This limitation could have been reduced by large sample size and keeping the type of surgery fixed.

V. Conclusion

In this study we reported that α2 adrenergic agonists may supplement the intrathecal local anaesthetic and it was observed that Dexmedetomidine provides longer duration of sensory and motor block as well as pronged time to demand for first rescue analgesia along with hemodynamic stability. Larger prospective studies are required to confirm our findings.

Tables

Table 1: Showing demographic profile of two groups.

Variable	Group A	Group B	P value	significance
Age	48.6± 8.25	47.4±10	0.955	NS
Gender (M:F)	07:23	10:20	0.869	NS
Weight	64.9 ± 6.53	65 ± 6.9	0.521	NS
ASA status (I:II)	25:05:00	23:07	0.519	NS

Table 2 : Showing Heart rate (HR) in both the groups.

Time Interval (minutes)	Group A		Group B		p value
	Mean	SD	Mean	SD	
Basal	81.3	6.07	80.1	6.66	0.52
0	80.6	6.73	79.6	6.75	0.58
5	79.1	6.11	75.9	5.21	0.03

10	77.6	6.21	74.6	5.1	0.046
15	76.33	6.28	72.9	6.04	0.04
20	74.9	4.96	71.4	5.51	0.02
30	74.3	4.39	69.4	5.81	0
40	73.9	4.9	68.8	5.75	0
50	73	4.8	68.1	6.12	0.001
60	72.8	4.9	68.1	5.8	0.001
70	72.73	4.81	68.1	5.66	0.001
80	72.43	5.03	67.2	5.74	0.0004
90	72.33	4.48	67.7	5.82	0.001

Table 3 : Showing Systolic Blood Pressure (SBP) in both the groups.

Time Interval (minutes)	Group A		Group B		p value
	Mean	SD	Mean	SD	
Basal	132.5	7.84	131	12.3	0.46
0	126.9	8.67	128	7.5	0.61
2	116.2	8.67	121	8.01	0.03
5	109.8	10.61	116	9.89	0.023
10	105.5	9.31	111	9.06	0.019
20	104.8	9.32	113	7.91	0.001
30	105.9	9.20	114	6.34	0.0002
40	107.2	9.27	113	7.45	0.009
50	107.03	10.8	116	6.83	0.0002
60	108.23	7.08	113	6.32	0.005
70	109.53	6.98	113	5.81	0.023
80	110.16	7.09	114	6.59	0.034
90	110.3	9.24	115	5.50	0.02

Table 4 : Showing Dystolic Blood Pressure (SBP) in both the groups.

Time Interval (minutes)	Group A		Group B		p value
	Mean	SD	Mean	SD	
Basal	76.99	4.76	76.7	4.62	0.85
0	76.73	4.54	74.6	3.61	0.052
5	69.43	5.8	72.5	4.48	0.026
10	62.36	4.26	70.8	6.98	0
15	62.13	4.58	71.2	6.48	0
20	64.66	5.88	71.4	4.47	0
30	66.33	6.99	71.8	3.82	0.00049
40	69.1	6.8	72.2	4.24	0.039
50	69.4	6.14	72.2	4.52	0.049
60	70.5	4.15	72.8	4.3	0.039
70	70.35	4.1	72.23	2.9	0.045
80	70.8	4.59	72.9	2.77	0.037
90	70.7	4.66	73.26	2.76	0.012

Table 5: Showing quality of block in two groups.

TOSB	3.48±0.42	3.37±0.45	0.332	NS
TOMB	6.56±1.5	6.42±1.2	0.69	NS
TRTS	118.3±9.1	125.7±16.2	0.034	S
DMB	214.1±10.9	224.3±22.4	0.03	S
TFRA	311±9.56	330±22.50	0.0001	VHS

TOSB: Time of onset of sensory block (to reach T10)
TOMB: Time of onset of motor block (to reach bromage scale 4)
TRTS: Time of regression of two segments.
DMB: Duration of motor block.
TFRA: Time to first rescue analgesia.
NS: Non significant
S: Significant
VHS: Very highly significant.

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