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A COMPARATIVE STUDY OF INTRATHECAL DEXMEDETOMIDINE AND CLONIDINE AS AN ADJUVANT TO INTRATHECAL BUPIVACAINE IN ELECTIVE LOWER LIMB SURGERIES

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ABSTRACT**Background and Aims**

To evaluate and compare intrathecal Dexmedetomidine and intrathecal Clonidine as an adjuvant to 0.5% hyperbaric bupivacaine for lower limb surgeries, with respect to block characteristics, efficacy, haemodynamic changes & adverse effects.

Materials and Methods: Ninety patients in the age group between 20 and 60 years of either sex belonging to ASA Grade I-II posted for elective lower limb surgeries were divided randomly into three groups (n=30). Group B: received 15mg of 0.5% hyperbaric bupivacaine with 0.5ml normal saline. Group C: received 15mg of 0.5% hyperbaric bupivacaine with 50µg Clonidine. Group D: received 15mg of 0.5% hyperbaric bupivacaine with 5µg Dexmedetomidine. The quality of block, total duration of analgesia, hemodynamic stability and side effects of the study drugs were recorded.

Results:

The mean time of onset of sensory blockade was shorter in group C (1.4±0.5mins) and group D (1.17±0.37mins) than group B (2.8 ± 0.66 mins). Two dermatomal regression time was longer in both Group C (136.33±10.9 mins) and D (136.33±10.9 mins) when compared to Group B (79.46±10.16mins). The mean duration of analgesia was 191±22.94 mins, 342.33±28.12 mins and 369.33±34.13 mins in group B, group C and group D respectively.

The mean time taken for the onset of motor blockade was 4.00 ± 0.69 mins, 1.63±0.49 mins and 1.13±0.346 mins in group B, group C and group D respectively. The mean time taken for attaining maximum motor blockade in Groups B, C & D was 6.57±0.93, 6.43±1.045 and 5.20±0.887mins. The mean duration of motor blockade was 166.16±20.95, 279±24.68 and 303.66±35.95 mins in group B, group C and group D respectively. The mean sedation score was 0.4±0.49 in group B, 0.50±0.682 in group C and 0.53±0.681 in group D.

Conclusion

Intrathecal dexmedetomidine Or intrathecal clonidine, when added as adjuvants with 15mg 0.5% hyperbaric bupivacaine they decrease the onset time, increase the duration of sensory & motor blockade and provide good postoperative analgesia.

KEYWORDS : spinal anaesthesia, clonidine, dexmedetomidine, lower limb surgeries.

INTRODUCTION

Hyperbaric bupivacaine 0.5% is extensively used in India for spinal anaesthesia. Though the duration of action of bupivacaine is prolonged, it will not produce prolonged post-operative analgesia. Hence an adjuvant is required for producing prolonged post-operative analgesia. Recently α -2 adrenoreceptor agonists have been used as adjuvants to local anaesthetic agents because of their sedative, analgesic and haemodynamic stabilizing effect.

Clonidine has been shown to result in prolongation of the sensory blockade and reduction in the amount or concentration of local anaesthetic required to produce post-operative analgesia. Dexmedetomidine also an α -2 adrenergic agonist is pharmacologically related to clonidine. Dexmedetomidine is a highly specific and selective alpha-2 adrenoceptor agonist with 8 times more affinity for alpha-2 adrenoceptor than clonidine. The ratio of alpha-1: alpha-2 receptor binding selectivity for dexmedetomidine is 1:1620 compared to 1:220 for clonidine.

The study was done to evaluate and compare the efficacies of clonidine versus dexmedetomidine with intrathecal hyperbaric 0.5% bupivacaine in patients scheduled for elective lower limb surgeries.

AIM OF THE STUDY

To evaluate and compare the following factors in two groups - intrathecal dexmedetomidine and intrathecal clonidine as an adjuvant to 0.5% hyperbaric bupivacaine for lower limb surgeries, with respect to block characteristics, efficacy, hemodynamic changes and adverse effects.

MATERIALS AND METHODS

Study design: Double blinded randomised case control study. The study was undertaken in Thanjavur medical college, Thanjavur, after obtaining ethical committee clearance as well as informed consent from all patients. Ninety patients in the age group between 20 and 60 years of either sex belonging to ASA Grade I-II posted for elective lower limb surgeries without any co-morbid illness were included randomly into three groups (n=30). Randomization was done

using simple sealed envelope technique.

Group B (control group): received 15mg of 0.5% hyperbaric Bupivacaine with 0.5ml normal saline. Group C (Clonidine group): received 15mg of 0.5% hyperbaric bupivacaine with 50µg clonidine. Group D (Dexmedetomidine group): received 15mg of 0.5% hyperbaric bupivacaine with 5µg dexmedetomidine.

EXCLUSION CRITERIA: Any contraindication for regional anaesthesia, Body weight more than 120 kg & height < 140 cm, Spinal deformity, History of allergy to study drugs, Coagulopathy, Cardiac, liver, or kidney diseases & Neurological disorders.

PREOPERATIVE PREPARATION:

Preoperative assessment was done for each patient one day before surgery. Patients were premedicated on the night before surgery with Tablet Ranitidine 150mg and Tablet Alprazolam 0.5mg. Half an hour before anaesthesia intravenous line was secured and preloaded with Ringer lactate 500ml. Under aseptic precautions subarachnoid block was performed at level of L3-L4 through a midline approach using 25G Quincke spinal needle and study drug was injected. Both the observer and the patients were blinded for the study drug. The study parameters were noted.

Sensory blockade was tested using pinprick method with a blunt tipped 27G needle at every minute for first 5 mins and every 5 mins for next 15 mins and every 10 mins for next 30 mins and every 15 mins till the end of surgery and there after every 30 mins until sensory block was resolved. Quality of motor blockade was assessed by Bromage scale. Level of sedation and incidence of side effects if any were noted. Hemodynamic monitoring was done during the block every 5 mins for first 15 mins and every 10 mins for next 30 mins and once in 15 mins till the end of surgery.

OBSERVATION AND ANALYSIS

All 90 patients in three groups completed the study without any exclusion. The collected data were analysed by chi square test and

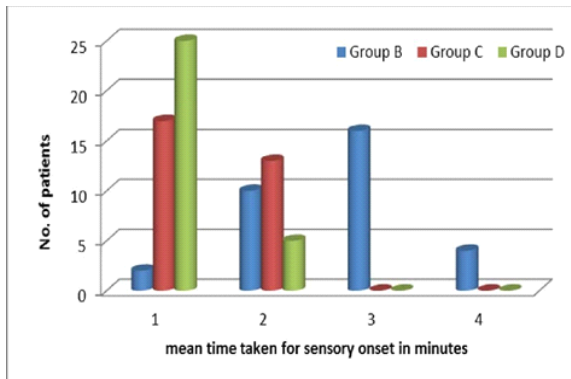
results obtained in the form of range, mean and standard deviation. The probability value p, of less than 0.05 considered statistically significant.

Patient demographic data that include age, sex and duration of surgery between groups were comparable ($p > 0.05$).

Table 1: Mean time taken for sensory onset in minutes

Groups	Time taken for sensory onset (Minutes)		
	Mean \pm SD	Range (mini)	Range (maxi)
Group B	2.80 \pm 0.664	2	4
Group C	1.43 \pm 0.504	1	2
Group D	1.17 \pm 0.379	1	2
Groups Versus	P values between groups (* $<$ 0.05)		
B vs C	0.000*		
B vs D	0.000*		
C vs D	0.024*		

Graph 1: Mean time taken for sensory onset in minutes

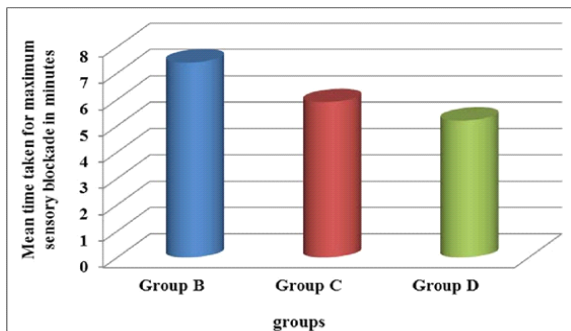


There was a statistically highly significant difference between groups B vs C & B vs D ($p=0.000$) and also between group C vs D ($p=0.024$).

TABLE 2: Mean time taken for maximum sensory blockade in minutes

Groups	Time taken for Maximum sensory Block (Minutes)		
	Mean \pm SD	Range (mini)	Range (maxi)
Group B	7.4 \pm 1.102	6	9
Group C	5.9 \pm 0.803	5	7
Group D	5.2 \pm 0.714	4	7
Groups Versus	P values between groups (* $<$ 0.05)		
B vs C	0.000*		
B vs D	0.000*		
C vs D	0.001*		

Graph 2: Mean time taken for maximum sensory blockade in minutes



There was a statistically highly significant difference between groups B vs C and B vs D ($p=0.000$), it was statistically significant difference between C vs D ($p=0.001$).

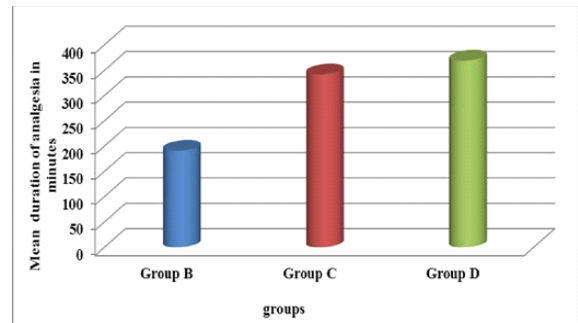
Mean time taken for regression of sensory block by two segments

It was 79.46 \pm 10.16 in group B, 136.33 \pm 10.90 in group C and 136.33 \pm 11.59 minutes in group D. There was a statistically highly significant difference between group B and group C and between group B and group D ($p=0.000$). There was statistically no significant difference between group C and group D ($p=1.000$).

Table 3: Mean duration of analgesia

Groups	Duration of analgesia (Minutes)		
	Mean \pm SD	Range (mini)	Range (maxi)
Group B	191 \pm 22.94	150	240
Group C	342.33 \pm 28.12	300	390
Group D	369.33 \pm 34.13	300	420
Groups Versus	P values between groups (* $<$ 0.05)		
B vs C	0.000*		
B vs D	0.000*		
C vs D	0.001*		

Graph 3: Mean duration of analgesia



There is a statistically highly significant difference between group B and group C ($p=0.000$) and between group B and group D ($p=0.000$) and between group C and group D ($p=0.001$). However there is no clinical significant difference between group C and group D.

Time taken for onset of motor blockade

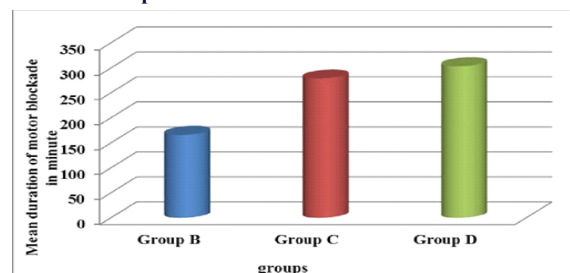
In group B it was 4 \pm 0.695 mins, in Group C 1.63 \pm 0.4 mins & in Group D 1.13 \pm 0.34 mins. P value was 0.000 on comparing between the groups.

The quality of motor blockade was similar in all the groups (Bromage grade 3). There was a statistically highly significant difference between group B and group C and between group B and group D and between group C and group D ($p=0.000$).

Table 4: Mean duration of motor blockade

Groups	Duration of Motor block (Minutes)		
	Mean \pm SD	Range (mini)	Range (maxi)
Group B	166.16 \pm 20.95	135	210
Group C	279 \pm 24.68	240	330
Group D	303.66 \pm 35.95	240	360
Groups Versus	P values between groups (* $<$ 0.05)		
B vs C	0.000*		
B vs D	0.000*		
C vs D	0.003*		

Graph 4: Mean duration of motor blockade



There is a statistically highly significant difference between group B and group C ($p=0.000$) and between group B and group D ($p=0.000$). However, there is no clinical significant difference between group C and D.

The mean sedation score was 0.4 ± 0.49 in group B, 0.50 ± 0.682 in group C and 0.53 ± 0.681 in group D. There was a statistically highly significant difference between group B and C and between group B and D ($p=0.000$). There was statistically no significant difference between group C and D ($p=0.850$).

There was no statistically significant difference in between the groups with respect to the incidences of side effects such as hypotension, bradycardia, nausea, vomiting & shivering.

DISCUSSION

Bupivacaine 0.5% heavy has more prolonged action compared to lignocaine, but the post-operative analgesic duration is limited. A number of adjuvants to local anesthetics for spinal anaesthesia like opioids, benzodiazepines, ketamine and neostigmine have been used. Spinal opiates prolong the duration of analgesia, but they do have drawbacks of late and unpredictable respiratory depression, pruritus, nausea, vomiting and urinary retention. Alpha 2 agonists may be a very useful drug along with the local anesthetic bupivacaine 0.5% hyperbaric for spinal anaesthesia. Various authors have studied clonidine for its analgesic action when it is used as an adjuvant along with local anesthetic without the side effects of opioids.²

Onset of sensory blockade

In our study the mean time taken for onset of sensory block was 2.8 ± 0.6 mins in the B group, 1.43 ± 0.5 mins in the C group and 1.17 ± 0.379 mins in Group D which is statistically significant. Our study is in concordance with the study conducted by Saxena H et al.³

Time taken for maximum sensory blockade

There was a statistically significant decrease in the mean time taken for the maximum sensory blockade in group C and group D compared to the control group. This was similar to the results of study conducted by Saxena H et al.³

Maximum level of sensory blockade achieved

There was no statistical significant difference in the maximum level of sensory blockade in the clonidine group and dexmedetomidine group compared to the control group. Similar results were obtained in studies conducted by Kanazi GE¹⁴ et al., Al-Ghanem⁹ SM et al.

The time taken for regression of sensory block by two segments

There was a statistically significant increase in the mean time taken for regression of sensory block by two segments in clonidine and dexmedetomidine groups compared to control group. This was comparable to the study conducted by Kanazi GE¹⁴ et al. Our study is also consistent with studies done by Dobrydnjov I et al.⁴, Saxena H³ et al., and Sethi BS et al.⁸

The time taken for sensory block to regress to S1

There was a statistically significant increase in the mean time taken for regression of sensory block to S1 in clonidine group and dexmedetomidine group compared to the control group. This compares with the study conducted by Kanazi GE¹⁴ et al, Al-Ghanem⁹ SM et al, Al-Mustafa MM et al and Gupta R et al.¹¹

Duration of analgesia

There was a statistically highly significant increase in the duration of analgesia in dexmedetomidine and clonidine group compared to the control group. Our study concurs with the study conducted by Grandhe RP et al. In studies conducted by Dobrydnjov I et al⁴ and Benhamou D et al in the clonidine group the duration of analgesia was 247 ± 75 mins and 153 ± 80 mins respectively.

Onset of motor blockade

There was a statistically highly significant decrease in the mean time for onset of motor blockade in the dexmedetomidine group and clonidine group compared to the control group.

In studies conducted by Kanazi GE et al¹⁴, Al-Mustafa MM et al., Gupta R et al.¹¹ and Shukla D15 et al. in the dexmedetomidine group and studies done by Saxena H et al.³ and in the clonidine group the authors observed a significant decrease in the mean time for onset of

motor blockade which concurs with our study.

Time taken for maximum motor blockade and grade of motor

blockade There was a statistically significant decrease in the time taken for maximum motor blockade in dexmedetomidine and clonidine group compared to the control group. But the grade of motor blockade in the study groups did not differ. All the groups had a motor blockade of Bromage grade 3. This was comparable with studies conducted by Kanazi GE¹⁴ et al, Al-Mustafa MM et al and Shukla D15 et al.

Duration of motor blockade

There was a statistically highly significant increase in the duration of motor blockade in dexmedetomidine group and clonidine group compared to the control group. This was comparable with study conducted by Kanazi GE et al¹⁴. Our study almost concurs with the study conducted by Kaabachi O et al⁷ who observed the mean duration of motor blockade to be 252 ± 79 mins when using clonidine of $1\mu\text{g}/\text{kg}$. Our study results were similar with studies conducted by Al-Mustafa MM et al., Al-Ghanem SM et al⁹, Gupta R et al.¹³, and Shukla D et al¹⁵ for dexmedetomidine group and in the study conducted by Saxena H et al³ for clonidine group.

Hemodynamic effects

Mean arterial blood pressure

There was no statistically significant difference in any of the three groups regarding fall in MAP. However it was found that there was a delay in maximum fall in MAP in the clonidine group and the dexmedetomidine group compared to the control group. Hemodynamic disturbances resulting from intrathecal Alpha 2 agonists depends upon other factors like segmental site of injection, patient position, preloading and baricity of local anaesthetic employed.

Heart rate

There was no statistically significant difference in any of the three groups regarding decrease in the mean heart rate. Our study was consistent with the studies done by Kanazi GE et al.,¹⁴ Al-Ghanem SM et al.⁹ and Al-Mustafa MM et al.

Sedation

In our study, sedation was assessed using a sedation scale according to the study done by Al-Ghanem SM et al⁹. There was a statistical significance in mean sedation scores between control group and clonidine group and between control group and dexmedetomidine group. There was no statistical significance between clonidine group and dexmedetomidine group. In our study we did not observe any evidence of respiratory depression, episodes of nausea, vomiting, shivering in any of the groups.

CONCLUSION

Intrathecal dexmedetomidine or intrathecal clonidine along with 15mg 0.5% hyperbaric bupivacaine decreases the onset time for sensory & motor blockade and also produces prolonged sensory & motor blockade, good postoperative analgesia with minimal haemodynamic changes.

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