International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Index Copernicus Value (2015): 78.96 | Impact Factor (2015): 6.391

To Study the Efficacy of 45µg of Clonidine Added to 0.5% Isobaric Ropivacaine For Spinal Anaesthesia in Lower Limb Orthopaedic Surgeries

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Abstract: ***Background: Not much data is available on the effect of clonidine added to 15 mg 0.5% isobaric ropivacaine in subarachnoid block. Aims: To evaluate the efficacy of 45 µg of clonidine with 15 mg isobaric ropivacaine in spinal anaesthesia for lower limb orthopedic surgery. Evaluation of effect on sensory and motor block characteristics which included onset, intensity, duration of block along with post-operative analgesia and patient safety. Patients & Methods: After Institutional Ethical Committee approval, double blind, prospective study was conducted. 100 ASA grade I-IIpatients (18-60 years) were equally randomized into group R (receiving 15 mg of isobaric ropivacaine) and group RC (receiving 15 mg of isobaric ropivacaine with clonidine 45 µg). Standard technique of administration and evaluation of subarachnoid block and postoperative analgesia were followed. Onset, duration and intensity of block and complications, VAS score in post-op period were recorded. Statistical Analysis: Fox Pro 2.6 model. RESULTS: There was significantly early onset, adequate and prolonged sensory & motor blockade in RC group when compared with R group. VAS score was also significantly less in RC group. Sedation level was more in RC group and cardiovascular changes were comparable in both groups. Conclusion: Addition of intrathecal 45 µg clonidine enhanced sensory & motor blockade & postoperative analgesia of isobaric ropivacaine safely.***

Keywords: Spinal anaesthesia, isobaric 15 mg ropivacaine 0.5%, 45 µg clonidine.

Key Message: clonidine 45µg with 15 mg isobaric ropivacaine

1. Introduction

Ropivacaine, an enantiomerically pure amide, has emerged as an attractive option in subarachnoid block because of its reduced CNS and cardiotoxic potential when compared to other racemic amide local anaesthetics, but this has also reduced its motor blockade intensity and post-operative analgesic duration[1]. To overcome these problems either a larger dose of ropivacaine or spinal additives can be used.

Clonidine, alpha-2 agonist, when added to subarachnoid local anaesthetic improves intensity & duration of sensory & motor block[2,3]. It also prolongs postoperative analgesia[4]. Unlike spinal opioids, clonidine does not produce pruritus or respiratory depression[5] . Moreover, intrathecal opioids have no effect on motor blockade and may worsen urinary retention.

In our study, we investigated ropivacaine and clonidine combination in spinal route for lower limb orthopaedic surgeries. Usual dose of intrathecal clonidine is 1-2µg/kg. The intention behind selecting 45µg of Clonidine as a fixed dose for intrathecal use was that lower doses such as 15 µg and 30 µg of Clonidine did not significantly enhance the quality and intensity of sensory and motor block and did not prolong post-opeartive analgesia, whereas, higher dose of 75 µg of intrathecal Clonidine did prolong sensory and motor block and gave a high quality anaesthesia, but was associated with systemic side effects like sedation and hypotension[6].

Therefore, 45 µg of intrathecal Clonidine was chosen as a fixed dose with effective prolongation of post-operative analgesia and minimal side effects[7].

2. Materials & Method

This prospective, randomized, study was carried out after approval by institutional ethical committee. Informed, valid, written consent was obtained from the patients.

100 ASA Gr I-II patients of age between 18 to 60 years, weighing > 50 kg, height > 150 cm scheduled for elective orthopaedic lower limb surgery under spinal anaesthesia were enrolled in the study. Patients with pregnancy and lactation, obesity, hypertension or Diabetes mellitus, local infection, severe hypovolemia, bleeding coagulopathy, neurological disorder, raised intracranial tension and deformities of spine, senitivity to local anaesthetics were excluded from the study.

100 patients were divided by computer generated randomization in 2 equal groups. Even numbered patients received 15 mg of 0.5% (3ml), isobaric ropivacaine – Group R (n=50). Odd numbered patients received 15 mg of 0.5% (3ml), isobaric ropivacaine + 45 µg , (0.3ml) of preservative free clonidine - Group RC (n=50).

Difference of 0.3 ml volume does not affect spread of subarachnoid block[8].

I.V. access was established and infusion of RL (10ml/kg) was started. Patients were monitored with ECG, pulse oximeter and NIBP. Under all aseptic precautions spinal anaesthesia was performed with the patient in the sitting position using a 25-gauge Quinke's needle at L3-L4 or L4-L5 interspace. Group R patients received 15 mg of Ropivacaine and Group RC patient received 45 µg Clonidine along with 15 mg of Ropivacaine

After the spinal block, intra-operatively the following parameters were observed and recorded.

1) HR, SpO2 and NIBP were recorded immediately after induction, ie, at 0 min after making the patient supine and thereafter at 5,10,15, 20,25 30, 40, 50, 60, 80,100, 120,140, 160 minutes time intervals.
2) Level of sensory block was be assessed by pinprick method and motor block by Modified Bromage scale. Surgery was allowed to start as soon as sensory block reached required level of anaesthesia for concerned surgery.

The following parameters were assessed:-

- The onset of sensory analgesia was tested using the loss of sensation to the pin prick. Highest sensory level that was achieved was noted.
- Time of onset of motor block was noted. Assessment of motor block was done using Modified Bromage scale.

MODIFIED BROMAGE SCALE[9]

0 - Able to perform a full straight leg raise over the bed for 5sec.
1 - Unable to perform a leg raise but can flex the leg on knee.
2 - Unable to flex knee but can flex ankle.
3 - Unable to flex ankle.
4 - Unable to move toes.

- Maximum level of sensory blockade attained and time taken for the same was noted.
- Maximum level of motor blockade attained and time taken for the same was noted.
- Two segment regression time of sensory blockade.
- Total duration of motor blockade.
- Total duration sensory blockade.
- Total duration of surgery.
- Any intraoperative side effect such as hypotension (decrease in mean arterial pressure more than 20% of base line value or less than 60mmHg), bradycardia (pulse rate less than 50 beats/min), and others like nausea, shivering, pruritis and urinary retention. Bradycardia was treated with Inj Atropine 0.6mg IV and hypotension was treated with IV fluids and if required Inj Mephentermine IV.
- Post operatively patients were observed for half an hour and oxygen was given by Hudson mask. Then the patients were monitored every 1 hour for 4 hours and recording of vital parameters and visual analogue scoring was done. Any adverse effects like urine retention, shivering, nausea, vomiting, transient radiating pain were also noted.
- Sedation: measured by Ramsay Sedation Scale and the patient is considered sedated if the score is ≥ 4

3. Statistics

Statistical analysis was done by using descriptive and inferential statistics using Chisquare test and Student's unpaired t test and software used in the analysis were SPSS 17.0 version, EPI-INFO 6.0 version and GraphPad Prism 5.0 version and $p<0.05$ is considered as level of significance.

4. Results

All the demographic data like weight, height, gender were comparable in between the groups and the difference was non-significant (p-value>0.05, NS), except age, the difference of which was significant in between the groups (p-value=0.0001). In spinal anaesthesia, age doesn't play any significant role in spread of the drug once the adult spinal anatomy is attained. Hence, in inclusion criteria the age group was between 18-60 years of either sex and the statistical significance was overlooked. (Table 1)

Table 1: Age wise distribution of patients in two groups

Age Group (yrs)	Group R	Group RC	ϰ2-value	p-value
Upto 20 yrs	2(4%)	8(16%)	27.22	0.0001,S
21-30 yrs	17(34%)	14(28%)		
31-40 yrs	21(42%)	5(10%)		
41-50 yrs	1(2%)	16(32%)		
51-60 yrs	9(18%)	7(14%)		
Total	50(100%)	50(100%)		
Mean±SD	34.76±11.96	35.84±13.04		

Table 2: Distribution of patients according to procedures

Procedures	Group R	Group RC	ϰ2-value	p-value
ACL Repair	2(4%)	3(6%)	11.49	0.64,NS
Antibiotic Bleed Removal	1(2%)	0(0%)		
CR and K-Wire Fixation	2(4%)	0(0%)		
Diagnostic Arthroscopy	2(4%)	0(0%)		
Dynamization for fracture tibia	1(2%)	0(0%)		
External Fixation	12(24%)	12(24%)		
External Fixator Removal	2(4%)	0(0%)		
Femur Nailing	2(4%)	8(16%)		
Implant Removal	4(8%)	7(14%)		
OR with DHS fixation	2(4%)	0(0%)		
ORF with ILN	1(2%)	1(2%)		
OR with plate Osteosynthesis	1(2%)	0(0%)		
Removal of illizarous fixation	2(4%)	0(0%)		
TBW	5(10%)	7(14%)		
Tibia Nailing	11(22%)	12(24%)		

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Table 3: Comparison of mean onset of sensory block (in mins)

Group	*N*	*Mean*	*Std. Deviation*	*Std. Error Mean*	*t-value*	*p-value*
Group R	50	4.66	1.82	0.25	9.67	0.0001,S
Group RC	50	1.86	0.92	0.13		

Table 4: Mean time required to achieve T12 level

Group	*N*	*Mean*	*Std. Deviation*	*Std. Error Mean*	*t-value*	*p-value*
Group R	50	7.60	2.23	0.31	14.63	0.0001,S
Group RC	50	2.64	0.87	0.12		

Table 5: Mean time for maximum sensory level in two groups

Group	*N*	*Mean*	*Std. Deviation*	*Std. Error Mean*	*t-value*	*p-value*
Group R	50	9.36	2.38	0.33	16.81	0.0001,S
Group RC	50	3.24	0.95	0.13		

Table 6: Mean time taken for two segment regression in two groups

Group	*N*	*Mean*	*Std. Deviation*	*Std. Error Mean*	*t-value*	*p-value*
Group R	50	70.76	11.44	1.61	15.81	0.0001,S
Group RC	50	114.28	15.70	2.22		

Table 7: Maximum level of sensory blockade attained in two groups

Sensory Level	*Group R*	*Group RC*	*ϰ2-value*
T6	6(12%)	7(14%)	8.83 p=0.031,S
T8	14(28%)	27(54%)	
T10	24(48%)	14(28%)	
T12	6(12%)	2(4%)	
Total	50(100%)	50(100%)	

Table 8: Median level of sensory block (dermatomal level)

Sensory Level	*Group R*	*Group RC*	*p-value*
Median Sensory level	T12	T8	p=0.021,S
Range	T6-T12	T6-T12	

Table 9: Mean total duration of sensory block (in mins)

Group	*N*	*Mean*	*Std. Deviation*	*Std. Error Mean*	*t-value*	*p-value*
Group R	50	134	17.34	2.45	21.88	0.0001,S
Group RC	50	229.48	25.50	3.60		

Table 10: Mean onset of motor block (in minutes)

Group	*N*	*Mean*	*Std. Deviation*	*Std. Error Mean*	*t-value*	*p-value*
Group R	50	2.96	1.71	0.24	6.18	0.0001,S
Group RC	50	1.38	0.56	0.08		

Table 11: Quality of motor blockade in two groups

Bromage S core	*Group R*	*Group RC*	*ϰ2-value*
Score 2	4(8%)	0(0%)	6.35 p=0.041,S
Score 3	29(58%)	24(48%)	
Score 4	17(34%)	26(52%)	
Total	50(100%)	50(100%)	

Table 12: Mean total duration of motor block (in min)

Group	*N*	*Mean*	*Std. Deviation*	*Std. Error Mean*	*t-value*	*p-value*
Group R	50	108.58	20.79	2.94	23.60	0.0001,S
Group RC	50	191.54	13.60	1.92		

Table 13: Mean VAS score at various time intervals post-operatively

Time Interval	*Group R*		*Group RC*		*t-value*	*p-value*
	Mean	SD	Mean	SD		
1 hour	2.34	1.15	0.00	0.00	14.34	0.0001**,S**
2 hour	3.64	1.12	0.14	0.35	21.08	0.0001**,S**
3 hour	4.74	1.13	0.98	0.89	18.37	0.0001**,S**
4 hour	5.56	1.05	1.84	0.97	18.31	0.0001**,S**

Table 14: Comparison of mean sedation score in two groups

Group	*N*	*Mean*	*Std. Deviation*	*Std. Error Mean*	*t-value*	*p-value*
Group R	50	2.08	0.38	0.05	2.42	0.017,S
Group RC	50	2.30	0.50	0.07		

Table 15: Intra-operative and Post-operative complications

	R group	*RC group*	*P value*
Intra-operative			
Bradycardia	0	2	0.15,NS
Hypotension	0	4	0.041,S
Shivering	0	0	-
Sedation	0	2	0.15,NS
Post-operative			
Nausea, vomiting	0	0	-
Headache	0	0	-
Transient radiating pain	0	0	-
Urine retention	0	0	-

The haemodynamic parameters heart rate and blood pressure were comparable between the two groups at various time intervals and had no statistical significance.

5. Discussion

Clonidine potentiates sub-arachnoid block through activation of post synaptic alpha -2 receptors in substantia gelatinosa of spinal cord, blocking the conduction of C and A delta fibers, increasing potassium conductance in isolated neurons in vitro and intensifies conduction block of local anesthetic[10].

The onset of sensory block and time taken for maximum sensory block was faster with the addition of clonidine as also reported by Swati Srivastava et al[11] and Sadhana Kulkarni et al[7]. In our study mean duration of sensory block was 134±17.34 min in group R and 229.48±25.50 min in group RC. Sadhana Kulkarni et al[7] also noted increased duration of sensory block which was 2.4 times the control group. De Kock et al[6] also observed prolongation of sensory blockade by 1.38 times the control group (132+38/183+52 min). This might be due to difference in dosages of Ropivacaine (8mg) used by them. Gonul et al[12] observed prolongation of duration by 1.2 times only as the dose of clonidine used was 30 micrograms. Thus, it shows that prolongation of sensory blockade by clonidine is dose dependant.

Onset and quality of analgesia produced by addition of clonidine was significantly better as compared to ropivacaine alone in our study. The median level of sensory block was T8 in group RC and T12 in group R, suggesting that the level of sensory anaesthesia was more with the addition of Clonidine intrathecally. 12% patients had a sensory level of T12 in group R as compared to only 4% in group RC. 10 patients did not have any sensory blockade in the study done by Sadhana Kulkarni et al[7] which was not comparable with our study which might be due to low dose of drug used in their study (2 ml) as compared to (3 ml) used in our study.

Similar effects were seen with the motor blockade. The grade of motor blockade was inferior (Table 11) in R group

as compared to RC group as also observed by De Kock et al[6]. The duration of motor block was 108.58±20.79 mins in group R where as it was 191.54±13.60 mins in group RC. Prolongation of motor blockade was less as compared to sensory blockade. This might be useful for patients undergoing day care surgery. Potentiation of intensity and duration of motor block may be ascribed to local anesthetic effect of clonidine itself. Alpha 2 adrenoreceptor agonists induce cellular modification in the ventral horn of spinal cord and facilitate the local anesthetic action[6].

In our study there was no statistical significant difference in the mean heart rate and blood pressure between groups at various intervals. However, two patients in group RC developed bradycardia which was managed by inj. atropine 0.6 mg IV. and 4 patients developed hypotension which was managed by fluids inj. Mephentermin 6 mg IV. Gonul et al[12] used 30 µg clonidine along with 10 mg ropivacaine and observed significant bradycardia and hypotension. Klimsha et al[13] suggested that when a larger dose of local anesthetic is used, the hypotensive action of clonidine is masked by dense axonal blockade produced by the local anesthetic. The relatively low dose of ropivacaine (8mg) used with 45µg clonidine by De Kock et al[6] ,might have unmasked the effect of clonidine leading to hypotension. In our study, hypotension was seen in the first half- hour which could be due to dense blockade by the local anaesthetic. Klimscha et al[13] stated that hypotension after 20-30 minutes of injection, is due to local spinal and systemic supraspinal actions as peak concentrations occur in CSF. Lipid solubility and elimination of clonidine in CSF results in lack of delayed hypotension.

Post-operative analgesia was enhanced with clonidine (table) as also observed by Sadhana Kulkarni et al[7], postoperative analgesia was 2.34 times (3.92+0.66/1.84+1.3 hours) prolonged by addition of 45 µg of clonidine, without any sedation or cardiovascular compromise. In the study done by Swati Srivastava et al[11], they found significant delay in “first rescue analgesic demand” in clonidine group. Total consumption of analgesics in first post-operative 24 hours was also low. Ghodki et al[14] added 30µg clonidine to intrathecal bupivacaine for laparoscopic surgeries and evaluated for shoulder tip pain. They found that incidence of shoulder tip pain was less and post operative analgesia was prolonged significantly. Clonidine significantly increased the duration and improved the post-operative analgesia in our study. Bajwa et al[15], Koul et al[16] and Forster et al[17] found similar results but these studies were done using caudal epidural route

Sedation was more with clonidine as by B.S.Sethi et al[18], which was in collaboration with our study, De Kock et al[6], including 120 patients, wherein various doses of clonidine were added to 8 mg ropivacaine. Sedation developed in two patients in the 75 µg clonidine group. In the study done by Gonul Sagiroglu et al[12], sedation was observed in five cases in the ropivacaine plus 30 µg clonidine group. Olfa Kaabache et al[19] observed sedation in 2% patients while using 1 µg /kg of clonidine intrathecally.

Nausea and vomiting are uncommon side effects associated with Clonidine administration. None in our Clonidine group experienced nausea. Urinary Retention and shivering are known side effects postoperatively in patients receiving spinal anesthesia. None in our study experienced urine retention or shivering. Striking advantage of intrathecal clonidine over intrathecal narcotics is absence of respiratory depression and pruritus. None of the patients in our studydeveloped any neurological complications postoperatively.

6. Conclusion

In conclusion, intrathecal 45µg of clonidine added to 15 mg of isobaric 0.5% of ropivacaine for lower limb orthopedic surgery significantly improved onset, quality and duration of sensory as well as motor blockade along with improvement in postoperative analgesia, safely.

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