Original Research Article

Comparative study between bupivacaine alone and bupivacaine plus clonidine in subarachnoid block in orthopaedic surgeries in lower limb

Anoop Singh Negi[1], Pritish Ranjan[2*]

[1]Assistant Professor, [2]Associate Professor, Department of Anaesthesia, ICU and Pain, Shri Guru Ram Rai Institute of Medical and Health Science, Dehradun. Uttrakhand, INDIA.
Email: dranoopnegi@gmail.com

Abstract

Background: Spinal anesthesia is widely practiced for providing sensory and motor block for lower limb surgeries. It was the demonstration of opiate receptors in the brain and substantia gelatinosa of spinal cord that revolutionized the concept of pain relief. The onset and the duration of anesthesia can be prolonged with addition of adjuvant drugs. To find out the efficacy of clonidine when combined with bupivacaine (0.5%) (hyperbaric). **Methods:** A Randomized controlled study, Patients scheduled for lower limb orthopaedic surgeries belonging to ASA I and II were included in the study. The study population was randomly divided into two groups with 50 patients in each group. Study period was June 2020 to April 2021. **Results:** Onset of motor blockade was in the range of 241-300 seconds in majority of patients in both groups (n=22, 44%) in group I and (n=23, 46%) in group II. The difference in onset of motor blockade among both the groups was not significant statistically (p value= 0.113) indicating that addition of clonidine had not shortened the onset of motor blockade. Level of sensory block obtained in both group were statistically not significant (p value= 0.835). In group I (n=28, 56%) of patients were having score of 1 which is significant. In group II (n=48, 96%) of the patients were having sedation score of 0. So, better sedation was achieved by addition of clonidine. **Conclusion:** Addition of clonidine to 0.5% hyperbaric bupivacaine in the dose of 75 µg significantly improves the quality of block, prolongs the onset as well as duration of motor blockade and increases the duration of analgesia as compared to bupivacaine alone.
Key words: spinal anesthesia, motor blockade, sensory block, sedation, bupivacaine, clonidine.

[*]**Address for Correspondence:**
Dr Pritish Ranjan, Associate Professor, Department of Anaesthesia, ICU and Pain, Shri Guru Ram Rai Institute of Medical and Health Science, Dehradun. Uttrakhand, INDIA.
Email: dranoopnegi@gmail.com
Received Date: 05/08/2021 Revised Date: 12/09/2021 Accepted Date: 26/10/2021

Access this article online

Quick Response Code:

Website: www.medpulse.in

DOI: https://doi.org/10.26611/10152037

INTRODUCTION

Spinal anesthesia is a popular anesthetic technique that is widely used across the world.[1] Spinal anesthesia was introduced into clinical practice by Karl August Bier in 1898.[2] Spinal anesthesia is widely practiced for providing sensory and motor block for lower limb surgeries. The onset and the duration of anesthesia can be prolonged with addition of adjuvant drugs. It was the demonstration of opiate receptors in the brain and substantia gelatinosa of spinal cord that revolutionized the concept of pain relief.[3] The quest for an ideal adjuvant continued because opioid adjuvants were associated with side effects such as pruritis, nausea, and delayed respiratory depression.

Bupivacaine is indicated for local infiltration, peripheral nerve block, sympathetic nerve block, and epidural and caudal blocks. It is sometimes used in combination with epinephrine to prevent systemic absorption and extend the duration of action. The 0.75% (most concentrated) formulation is used in retrobulbar block.[4] It is the most commonly used local anesthetic in epidural anesthesia during labor, as well as in postoperative pain

How to site this article: Anoop Singh Negi, Pritish Ranjan. Comparative study between bupivacaine alone and bupivacaine plus clonidine in subarachnoid block in orthopaedic surgeries in lower limb. *MedPulse International Journal of Anesthesiology.* December 2021; 20(3):105-109. http://medpulse.in/Anesthsiology/index.php

management.[5] Liposomal formulations of bupivacaine are no more effective than plain solutions of bupivacaine.[6]

Clonidine was patented in 1961 and came into medical use in 1966.[7] It is available as a generic medication. As of 2019 a month of medication costs the NHS about £8. In 2017, it was the 79th most commonly prescribed medication in the United States, with more than ten million prescriptions.[8] Clonidine is used to treat high blood pressure, attention deficit hyperactivity disorder (ADHD), drug withdrawal, menopausal flushing, diarrhea, and certain pain conditions. Clonidine may be effective for lowering blood pressure in people with resistant hypertension. Clonidine may improve symptoms of attention deficit hyperactivity disorder in some people but causes many adverse effects and the beneficial effect is modest.[9]

METHODS

A Randomized controlled study, Patients scheduled for lower limb orthopaedic surgeries belonging to ASA I and II were included in the study. The study population was randomly divided into two groups with 50 patients in each group. Study period was June 2020 to April 2021. Study conducted in the department of Anaesthesia, Shri Guru Ram Rai Institute of Medical and Health Science, Dehradun. Uttrakhand,

Group I (n=50): Received 3.0 ml of subarachnoid bupivacaine (hyperbaric) (0.5%) with 0.5 ml (75µg) of preservative - free Clonidine.

Group II (n=50): Received 3.0 ml of subarachnoid bupivacaine (hyperbaric) (0.5%) alone

Exclusion Criteria: Patients refused to give consent. Patients with spinal deformities. Patients with bleeding disorders / on anticoagulant medications. Patients with neurological deficit. Patients with local skin sepsis around the site of needle insertion.

Study Variables: Name of the patient, age, sex, weight, height, name of surgery, systolic blood pressure (SBP), diastolic blood pressure (DBP).

Pre-operative Preparation: Tablet- Ranitidine (150mg) per orally at the night before surgery. Tablet- Alprazolam (0.5mg) per orally at night surgery. Nil per orally for 6 hrs prior to surgery.

Methodology: Informed consent was obtained from all patients followed by pre-anaesthetic check-up where detailed history was taken and initial pre-operative counselling and reassurance was given to gain their confidence. The nature of the procedure was explained and the patients were taught to assess the intensity of pain using the visual analogue scale (VAS). Patients were physically examined and relevant routine and special investigations were carried out.

Statistical Analysis: The demographic data were analyzed using either Student's t-test or Chi-square test. Quantitative data was analyzed by student's t test and qualitative data was analyzed by Chi-square test. All values were expressed as mean ± standard deviation. $P < 0.05$ was considered statistically significant. All statistical tests were done by "SPSS-IBM" version 23.

RESULTS

Table 1: Age Distribution

Age Group (years)	Group I		Group II		p value
	Frequency	Percentage	Frequency	Percentage	
20-30	13	26.0	11	22.0	0.502
31-40	21	42.0	23	46.0	
41-50	10	20.0	9	18.0	
51-60	6	12.0	7	14.0	
Total	**50**	**100.0**	**50**	**100.0**	
Mean Age	**36.120±9.99**		**37.600±9.01**		

Table 1 shows the age distribution of the study participants. The most common age group in both arms was 31-40 years involving 42% (21) of Group I and 46% (23) of Group II. The mean age for group I and II was 36.12 and 37.6 years respectively and regarding age group the two groups were comparable (p value= 0.502).

Table 2: Sex Distribution

Sex	Group I		Group II		p value
	Frequency	Percentage	Frequency	Percentage	
Male	31	62.0	33	66.0	0.67
Female	19	38.0	17	34.0	
Total	**50**	**100.0**	**50**	**100.0**	
Chi-Square	**0.173**				

The sex distribution of the study subjects according to their respective group. We observed a male predominance in both groups as 62% (31) of group I and 66% (33) of group II were male. Difference between both groups for sex wise distribution was statistically not significant(p value =0.67).

Table 3: Duration of Surgery

Duration (min)	Group I		Group II		p value
	Mean	±SD	Mean	±SD	
	75.540	±6.50	90.020	±12.42	0.001

The comparison of mean duration of surgery between two groups. The mean duration of surgery in group I and group II was 75.54±6.50 minutes and 90.02±12.42 minutes respectively. Difference between both groups for duration of surgery was statistically significant (p value =0.001).

Table 4: Onset of Sensory Blockade

Onset in seconds	Group I		Group II		p value
	Frequency	Percentage	Frequency	Percentage	
61-120	3	6.0	5	10.0	0.699
121-180	34	68.0	32	64.0	
181-240	11	22.0	9	18.0	
241-300	2	4.0	4	8.0	
Total	**50**	**100.0**	**50**	**100.0**	
Chi- Square		**1.427**			

The distribution of study subjects in both groups according to the onset of sensory blockade. Onset of sensory blockade was in the range of 121-180 seconds in majority of patients (n=34, 68%) in group I and (n=33, 66%) in group II. The difference in onset of analgesia among both the groups was statistically not significant (p value= 0.699), indicating that addition of clonidine had not shortened the onset of sensory blockade.

Table 5: Onset of Motor Blockade

Onset in seconds	Group I		Group II		p value
	Frequency	Percentage	Frequency	Percentage	
121-180	2	4.0	5	10.0	0.113
181-240	12	24.0	3	6.0	
241-300	22	44.0	23	46.0	
301-360	8	16.0	11	22.0	
361-420	6	12.0	8	16..0	
Total	**50**	**100.0**	**50**	**100.0**	
Chi- Square		**7.467**			

The distribution of study subjects in both groups according to the onset of motor blockade. Onset of motor blockade was in the range of 241-300 seconds in majority of patients in both groups (n=22, 44%) in group I and (n=23, 46%) in group II. The difference in onset of motor blockade among both the groups was not significant statistically (p value= 0.113) indicating that addition of clonidine had not shortened the onset of motor blockade

Table 6: Grade of motor blockade (Bromage scale 1962)

Grade	Group I		Group II		p value
	Frequency	Percentage	Frequency	Percentage	
0	0	0.0	0	0.0	NA
1	0	0.0	0	0.0	
2	50	100.0	50	100.0	
Total	**50**	**100.0**	**50**	**100.0**	

The distribution of study subjects in both groups according to the grade of motor blockade. All patients had a grade 3 motor blockade in both groups.

Table 7: Level of Sensory Block

Level of Sensory Block	Group I		Group II		p value
	Frequency	Percentage	Frequency	Percentage	
T7	32	64.0	31	62.0	0.835
T8	18	36.0	19	38.0	
Total	**50**	**100.0**	**50**	**100.0**	
Chi-Square-			**0.042**		

The distribution of study subjects in both groups according to the level of sensory block. Majority of patients in both group had level of sensory block up to T7 level. Level of sensory block obtained in both group were statistically not significant (p value= 0.835).

Table 8: Level of Motor Block

Level of Motor Block	Group I		Group II		p value
	Frequency	Percentage	Frequency	Percentage	
T8	36	72.0	30	60.0	0.205
T9	14	28.0	20	40.0	
Total	**50**	**100.0**	**50**	**100.0**	
Chi-Square			**1.604**		

The distribution of study subjects in both groups according to the level of motor block. Majority of patients in both group had level of motor block up to T8 level. Level of motor block obtained in both group were statistically insignificant (p value= 0.205).

Table 9: Sedation Score

Sedation Score	Group I		Group II		p value
	Frequency	Percentage	Frequency	Percentage	
0	15	30.0	48	96.0	<0.001
1	28	56.0	0	0.0	
2	7	14.0	2	4.0	
3	0	0.0	0	0.0	
Total	**50**	**100.0**	**50**	**100.0**	

Comparison of sedation score between two groups is mentioned. In group I (n=28, 56%) of patients were having score of 1 which is significant. In group II (n=48, 96%) of the patients were having sedation score of 0. So, better sedation was achieved by addition of clonidine.

Table 10: Comparison of Mean VAS Score

Duration (hrs)	Group I		Group II		p value
	Mean	±SD	Mean	±SD	
2 hrs	00	-	1.858	0.78	-
4 hrs	1.710	±0.36	16.656	±2.62	<0.001
6 hrs	7.832	±0.60	75.160	3.15	<0.001

The comparison of mean VAS score between two groups at different time intervals. Mean VAS score was significantly lower in group I as compared to group II. The difference between the mean VAS score at different time, among both the groups, was statistically significant ($p < 0.001$).

DISCUSSION

The present study was carried out to evaluate the efficacy of clonidine administered in subarachnoid space with 0.5% bupivacaine (heavy) and its influence on the extent of postoperative analgesia.100 patients of either sex belonging to ASA I and II in age group of 20-60 years and body weight between 45-80 kg were included. All the patients underwent elective lower limb surgical procedures. The patients were divided into two groups of 50 each according to drug administered. The group I received 3ml of 0.5% bupivacaine (heavy) with 0.5ml (75µg) of clonidine. The group II received 3 ml of 0.5% bupivacaine (heavy) alone. Our findings were in consonance with the studies by B.S. Sethi *et al.*8 and L Niemi.[10] In the study of L Niemi µg.kg-1 of clonidine was added to 15mg of 0.5% bupivacaine administered intrathecally in patients undergoing knee arthroscopy.[11] This is consistent with the studies done by Strebel S, *et al*[12] Sethi BS, *et al.*[13] and Saxena H *et al.*, who observed the complete motor blockade of the lower extremity in all patients.[14] Our study almost concurs with the study conducted by Kaabachi O. *et al.*[15] who observed the mean duration of motor blockade to be 252±79mins when using clonidine of 1µg/kg. Subarachnoid clonidine alone even in doses up to 450 µg, does not induce motor block or weakness. In contrast subarachnoid clonidine combined with local anaesthetics significantly potentiates the intensity and duration of motor blockade. The explanation could be that alpha$_2$ adrenergic agonists induce cellular modification in the ventral horn of the spinal cord (motor neuron hyperpolarisation) and facilitates local anaesthetic action. In the present study 15 patients in group I were wide awake (SS-0) compared to48 patients in group II during the intraoperative period. There were 28 patients who had Sedation score 1 and 7 patients had Sedation score 2 in group I. It is quite clear that addition of clonidine has improved sedation in group I which is often a desirable effect during the intra and post operative period. In a study conducted by Saxena H *et al.*,[14] higher incidence of sedation was seen in the clonidine group (37.5 µg). The authors found 90% of the patients were asleep but arousable in the clonidine group (37.5µg). Jain P N *et al.* 2003 reported that 60% patients were sedated after 75µg

subarachnoid clonidine. Clonidine produces dose-dependent sedation over the dose range 50-900 µg of rapid onset (<20 min) regardless of route of administration.[16] Sedation commonly accompanies the use of clonidine for regional anesthesia, consistent with the known sedative/anesthetic sparing properties of alpha$_2$ adrenergic agonists by action in the locus cereleus. This brain stem nucleus is associated with a wide variety of physiologic regulatory process, including regulation of sleep and wakefulness and is inhibited by alpha$_2$ adrenergic agonists via a G-protein mediated mechanism that involves inhibition of adenylatecyclase. In this study patients were closely monitored intraoperatively and postoperatively for complications if occurred. In group I there were 5 patients had hypotension and 5 patients had bradycardia while in group II, 4 patients had hypotension and 5 patients had bradycardia. Incidence of hypotension was not statistically significant and was well control by ephedrine. Two patients in each group had nausea and vomiting. Equal number of patients had shivering in both the groups. No incidence of backache, headache, pruritus, respiratory depression and urinary retention occurred throughout the study. Hence, overall we observed that addition of clonidine (75µg) in subarachnoid block produces excellent intraoperative and postoperative prolonged analgesia with minimal side effects in lower abdominal surgery.

CONCLUSION

Addition of clonidine to 0.5% hyperbaric bupivacaine in the dose of 75 µg significantly improves the quality of block, prolongs the onset as well as duration of motor blockade and increases the duration of analgesia as compared to bupivacaine alone. These outcomes not only decreased the dose of bupivacaine required but also the need of sedatives and other analgesics with minimum acceptable side effects.

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Source of Support: None Declared
Conflict of Interest: None Declared