



ADJUNCTIVE USE OF CLONIDINE OR DEXMEDETOMIDINE WITH 0.25% ROPIVACAINE IN PNS GUIDED FEMORAL NERVE BLOCK FOR POST OPERATIVE ANALGESIA AFTER LOWER LIMB PROCEDURES : A RANDOMISED COMPARATIVE CLINICAL TRIAL

Anaesthesiology

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ABSTRACT

Background: The quality and duration of analgesia is improved when a local anesthetic is combined with alpha 2 adrenergic agonist. Though, the effects of clonidine on local anesthetics have been extensively studied, there are limited studies demonstrating the effects of epidural dexmedetomidine on local anesthetics. The aim of our study is to compare the effect of clonidine and dexmedetomidine when used as an adjuvant to ropivacaine for post operative analgesia after lower limb surgeries. **Materials and Methods:** Primary anesthetic technique in all the patients was spinal anesthesia. However femoral nerve block was placed at the completion of surgery by randomizing patients in two groups: Group C (20ml 0.25% Ropivacaine +1mcg/kg Clonidine) and Group D (20ml 0.25% Ropivacaine +1mcg/kg Dexmedetomidine) both containing 35 patients Onset of analgesia , duration of analgesia (It is time interval between administration of FNB & demand of first rescue analgesic ,total no of Rescue analgesics required in 24 hrs and quality of analgesia ,hemodynamic stability, post operative sedation scoring ,failure rate of technique and complications were recorded. **Results:** We found significant difference in onset(9.41 ± 0.73 mins) and duration(7.69 ± 0.69 mins) of analgesia in group C as compared to onset(3.08 ± 0.61 mins) and duration(11.16 ± 0.58 mins) of analgesia in group D. No significant complications were seen in either of the group. **Conclusion:** Dexmedetomidine at doses of 1 $\mu\text{g/kg}$ is an effective adjuvant to ropivacaine for post operative analgesia after lower limb procedures .

KEYWORDS

Clonidine, dexmedetomidine, lower limb surgery , analgesia ropivacaine

INTRODUCTION

Femoral Block is one of the most commonly practiced blocks, as it offers almost complete anaesthesia and analgesia and an excellent operative field for surgeries of the lower extremities. The various local anaesthetics have been tried like bupivacaine, Ropivacaine and levobupivacaine in peripheral nerve block for postoperative analgesia.¹ Ropivacaine is a pure S[-] enantiomer developed for the purpose of reducing potential cardiovascular and central nervous system toxicity and improving relative sensory and motor block profiles.²

Addition of adjuvants decreases the dose of local anaesthetics and thereby decrease the potential local anaesthetic toxicity. There has been a quest for finding never and better adjuvants which can be added to the local anaesthetics in peripheral nerve block so as to improve the duration and quality of analgesia . Literature has evident several such adjuncts, including opioids, clonidine, neostigmine, hyaluronidase and dexamethasone.³

Clonidine, is a selective α_2 adrenergic agonist with some α_1 agonist property and act by enhancing the sodium channel blockade action of local anesthetics by opening up the potassium channels resulting in membrane hyperpolarisation, a state in which the cell is unresponsive to excitatory input⁴

Dexmedetomidine is a potent α_2 adrenoceptor agonist, and produce analgesia by reducing the release of norepinephrine and also causing inhibitory effects on the receptor independent nerve fibre action potentials.⁵

Both the agents have been used at various strengths as an adjunct to local anesthetics to prolong the duration of block and post- operative analgesia in various peripheral blocks. The anaesthetic and analgesic requirement of local anaesthetics gets reduced by the use of these two adjuvants because of their analgesic property and augmentation of local anaesthetics effects.⁶

Keeping all this into consideration, this current study was designed to study effects of Clonidine and Dexmedetomidine as adjuvants to 0.25 % Ropivacaine in femoral nerve block.

MATERIAL AND METHODS

The present study was carried out prospectively from January 2021 to January 2022 in the Department of Anaesthesiology in a tertiary care hospital after getting approval from Institutional Ethical Board .The total population of 70 patients was selected based on our previous pilot study on 10 patients, wherein the first demand dose of rescue analgesia

was considered as a point of estimation and calculated Cochran's formula ($p=0.25\%$; 5% level of significance 80% power and 10% drop out rate).

All the patients scheduled for elective lower limb surgeries e.g. Tibia interlocking nail, debridement, Total knee replacement, patella fracture, hip and knee surgery having ASA Grade I and II and having no neurological lesion on the operated lower limb site, absence of diabetic neuropathy ,psychiatric issues, bleeding disorder , no history of local anaesthetic allergy and no active analgesic therapy were included in the study . The patients were briefly informed about the need of the study and consent was obtained for the same prior to their inclusion in the study.

Primary anesthetic technique in all the patients was spinal anesthesia using bupivacaine 0.5 % , 3cc. After completion of surgery, when the effect of subarachnoid block is at L1 level with patient perceiving mild pain, PNS guided femoral block was given with the aid of nerve stimulator (organon), using a short beveled, Teflon coated stimulating 21 Gauge needle. Stimulation frequency was set at 2 Hz. The intensity of stimulating current was initially set at 1mA, and then gradually decreased to 0.5 mA.

Femoral nerve block was placed at the completion of surgery by randomizing patients in two groups: Group C (20ml 0.25% Ropivacaine +1 $\mu\text{g/kg}$ Clonidine) and Group D (20ml 0.25% Ropivacaine +1 $\mu\text{g/kg}$ Dexmedetomidine) both containing 35 patients each.

The Primary systemic investigations including blood profile, kidney and liver function test ,cardiac activity were carried out , following which , the patients were deemed fit for the surgery.

Time 0 for clinical assessments was deemed as the completion of anaesthetic injection at the femoral nerve.

The Onset of analgesia was observed using pin prick method (Hollmen scale) wherein score 1 was Normal sensation to pinprick and score 4 was no perception to pinprick. The evaluation was made at an interval of every 2 mins until complete sensory block was achieved.

Onset of sensory block was defined as the time interval in minutes from the end of administration of local anaesthetic solution in femoral nerve (time-0) till sensory block started appearing i.e. Hollmen score = 2.

Total duration of analgesia was taken till the time patient asked for rescue analgesia i.e. VAS ≥ 4 . Pain was assessed by Visual Analogue

Scale (VAS). VAS was recorded and assessed at an interval of every 30 minutes till the score ≥ 4 . Time of first dose of post-operative systemic analgesic was on the basis of VAS score ≥ 4 and was noted for use as duration of analgesia.

Visual analogue scale consists of a 10 cm line, marked at 1 cm each. The patient makes a mark on the line that represents the intensity of pain he or she experienced. Mark "0" represents no pain and mark "10" represents worst possible pain. The numbers marked by the patient was taken as units of pain intensity.

Rescue Analgesia required in 24 hours was given if VAS score is equal to 4 or >4 , they received a dose of inj diclofenac sodium 75mg intramuscularly. Additional analgesic of inj.tramadol hydrochloride 100 mg intramuscular was given.

Quality of analgesia was assessed every 5 minutes after the onset established. It was assessed using pin prick and application of ice cold water. At the end of 30 minutes, the quality of sensory block was assessed by number of dermatomes having a full block. The sensory block in each dermatome was graded as partial (reduced sensation) or Complete (absence of sensation).

Postoperative hemodynamic stability were analyzed using Heart rate (HR), Systolic and Diastolic Blood pressure (SAP, DAP), Mean arterial pressure (MAP), Respiratory rate (RR) and oxygen saturation monitoring at various time intervals.

Postoperative Sedation was recorded using Ramsay sedation score⁷ wherein score 1 was awake and alert and score 5 was not arousable.

Complication like Nausea vomiting, respiratory depression, hypotension, bradycardia, horner's syndrome, accidental intravascular puncture and local anesthetic toxicity

Failure rate of technique was noted if the patients pain is persistent for 30 minutes, and it was considered as block failure and treated with rescue analgesics.

Statistical Analysis

SPSS ver. 22.0 was used for statistical analysis. Data were presented as mean $\pm$ standard deviation. To estimate differences in non continuous variables like demographic and analgesia characteristics chi square test was performed whereas for estimating post operative hemodynamic parameters student t test was performed. A p value < 0.05 was considered statistically significant.

OBSERVATION AND RESULTS

Demographic Characteristics

This study was carried out on 70 patients divided into two groups of 35 each of age group of 18–65 years with a mean age of 36.77 ± 13.07 years (Group C) and 38.20 ± 12.96 years (Group D) ($p=0.715$). No significant difference between the gender and weight of the patients in the groups. Also, maximum number of patients in both the groups were in ASA grade 1. The most common diagnosis among both the groups was tibia fracture. Both the groups were comparable with respect to surgeries performed. Among both the groups, nailing was the most common procedure done. (Table 1)

Analgesia Characteristics

The analgesia characteristics of the patients were summarized in Table 2. We found that except at baseline and at 24 hours, the HR in Group D was significantly low as compared to Group C ($p<0.05$). The DAP was significantly lower in Group D at Baseline and higher at 30 minutes, 2 hour and at 12 hours in comparison to Group C. ($p<0.05$)

The SAPs was significantly lower in Group D at Baseline and higher at 30 minutes in comparison to Group A. ($p<0.05$) The MAP was significantly lower in Group D at Baseline and at 20 hours while it was higher at 30 minutes, 2 hour and at 12 hours in comparison to Group C. ($p<0.005$). Though fall in HR and blood pressure was statistically significant in Group D but it is not clinically significant to treat with medications.

The respiratory rate was significantly lower in Group D than Group C during all the tested time intervals ($p<0.05$) No statistically significant difference in the oxygen saturation level in the patients of both the groups was observed during all the tested time intervals (Figure 1)

During the course of the study, only one case had failure among Group D and none has in Group C. The difference is not statistically significant. ($p=1.000$)

DISCUSSION

The femoral nerve block anesthetizes the femoral nerve distribution, and surgeons use it for lower limb surgical procedures. It can provide effective analgesia with less opioid intake, which consequently reduces the adverse effects from opioid consumption, and promote earlier hospital discharge.

In our study, the dexmedetomidine group showed longer mean duration of analgesia, earlier onset of duration, lower rescue analgesia, lower intraoperative mean blood pressure, respiratory pressure as compared to the clonidine group. Significantly whereas there was an insignificant difference in MAP and oxygen saturation and incidence of side effects. Such as bradycardia, hypotension, nausea, vomiting, drowsiness or convulsions.

In our study, ropivacaine was chosen as the local anesthetic because of its low cardiotoxicity. According to Rashique et al.⁸ maximum dose of ropivacaine was 4 mg.kg^{-1} and according to Shonfeld et al.⁹ it was 3 mg.kg^{-1} . For our patients, we selected a dose of 20 ml of 0.25% ropivacaine which coincides with the study of Sharma B et al.¹⁰ Bafana U et al.¹¹ studied 0.5 % ropivacaine alone and in combination of with clonidine in supraclavicular block. Concluded that duration of analgesia was prolonged in Ropivacaine clonidine group ($1016.9 \pm 170.1 \text{ min}$) than Ropivacaine group ($488 \pm 65.04 \text{ min}$). The difference was highly significant ($p=0.000$)

There have been four proposed mechanisms for the action of clonidine in peripheral nerve blocks. These mechanisms are centrally mediated analgesia, $\alpha_2\beta$ adrenoceptor-mediated vasoconstrictive effects, dwindling of inflammatory response and direct action on peripheral nerve. The direct action of clonidine on the nerve can be explained on the basis of a study conducted by Dalle et al.¹² They proposed that clonidine, by minimizing or blocking the Na/K pump hyperpolarisation generated during repetitive nociceptive stimuli. Kosugi et al.¹³ examined the effects of various adrenoceptor agonists including dexmedetomidine, tetracaine, oxymetazoline and clonidine, and also an α_2 adrenoceptor antagonist (atipamezole) on compound action potential (CAP) recorded from frog sciatic nerve, and found that both dexmedetomidine and clonidine effectively blocks this potential. A study by Brumett et al.¹⁴ showed that dexmedetomidine enhances duration of bupivacaine anaesthesia and analgesia of sciatic nerve block in rats without any damage to the nerve. The histopathological evaluation of these nerve axons and myelin were normal in both control and dexmedetomidine + bupivacaine groups.

In another study, perineural dexmedetomidine added to ropivacaine for sciatic nerve block in rats prolonged the duration of analgesia by enhancement of the hyperpolarisation-activated cation current, which prevents the nerve from returning from a hyperpolarized state to resting membrane potential for subsequent firing.¹⁵

Future studies may be undertaken to find out if hemodynamic response could be further attenuated with lower dose of dexmedetomidine as an adjunct with local anesthetics in supraclavicular brachial plexus block.

CONCLUSION

It can be concluded from present study that, Dexmedetomidine with Ropivacaine has faster onset of analgesia, longer duration of analgesia, less number of rescue analgesic required in 24 hours and better patient acceptance. Our study recommends that Dexmedetomidine with Ropivacaine is better than Clonidine with Ropivacaine in femoral nerve block for post operative analgesia in lower limb procedures.

Table 1. Demographic characteristics of the patients

Age group (Years)	Group A (n=35)		Group D (n=35)		P value
	Nor	%	Nor	%	
<20	4	11.43	0	0	0.110
21 to 30	7	20.00	5	14.29	9a
31 to 40	10	28.57	7	20.00	
41 to 50	6	17.14	12	34.29	
51 to 60	6	17.14	5	14.29	
>60	2	5.71	6	17.14	

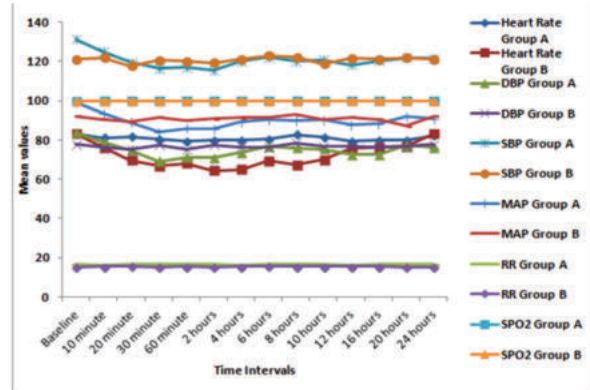
Gender					
Females	11	31.43	8	22.86	0.423
Males	24	68.57	27	77.14	3a
ASA Grades					
Grade 1	31	88.57	30	85.71	0.721
Grade 2	4	11.43	5	14.29	0a
Weight	54.83±4.97	55.51±4.74		0.4233b	
Diagnosis					
ACL injury	1	2.86	0	0	0.789
Both bone fracture	12	34.29	10	28.57	5
OA knee	1	2.86	1	2.86	
Patella fracture	5	14.29	3	8.57	
Tibia fracture	15	42.86	19	54.29	
Tibia nailing	1	2.86	1	2.86	
Tibia OM	0	0	1	2.86	
Operative Procedure					
ACL injury	1	2.86	0	0	0.821
CC screw fixation	1	2.86	2	5.71	9
Debridement	4	11.43	6	17.14	
Expert tibia nailing	0	0	1	2.86	
Implant removal	1	2.86	1	2.86	
Nailing	14	40.00	10	28.57	
Plating	8	22.86	11	31.43	
TBW	5	14.29	3	8.57	
TKR	1	2.86	1	2.86	

Nor-Number; %-Percentage; a-Chi square test; b-Student t test applied; SD- Standard deviation

Table 2. Analgesia Characteristics

	Group C		Group D		p value
	Mean	SD	Mean	SD	
Onset of analgesia (minutes)	9.41	0.73	3.08	0.61	<0.001b
Duration of Analgesia	7.69	0.69	11.16	0.58	<0.001b
Post operative sedation (Ramsay sedation score)	1.00		1.00		-
Quality of Block	No.	%	No.	%	
One (partial block)	2	5.71	1	2.86	0.5510a
Two (complete block)	33	94.29	34	97.14	
Total number of rescue analgesia (in 24 hours)					
One	1	2.86	8	22.86	<0.001a
Two	9	25.71	26	74.29	
Three	25	71.43	1	2.86	
Complications					
Nausea/vomiting	2	5.71	0	0	0.4521

Nor-Number; %-Percentage; a-Chi square test; b-Student t test applied; SD- Standard deviation



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