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Verapamil as an Adjunct to Local Anesthetic Solution for Supraclavicular Brachial Plexus Block

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Abstract

Introduction: Calcium permeability is reduced by local anesthetics, and calcium ions play an important role in opioid-receptor mediated analgesia. The aim of this study is to evaluate whether addition of verapamil into local anesthetic for brachial plexus block provide additional anesthetic and analgesic effects. *Methodology:* Sixty patients undergoing upper extremity surgery were randomized to either Group A (*20 ml* of 1% lignocaine, *20 ml* of 0.25% bupivacaine, *1 ml* normal saline) or Group B (*20 ml* of 1% lignocaine, *20 ml* of 0.25% bupivacaine, *1 ml 2.5 mg* verapamil). *Results:* Baseline characteristics like age, gender distribution and body weight were similar in both the study groups. Mean duration of sensory block was found to be significantly higher in the group of patients receiving verapamil (191 ± 45.59 minutes vs 163 ± 45.72 minutes; p value < 0.01). Rest of the parameters like mean time of onset of sensory and motor block, duration of motor block and duration of analgesia were similar in both the study groups. There was no difference in the proportions of hemodynamic complications like heart rate, systolic blood pressure and oxygen saturation among the patients in the two groups as well. *Conclusions:* Our results show that adding verapamil to brachial plexus block can prolong sensory block. However, no change in analgesic properties or hemodynamic changes was observed.

Keywords: Brachial plexus block; Levobupivacaine; Verapamil.

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Introduction

Peripheral neural blockade is now a well accepted component of comprehensive anesthetic care. Its role has expanded from the operating suite into post-operative and chronic pain management. The first brachial plexus block was performed by William Stewart Halsted in 1885,[1] less than a year after Koller demonstrated the anesthetic properties of Cocaine.[2] Halsted exposed the roots surgically under local infiltration and injected each of them with a small amount of 0.1% cocaine under direct vision. In an attempt to improve peri-operative analgesia, variety of adjuncts such as opioids, clonidine, neostigmine and tramadol have been administered concomitantly with local anesthetics in nerve blocks. Calcium permeability is reduced by local anesthetics,[3] and calcium ions play an important role in opioid-receptor mediated analgesia. After binding to mu-receptor, opioids increase potassium permeability and decrease

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calcium influx, which can lead to inhibition of neuronal transmission. Several studies suggest that the analgesic effects of opioids might be increased by concomitant administration of calcium channel blockers and these drugs by themselves may possess analgesic properties. The aim of this study is to evaluate whether addition of verapamil into local anesthetic for brachial plexus block provide additional anesthetic and analgesic effects.

Materials and Methods

Study Design and Sampling

A double blinded randomized controlled trial was conducted on patients undergoing upper limb surgery over a period of *two years* at a tertiary level hospital. We included patients of American Society of Anesthesiologists (ASA) physical status classification I and II, aged *18* to *60 years*, undergoing elective surgery of upper limb. Patients with medical history of peripheral neuropathy, coagulation disorders, cardiac conduction abnormalities and hypersensitivity to local anesthetics were excluded from the study. We also excluded patients receiving verapamil or anticoagulants. The study was approved by the Institutional Ethics Committee. The study participants were explained the purpose of the study and a separate informed written consent was obtained before being enrolled in the study.

Pre-anesthetic preparation

All patients were subjected to thorough pre-anesthetic evaluation and relevant laboratory investigations. The anesthetic procedure was explained to the patients and an attempt was made to alleviate the anxiety of the patients. All patients were kept on overnight fasting and oral diazepam *10 mg* was given the night before the surgery.

Randomization

Eligible patients were randomized (using random number method) to receive either:

Group A: *20 ml* of 1% lignocaine + *20 ml* of 0.25% bupivacaine + *1 ml* normal saline;

Group B: *20 ml* of 1% lignocaine + *20 ml* of 0.25% bupivacaine + *1 ml 2.5 mg* verapamil.

The anesthetic solutions were prepared by an anesthesiologist not participating in the study. Thus neither the patient, nor the administering anesthesiologist were aware of the medication.

Outcome measures

Brachial plexus block was performed by supraclavicular approach (classical technique), with patient in the supine position.

Onset of sensory blockade: Time between injection and total abolition of pinprick response and temperature testing.

Onset of motor blockade: Was assessed by Bromage three point score.[4]

Duration of sensory blockade: Time between onset of action and return of pinprick response, assessed every *30 minutes* in at least three major nerve distributions.

Duration of motor blockade: Time till return of complete muscle power in three major nerve distributions.

Duration of analgesia: Time between onset of action and onset of pain after receiving first dose of analgesic.

Hemodynamic parameters: Heart rate, systolic blood pressure and oxygen saturation was monitored every *5 minutes* during the procedure and every *30 minutes* post-operatively.

Data Collection and Data Analysis

Using a pre-designed semi-structured case report form, patient related data were noted. Data were codified in Microsoft Excel sheet and analysed in SPSS software (IBM, version 21). Quantitative and qualitative data were described as means ± standard deviations and frequency distribution respectively. Means were compared using unpaired *t*-test and frequency distribution was compared using Chi-squared or Fisher's exact test. Probability value of less than 0.05 denoted statistical significance.

Results

During the study period, brachial plexus block was carried out as an elective procedure in sixty patients undergoing upper limb surgery, 30 in each study group. Mean age of the patients in both the groups was comparable shows in Table 1.

Table 1: Comparison of baseline characteristics of patients included in the study

	Group A	Group B	*p* value*
Mean age (in years)	33.7 ± 11.49	31.76 ± 10.64	0.25
Gender distribution			
Females	7	8	0.76
Males	23	22	
Body weight (in kg)	64 ± 8	64.2 ± 8.01	0.46

*Calculated by unpaired *t*-test or Chi-square test

Group A = 33.7 ± 11.79 *years* ***vs*** Group B = 31.76

± 10.64 *years, p* value > 0.05). Similarly, the gender distribution and the mean weight of the patients among the two study groups was comparable as well (*p* value > 0.05). Table 2 describe the anesthesia related parameters of the patients. Mean onset of sensory duration was faster in Group B (23.1 ± 3.53 *minutes*) as compared to Group B (23.6 ± 3.91 *minutes*), however, the difference was not statistically significant. Duration of sensory blockade was significantly longer in Group B (191 ± 45.59 *minutes*) as compared to those in the Group A (163 ± 45.72 *minutes*), *p* value < 0.01. Onset of motor blockade was found to be faster among patients in Group B as compared to Group A (26.2 ± 2.94 minutes vs 26.8 ± 3.43 minutes), though the difference was not statistically significant (*p* value = 0.4). Similarly, duration of motor blockade was not statistically different among the patients in the two study groups (Group A 151 ± 43.5 *vs* Group B 155 ± 43.92 *minutes*, *p* value = 0.72). Duration of analgesia was found to be comparable among patients in the two study groups are well (*p* value = 0.41). Figure 1 illustrates the comparison of various hemodynamic profile of patients. Mean pulse rate of Group A and Group B ranged from 7.6 ± 6.0 to 77 ± 7.0 *beats/minute* and 78 ± 7.0 to 79 ± 7.0 *beats/minute* respectively. At no point during the follow up period, the pulse rate was significantly different between the patients in the two study groups. Mean systolic blood pressure in Group A and Group B ranged from 117 ± 9.85 *mm Hg* to 118 ± 10.38 *mm Hg* and 117 ± 10.53 to 118 ± 11.19 *mm Hg* respectively. The systolic blood pressure was comparable between the two study groups throughout the follow up period. Last hemodynamic parameter noted was oxygen saturation. Mean oxygen saturation in Group A and Group B ranged from 98 ± 0.5% to 99 ± 0.57% and 98 ± 0.5% to 99 ± 0.49% respectively. The oxygen saturation was not statistically different at any point during the entire follow up period.

Table 2: Comparison of block related and analgesia among patients included in the study

	Group A	Group B	*p* value*
Sensory block			
Mean time of onset (in *minutes*)	23.6 ± 3.91	23.1 ± 3.53	0.6
Mean duration (in *minutes*)	163 ± 45.72	191 ± 45.59	<0.01
Motor block			
Mean time of onset (in *minutes*)	26.8 ± 3.43	26.2 ± 2.94	0.4
Mean duration (in minutes)	151 ± 43.5	155 ± 43.92	0.72
Duration of analgesia (in *minutes*)	307 ± 63.85	321 ± 69.19	0.41

*Calculated by unpaired *t*-test

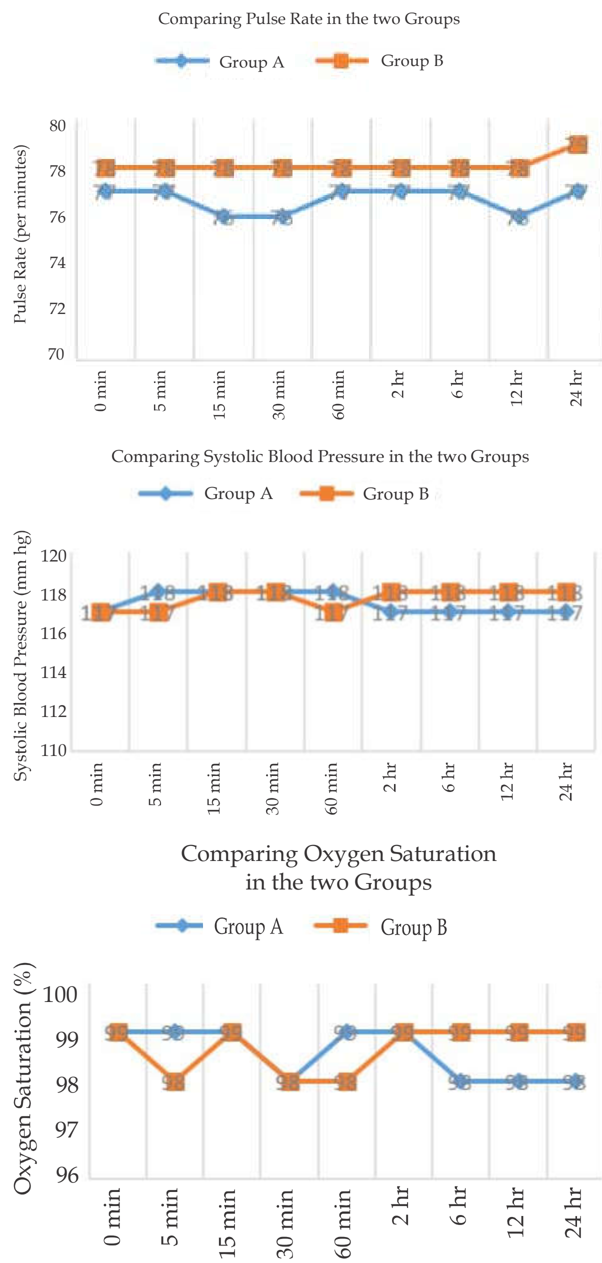

Fig. 1: Comparing hemodynamic variables among patients in the two treatment groups

Discussion

Supraclavicular brachial plexus block not only provides an efficient form of regional anesthesia but is also useful for controlling post-operative pain by acting at the level of the trunks. These trunks are relatively superficial, making supraclavicular approach easy to perform for a prompt form of nerve block. Using calcium channel blockers along with local anesthetics is not a new phenomena. Nowycky *et al.* Demonstrated L, T and N types of calcium channels in sensory neurons. Of these, the L and N types of channels regulate the release of neurotransmitter from neurons.[5] Though anti-nociceptive effects of N type channels are more than L type channel, N type channel blockers being severely neurotoxic have limited clinical utility. Hara *et al*.[6] demonstrated that the L-type channel blockers like verapamil and diltiazem produce both somatic as well as visceral pain relief in a dose-dependent manner, suggesting the relevance of L-type channel blockers in pain management. Similar observations were made in animal models, as Iwasaki *et al.* showed that local sensory block produced by lidocaine injection at the tail base was potentiated by verapamil, diltiazem, and nicardipine in a dose-dependent manner in rats.[7]

In the present study, baseline characteristics like age, gender distribution and body weight were similar in both the study groups. As for the anesthesia related parameters, mean duration of sensory block was found to be significantly higher in the group of patients receiving verapamil. Rest of the parameters like mean time of onset of sensory and motor block, duration of motor block and duration of analgesia were similar in both the study groups. There was no difference in the proportions of hemodynamic complications among the patients in the two groups as well. Mosaffa and colleagues found the onset of motor block to be quicker and duration of sensory and motor block to be statistically higher in the group of patients receiving verapamil.[8] However, they used two doses of verapamil with bupivacaine in supraclavicular brachial plexus block. The authors concluded that verapamil (both *2.5 mg* and *5 mg*) decreased the onset of sensory and motor block and increased the duration of analgesia. Routray *et al.* found that in group receiving verapamil, the time for a request for rescue analgesia was significantly higher, the mean of sensory and motor block onset time was significantly lower and mean duration of sensory block was significantly lower.[9] Choe *et al*. also found decreased requirement of analgesics in post-operative period when verapamil used as adjuvant epidurally.[10] However, Ruben found no effect on post-opreative analgesic requirement when verapamil used as adjuvant in brachial plexus block.[11]

The site and approach of verapamil administration has been shown to affect its role as an adjunct to anesthetic agent. Laurito *et al.* demonstrated that verapamil failed to prolong the duration of lignocaine anesthesia when given subcutaneously.[12] While, Del Pozo *et al.* also failed to exhibit anti-nociceptive effects with subcutaneous verapamil, analgesic effect was seen when administered by intracerebroventricular route in rats.[13] This may be due to decreased central nervous system concentration when verapamil was administered by peripheral route. Perhaps, the analgesic effects of verapamil were short-lived and masked by the local anesthetic effect of lignocaine/bupivacaine solution in our study. Pharmacokinetic studies are required to further investigate these observations.

Conclusion

Our results show that adding verapamil to lignocaine/bupivacaine solution for brachial plexus block can modify the action of local anesthetic solution to some extend, without increasing complications. However, there is scope for further study using solution of different local anesthetics in different strengths and with different calcium channel blocking drugs and other adjuncts in different dosage strengths.

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Conflict of interest: None

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