



## EFFECT OF VERAPAMIL AS AN ADJUVANT TO LOCAL ANAESTHETIC SOLUTION ON THE EFFICACY AND THE DURATION OF SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK

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### ARTICLE INFO

#### Article History:

Received 9<sup>th</sup> December, 2017

Received in revised form 21<sup>st</sup>

January, 2018

Accepted 05<sup>th</sup> February, 2018

Published online 28<sup>th</sup> March, 2018

#### Key words:

Adjuvants, analgesia, verapamil, supraclavicular block

### ABSTRACT

**Background:** Many drugs have been studied as adjuvant to local anaesthetic solution for peripheral nerve blocks in order to increase the quality of block and to increase the duration of analgesia. This study used verapamil, a calcium channel blocking drug as adjuvant for supraclavicular block  
**Aim:** To evaluate the effect of verapamil as an adjuvant to local anaesthetic solution in supraclavicular block.

**Methodology:** In this randomised prospective double blind control trial study we divided 60 ASA grade I,II patients undergoing elective upper limb surgery into two equal groups of 30 (n=30) each. Group A received brachial block with 2% lignocaine 10cc and 20 cc 0.5% bupivacaine with added NS .9% 1cc. Group B received 10 cc of 1.5% lignocaine and 20 cc of 0.5% bupivacaine with 1 cc verapamil (2.5 mg). Observations made regarding onset of sensory block and motor block, duration of sensory and motor block and duration of analgesia. Also haemodynamic parameters monitored to see any difference.

**Results:** Results are calculated using statcal software SPSS version 17, unpaired 't' test and chi square test are used to compare numerical and categorical variables respectively. There was no difference in both the groups regarding onset of sensory, motor block, duration of motor block and duration of analgesia ( p>0.05). Duration of sensory block is found to be significantly greater in group B(191± 45 ) than in group A (163± 4) this difference is statistically significant (p=0.01)

**Conclusion:** Addition of verapamil as an adjuvant to local anaesthetic for supraclavicular block results in prolonged duration of sensory block without any effect on analgesic duration.

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### INTRODUCTION

Since 1884 when Halsted performed first brachial plexus block[1], and in 1911 Hirshell[2] described its percutaneous technique, this type of regional anaesthesia being widely used for upper limb procedures with or without general anaesthesia and of many approaches supraclavicular approach has distinct advantage of dense, complete, reliable anaesthesia [3,4,5]. As it is performed at trunks level where plexus is compactly arranged over first rib. Use of ultrasound for giving peripheral blocks has increased its use and outcome due to precise location of administering the drug near to nerve. While catheter based techniques allows for sustained pain relief it comes with its own disadvantages and complications like catheter displacement , infection overall skill and cost [6].So adding adjuvant to enhance peripheral nerve block efficacy and duration of analgesia still remains sought for option. Use of adjuvants for its synergistic action allows us to use lower concentrations of local anaesthetics and thereby reducing its systemic (cardiac and central nervous system) toxicity as well as local neural toxicity, it reduces postoperative opioid

requirements and side effects associated with it. Various groups of drugs have been tried so far to find the ideal adjuvant .Use of vasoconstrictor like epinephrine has raised query for its potential neurotoxicity and its role is now limited to give test dose to rule out intravascular injection [7,8,9]. Wide range of opioids like morphine, fentanyl, tramadol ,buprenorphine have been tried with variable results [10,11,12,13,14,15,16,17 ] main concern using opioids is their side effects like nausea, vomiting, sedation, pruritus and potentiation of lignocaine mediated nerve toxicity .Clonidine  $\alpha_2$  adrenoreceptor antagonist has shown to prolong the duration of analgesia but associated with haemodynamic effects like hypotension, bradycardia in postoperative period and warns its use in high concentration and in high risk patients[18,19,20]. Use of dexmedetomidine is good choice [21] but requires post operative monitoring for bradycardia and still further studies are required to make its use routine. Dexamethasone a potent anti inflammatory agent has been tried as an adjuvant though there is increased duration of analgesia further well powered studies are required to establish its safety in terms of neurological complications [22].Other

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many drugs tried like magnesium, neostigmine and midazolam, ketamine but none proved ideal[23,24,25,26] As we know calcium ions have an important role in analgesia mediated by local anaesthetics. Calcium permeability is reduced by local anaesthetics. In addition calcium ion play an important role in opioid -receptor mediated analgesia .Various studies have shown that verapamil a calcium channel blocking drug can potentiate analgesic effect of local anaesthetic solution in epidurals or in regional blocks [27,28,29]. With this background we decided to investigate the effect of verapamil as an adjuvant to local anaesthetic in brachial plexus block, as not sufficient work has been done on this. Aim of our study was to evaluate effect of verapamil as an adjuvant to local anaesthetic solution on the efficacy and duration of supraclavicular brachial plexus block. Objectives: To see the effect of verapamil as an adjuvant on onset of sensory and motor block, duration of sensory and motor block and duration of analgesia.

## MATERIALS AND METHODS

This was randomised double blind prospective controlled trial study conducted in Dr D.Y. Patil Medical College, Kolhapur; from may 2011 to may 2013. After institutional ethical committee approved the project 60 patient of ASA grade I ,II of either sex, aged between 18-60 yrs and weighing 50-100 kgs, to be undergoing upper limb elective surgery mainly orthopaedic, plastic and reconstructive surgery requiring >30 min time for procedure were enrolled in study. Patients who refused permission for study, were on oral verapamil, with history of peripheral neuropathy, with cardiac conduction abnormality ,with deranged coagulative profile were excluded from study .All patients were clinically thoroughly evaluated and appropriately investigated on previous day of surgery in preanaesthetic checkup clinic and written informed consent obtained for surgery and study, patients were given tab. Diazepam 10 mg at night and were kept nil by mouth overnight. Patients were randomly divided in two groups of 30 each by computer generated random number method i.e. Group A and Group B. All drug solutions required for block were prepared by anaesthesiologist colleague who was not involved in study or in giving anaesthesia.

Group A: Received brachial block with 10 ml of lignocaine 2% and 20 ml of .5% bupivacaine with normal saline 1ml added to it .This was control group.

Group B: Received brachial block with 10 ml of 2% lignocaine and 20 ml of .5% bupivacaine with 1ml inj verapamil (2.5mg) added to it. This was study group.

On arrival to operation theatre multipara monitor attached and iv line secured with 20 g IV cannula on opposite dorsum of hand and RL started. Baseline parameters like pulse rate, SBP, DBP, MBP, SPO2 recorded as preop values. After giving proper position to the patient brachial block by supraclavicular approach (2 cm above the midpoint of clavicle, lateral to subclavian artery pulsations on first rib) with 22g, 5 cm stimuplex needle was given under all aseptic precautions using PNS, taking fingers flexion to 0.3 mv as end point response. And total 30 cc volume of drugs given as mentioned above. Time of injection is noted. After the block following observations are made every 3 min interval about sensory and motor block till surgery is started, to note the onset of block and at every 30 min interval once surgery is over to note the duration of block . Sensory block assessed with pin prick on

palmer aspect of little finger (ulnar nerve), on palmar aspect of index finger (median nerve) and dorsum of thumb for radial nerve. Using Hollmens scale 1.-normal sensation to pin prick, 2.- weak sensation but prick felt,3.- prick felt as blunt touch, 4.- no sensation. Motor block assessed by conventional muscel power grading from 0- complete paralysis to 1- reduced mobility 2- no force but mobility present , 3- pronounced reduction in force, 4- slightly reduced muscular force and 5 - normal muscel power. We checked Thumb abduction for radial nerve, thumb adduction for ulnar nerve, thumb opposition for median nerve and elbow flexion by musculocutaneous nerve. We asked surgeon to proceed with scrubbing the limb once sensory block scale was 3 and motor power was 3. Observations recorded as follows 1.Onset time for sensory block: it was taken as time interval between injection of drug and sensory block to scale 2. 2.-onset time for motor block: it was taken as time interval between injection of drug and motor block of grade 3. 3-duration of sensory block defined as time interval between complete block and return of normal sensation i.e. pinprick .4.- duration of motor block was defined as time interval between complete paralysis to complete recovery of motor function to grade 5 . 5- duration of analgesia is assessed by evaluating pain post operatively every 30 min when VAS score is >4 it is taken as need to provide supplementary analgesia and is provided with 100 mg of tramadol intramuscularly and time is noted . Time between onset of block and supplementary analgesia given was taken as duration of block .We monitored pulse, SBP, DBP, MBP, Spo2 every 5 min interval during surgery and every 30 min interval postoperatively .We sedated patients with inj pentazocine 0.3 mg/ kg iv and inj midazolam 0.04 mg /kg . We observed no untoward reactions, complications or failed block .

### Statistical analysis

The data was statistically analysed using statcal software-SPSS version 17.0. The various mentioned parameters and patients characteristics were compared using students unpaired 't' test and chi-square test . With  $p < 0.05$  was taken as significant difference and  $p < 0.01$  wa taken as highly significant difference. Numerical data variables were presented as mean and standard deviation while categorical variables were presented as frequency and percentage. As regards to numerical variables unpaired students 't' test was used while for categorical variables chi-square test was used. For analysis of demographic data for gender distribution chi- square test was applied along with calculation of degree of freedom (df) where as for age and weight distribution unpaired students 't' test was applied .

## Observations and results

### Demographic Data

Table 1 Age wise distribution of patients

Group	N	Mean Age(yrs)	SD ±	Min	Max	t value	P value#	Significance
Group A	30	33.70	11.49	18	60	0.67	0.25	Not significant
Group B	30	31.76	10.64	18	60			
# Unpaired t test								

Table 1 showed Mean age of both the groups were comparable and showed no statistical difference ( $p > 0.05$ )

**Table 2** Sexwise distribution of patients in two groups

Group	Sex		Total
	Male	Female	
Group A	23 76.67%	07 23.33%	30 100%
Group B	22 73.33%	08 26.67%	30 100%
Total	45 75%	15 25%	60 100%

  

Chi-square test	df	P value
0.089	1	0.76

**Table 2** Showed overall there was no significant difference in both the groups as per sex distribution of patients.

**Table 3** Group wise weight distribution of patients

Group	N	Mean wt(kg)	SD±	t value	P value#	Significance
A	30	64	8	0.095	0.46	Not significant
B	30	64.2	8.01			

# Unpaired 't' test

It was very clear from Table 3 that mean weight of the patients in both the groups was statistically comparable.

**Table 4** Onset of sensory blockade in min in two groups

Group	Onset of block in min		t value	P value #	Significance
	Mean	SD ±			
Group A	23.6	3.91	0.51	0.60	Not significant
Group B	23.1	3.53			

# Unpaired 't' test

Table 4 compared the time taken for onset of sensory blockade in the two groups, though onset of blockade was little early in Group B it was statistically not significant.

**Table 5** Onset of motor blockade in both the groups

Group	Onset of motor blockade in min		t value	P value	Significance
	Mean	SD ±			
Group A	26.8	3.43	0.72	0.4	Not significant
Group B	26.2	2.94			

Table 5 showed time taken for onset of motor block and was comparable without statistical significant difference.

**Table 6** Duration of sensory block in both the groups in mins.

Group	Duration of sensory block (min)		t value	P value #	Significance
	Mean	SD ±			
Group A	163	45.72	2.37	0.01*	Significant*
Group B	191	45.59			

# Unpaired 't' test \* Statistically significant

When duration of sensory blockade compared as seen in table 6 we found significantly longer duration of action in group B (P=0.01 statistically significant)

**Table 7** Duration of motor block in both the groups

Group	Duration of motor block (min)		't' value	P value #	Significance
	Mean	SD±			
Group A	151	43.5	0.35	0.72	Not Significant
Group B	155	43.9			

# Unpaired 't' test

Table 7 compared the duration of motor blockade in both the groups and it was not found to be significantly different statistically.

**Table 8** Duration of analgesia in both the groups in mins.

Group	Duration of analgesia (min)		t value	P value #	Significance
	Mean	SD±			
Group A	307	63.8	0.8	0.41	Not significant
Group B	321	69.1			

#Unpaired 't' test

When we compared duration of analgesia in both the groups above Table 8 showed the difference is statistically not significant, though there was little longer duration of analgesia in group B.

Also we recorded and observed any significant difference in between the groups regarding systolic, diastolic and mean blood pressure as well as pulse rate and oxygen saturation for every 5 min interval during procedure and every half an hr post operatively till 6 hrs. We did not note any significant difference. Neither any untoward reaction or side effect was not noted in any of the groups.

## DISCUSSION

A variety of receptor mediate nociception on peripheral sensory axons, and peripheral administration of appropriate drugs (adjuvants along with local anaesthetics) may have analgesic benefits and reduced systemic adverse effects. In an attempt to improve perioperative analgesia, variety of adjuvants such as opioids, clonidine, neostigmine have been administered concomitantly with local anaesthetic into the brachial plexus sheath but none proved ideal. The aim of this study was to evaluate whether additional anaesthetic and analgesic effect could be derived from administration of verapamil, a calcium channel blocker when used as adjuvant to local anaesthetic solution into brachial plexus sheath. Verapamil is a synthetic papavarine derivative, a L type of calcium channel blocker. It also inhibits fast sodium channel and has shown to have similar effect like local anaesthetic[30]. There are three different types of voltage gated calcium channels namely L,T and N. L and N type has significant role in regulation of release of neurotransmitter from neurons [31]. Amongst all N type are most potent antinociceptives but because of their neurotoxicity they are not suitable for clinical use. Pirec *et al* had shown its application with morphine in invitro experiments in rats where it attenuated a-delta and C fibres mediated nociception [32]. Somatic and visceral pain may be attenuated in dose dependant manner with L type of calcium channel blockers was the conclusion of Hara *et al* [33]. Ometo when used verapamil intrathecally found that by itself it doesn't have and sensory or motor blockade but when combined with lignocaine it significantly prolongs analgesia [34]. Laurito found no difference when verapamil is injected subcutaneously with local anaesthetic [35]

We conducted double blind study using verapamil as adjuvant to local anaesthetic for supraclavicular brachial plexus block and our results demonstrated significant prolongation of duration of sensory block but onset of sensory and motor block as well as duration of analgesia were not significantly affected. Our results are similar to results of Lall *et al*, where verapamil was used as adjuvant for brachial block.[29] Similarly Tabaeizavareh *et al* when used verapamil as adjuvant in epidural analgesia failed to find any difference in sensory and motor block characteristics[28]. Two different dose (2.5 and 5 mg) of verapamil as an adjuvant have been tried by Mosaffa who found that though onset of sensory and motor block was

hastened in verapamil group dose wise there was no difference.[27] Kim and Choe also found decreased requirement of analgesics in postoperative period when verapamil used as adjuvant epidurally. [36,37]. Ruben found no effect on postop analgesic requirement when verapamil used as adjuvant in brachial plexus block.[38] Multiple other studies by Miranda, Carta, Hasegava favours use of verapamil as adjuvant as they found increased analgesic effects [39,40,41] Our results suggests that analgesic effect of verapamil may have been short lived due to overdilution of drug or may have been masked by long acting bupivacaine. Verapamil epidurally gives better results may be due to action on spinal cord by attenuating neurotransmitters release. There is recent concept of 'multimodal perineural analgesia' where multiple agents with different mechanisms of action used with goal of providing perineural analgesia while avoiding exposure to high and potentially toxic levels of individual agents. There is still scope for further studies by using different calcium channel blocker or different dose of verapamil or may be verapamil with opioids as a part of multimodal perineural analgesia.

## CONCLUSION

Addition of verapamil to lignocaine bupivacaine solution for brachial plexus block can modify the action of local anaesthetic by increasing duration of sensory block. Although dose used in our study failed to demonstrate any difference in onset of block or analgesia duration. So it does suggest that there is further scope for studies using different dose or different calcium channel blocker or verapamil with other opioid as a part of multimodal perineural analgesia

## Acknowledgement

Study not been funded.

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#### How to cite this article:

Rashmee Vijay Chavan and Samrat S Madanaik (2018) 'Effect of Verapamil As An Adjuvant To Local Anaesthetic Solution On The Efficacy And The Duration of Supraclavicular Brachial Plexus Block', *International Journal of Current Medical And Pharmaceutical Research*, 04(3), pp. 3166-3170.

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