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Verapamil as An Adjunct to Local Anaesthetic for Brachial Plexus Blocks

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ABSTRACT

Background: Upper extremity surgeries are recently performed under regional anesthesia. Regional anesthesia of the upper extremity has several advantages over general anesthesia, such as improved postoperative pain, decreased postoperative narcotic consumption, and reduced recovery time. Supraclavicular approach of the brachial plexus block has gained importance for surgical and interventional pain management purposes. Supraclavicular brachial plexus block provides an ideal condition for surgery of the upper limb, maintains hemodynamic stability, decreases postoperative pain and allows for early ambulation. However, the duration of the supraclavicular brachial plexus block is limited by the duration of action of the local anesthetic used in the block.

Aim of the Work: The aim of this study is to evaluate whether additional anesthetic effects could be derived from addition of verapamil into local anesthetics injected into brachial plexus sheath.

Patients and Methods: This study was a prospective, randomized, controlled, double blind study had been carried out in Matareya Teaching Hospital on 60 adult patients with a physical status ASA I & II classification scheduled for upper limb surgeries for 6 months. *Patients were randomly classified using sealed envelopes into two equal groups (group I & group II) each of 30 patients*. Group I: 30 patients who received 40 ml of 1% lignocaine (20ml) with 0.25% bupivacaine solution (20ml), Group II: 30 patients who received 40 ml of 1% lignocaine(20ml) with 0.25% bupivacaine solution with 2.5mg verapamil (20ml).

Results: Onset of sensory blockade time was marginally faster in Group II (12 ±1.8minutes) as compared to Group I (12.6 ± 1.4 minutes). However this difference was statistically not significant. The increase in duration of sensory blockade in Group II (209.90 ± 13.22 minutes) as compared to Group I (183.80 ± 11.68 minutes) was statistically significant ($p < 0.001$). Increase in duration of motor blockade in Group II (172.00 ± 9.32minutes) as compared to Group I (168.20 ± 8.91 minutes) was statistically not significant ($p = 0.112$).

Conclusion: we conclude that adding 2.5 mg verapamil with 0.25% bupivacaine solution (20ml) with 1% lignocaine (20ml) to brachial plexus block can prolong sensory anesthesia without significant effect on duration of motor block, onset of sensory and motor block.

Keywords: Verapamil, Brachial Plexus Blocks.

INTRODUCTION

Upper extremity surgeries are recently performed under regional anesthesia. Regional anesthesia of the upper extremity has several advantages over general anesthesia, such as improved postoperative pain, decreased postoperative narcotic consumption, and reduced recovery time [(1)].

Supraclavicular approach of the brachial plexus block has gained importance for surgical and interventional pain management purposes. Supraclavicular brachial plexus block provides an ideal condition for surgery of the upper limb, maintains hemodynamic stability, decreases postoperative pain and allows for early ambulation. However, the duration of the supraclavicular brachial plexus block is limited by the duration of action of the local anesthetic used in the block [(2)].

The interest in peripheral nerve blocks has increased due to the availability of ultrasound machines. Ultrasound guided supraclavicular block has been shown to be a safe alternative to the blind supraclavicular brachial plexus block as it bypasses its complications, however there is a little evidence as yet to support the superiority of ultrasound compared to any other method of nerve localization [(3)].

The advantage of the ultrasound guidance in peripheral nerve block is the ability to confirm local anesthetic spread around the target nerve. This is the difference from blind techniques, which can easily fail because local anesthetic does not surround the target nerve uniformly [(4)].

The operator can manipulate the needle under direct vision to the appropriate depth and place the needle tip immediately adjacent to the target nerve. With ultrasound imaging, the needle

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position can be changed freely if needed. Ultrasound imaging has revealed that nerves are often displaced by light pressure or local anesthetic injection, which likely contributes to the failure rate of the blind techniques [(4)].

Preliminary experience with ultrasound imaging has revealed that nerves are often displaced by light pressure or injection of local anesthetic, which likely contributes to the failure rate of the blind techniques [(5)].

Calcium ions have an important role in analgesia mediated by local anesthetics. Local anesthetics reduce calcium permeability and various studies have shown that verapamil can potentiate the analgesic effects of local anesthetics. Pain is a highly subjective phenomenon and a variety of receptors mediate pain perception. Nowycky et al [16] in 1985 reported the evidence of three distinct types of calcium channels in sensory neurons namely L, T, and N type. Of these L and N type of channels have a significant role in regulating neurotransmitter release from neurons. The N type has much more potent antinociceptive effects than L type. Studies in rats have shown that application of morphine and N type calcium channel blockers attenuate pain mediated by A delta and C fiber [16]. N type channel blockers were not clinically suitable for use because of their severe neurotoxicity

The aim of this study is to evaluate whether additional anesthetic effects could be derived from addition of verapamil into local anesthetics injected into brachial plexus sheath.

PATIENTS AND METHODS

This a prospective, randomized, controlled, double blind study included a total of 60 adult patients with a physical status ASA I & II classification scheduled for upper limb surgeries for 6 months was conducted between August 2017, and February 2018 , attending at Matareya Teaching Hospital. Approval of both the institutional and the regional ethical committees was obtained. A written informed consent had been obtained from all patients. Every patient received an explanation to the purpose of the study and had a secret code number.

Inclusion Criteria: Sixty adult patients with age between 16 and 60 years of both sexes, physical status ASA I & II classification scheduled for upper limb surgeries.

Exclusion Criteria: Patients refusal, myasthenia gravis, peripheral vascular disease and peripheral neuropathy, COPD, patients with neck abscess, coagulopathy and bleeding tendency**,** patients with decompensated chronic liver disease, underweight or cachectic patients, and patients with history of any used drug allergy.

Patients were randomly classified using sealed envelopes into two equal groups (group I & group II) each of 30 patients; Group I: included 30 patients who received 40 ml of 1% lignocaine(20ml) with 0.25% bupivacaine solution (20ml). Group II: included 30 patients who received 40 ml of 1% lignocaine(20ml) with 0.25% bupivacaine solution with 2.5mg verapamil (20ml).

Anesthetic technique:

All patients received anesthesia through supraclavicular approach guided by ultrasonography.

The following parameters were observed: onset time of sensory blockade (time between injection and total abolition of pin prick response), duration of sensory blockade (time between onset and return of pin prick response) and duration of analgesia (time between onset of action and onset of pain) and duration of motor blockade (return of complete muscle power). Observations were made every 30 minutes. All observations were made in 4 major nerve distribution areas (Radial, Median, Ulnar and Musculocutaneous.

Statistics

Statistical presentation and analysis of the present study was conducted, using the mean, standard deviation and chi-square test by SPSS (Statistical Package for Social science) software V.20. P-value was considered significant if < 0.05.

RESULTS

The age, sex and weight distribution is given in Table 1. The results were statistically analyzed using the student's t-test. In the two groups, there was no significant difference according to demographic data (age, weight, sex).

Table (1): Demographic data of the patients.

Patient Number		Age (years)		Sex		Weight (Kg)	
		roup I	roup II	Group I	roup II	roup I	roup II
Range		25-40	27-41	(40%)	(36.6%)	65-90	65-89
Mean± SD		80±3.78	23±3.96	(60%)	(63.3%)	07±7.04	50±7.21
test	T	-0.433		X^2=0.86		-0.236	
	value	0.666		0.837		0.815	

As regard duration of operations there was no significant difference between the two groups as shown in table 2

Table (2): Duration of the operation of each patient in both groups (hrs. min).

Patient number		Group I	Group II
Range		1.15-2.20	1.10-2.30
Mean±SD		1.52±0.32	1.48±0.30
T-test	T	0.569	
	P-value	0.572	

As regard onset of sensory block there was no significant difference between two groups as shown in table 3

Table (3): Onset of sensory block (min).

Patient number		Group I	Group II
Range		11 - 15	9 - 15
Mean±SD		12.6 ±1.4	12.0 ± 1.8
T-test	T	1.439	
	P-value	0.155	

Onset of motor block was marginally faster in group II but the difference was statically insignificant as shown in table 4

Table (4): Onset of motor block (min).

Patient number		Group I	Group II
Range		16 – 25	14 – 19
Mean±SD		18.07 ± 2.15	17.0 ± 1.75
T-test	T	1.911	
	P-value	0.061	

The increase in duration of sensory block in group II was statistically significant as shown in table 5

Table (5): Duration of sensory block (min).

Patient number		Group I	Group II
Range		160 – 210	187 – 230
Mean±SD		183.80 ± 11.68	209.90 ± 13.22
T-test	T	-8.103	
	P-value	<0.001*	

Duration of motor block in group II more than group I but the difference was statistically insignificant as shown in table 6

Table (6): Duration of motor block (min).

Patient number		Group I	Group II
Range		150 – 180	155 – 187
Mean±SD		168.20 ± 8.91	172.00 ± 9.32
T-test	T	-1.614	
	P-value	0.112	

DISCUSSION

The first brachial plexus block was performed in 1885 with cocaine by Halstead. In 1911, **Hirschell** [15] described the first percutaneous technique for performing the block. In recent years it has gained popularity with addition of various adjuncts to local anesthetic solution in an attempt to increase its efficacy and duration. Systemic adverse effects and prolonged motor block are avoided along with a reduction in total dose of local anesthetic used. Adjuncts like epinephrine, bicarbonate opioids, clonidine, neostigmine and tramadol have been injected concomitantly with local anesthetic solution. Calcium ions have an important role in analgesia mediated by local anesthetics. Local anesthetics reduce calcium permeability and various studies have shown that verapamil can potentiate the analgesic effects of local anesthetics. The aim of this study is to evaluate whether additional anesthetic effects could be derived from addition of verapamil into local anaesthetics injected into brachial plexus sheath.

Pain is a highly subjective phenomenon and a variety of receptors mediate pain perception. In 1985 **Nowycky *et al.*** [16] reported the evidence of three distinct types of calcium channels in sensory neurons namely L, T, and N type. Of these L and N type of channels have a significant role in regulating neurotransmitter release from neurons? The N type has much more potent antinociceptive effects than L type. Studies in rats have shown that application of morphine and N type calcium channel blockers attenuate pain mediated by A delta and C fibre. N type channel blockers were not clinically suitable for use because of their severe neurotoxicity.

Various adjuncts have been attempted to prolong duration of analgesia. **Hara *et al***. [11] showed that L type channel blockers verapamil and diltiazem produced both somatic and visceral pain relief in a dose dependent manner suggesting the relevance of L type channel blockers in pain management. Verapamil, a synthetic papaverine derivative, is an L type calcium channel blocker. Verapamil has been shown to have potent local anaesthetic activity, reflecting inhibition of fast sodium channels. It induces fast channel blocking effects similar to local anaesthetics.

Omote *et al*. [12], showed that although intrathecal verapamil alone demonstrated neither sensory nor motor block, combination of lidocaine-tetracaine solution and verapamil produced potent and prolonged pain relief with motor blockade when compared with the local anesthetic solution alone.

Choe *et al*. [13], demonstrated that addition of verapamil to bupivacaine administered epidurally resulted in less post-operative analgesic requirement. **Laurito *et al***. [17], demonstrated that verapamil failed to prolong duration of lignocaine anaesthesia when given subcutaneously. Some researchers have suggested that the analgesic effect of verapamil is centrally and not peripherally mediated.

Delpozo *et al*. [14] found that subcutaneous verapamil failed to exhibit anti-nociceptive effects, 2but was clearly analgesic when administered by intracerebroventricular route in rats. Effect of lignocaine/ bupivacaine.

As regard to the study of **Williams *et al.*** (6), the pleural puncture was very common and the risk of pneumothorax was very high (6.1%). A study done on 80 patients allocated into 2 equal groups to receive supraclavicular nerve block by ultrasound or nerve stimulator, using the same anesthetic mixture, reported that supraclavicular blocks performed by ultrasound guided technique were of more rapid onset than those with nerve stimulator, fewer needle passes and less patient discomfort (6).

Also another study was done by **Daniel *et al.*** (7), stated that the use of ultrasound guidance in the supraclavicular brachial plexus block decrease the risk of pneumothorax after a study done on 50 adult patients classified into two equal groups each of 25 adult patients with a physical status ASA I and II. In the first group the supraclavicular block was done blindly, where, in the second group the block was done under the ultrasound guidance, and the incidence of pneumothorax was higher in the first group (7).

Moreover, a study by **Perlas *et al.*** (8) reported that ultrasound guided supraclavicular block is associated with a higher success rate with lower complication rate with no pneumothorax in a series of 510 consecutive patients. They suggested that ultrasound guided supraclavicular block might reduce the risk of pneumothorax because the pleura and first rib are often easy to visualize during the approach (8).

As regard to **Cornish *et al.*** (9) checked and evaluated complications, particularly dyspnea by hemidiaphragmatic paresis and observed the possibility of decreased incidence of hemidiaphragmatic paresis in supraclavicular

block with a lower local anesthetic volume. Only one patient who received 21 ml of local anesthetic complained of chest discomfort and showed hemi-diaphragmatic paresis on the post-operative chest X-ray. No hemidiaphragmatic paresis was observed in the patients who received a local anesthetic volume < 21 ml. Previous studies have reported a 35-60% incidence of hemi-diaphragmatic paresis after supraclavicular block using typical volumes of local anesthetics [(9)].

Also**, Wedel *et al.*** [(10)] systemic local anesthetic toxicity are still frequent and dose dependent. Therefore, reducing the dose of local anesthetic in regional anesthesia can contribute to the safety of regional anesthesia [(10)]**.**

In our study the patients were randomly divided into two groups of 30 patients each. All patients were administered brachial plexus block by supra-clavicular approach ultrasound guided. Group I patients received 40 ml of 1% lignocaine with 0.25% bupivacaine solution. Group B patients received the same solution with 2.5 mg verapamil added.

The following parameters were observed: onset time of sensory blockade (time between injection and total abolition of pin prick response), duration of sensory blockade (time between onset and return of pin prick response) and duration of motor blockade (return of complete muscle power). Observations were made every 30 minutes and rescue analgesia was given with Injection paracetamol 1gm when visual analog scale (VAS) score was more than 4. All observations were made in 4 major nerve distribution areas (Radial, Median, Ulnar and Musculocutaneous).

In the two groups, there was no significant difference according to demographic data (age, weight, sex, type and duration of surgery) and according to the hemodynamics (heart rate and mean arterial blood pressure) intraoperative and postoperative.

There was no significant difference (P >.05) between the two groups regarding the onset of sensory block. There was also no significant difference (P >.05) between the two groups regarding the onset of motor block.

The difference in duration of sensory block between the two groups was statistically significant ($p < 0.05$). The difference in duration of motor block between the two groups was not statistically significant ($p > 0.05$).

In conclusion, addition of verapamil to local anaesthetic solution for brachial plexus block can modify the action of the local anaesthetic., there was a statistically significant increase in duration of sensory blockade. There is scope for further study using different calcium channel blocking drugs or in different dosage strengths.

According to complications there were two patients who developed Horner syndrome and one patient developed phrenic nerve paralysis and all three patients improved spontaneously.

CONCLUSION

We conclude that adding 2.5 mg verapamil with 0.25% bupivacaine solution (20ml) with 1% lignocaine (20ml) to brachial plexus block can prolong sensory anesthesia without significant effect on duration of motor block, onset of sensory and motor block.

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