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Evaluation of the analgesic effect of 2 doses of verapamil with bupivacaine compared with bupivacaine alone in supraclavicular brachial plexus block

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Abstract

Background: Different adjuvant drugs have been used with local anesthetics in order to decrease the time of onset and elongate the duration and quality of regional blocks. This study was performed to study the effects of one of the adjuvants, verapamil, in supraclavicular block.

Methods: In this double blinded clinical trial, we divided 60 ASA class I and II patients who were to undergo upper extremity surgery (aged between 18-40 yrs) into 3 different groups randomly. In group I the patients received 30ml Bupivacaine 0.5% plus 2ml normal saline for injection. Group II included patients who received 30ml bupivacaine 0.5% plus 2.5mg verapamil locally and 1ml normal saline for injection. In group III the patients got 30ml bupivacaine 0.5% plus 5mg of local verapamil. All blocks were performed through a supraclavicular brachial plexus procedure, and time of initiating sensory and motor blocks and onset of complete anesthesia and also blood pressure alterations and heart rates were studied and taken into consideration. For data analysis we used SPSS 11.5 software.

Results: Our results clarified that verapamil decreased the onset time of anesthesia, motor block and total anesthesia but there was no statistical difference between 2.5 and 5mg doses of verapamil (P>0.05). Among patients who received verapamil in the block, variation of more than 20% from baseline wasn't detected in blood pressure and heart rate.

Conclusion: According to our findings, verapamil causes a decrease in onset times of sensory and motor block and the initiation of complete anesthesia of bupivacaine in supraclavicular block, but there were no significant differences between groups II (verapamil 2.5mg) and III (verapamil 5mg). Blood pressure and heart rate fluctuations were not more than 20% in group II and III.

Keywords: supraclavicular block, verapamil, onset time of sensory and motor blocks, initiation time of complete analgesia

Introduction

Various adjuvant drugs have been used with local anesthetics in order to decrease the time of onset and elongate the duration and quality of regional blocks. It is clear that each drug has its advantages and disadvantages, so efforts were made to combine the adjuvant with local anesthetics to improve patient and surgeon satisfaction. Although verapamil is known as a calcium channel blocker, it can affect Na^+ channels. For the

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first time in 1982 Kraynack and colleagues by working on animal models defined that verapamil can block fast channels dose dependently and augment the effect of procaine as a local anesthetic drug [1]. In 1998 Choe [2] suggested that verapamil can block slow Na^+ - K^+ channels in cardiac muscles and vessels. Besides that, verapamil can block fast channels similar to the process of local anesthesia.

Regarding the obvious role of calcium ion in pain formation, calcium channel blockers emerged as adjuvant for analgesia and anesthesia. These drugs were proposed as new options for peripheral and central nerve blocks.

The aim of the study was to assess the effects of verapamil on peripheral nerve block regarding its consequences on the onset of sensory and motor block and initiation of time of complete anesthesia and also the effects on hemodynamic alterations.

Methods

This study is a double blinded clinical trial revealing the effects of 2 doses of verapamil (5mg and 2.5mg on the analgesic effect of bupivacaine during supraclavicular block.

Entrance criteria were:

-Age between 18-40 years.

-ASA class I and II and not having any other disease.

-No emergency surgery or fractures of arm or elbow.

-No history of addiction to drugs and any evidence of alcohol or drug consumption.

-No sedatives or analgesics before operation.

-No history of chronic obstructive pulmonary disease in which supraclavicular block is relatively contraindicated.

-No history of preoperative coagulation disorder in which any regional block is contraindicated.

-The patients who were qualified for the survey were divided into 3 groups by a technician according to the last number of their file figure. The same individual prepared the solutions in equal volume and offered them to the physician.

Control group: 30ml bupivacaine 0.5% plus 2ml normal saline for injection.

30ml bupivacaine 0.5% plus 2.5mg verapamil and 1ml normal saline .

30ml bupivacaine 0.5% plus 5mg verapamil.

Blood pressure, heart rate, sense and motion were all checked before the block. For performing the block, a nerve stimulator was used and the point of puncture was situated at the junction of the upper two-thirds of the clavicle and Chassainac's tubercle, approximately 1.5-2cm above the midpoint of the clavicle in the interscalene groove*. Twitch response in the muscles of arm and forearm by 0.2-0.5mA electrical stimulation with an insulated needle (24G/O, 35mm) was obtained and then the solution was injected [3].

During the operation, blood pressure and heart rate were controlled and recorded respectively by manual cuff and pulse oximetry.

The intensity of pain was assessed by Pin Prick test according to the numerical score from 0 to 10 in the time of entrance and after 10 minutes and then in every minute from the tenth minute to thirtieth minute and all information was recorded.

The information was assessed by ANOVA and Scheff's post Hoc methods; in all conditions $P<0.05$ was significant.

Results

Totally 60 patients (20 patients in each group) were evaluated. Age and sex in the 3 groups didn't show any statistical differences.

Mean time required for the onset of the sensory block in control group (group I) was 12.8±3.5min, 10±0.8min in group II(bupivacaine plus 2.5mg verapamil) and 9± 0.8min in group III (bupivacaine plus 5mg verapamil). By comparison we perceived that the onset time

* This approach was designed as modified parascalene block by F. Mosaffa.

of sensory block in group I was significantly shorter than the other 2 groups, but regarding the relative shorter onset time in group III, there was no difference between groups II and III statistically.

The mean onset time of motor block in group I was 20.4±8min, and 11.6±2.7min in group II and 10±1min in group III. By evaluating these times, we understood that the required time for initiating motor block in group I was significantly longer than groups II and III, but despite the relatively shorter time for group III, there was no difference between groups II and III statistically.

Mean duration of complete analgesia was 25±5min in group I, 12.7±3min in group II and 10.5±1min in group III, so the required time for beginning complete analgesia was significantly longer in group I but there was no difference between group II and III regarding relative shorter time in group III.

Maximum blood pressure alteration and heart rate fluctuations for every patient were recorded as percentage. We did not detect more than 20% of alteration compared to the baseline in any patient. Maximum alteration of BP in group I was 0.09±0.04mmHg and 0.1± 0.04mmHg and 0.1±0.03mmHg in groups II and III respectively.

ANOVA method used to compare BP fluctuations showed that regarding less fluctuation of BP in group I, there were no statistical differences between the 3 groups (P=0.236, F=1.48).

Maximum heart rate alteration in group I was 0.04±0.01 and 0.056±0.02 and 0.06±0.02 in groups II and III.

By ANOVA method it was revealed that regarding less fluctuation of HR in group I, there were no significant differences between all 3 groups (P=0.393/F=0.95)

Conclusion

Our survey revealed that using bupivacaine in combination with verapamil significantly decreases the onset time of sensory and motor block as well as the initiating time of complete analgesia. There was no significant difference between 2 doses of 2.5 and 5mg of verapamil. Moreover, the findings showed that using verapamil with the mentioned doses couldn't alter hemodynamic indices.

The dose dependency was not revealed in our survey which could be due to the lack of samples. Verapamil can prolong intrathecal lidocaine and tetracaine anesthetic effects as synergism. Choe et al [2] found that verapamil and bupivacaine in the form of epidural application caused less postoperative analgesic consumption. But Reuben [4] in one surgery suggested verapamil plus a local anesthetic can increase the duration of local anesthesia by injection into the brachial plexus sheath, but additional effects of verapamil as an analgesic in combination with morphine were not approved.

Multiple Investigations by Hasegawa [5], Mirande [6] and Corta [7] suggested that verapamil combined with local anesthetics could increase analgesic effects, although we should consider that Corta used Nifedipine (one of the dihydropiridinic compounds) instead of verapamil (a diphenyl alkylamine derivative). Altogether, the effects of these drugs would be due to their effects on nociceptor C fibers and sensory fibers. For example substance P that stimulates C fibers, can activate the neurokinin I receptor and consequently create a slow and long depolarization and aggregate calcium flow through calcium channels, NMDA and phospholipase C activity that subsequently release calcium through the sarcoplasmic reticulum. Increase of intracellular calcium causes the increase of dynorphine gene explanation and central sensitivity such as wind up phenomenon and augments longer efficacy. So for making a painful message intact the calcium channel is essential and any disturbances of calcium ion transmission can interfere with pain sensation [8]. Meanwhile verapamil is one of the phenylalkylamine derivatives produced as racemic mixture and R- rotatory of verapamil has in-

hibitory effects on fast sodium channels and would be regarded as a local anesthetic [9].

For this reason verapamil and bupivacaine combination in supraclavicular block can increase the total number of anesthetic molecules near the nerve. In other words addition of local anesthetics in the site of action can increase the rate of drug distribution and decrease the time of onset.

The survey revealed that verapamil can be used as an adjuvant to decrease the onset time of sensory and motor blocks of bupivacaine in supraclavicular block. Moreover, verapamil in 2.5mg and 5 mg doses in regional blocks did not show any hemodynamic side effects.

References

1. Kraynack BJ, Gintauta SJ, Lawson NW. Effects of verapamil on excitable membranes. Proc West Pharmacol Soc 1982; 25:61-8.

2. Choe H, Kim JC, Ko SH. Epidural verapamil reduces analgesic consumption after lower abdominal surgery. Anesthesia Analgesia 1998 Apr; 86(4)786-90.

3. Mosaffa F, et al. Using physical examination in supraclavicular brachial plexus block with modified parascalene approach. MJIRI 2006; 19 (4): 313-317.

4. Reuben SS, Reuben JB. Brachial plexus anesthesia with verapamil and/or morphine. Anesthesia Analgesia 2000 Aug; 9(2): 379-83.

5. Hasegawa AE, Zancy J. Influence of 3 L-type calcium channel blocker on morphine effects in healthy volunteers. Anesth Analg 1997; 85:633-8.

6. Miranda HF, Bustamante D, Kramer V, et al. Antinoticeptive effects of Ca channel blockers. Eur J Pharmacol 1992; 217:137-41.

7. Corta F, Bianchi M, Argento S. Effect of nifedipine on morphine-induced analgesia. Anesthesia Analgesia 1990; 70:493-8.

8. Saied EL, Steyn MP, Aneserino JM. Clonidine prolongs the effect of ropivacaine for axillary brachial plexus block. Can J Anesthesia 2000 ; 47(10):962-7.

9. Bouderka MA, Al-Harrer R, Bouaggad A. Neostigmine added to bupivacaine in axillary plexus block. Ann Fr Anesthesia and Reanimation 2003; 22(6):510-13.