

The effect of verapamil as an adjuvant agent with local anesthetic on sensory block level, hemodynamic and postoperative pain

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ABSTRACT

Objective: Coadministration of verapamil with local anesthetics could potentiate the sensory block of peripheral nerve, increase the duration of sensory nerve block and reduce postoperative pain and analgesic consumption. The aim of this study was to investigate the effect of verapamil as an adjuvant with bupivacaine on level of sensory block, post-operative pain and analgesic consumption among patients undergone elective surgery in Isfahan.

Methodology: In this prospective randomized interventional clinical double-blind study ASA physical status I or II male patients referred for elective lower abdominal surgery were enrolled. They randomized in group A (20cc of 0.5% bupivacaine plus 5 mg verapamil) and B(20cc of 0.5% bupivacaine plus 2cc normal saline). The sensory level block, postoperative pain, opioid consumption and vomiting and nausea and hemodynamic state was recorded and compared in two groups.

Results: Sixty two patients were studied. Mean of the sensory level block 20 minutes after stating epidural anesthesia and immediately after surgery, postoperative pain score, opioid consumption and nausea and vomiting and fluid intake was not significantly different in two groups ($P>0.05$). Mean of systolic and diastolic blood pressure and pulse rate changes was not significantly different in two groups ($P>0.05$).

Conclusion: Verapamil as an adjuvant with bupivacaine could not significantly increase the level of sensory block and attenuate post-operative pain and analgesic consumption and hemodynamic condition of the patients. For more accurate results it is recommended to determine the effect of different dose of verapamil in larger sample size of the patients. Studying the effect of other Ca channel blockers would be favorable in this regard.

KEY WORDS: Verapamil, Epidural anesthesia, Pain, Sensory Block, Hemodynamic.

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INTRODUCTION

Perioperative pain management and efficiency is an important phenomenon in the practice of anesthesiology. Anaesthesiologists have a crucial role in providing optimal surgical conditions to reduce related postoperative early complications and side effects in a way that patients with coexisting medical conditions are managed well during the procedure. Many studies have investigated the efficacy of different multimodal analgesia and perioperative medical care in different methods of analgesia.^{1,2}

Epidural anesthesia is one of the popular methods which are used for surgical procedures. Though this method have more significant effects such as postoperative pain relief more effectively than any other anaesthetic method and perioperative reducing of stress responses but it seems that for more effective perioperative result this method should be optimized.³

Based on type and duration of surgery, different kinds of local anesthetics have been used for this purpose and many studies have investigated the consequences of different anesthetics in this regard. Improvements of understanding the underlying mechanisms of postoperative pain led to the use of different analgesic agents and examine the effects of adjuvant agents with local anesthetics in different regional anesthesia techniques.

Calcium has an important role in local analgesia. Evidences indicated that activation of N-methyl-D-aspartic acid (NMDA) receptors leads to Ca^{++} entry into the cell and initiates a series of central sensitization such as wind up and long term potentiation in the spinal cord. So, it seems that Ca channel blockers would be effective in preventing the central sensitization.⁴

The role of Magnesium sulphate in this regard as a physiologic calcium channel blocker and Methyl D Aspartate antagonist has established in some studies. Accordingly it leads to better sensory nerve block and low postoperative analgesic consumption.⁵

The role of verapamil, a Ca channel blocker, in improving the analgesic effects of local anaesthetics have been reported in many studies.⁶⁻¹⁰ Coadministration of verapamil with local anesthetics could potentiate the sensory block of peripheral nerve, increase the duration of sensory nerve block and reduce postoperative pain and analgesic consumption.⁶⁻¹⁰

Bupivacaine is a long acting agent that is usually used for lengthy surgical procedures. But factors such as patient discomfort and inadequate sensory level block during surgery and termination analgesic effects of bupivacaine which result in significant pain after surgery have limited its use.¹¹ Some studies recommended the combination use of bupivacaine with other agents.¹²

The aim of this study was to investigate the effect of verapamil as an adjuvant with bupivacaine on level of sensory block, post-operative pain and analgesic consumption among patients undergone elective lower abdominal surgery in Isfahan.

METHODOLOGY

In this prospective randomized interventional clinical double-blind study (Research project No:79094) ASA physical status I or II male patients referred for elective lower abdominal surgery in affiliated hospitals of Isfahan University of Medical Sciences, were enrolled. All selected patients were aged 20-70 years, with body weight ranged 50-90 kg and height ranged >150 cm.

Patients with history of conductive heart disturbance, cardiovascular disease, opioid consumption or any contraindication for neuroaxial block failure in epidural anesthesia and need to general anesthesia for surgery excluded.

The protocol was approved by Medical Ethics Committee of Isfahan University of Medical Sciences. Written consent was obtained from all patients. Demographic characteristics of selected patients recorded using questionnaire. All patients were NPO eight hours before surgery and received 2cc/kg ringer solution during NPO Period.

Epidural anesthesia and data collection performed by two anesthesiologists as each of them was blinded to another. Patients were randomized in two groups. One group received epidural anesthesia using 20cc of 0.5% bupivacaine plus 5 mg verapamil (total volume 22cc) (Group A) and another one 20cc of 0.5% bupivacaine plus 2cc normal saline (Group B).

Epidural anesthesia was performed keeping patients in sitting position and using 18 gauge touchy needle insertions at L3-L4 level. Confirmation of suitable needle place insertion in epidural space are achieved by hanging of drop technique. ECG-Pulse Oxymetry and Non invasive Blood Pressure monitoring was performed in patients before epidural block.

Five cc solutions include lidocaine 2% with 1/200000 Epinephrine injected as test dose and after 3 minutes solution A or B injected slowly. Continuous pulse rate and ECG monitoring, and BP in 5 minutes interval performed every 5 minutes during surgery and recorded. Hypotension (defined as drop in Mean arterial pressure more than 20% of basic amount) was treated with bolus doses of 3 mg ephedrine and infusion of Ringer solution. Bradycardia (heart rate <50/min) was treated with 0.5 mg atropine.

The sensory level block is determined with needle 20 minutes after stating epidural anesthesia and pain scoring evaluated by numerical rating scale (0=no pain and 10=worst possible pain) and Prince Henry Score (PHS defined as 0=no pain, 1=pain

on cough, 2=pain on deep brathing, 3=moderate resting pain,4=sever resting pain.) 24 hours post-operatively at 2,6,12,24, hours after surgery.¹³ Post-operative opioid consumption in each groups are recorded. Also postoperative nausea and vomiting checked for 24 hours after surgery.

Statistical Analysis: Obtained data analyzed using SPSS (Ver 16) software and t-Test and chi-square manwithny test. Values are represented as mean \pm SD and P Value <0.05 was considered statistical significant.

RESULTS

In this study 62 ASA physical status I or II male patients were studied. Demographic characteristics of studied population in two groups are presented in Table-I. Two groups were similar regarding age, weight, height and duration of surgery ($P>0.05$).

Mean \pm SD of the sensory level block 20 minutes after stating epidural anesthesia and immediately after surgery(recovery), pain score at 2, 6, 12 and 24 hours after surgery, postoperative opioid consumption, postoperative nausea and vomiting and fluid intake for assessing hemodynamic status, checked for 24 hours after surgery, presented in Table-II.

Mean \pm SD of systolic and diastolic blood pressure and pulse rate changes at 2, 6, 12 and 24 hours after surgery/before surgery was not significantly different in two groups($P>0.05$).

DISCUSSION

In this study the effect of verapamil as an adjuvant with bupivacain on the level of sensory block, post-operative pain and analgesic consumption among patients undergone elective surgery was investigated and the findings indicated that it had

Table-I: Demographic characteristics of studied population in group A (20cc of 0.5% bupivacaine plus 5mg verapamil) and B (20cc of 0.5% bupivacaine plus 2cc normal saline).

	Group A	Group B
Age(yrs)	49.7 \pm 4.6	50.4 \pm 3.9
Weight(kg)	61.5 \pm 8.2	63.6 \pm 6.3
Height(cm)	164.1 \pm 5.6	165.8 \pm 6.4
Duration of surgery(min)	100.3 \pm 43.7	105.1 \pm 49.0

not significant effect on studied factors related to epidural anesthesia. Considering the role of Ca ion on the mechanism of post operative pain, in this study the role of verapamil as a non-opioid adjuvant agent was investigated.

Voltage-gated calcium channels (VGCC) first described in 1985 by Nowycky et al they reported three types of L, T and N VGCC in sensory neurons.¹⁴ In various pathologic conditions the expression and activities of VGCC may dysregulate and result in the development of pain. From identified VGCC, the L and N types have significant role in regulating neurotransmitter release. N type VGCC has much more potent antinociceptive effects than L ones and they reduce pain mediated by A delta and C fibre.¹⁵ But they are not clinically suitable for use due to their severe neurotoxicity. Animal studies indicated that L type channel blockers such as verapamil and diltiazem could attenuate both somatic and visceral pain.¹⁶

Verapamil is a synthetic papaverine derivative and L type Ca channel blocker. It has a potent local anaesthetic activity by inhibiting the fast sodium channels similar to local anaesthetics. Previous studies reported that intrathecal verapamil alone had not sensory and motor block effect but its combination with other local anaesthetics such as

Table-II: Mean \pm SD of the sensory level block 20 minutes after starting epidural anesthesia and immediately after surgery, pain score at 2, 6, 12 and 24 hours after surgery, postoperative opioid consumption, postoperative nausea and vomiting and fluid intake in group A(20cc of 0.5% bupivacaine plus 5 mg verapamil) and B(20cc of 0.5% bupivacaine plus 2cc normal saline).

	Group A	Group B	P value
Sensory level block			
-20 minutes after starting epidural anesthesia	T8.7 \pm 2.4	T9.7 \pm 1.1	0.18
-Immediately after surgery	T9.9 \pm 1.9	T11 \pm 1.1	0.26
Pain score			
-Immediately after surgery	0.3 \pm 0.9	0.1 \pm 0.3	0.62
-2 hours after surgery	3.7 \pm 2.4	1.44 \pm 1.9	0.03
-6 hours after surgery	4.8 \pm 3.3	3.3 \pm 1.8	0.35
-12 hours after surgery	4.2 \pm 2.9	3.8 \pm 2.3	0.84
-24 hours after surgery	4.3 \pm 2.1	5.2 \pm 2.6	0.42
Postoperative opioid consumption(mg)	5.7 \pm 4.5	5.8 \pm 4.9	0.87
Postoperative nausea and vomiting(times/24 hours)	0.7 \pm 0.3	0.8 \pm 0.2	0.45
Postoperative fluid intake(ml)	1340.9 \pm 498.4	972.2 \pm 423.6	0.24

lidocaine-tetracaine solution could have potent and prolonged pain relief effect with motor blockade when compared with the local anaesthetic solution alone.¹⁷

In current study verapamil had not the mentioned effects in reducing pain, the level of sensory block, analgesic consumption, post operative nausea and vomiting and hemodynamic status of the patients. Only two hours after surgery the pain score was higher in verapamil group, considering that it was not continued in 6, 12 and 24 hours after surgery, the findings was not significant enough. Whereas in two similar studies verapamil has indicated the mentioned effects.

Kim et al in Korea have indicated that addition of verapamil to preoperative epidural bupivacaine would decrease postoperative pain possibly by preventing the establishment of central sensitization.⁷ Choe et al demonstrated less post-operative analgesic requirement in cases that verapamil was added to bupivacaine which administered epidurally.⁸

In the study of Laurito et al subcutaneous verapamil did not prolong duration of lignocaine anaesthesia. It may be due to the method of injection i.e. subcutaneous injection.⁹ Evidences suggest that subcutaneous verapamil has not anti-nociceptive effects.¹⁸

Lalla et al in India showed that adding verapamil to brachial plexus block can increase the duration of sensory blockade without any effect on duration of motor blockade and prolongation of analgesic duration.¹⁰ The difference between our results and those reported by Kim et al. and Choe et al may be due to that in the study of Choe et al postoperative analgesic consumption was determined by patient controlled analgesia (PCA) device.⁸ In this study the fluid intake after surgery was not different significantly in two groups, which showed that the hemodynamic state of the patients was not changed by using verapamil as adjuvant agent.

Hypotension is considered one of the complication of epidural anesthesia which is caused by rostral spread of the local anesthetic with subsequent sympathetic blockade.¹⁹ In this study the rate of postoperative hypotension was not different in two studies. Considering that factors such as patients' pre-existing circulation state, dose of local anesthetic and the site of drug injection influence the degree of sympathetic blockade and consequently the occurrence of hypotension¹⁹ for more conclusive results mentioned factors should be considered in future studies. The limitation of this study was small sample size and short duration of follow up

(24 hours). Previous studies mostly follow up their patients for 48 hours.^{7,8}

In conclusion, our findings indicated that though verapamil as an adjuvant with bupivacaine could not significantly increase the level of sensory block and attenuate post-operative pain and analgesic consumption but it had positive effect on hemodynamic condition of the patients. For more accurate results it is recommended to determine the effect of different dose of verapamil in larger sample size of the patients. In addition studying the effect of other Ca channel blockers would be favourable in this regard.

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