

The effect of pre-operative administration of gabapentin on post-operative pain relief after herniorrhaphy

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ABSTRACT

Background: Gabapentin, an anticonvulsant, recently has been suggested as an effective post-operative "analgesic" agent. The objective of the present study was to examine the analgesic effectiveness and opioid-sparing effects associated with the use of a single dose of gabapentin as a prophylactic analgesic. **Materials and Methods:** In a randomized double-blinded clinical trial, 50 American Society of Anesthesiologists I and II patients with an age range of 40-60 years who were the candidate for inguinal herniorrhaphy under spinal anesthesia were randomly assigned to receive 400 mg gabapentin or placebo 2 h prior to surgery. Post-operatively, the pain was assessed on a visual analog scale (VAS) at 2, 4, 12 and 24 h at rest. Morphine 0.05 mg/kg intravenously was used to treat post-operative pain on patient's demand. Total morphine consumption in the first 24 h after surgery was also recorded. **Results:** Patients in the gabapentin group had significantly lower VAS scores at the all-time intervals of study than those in the placebo group ($P < 0.05$). The total morphine consumption in the first 24 h after surgery was also significantly lower in gabapentin group than in the placebo group (0.9 ± 1.23 vs. 1.8 ± 1.5 ; $P = 0.003$). There was no significant difference between the first time of analgesic request among the two groups. **Conclusion:** In conclusion, prophylactic administration of gabapentin decreases pain scores and analgesic consumption in the first 24 h after repair of inguinal hernia.

Key words: Analgesic requirement, gabapentin, herniorrhaphy, post-operative pain

INTRODUCTION

According to the definition of International Association for the Study of Pain, pain is an emotional experience accompanying a physical injury or psychosomatic problems.^[1] In spite of the use of new drugs and novel drug delivery modalities, studies have shown that acute post-operative pain continues to be undermanaged. Approximately, three of every four patients experience acute pain after surgery and 80% of these have moderate to severe pain.^[2] Since post-operative pain management is important in early mobilization and well-being of surgical patients,^[3] it is now widely accepted that appropriate

attention must be paid in both pediatric and adult patients specially in critically ill groups.^[1] Non-steroidal anti-inflammatory drugs, local anesthetics, alpha2 agonists and N-methyl-D-aspartate receptor antagonists are the main pharmacologic groups, which have been investigated for their synergic effects in association with opioid analgesics in the management of post-operative pain.^[4]

Gabapentin, which is basically known as an anti-convulsive agent, has shown promising results for the treatment of chronic neuropathic pain like diabetic neuropathy and also in conditions such as post herpetic neuralgia or cancer pain. It has synergic effects with morphine in managing chronic neuropathic pain.^[5] On the other hand, there is considerable overlap between the pathophysiology of post-operative pain and that of neuropathic pain. Allodynia and hyperalgesia, which are the cardinal signs and symptoms of neuropathic pain, are also present after trauma and surgery.^[6] In this study, we are aimed to investigate the effect of pre-operative use of gabapentin on a post herniorrhaphy pain in patients underwent spinal anesthesia.

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MATERIALS AND METHODS

A total of 50 male patients aged between 40 and 60 years who were scheduled for unilateral herniorrhaphy under spinal anesthesia with class 1 or 2 physical status according to the classification system of American Society of Anesthesiologists were enrolled in our randomized double-blinded clinical trial. Subjects were randomly assigned into two groups (case and control) using a computer generated table of random numbers to receive the medication. In the case group, 400 mg gabapentin tablet and in the control group similar placebo tablet were used. Patients have had the tablet with 150 cc water 2 h prior to the herniorrhaphy. They received no other pre-medications. After patients were transferred to the operation room, they received 1000 cc Ringer solution and after prepping and draping the injection site, they underwent spinal anesthesia with 100 mg hyperbaric lidocaine using 25 gauge Queenke needle in a sitting position. The operation was initiated after providing adequate analgesia for surgery. Electrocardiography, pulse rate, pulse oximetry and non-invasive arterial blood pressure were monitored and registered for all the patients during the surgery. After the operation was completed, patients were transferred to the recovery room and then, transferred to surgery ward. In the ward one of the staff, which were not among surgery team, registered at-rest pain scores of hours 2, 4, 12 and 24 after operation using visual analogue scale (VAS). The pain scale consisted of a 10 cm horizontal line marked from 0 (denoting no pain) to 10 (denoting worst possible imaginable pain). And in the same time side-effects such as drowsiness, nystagmus, tremor, diplopia and nausea were evaluated. Morphine 0.05 mg/kg intravenously was used to treat post-operative pain on patients' demand. The time for the first dose of morphine and total morphine consumption in the first 24 h after surgery was also recorded. Data were analyzed using Statistical Package for the Social Sciences statistical software version 16 (Chicago, IL, USA). Pain scores in 2, 4, 12 and 24 h after herniorrhaphy operation, morphine demand during 24 h after surgery and the time of first need for analgesic were compared between two groups using independent *t*-test. *P* < 0.05 was considered to be statistically significant.

RESULTS

A total of 50 male patients who were candidates for unilateral herniorrhaphy under spinal anesthesia were enrolled in our double-blinded clinical trial to evaluate the effect of pre-operative prescription of gabapentin on the post-operative pain. As demonstrated in Table 1, the mean age was 44.40 ± 15.09 years in case group and

51.00 ± 10.29 years in the control group (*P* = 0.07). Duration of surgery was not different among two groups (83.4 ± 10 min in case vs. 84 ± 9.6 min in the control group; *P* = 0.87).

Morphine consumption dosage was 1.8 ± 1.5 mg/kg in the control group and 0.9 ± 1.22 mg/kg in gabapentin group during first 24 h after herniorrhaphy, which the difference was statistically significant (*P* = 0.003) [Table 2]. The time for first analgesic request was 40.8 ± 84 min after herniorrhaphy in the control group and 86.4 ± 82.2 min after surgery in the case group. Although time for the first request for analgesics is shorter in the control group compared with the others, but no statistically significant difference was observed between groups (*P* = 0.06). The VAS pain scores in 2, 4, 12, 24 h after surgery in two groups were summarized in Table 2 and Figure 1.

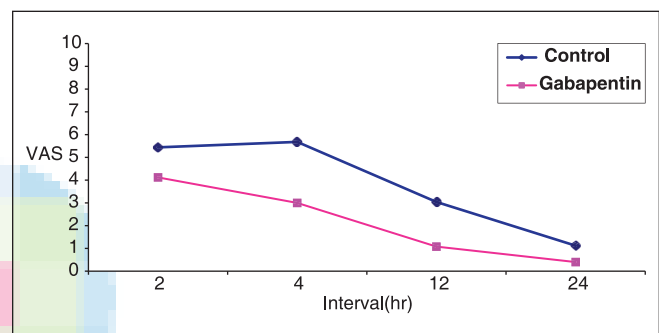


Figure 1: Intensity post-operative pain in two groups at 2nd, 6th and 12th h after surgery

Table 1: Patients' characteristics between two groups

Characteristics	Gabapentin group	Control group	<i>P</i> value
Age (mean±SD)	44.40±15.09	51.00±10.29	0.07
Duration of surgery (min)	83.4±10	84±9.6	0.87

SD: Standard deviation

Table 2: Pain scores according to VAS in 2, 4, 12, 24 h after surgery and total morphine consumption and time for first opioid request

Variabls	Gabapentin group	Control group	<i>P</i> value
VAS			
2 h after surgery	4.12±1.09	5.44±1.50	0.001*
4 h after surgery	3.00±1.58	5.68±1.14	0.001*
12 h after surgery	1.08±1.11	3.04±1.83	0.001*
24 h after surgery	0.4±0.7	1.12±1.23	0.01*
Total morphine consumption first 24 h (mg/kg)	0.90±1.22	1.80±1.50	0.003*
Time for first morphine request (min)	86.4±82.2	40.8±84	0.06

VAS: Visual analog scale, **P* < 0.05

DISCUSSION

Pain after surgery is predominantly nociceptive in nature. However, prolonged central sensitization manifesting as hyperalgesia does occur after surgical trauma.^[7] Gabapentin was introduced initially by Pfizer Inc., in the early 1990s as an anticonvulsant, but is better known as an effective treatment for neuropathic pain^[2] especially in diabetic neuropathy patients.^[5] As mentioned above, There is considerable overlap between the pathophysiology of post-operative pain and neuropathic pain.^[6] Gabapentin is a 3-alkylated analog of γ -aminobutyric acid (GABA).^[5] Several hypotheses have been proposed for mechanisms of anti-nociceptive, anxiolytic and neuroprotective activity of gabapentin such as increasing the concentration and probably the rate of synthesis of GABA in brain, reduction of the releasing monoamine neurotransmitters, modulating certain types of Ca^{2+} channels and inhibiting voltage-activated Na^+ channels and increasing serotonin concentrations in the blood, which may be relevant to neurobehavioral actions.^[8] The peak plasma level of gabapentin is achieved 2-3 h after ingestion; it is not metabolized and is eliminated unchanged in the urine. The absence of hepatic metabolism and the low level of protein binding of gabapentin contribute to its lack of clinically relevant drug interactions. Until now, several studies have been conducted about effects of pre-operative gabapentin on the post-operative pain and opioid demand, which vary in dosage and type of surgery and time of administration.^[6] In the review made by Ho *et al.*, using 1200 mg of gabapentin pre-operatively has led to lesser demand for opioid administration after surgery. In this dosage, gabapentin had a higher risk of sedation, but was associated with lesser opioid-related side-effects such as vomiting and pruritus.^[7] In the study of Pandey *et al.*, increasing dosage of gabapentin from 600 mg to 1200 mg, did not show a reduction in pain scores after discectomy, then 600 mg gabapentin was determined as favorite dose for post discectomy pain reduction.^[9] In our study, regarding to type of surgery, which was a lower abdominal surgery, 400 mg of gabapentin determined favorite in reducing post-operative pain.

Using gabapentin in multiple dosages was assessed in the systematic review of Seib and Paul. According to this review, pre-operative 1200 mg or less gabapentin as a single dose was associated with lesser post-operative pain and opioid demand during first 24 h after surgery, but multiple dosage of gabapentin before and after surgery did not cause a reduction in VAS score for pain, in this regard it suggests single pre-operative dose of gabapentin to reduce post-operative pain, as conducted in our study.^[4]

On the other hand, post-operative analgesic effect of gabapentin has been controversial some times. In the review of Kissin, it has been stated that pre-operative gabapentin has not shown significant reduction in pain score after mastectomy in contrast with the findings of Fassoulaki *et al.* and Dirks *et al.*, which in their studies 1200 mg pre-operative gabapentin lead to both acute and chronic pain reduction after mastectomy.^[10,11] The wide variability of gabapentin dosing regimens, which varied between 300 and 1200 mg and the differences in pain score and side-effect evaluating systems and type of surgeries undoubtedly influences the outcome of these studies.^[3] Therefore to determine definite effect of gabapentin, more trials is needed considering favorite dosage for each type of surgery especially for major surgeries.

According to former studies, it has been highly supported that preventive analgesic effects of gabapentin is more significant than post-operative administration of it, but a study by Pandey *et al.* demonstrated that there is not a significant difference in pain scores and opioid request in administration of 600 mg gabapentin prior to beginning of the surgery or after incision in open donor nephrectomy.^[12] Considering the type of surgery in our study, gabapentin was given 2 h pre-operatively to yield the optimum serum drug level prior to initiation of the tissue injury. 400 mg pre-operative gabapentin showed a significant reduction in pain score and patient's request for analgesics in first 24 h after unilateral herniorrhaphy. We used low single dosage of gabapentin and no obvious side-effect was reported in our study. Further clinical trials and systematic reviews are necessary to determine suitable dosage according to type of surgery.

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