

Effectiveness of Short-term Use of Gabapentin as Pre-emptive Analgesia in Reducing Pain after Video Assisted Thoracoscopic Surgery

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Background: Pain control after thoracoscopy is one of the important issues in patient health care. Pre-emptive analgesia can reduce acute postoperative pain and also prevent chronic pain. This study aimed to evaluate the effectiveness of gabapentin (GABA analog) as pre-emptive analgesia in reducing pain and reducing opiate consumption after video-assisted thoracoscopic surgery (VATS) surgery.

Materials and Methods: In this study, 67 patients undergoing thoracoscopic surgery were randomly divided into two groups (31 placebos and 36 gabapentin). Patients received two capsules (300 mg gabapentin capsules or placebo) on the night before surgery and again one hour before surgery. After completion of the operation, all patients were transferred to the recovery. Evaluation of postoperative pain was performed using the visual analog scale (VAS) every 30 minutes and then after 2, 4, 6, 10, 24 hours. If patients had pain (VAS above 3), intravenous morphine was injected to relieve pain and the number of injections and the total dose of morphine administered was recorded.

Results: There was no significant difference between the two groups regarding VAS, blood pressure (BP), heart rate (HR), respiratory rate (RR) and saturated oxygen level (SaO₂), urea, creatinine, and adverse effects.

Conclusion: Preoperative gabapentin administration did not affect postoperative pain reduction, but morphine consumption in the gabapentin group was decreased during the first 24 hours after VATS.

Key words: Video-assisted thoracoscopic surgery; Pain control; Pre-emptive analgesia; Morphine; Gabapentin

INTRODUCTION

Video-assisted thoracoscopic surgery (VATS) is a kind of minimally invasive thoracic surgery that provides sufficient incision despite confined access to the thorax, allowing the method to be performed in patients who are debilitated or have a marginal pulmonary supply (1-5). VATS is employed in cases such as the management of mediastinal, pulmonary, and pleural pathology(6).

However, its basic gain has been the shirk of a thoracotomy incision, which allows a shorter operating time, less postoperative morbidity, and earlier reversal to normal actuality than can be achieved with thoracotomy (7). This method however, also has risks such as pain (8).

One of the methods of pain management is multimodal analgesia, which is based on the use of various drugs for pain sedation (9). In other words, it can be said that the

basic principle of this method is the simultaneous use of multiple analgesics with different functional states (10). Using this method can reduce the pain of patients to some extent, which reduces the dose of individual drugs, which in result will reduce the amount and severity of side effects (11,12).

Gabapentin is an anticonvulsant drug used to treat hot flashes, neuropathic pain, partial seizures, and restless legs syndrome (13). On the other hand, it is one of the first-line drugs used to treat neuropathic pain such as diabetic neuropathy, post-heat neuralgia, and central neuropathic pain are recommended (14, 15). Due to the low adverse effect rate and its acceptable safety profile, it is a suitable candidate for pain management (16). Its mechanism of action as analgesic and anticonvulsant is unknown (17).

Given the increasing prevalence of VATS, there have been few studies on the efficacy of gabapentin as an antidote to VATS and the results have been conflicting. Therefore, the current study was designed to investigate the effectiveness of gabapentin as pre-emptive analgesia in reducing the pain after VATS.

MATERIALS AND METHODS

This clinical trial study was registered at the Iranian clinical trials registry with the following code: IRCT20160813029327N12, and was approved by the institutional ethics committee (Code: IR.IAU.PS.REC.1396.73).

Sample collection

This research was designed as a double-blind prospective randomized clinical trial. The sample population consisted of 67 thoracoscopy patients, who were randomly divided into two groups of 36 and 31. Written informed consent was obtained from all patients. This study was conducted at the surgical ward, Masih Daneshvari Hospital, Tehran, Iran from August 2017 until November 2018.

Patients were reassured that they would get the required medication in case of pain after surgery.

Inclusion criteria were ASA class I, II, III, age between 18 to 65, and being a VATS candidate.

Exclusion criteria were pregnancy, lactation, taking drugs affecting the central nervous system, substance use disorder, sensitivity to gabapentin, ketorolac or opioids, recent consumption of gabapentin or pregabalin, renal failure, liver failure, and history of cardiothoracic surgery.

Preoperative candidates were divided into 2 groups (gabapentin and placebo) using a random numbers table created by www.randomization.com.

Bottled capsules were given to the patients by pain management nurses who were blinded about the groups. Patients and surgeons were also blinded.

All the patients were explained briefly about the procedure and this study. Before any medical intervention, a complete patient history along with medications used and demographic information was taken from each patient. All patients underwent the physical and para-clinical examination.

Study design

Based on the group they were assigned to, patients were given 2 capsules, either 2 gabapentin (300 mg) cap or 2 placebo caps on the night before surgery and again one hour before surgery.

To anesthetize patients, Sodium Thiopental 3-5mg/kg, fentanyl 2-4 mcg/kg, and midazolam 1-2 mg were administered intravenously. On the other hand, to relax the muscles, atracurium 0.6 mg/kg was injected into all patients. The anesthesia was maintained using propofol 100-200 mcg/kg/min infusion. For all patients, mechanical ventilation was done and during surgery, the dose of anesthetics was adjusted accordingly.

After surgery, all patients were transferred to the recovery room and given Ketorolac by PCA (90 mg per 100 ml, 4 ml per hour). PCA was mechanical and disposable. 0.5 mL solution was injected into the patients every time they pushed the bolus button within 15 min intervals.

Visual Analogue Score (VAS) was used to assess the patients' pain every 30 min up to the first two hours after

the surgery and then, 2, 4, 6, 10, and 24 hours after surgery. This index can be determined by asking the patients during rest and after coughing. In this method, 0 indicates no pain and 10 indicates intolerable pain. If patients had VAS>3, they were given IV morphine.

Furthermore, respiratory rate (RR), heart rate (HR), blood pressure (BP), oxygen saturation (SaO2), and reported adverse effects were recorded for each patient.

All the information regarding the patient's demographics, adverse drug reactions, dose and times of morphine usage, and other pain killers were recorded in the form of a questionnaire.

Statistical analysis

The sample size was calculated by a biostatistician based on previous studies and the Designing Clinical Research book. The number of patients for each group was determined to be 45 based on the hypothesis. Type I (α) and type II (β) error were 5 and 20%, respectively and the effect of size/standard was 0.6. T-test, Mann Whitney U, and Chi-square tests were used to analyze the data.

RESULTS

One hundred thirty-four patients were assessed and 67 completed the study; 31 patients in the placebo group and 36 patients in the treatment group.

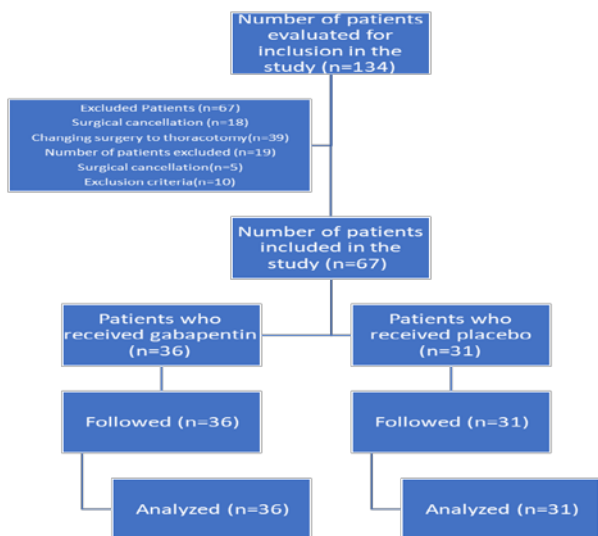


Figure 1. Diagram of how patients are enrolled

Table 1 shows demographic information of the patients. There was no significant difference between the two groups at the baseline.

Table 1. Demographic information of the study patients

	Placebo	Gabapentin	P value
Drug	31	36	-
Age (Mean ± SD)	41 ± 16.18	40 ± 15.69	0.925
Sex			0.867
Male	17	19	-
Female	14	17	-
Weight(kg)	72.90	67.17	0.083
Height(cm)	169.81	167.63	0.389
Underlying Disease			0.459
No	11	16	-
Yes	20	20	-
Type Of VATS			0.194
Diagnostic	10	16	-
Therapeutic-Pulmonary	12	13	-
Therapeutic-Mediastinal	9	7	-
Duration of Anesthesia (Mean ± SD) hour	3.22 ± 2.3	2.38 ± 1.0	0.071
Duration of Surgery (Mean ± SD) hour	2.31 ± 1.4	1.84 ± 1.0	0.133
ASA Score			0.459
1	6	8	-
2	25	23	-
3	0	5	-
RR (breathes/min)	15	14	0.699
HR (beats/min)	80	83	0.527
BPs (mmHg)	118	116	0.630
BPd (mmHg)	73	75	0.338

Based on the Mann-Whitney test, VAS of 1.5-hour post-op during resting and the VAS of 1.5- and 2-hours post-op during coughing were significantly different in the gabapentin group compared to placebo (Figure 2A and 2B). There was no significant difference at other time frames.

Regarding the amount of morphine taken by the patients after surgery, there was a significant difference between these groups (Table 2). The amount of morphine taken by the placebo group was significantly higher than the gabapentin group (Figure 3).

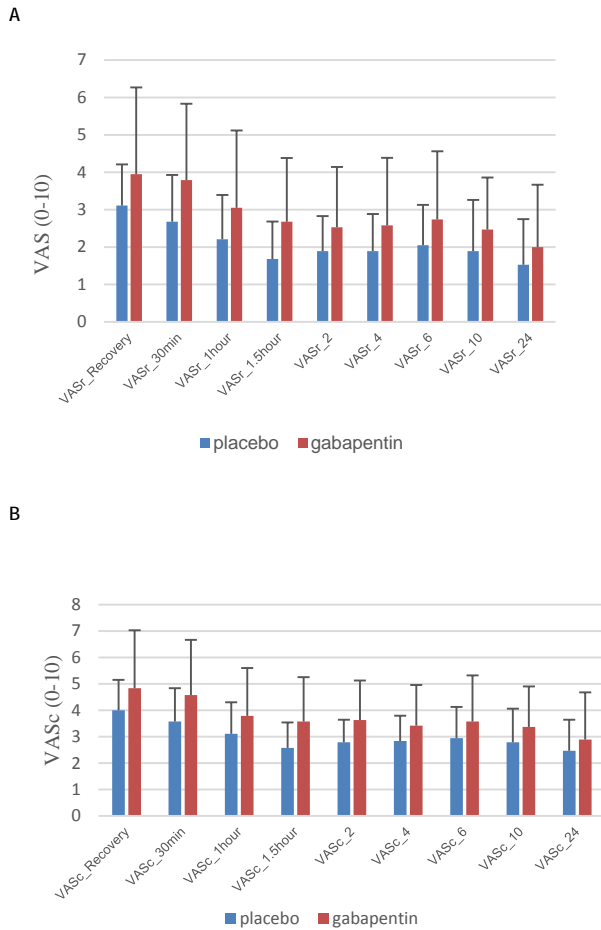


Figure 2. Comparison of resting pain (A) and cough (B) scores between the two groups

Table 2. Comparison of mean morphine dose between the two groups

Drug Name	N	Mean	Std. Deviation	Std. Error Mean	P-value
Placebo	31	10.65	7.662	1.376	0.048
Gabapentin	36	7.33	7.147	1.191	

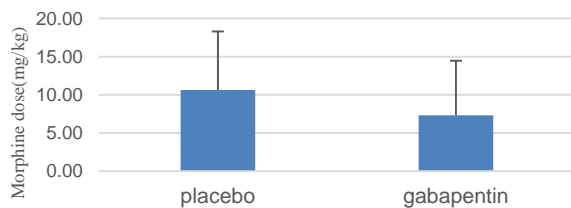


Figure 3. Comparison of morphine requirement between the two groups in the first 24 hours after surgery

DISCUSSION

The antinociceptive effects of gabapentinoids have been controversial for various surgeries and there have always been conflicting results. The positive efficacy of this drug group has been reported in many surgeries (18-20), while some reports have shown no positive effects in many surgeries (20-23).

In this study, gabapentin was used as a pre-emptive analgesic to reduce the pain in patients after VATS. Based on the results, even though there was no significant difference between the VAS of both placebo and gabapentin groups, the total dose of morphine taken by the gabapentin group had significantly decreased during 24 hours after surgery compared to the placebo group.

Amr and Yousef published an article in 2010 which in this study, one group of patients received 611 mg preoperative gabapentin and 211 mg every 3 to 2 days postoperatively. Pain scores, morphine intake, and patient satisfaction were similar between the gabapentin and placebo groups. The results of this study were similar in comparison with our study in comparison of pain scores in both groups, but there was a difference in morphine consumption (21).

An article was published on the efficacy of gabapentin as preventive analgesia for 121 patients undergoing thoracotomy. In this study, one group received 600 mg gabapentin and the other group received 12.5 mg diphenhydramine as active placebo 2 hours before surgery. This dose of gabapentin did not reduce pain and opioid use after the first 48 hours (23). These results contradict the results obtained in our study.

A study in 2018 showed that gabapentin was not effective in alleviating the pain after hysterectomy and reducing the total dose of opioids for pain management. In this study, the gabapentin group (21 patients) had taken gabapentin 600 mg as a single dose (age under 65 years old) and 300 mg as a single dose (age over 65 years old) 2 hours before surgery (24).

Another study showed that 1200 mg gabapentin before surgery and 600 mg three times a day for three days had a

significant effect on reducing the opioid required for pain relief in patients. This study was conducted in a hospital at Stanford University and the placebo group had taken 0.5 mg lorazepam as an active placebo before surgery and inactive placebo three times a day for three days. VAS was not different in these groups but the results are in line with our findings (20).

Singh et al. showed that the oral gabapentin can play an effective role in reducing pain and inducing sedation during knee arthroplasty (25). Tomar et al. also stated that the optimal use of gabapentin to induce analgesia in subarachnoid block surgery can be effective (26).

Even though low dose gabapentin was proved to have no efficacy in reducing the pain level in patients after surgery and the fact that most clinical trials have not optimized the dose, it seems like high dose gabapentin before and after surgery could be beneficial. Pregabalin and gabapentin were shown to have limited efficacy in reducing the pain but they are effective in reducing opioid use after surgery (27). This conclusion is also clearly confirmed in the present study.

CONCLUSION

The difference in VAS between the two groups was not significant because patients in both groups received adequate analgesia. Preoperative gabapentin administration did not affect postoperative pain reduction, but morphine consumption in the gabapentin group was decreased during the first 24 hours after VATS.

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Conflict of Interest

The authors declare that there's no conflict of interest.

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