SUPPLEMENT ISSUE

ARTICLE

THE EFFECT OF PREOPERATIVE SINGLE DOSE OF ORAL PREGABALIN ON POSTOPERATIVE PAIN OF ORTHOPEDIC SURGERY OF LOWER LIMBS

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ABSTRACT

Introduction: *Postoperative pain is one of the problems in which lack of adequate controls cause many complications. Pregabalin, as gamma-amino-butyric acid, has shown sedative effects on postoperative pain. Therefore, this article aimed to study the effect of preoperative single dose of oral pregabalin on postoperative pain of patients undergoing orthopedic surgery of lower limbs.* ***Method:*** *This is a randomized double-blind clinical trial on 34 candidates of orthopedic surgery of lower limbs of Peymanieh Hospital of Jahrom, Iran. The patients were split in two groups. The patients in the first group received one 150-mg pregabalin capsule prior to the surgery. The second group received a placebo. The existence of postoperative pain was assessed at 2, 4, 6, 8, and 10 hours after the surgery and the pain was assessed according to VAS. Data were analyzed using SPSS 21, descriptive statistics, and ANOVA.* ***Findings:*** *A total of 34 patients with mean age of 38.53±18.77 were enrolled. 82.4% of the patients were males and the rest were females. Experiment and control groups (pregabalin) were similar concerning the age and gender. No significant difference was found among them. The effect of pain was significant at different times in pregabalin and control groups (P<0.001). Pain reduction was greater in pregabalin group than in control group.* ***Conclusion:*** *Prescribing a 150-mg single dose of oral pregabalin one hour prior to the orthopedic surgery of lower limbs undergoing spinal anesthesia reduces the postoperative pain.*

KEY WORDS
Pregabalin, Pain, Orthopedics, Spinal Anesthesia

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INTRODUCTION

Adequate control of postoperative pain has still remained one of major challenges of surgery. Such pain causes physical complications, increased metabolism, underlying disease exacerbation, and hypertension. As a result, increased length of stay, increasing costs, patient dissatisfaction, lack of coordination by patient, and chronic pain are expected [1, 2]. Postoperative pain mechanism includes inflammation, trauma to the tissue due to surgical incision, lacerations, burns, and nerve damage, cut or pulls, or pressure on a nerve [3]. Postoperative pain causes some complications such as tachycardia, hypertension, myocardial ischemia, decreased pulmonary ventilation, and poor wound healing. Acute pain can increase the sensitivity of neurons and the release of inflammatory mediators [4-6]. Proper control of postoperative pain is still one of important topics of postoperative care. Although opiate drugs are the major postoperative pain treatment, using them brings about some complications. That is why numerous efforts have been made in order to prescribe other drugs for improving postoperative pain [7]. Advances in molecular mechanisms caused the development of multi-dimensional painlessness and the use of new medicinal products for postoperative pain control. Pregabalin is one of these new products [8]. Pregabalin, as gamma-amino-butyric acid, is initially used as anticonvulsants. Pregabalin reduces the entry of calcium to the terminals of peripheral and central nervous system and lowers levels of Substance P, glutamate, and noradrenaline, which play a major role in creating a sense of pain. Today, pregabalin is used for neuropathic and even inflammatory pain reduction, tissue stimulation, neurology, and fibromyalgia [6, 9-13]. Considering the importance of pain control especially acute postoperative pain, acute postoperative pain seems not to be effectively controlled [14]. Therefore, it is essential to study and assess different methods to reduce postoperative pain. This article aimed to study the effect of preoperative single dose of oral pregabalin on postoperative pain of orthopedic surgery of lower limbs.

MATERIALS AND METHODS

This is a randomized double-blind clinical trial on 34 candidates of orthopedic surgery of lower limbs of Peymanieh Hospital of Jahrom, Iran. Written inform consent was taken from the participents. The patients were split in two groups (14 Placebo and 20 pregabalin) using convenience sampling. The patients in the first group received one 150-mg pregabalin capsule 2 hours prior to the spinal anesthesia (Pre-anesthetic drug). The second group received a placebo.

Inclusion Criteria

All patients in Peymanieh hospital of Jahrom who underwent the orthopedic surgery of lower limbs were enrolled as the sample. They underwent spinal anesthesia.

Exclusion Criteria

Weight over 100 kg
Older than 75 or younger than 15
A history of drug dependence
History of migraine
Inability to communicate with patients to evaluate the postoperative pain
The need for postoperative ICU hospitalization
ASA 3 or 4 Patients
ASA 2 patients with development of hemodynamic instability, bradycardia or tachycardia and other complications which might be life-threatening.

All patients underwent similar spinal anesthesia. After determining the needle entry site which is generally between the fourth or third lumbar inter-vertebral space, the site was disinfected by betadine and then dried. Then the special needle entered from the inter-vertebral space into spinal subarachnoid space. After the withdrawal of cerebrospinal fluid from the bottom of needles, drugs were injected. Upon the completion of the technique, the patients were left in supine position. The onset of anesthesia was calculated from the patient's inability to feel the painful stimuli such as pinch in the lower extremities. T10 was considered the base. Blood pressure, pulse, and respiration of patients were measured and recorded immediately after the injection and at 5, 10, 20 and 60 minutes. The patients were asked concerning the pain. The onset of pain was recorded. The pain was assessed 2, 4, 6, 8, and 10 hours after the surgery. In case of failure for spinal block, the patients underwent general anesthesia and were excluded. The severity of pain was measured using VAS. The pain was categorized in three: Mild, Medium, and Severe. The data were analyzed using SPSS 21, descriptive statistics, and ANOVA.

RESULTS

A total of 34 patients with mean age of 38.53±18.77 entered the study. 82.4% of the patients were males and the rest were females. Experiment and control groups (pregabalin) were similar concerning age and gender. No significant difference was found among them. [Table 1] shows the ANOVA with repeated measures. The results showed that the effect of pregabalin intervention was not significant on postoperative pain of the patients undergoing orthopedic surgery of lower limbs using spinal anesthesia at different times in both groups (P=0.610). Pain reduction was, however, significant at different times in pregabalin and control groups (P<0.001). [Fig. 1] shows that pain reduction was greater in pregabalin group than the control group. In pregabalin group, pain increased up to four hours after the surgery and then decreased.

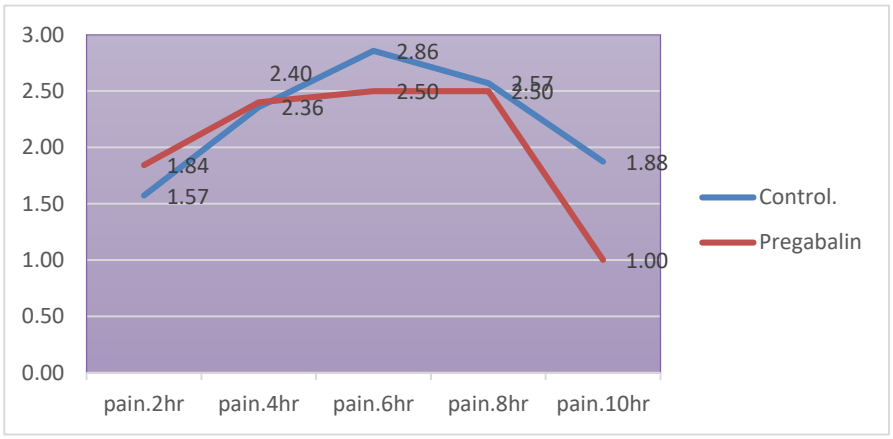

Fig. 1: Comparison of Pain at Different Times in Two Groups (Pregabalin and Control)

A significant difference was found between experiment and control groups concerning respiratory changes. No significant difference was found concerning changes in heart rate, systolic and diastolic blood pressure, heart rate and 02. The effect of changes in diastolic blood pressure and heart rate was significant at different times in both groups (P<0.001). Changes in increasing diastolic blood pressure and heart rate were declining after the surgery [Table 2].

Table 1: Comparison of Pain at Different Times in Two Groups (Pregabalin and Control)

	group				Time Effect	Time*group Effect
	Control(N=14)		Pregabalin(N=20)			
	Mean	SD	Mean	SD		
pain.2hr	1.57	.65	1.84	0.96	<0.001	0.610
pain.4hr	2.36	1.15	2.40	1.10		
pain.6hr	2.86	1.10	2.50	1.19		
pain.8hr	2.57	1.28	2.50	1.31		
pain.10hr	1.88	.64	1.00	.		

Table 2: Comparison of Vital Signs at Different Times in Two Groups (Pregabalin and Control)

	group				Time Effect	Time*group Effect
	Control(N=14)		Pregabalin(N=20)			
	Mean	SD	Mean	SD		
BP SISTOL Pre	116.23	12.08	113.17	32.99	0.565	0.051
BP SISTOL 5min	110.67	33.72	123.40	20.14		
BP SISTOL 10min	117.79	16.29	118.45	16.92		
BP SISTOL 20min	113.23	15.16	114.40	14.08		
BP SISTOL 60min	115.62	15.32	116.39	13.96		
dystol	69.77	10.83	73.67	11.18	0.018	0.569
dystol5	72.00	12.17	74.30	12.30		
dystol10	71.07	11.38	69.35	11.02		
dystol20	67.92	11.53	66.75	13.02		
dystol60	72.31	13.24	66.89	11.47		
HR.reoperative	83.23	21.71	79.00	8.86	0.001	0.139
HR.5min	78.93	18.79	84.30	15.88		
HR.10min	77.00	16.95	82.80	14.09		
HR.20min	75.36	15.11	76.30	12.66		
HR.60min	70.93	17.56	72.95	13.22		
Breath.reoperative	19.86	1.17	18.56	3.05	0.142	0.027
Breath.5min	19.14	.95	18.80	3.98		
Breath.10min	19.43	1.50	17.70	2.74		
Breath.20min	18.86	1.03	17.75	4.54		
Breath.60min	20.21	2.15	17.18	3.19		
O2.reoperative	96.58	3.12	97.29	1.27	0.052	0.237
O2.5min	97.85	.55	96.20	3.30		
O2.10min	97.29	2.33	97.21	1.87		
O2.20min	98.07	.83	97.70	1.42		
O2.60min	98.07	1.33	98.11	1.13		

DISCUSSION

Pregabalin, as gamma-amino-butyric acid is mainly used in controlling neuropathic pains [15]. Its mechanism is the pre-synaptic connection to voltage-gated calcium channels in the central nervous system. Pregabalin inhibits the over-stimulation of neurons by affecting the calcium channels [6, 16-20]. The results of our study showed that pain reduction was lower in patients who received preoperative pregabalin than those who received placebo. The results are consistent with other studies. The study by *Choubsaz et al.* showed that pain in pregabalin group was lower at 6 and 12 hours after the surgery than the placebo group [21]. The study by *Hazem et al. (2014)* showed that preoperative prescription of pregabalin can well reduce the postoperative LASIK pain [22]. The study by *Naderi et al.* showed that prescribing 150mg oral pregabalin one hour prior to the orthopedic surgery of lower limbs decreased the postoperative pain dramatically [23]. Another study by *Joe Kola and Ahounen* showed that prescribing 150 mg pregabalin decreased the postoperative pain of patients undergoing gynecological laparoscopy [24]. The study by *Backonja et al.* showed that prescribing 300 mg preoperative pregabalin prior to orthopedic surgery controls pain and reduced the drug intake by 50%. A study on small gynecologic surgeries showed that prescribing 150 mg preoperative pregabalin was not effective in pain reduction [25], which might be associated with the type of surgery. Other studies including Jakala and Matthiessen showed that no significant difference was found

between pregabalin and control groups concerning the pain severity, which is inconsistent with our study [26, 27]. According to the results, it is recommended to study higher doses of preoperative pregabalin on postoperative pain and complications. Since the patients were assessed for 10 hours after the operation, longer periods of assessment are advised.

CONCLUSION

According to the findings, prescribing 150 mg oral pregabalin 2 hours before the orthopedic surgery of lower limbs reduced postoperative pain severity.

CONFLICT OF INTEREST
There is no conflict of interest.

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FINANCIAL DISCLOSURE
None

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