RESEARCH ARTICLE

The Preemptive Effect of Pregabalin Single Dose on Opioid Consumption after surgery of Mandible Fracture: The Double-Blinded Clinical Trial

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Background: Currently, the administration of non-opioid analgesics as a preemptive treatment has been approved by the surgeons of jaw due to lack of side effects of opioids in jaw surgery. However, which medicine as a pre-medication has a good result, is a controversy. Therefore, the aim of this study was to investigate the effect of preemptive therapy by pre-gabalin single dose on opioid consumption rate after surgery on mandibular fractures.

Methods: This double-blind clinical trial was conducted in Tabriz Imam Hospital in 2012 on 60 patients who were undergoing mandibular fracture surgery. Patients were classified as intervention and control groups and the intervention group consumed one pregabalin capsule 300 milligrams with 50 ml of water half an hour before surgery. The amount of opioid use in the first eight hours after surgery was measured and recorded in both groups.

Results: Opioid use in both groups was decreased with time- spending. There was also a significant relationship between opioid use in both intervention and control groups (P <0.001).

Conclusion: Pregabalin premedication could have analgesic effects in lower jaw fracture surgery and decrease opioid use after surgery.

Keywords: Pregabalin; Preemptive; Mandible; Fracture; Opioid

Based on the absence of protection in the lower mandible area, this area is considered as one of the most sensitive areas of the body, with high frequency of fractures [1] and its prevalence varies from country to country [2]. The treatment of jaw fractures is very important because of the close proximity to head and vital elements, as well as beauty features [3]. Because mandible fractures are extensive in most cases, they require surgical treatment and therefore, mandible surgery is unavoidable [4]. In comparison with other therapeutic options, the surgery of fracture could reduce cost of treatment, induce comfort and satisfaction of patients, reduce visits to physicians, and there are many complications in correlation with its high benefits [5]. Inability to eat and drink, movement constraints, inability to speak, pain and to relieve pain are very undesirable and sometimes unstable complications in the first week after surgery [6], among which of them, pain and inability to discuss about it over first 24 hours after surgery are considered as main part of claims [7]. Based on inability of patients to use oral analgesic drugs for control of postoperative pain, the use of intravenous opioids is one of the most common methods for controlling and management of pain in these patients [7], but with regard to opioids-induced complications such as respiratory apnea and vomiting, which are prescribed by physicians with obsession and fear [8]. The need to intubation after apnea and vomiting after opioid administration increases probability of patients returning to the operating room and requiring further surgery [7,9]. Different protocols have been presented by specialists for the management of pain after jaw fracture surgery, preemptive treatment is proposed more advisable than other methods. One of these methods is the use of pre-surgical oral medications, which is favored with many surgeons [7]. The use of this method could reduce postoperative pain, need to opioid administration and patient satisfaction; however, there is controversy [10-13]. Due to its high fat solubility and high penetration in blood-brain barrier, pregabalin has good antinociceptive effects, which have been suggested in some studies for controlling of postoperative pain [14]. This drug has been introduced as an oral medication to control and management of postoperative jaw fracture surgery. There are very few studies to confirm the analgesic effects, and based on the controversial results about positive effects of oral drugs on postoperative pain control and management after jaw fracture surgery, we aimed to evaluate the effect of preemptive therapy with pre-gabalin single dose administration on opioid use after surgery of mandibular fracture.

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Methods

In this double-blind clinical trial (IRCT201202281772N10, ethical no: 90.1-6.12) and 60 patients undergoing mandibular surgery through April 2011 until April 2013 were included. Inclusion criteria were age 16-60, ASA I-II, mandible fracture. Drug abuse, drug sensitivity to pregabalin, psychiatry disorders were exclusion criteria and patients were randomly classified into intervention and control groups. All patients did not visit Tabriz Imam Reza Hospital at the same time, random allocation of samples was conducted with 60 cards with the terms "group A" and "group B " written and folded up to be readable and observable for patients. Group A was the control group and the intervention group were B group. Cards were provided to patients. Each patient received one card in the same way as control card. The patients were referred to mandibular surgery clinic. For the intervention group, half an hour before the surgery, a 300-mg pregabalin capsule with 50 mL of water was given by nurse who was aware of study; it should be noted that patients had no information about capsule type. The control group did not receive this medication. Afterwards, patients were transferred to operating room and received fentanyl (2µg/ kg) and midazolam (0.01 µg/ kg) for premedication and induction with propofol (2mg/ kg) and cisatracurium (0.4mg/ kg); then intubated. Maintenance of anesthesia was continued with TIVA (i.e. propofol and remifentanil). Researchers, patients, anesthesiologists and surgeons were blind to the study. At the end of surgery, the patients were reversed with i.v. atropine 1.5mg and neostigmine 2.5mg and then extubated. The patients were transferred to the recovery unit after stability of patients; they were transferred to mandibular surgery department after being fully conscious in post anesthesia care unit. The amount of opioid intake (e.g. morphine/ mg) was recorded at the second, fourth, sixth and eighth hours after surgery. Finally, after data collection in SPSS 21, was analyzed by descriptive statistics (mean and standard deviation) To compare the mean before and after the quantitative variable, the Paired Sample T-test and the mean comparison of the two groups independent of the Independent T-test were used. The Kolmogorov-smirnov test was used to determine the normal gravity of the varieties.

Chi-square test was used to compare qualitative data. It should be noted that P <0.05 was considered significant.

Results

The results of the study indicated that 41 patients were male, mean age ± SD of patients was 49.13 ± 53.31 years old. Systolic and diastolic blood pressure, heart rate before and after surgery, height and weight are given in (Table 1).

Opioid use in both groups was associated with decrease in time from the second hour to the next hour; there was also a significant association between opioids consumption between intervention and control groups (Table 2).

Table 1- Height, Weight, Systolic Blood Pressure, Diastolic and Heart Rate Before and After Surgery

		Mean±SD	p-value
Systolic Blood Pressure	Before	117.71±12.09	<0.001
	After	107.96±11.48	
Diastolic Blood Pressure	Before	76.05±9.43	<0.001
	After	72.52±6.17	
Heart Rate	Before	92.33±11.66	<0.001
	After	87.72±9.39	
Height(cm)		173.25±9.43	
Weight (kg)		80.40±9.55	

Table 2- Consumption of opioids in milligrams

	Groups		p-value
	intervention	control	
At 2 o'clock after surgery	0.16±0.11	0.16±0.11	1.00
At 4 o'clock after surgery	1.07±0.33	2.19±1.21	0.001
At 6 o'clock after surgery	0.00	0.75±0.22	0.01
At 8 o'clock after surgery	0	0	-
Received in the first eight hours after surgery	1.16±1.82	3.07±1.9	<0.001

Discussion

The aim of this study was to evaluate the effect of preemptive therapy by pregabalin single dose on opioid consumption after surgery of mandible fracture. The results show preoperative pregabalin administration effects on opioid reduction after surgery. Based on the results of present study, there was no significant difference in systolic, diastolic blood pressure and pulse rate before and after surgery between two intervention and control groups but there was a significant difference in postoperative heart rate between control and intervention groups so that heart rate of control group was higher than intervention group, which indicates pain in the control group; the pregabalin drug, due

to the effects of postoperative pain relief, reduces heart rate, which is consistent with the results of this study by Baffen et al. [15]. Other results showed a significant difference in postoperative opioid use between intervention and control groups, so that control group received opioid three times in relation to intervention group. The results of this study were consistent with results of the study by Alimian et al. In their study, positive effects of preoperative pregabalin administration on reduction of pain and opioid use in laparoscopic patients were demonstrated and suggested further studies in other surgeries [16]. Carolina et al. stated positive effects of pregabalin on the reduction of opioid use in patients undergoing laparoscopic surgery, and suggested that pregabalin can cause analgesic effects in patients undergoing surgical intervention [17]. Zang et al., in their meta-analysis, concluded that pregabalin in most studies had postoperative antinociceptive effects, which is consistent with the results of the present study, but it seems that for suggestion of drug in different patients, surgeries, races and ethnicity, we must conduct further surveys on higher sample sizes with most similar to the community [14].

Limitations:

The lower sample size in this study was not a good indication of generalization to the community; also, the study of opioid use in the early hours after surgery, where the effects of anesthetic drugs have not been fully addressed and the lack of the study of opioid use for up to 48 hours after surgery is another limitation in this study. Therefore, the researchers suggested that further studies should be conducted with a larger sample and opioid use up to two days after surgery. The researchers also believed that Tabriz University of Medical Sciences in the northwestern region of Iran has the highest proportion of patients from other provinces that are of other ethnicities and races. In all interventional studies, in addition to the appropriate sample size, ethnicity should also be considered in selecting samples so that different patients will be enrolled in the study and thus the results of clinical trials can be more generalized to the community.

Conclusion

The use of pregabalin preemptive therapy could have analgesic effects in mandible fractures and reduce opioid use after surgery.

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