RESEARCH ARTICLE

Effect of Single Dose of Pregabalin on Post Tracheal Intubation Sore Throat after General Anesthesia

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Background: Sore throat is one of the major complications of tracheal intubation after general anesthesia. Pregabalin is an analgesic, the anti neuropathic pain and analgesic effects of which have been demonstrated in various studies. This study examined the effects of single dose pregabalin one hour before tracheal intubation, to prevent sore throat after extubation.

Methods: In a double-blind, randomized clinical trial, 60 patients who had undergone general and urologic surgeries at Imam Reza hospital in Tabriz, Iran, since March to July 2015 that required tracheal intubation, were included in the study. The patients were randomly divided into two groups (group A, 30 patients and group B, 30 patients). In the group A, an hour before anesthesia, one pregabalin tablet (300mg) was given to the patients. For the patients of the group B, the placebo was given. After awareness of patients, the severity of sore throat was measured and recorded by VAS scale after 2, 6 and 24 hours of the surgery.

Results: Severity and incidence of sore throat after tracheal intubation were not significantly different between two groups. Meanwhile, no side effects of pregabalin were observed in the group A.

Conclusion: Administration of pregabalin as a single dose of 300 mg one hour prior to anesthesia and intubation decreased the incidence and severity of sore throat in the case group than the control group, although the amount of this reduction was not statistically significant between the two groups.

Keywords: Extubation; General anesthesia; Pregabalin; Sore throat; Tracheal intubation

Endotracheal intubation during general anesthesia is done in order to achieve two major objectives: first, creating safe airway and second, prevention of aspiration during surgery.

Endotracheal intubation is performed in various ways, including intubation through the mouth and nasal. Postoperative sore throat is a common and unpleasant complication in patients who undergo surgery with general anesthesia with endotracheal intubation or laryngeal mask. Postoperative sore throat has been reported to be 14/4%-57% in patients who had endotracheal intubation and 3/5%-34% in patients with laryngeal mask [1-3]. Several factors are involved in causing the complication including age over 60 years, use of a pharyngeal pack, appropriate size of endotracheal tubes, high pressure of the laryngeal masks and endotracheal tube cuff, duration of surgery, the patient's position during surgery and the degree of difficulty of intubation. These factors cause airway irritation and inflammation and pain [2-4]. However, the pain in some patients is so severe that causees patients' discomfort. Different drug and non-drug preventative methods are recommended to reduce the incidence and severity of pain and improve the quality of post-operative care [2, 4-5]. Non-drug approaches include: the use of small endotracheal tube, lubricating endotracheal tube with a lubricant that is insoluble in water and careful techniques of suction of patient's throat and extubation when the tracheal tube cuff is completely empty [5-6]. Drug preventative methods include the use of magnesium tablets, benzydamine hydrochloride spray, 10% and2% lidocaine spray on the endotracheal tube cuff, the use of lidocaine 2% gel, and the use of inhaled beclomethasone and dexamethasone [1-2, 5, 7].Given the prevalence of this complication it seems that extensive research needs to be done. The use of certain drugs in the postoperative period may cause undesirable side effects. For example, nonsteroidal anti-inflammatory drug (NSAID) has such side effects as platelet dysfunction, stress ulcer; etc. The routine use of them has not dealt well in controlling sore throat. The use of a variety of analgesics seems acceptable because they don't have the mentioned side effects [6]. Many studies showed that pregabalin has analgesic effects which are used at doses of 300 mg up to 1,200 mg in separated doses or with other analgesics before the onset of pain [8-9]. Pregabalins, strong connection to the Delta α^2 shows that by reducing the depolarization-induced calcium influx at nerve terminals induction and consequently decrease of the number of stimulatory mediators, such as

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glutamate, norepinephrine, substance P and calcitonin gene-related peptide (CGRP) happens [10]. It is probable that this modulation of neurotransmitter released by pregabalin contributes to the drug's anticonvulsant, analgesic, and anxiolytic effects [9-10]. Agarwal et al. [8], research showed that single preoperative oral dose of pregabalin 150 mg is an effective method for reducing postoperative pain and fentanyl consumption in patients undergoing laparoscopic cholecystectomy. Tippana et al. [7] showed that single dose of gabapentin 300-1200 mg; effectively reduces postoperative pain and opioid consumption. Jokela et al. [9] in a clinical trial showed that 50 to 300 mg doses of pregabalin in comparison with ibuprofen 400 mg in a dental pain model, the 300 mg dose of pregabalin induced considerably more side-effects than ibuprofen. The most common side-effects were dizziness, visual disturbances, and vomiting [10-11]. The effect of pregabalin has not been studied on sore throat after tracheal extubation. This study evaluated the effect of pregabalin on sore throat after tracheal extubation.

Methods

In this study, 60 patients from Imam Reza Hospital, Tabriz, Iran, since March to July 2015 that required tracheal intubation were selected through randomized sampling. The patients were trained on the measurement of pain to manner visual analog scale (VAS). After ethics committee approval of all the patients, written consent to the use of pregabalin was obtained. The patients were divided into two groups with simple random sampling. Group A received one tablet pregabalin 300 mg with 50 ml of water one hour before anesthesia and intubation, and group B received placebo instead of pregabalin. The patients in both groups had similar premedication with fentanyl (1µg/kg) and midazolam (0.02 mg/kg), and were similarly inducted with propofol (2-2.5 mg/kg), atracurium (0.5 mg/kg). The patients were gently intubated with cuffed oral endotracheal tube with a diameter of 7-8 mm by an anesthesiologist. Anesthesia was continued with a continuous infusion of propofol 100 µg/kg/min, and remifentanil 0.0625-0.25 µg/kg/min. After completion of the operation the patient's throat was gently suctioned, and then endothrachal tube was extubated after deflation of cuff. The postoperative analgesic regimen was similarly chosen in the ward. The patients' sore throats were recorded after awareness of patients by one medical student who was unaware of the group of patients, 2-6 and 24 hours after surgery, and data were collected by questionnaires.

Statistical analysis

In order to study qualitative variables X^2, and quantitative variables t- test were employed. For data analysis, Social Sciences (SPSS) software (version 15.0 for Windows; SPSS Inc., Chicago was used. If P=0.05 or less then it was considered statistically significant. Data obtained from the study by descriptive statistics (frequency-percentage - Mean and standard deviation) were analyzed and the mean difference test for independent groups was employed. For normality of distribution of data Kolmogorov-Smirnov test and Q-Q charts was used.

Results

Sixty patients were included in this study. Information (demographic) related to the patients' general characteristics are presented in (Table 1).

The patients in the groups A and B were ASA of physical status classification I and II, No statistically significant difference was found between the physical conditions (P=0.17).

Prevalence of postoperative sore throat in patients of both groups was measured by a medical student and using a VAS. Incidence of sore throat was measured in 2, 6 and 24 hours after surgery. There was no statistically significant difference (P= 0.45) in prevalence of pain at different times after surgery (Table 2).

Incidence of postoperative sore throat severity and pain intensity according to VAS was measured in the hours of 2-6- 24 postoperative (after surgery) and was recorded. Severity of sore throat was divided to; without, mild, moderate and acute sore throat. There was no statistically significant difference in Pain severity average at different times after surgery (Table 3).

Table 1- Demographic characteristics of patients in both groups

Parameters	Group A(n)	Group B(n)	P values
Patients (n)	30	30	
Female (n)	13	18	
Male (n)	17	12	
Mean age (years)*	35.5±12.2	42.4±12.8	P=0.3

*Results are shown as Mean ± SD.

Table 2- Prevalence of sore throat among patients in both groups.

Time (Hour)	patients in Group A(n)	patients in Group B(n)	P values
2	23	17	P=0.1
6	19	15	P=0.19
24	4	6	P=0.45

Table 3- Prevalence of postoperative sore throat severity and pain intensity in both groups.

Time	Pain in group A(n)					Pain in Group B(n)					P value
hours	Without	mild	moderate	acute	Mean*	Without	mild	moderate	acute	Mean*	
2	7	6	13	4	3.9±2.9	13	2	9	5	3.2±3.3	P=0.41
6	11	16	3	1	1.7±1.8	15	9	4	1	1.5±2	P=0.59
24	26	4	0	0	0.5±1.7	24	3	1	2	0.7±1.6	P=0.67

*Results are shown as Mean ± SD.

Discussion

The present study assessed preventive effect of a single dose of pregabalin on the sore throat at two, six and twenty-four hours after intubation, and the results obtained from the two groups who had received single dose of pregabalin (group A) and placebo (group B) were compared. In this study, the frequency of sore throat in two, six and twenty-four hours after intubation had no significant difference (P value respectively P=0.1, 0.19 and 0.45) between the two groups. The severity of sore throat was not significantly different in two, six and twenty-four hours after intubation in two groups (P value respectively P=0.41, 0.59 and 0.67), and no adverse effects such as; dizziness, visual disturbances, insomnia, dry mouth, swelling of the hands and feet and vomiting were observed in this study related to pregabalin.

Few studies have been done on the analgesic effect of preoperative single dose of pregabalin [8-9].

Aydogan et al. [10] studied 60 patients who were candidate for percutaneous nephrolytetomy showed that analgesic effects of a single dose of 75 mg of pregabalin in the prevention of postoperative pain in 30 minutes and 1 and 2 hours after surgery was effective. Aydogan et al. [10] stated that VAS is used to assess the severity of pain after surgery. In this study, single dose of pregabalin decreased rate of postoperative sore throat in the intervention group, although this reduction was not statistically significant (P=0.45). Another study by Cabrera et al. [12] on 80 patients undergoing laparoscopic gastrectomy showed that administration of a single dose of pregabalin prior to surgery significantly reduces morphine consumption during the first 24 postoperative hours in pregabalin group versus the placebo group (11.51 ± 7.93 mg vs 23.07 ± 9.57 mg), (P< 0.05). The incidence of nausea and vomiting and the use of antiemetic drugs were also significantly (P < 0.05) were lower in patients that received the pregabalin. Several studies have shown the effects of various drugs on the sore throat after general anesthesia and intubation [1-2, 5-6]. However, no study has yet investigated the effects of pregabalin on the sore throat.

Another study by Canbay et al. [13] on 46 patients who were scheduled for septorhinoplasty showed that ketamine gargle with a dose of 40 mg, 5 minutes before induction of anesthesia, reduce the frequency and severity of postoperative sore throat significantly. However, in Canbay et al. [13] study, ketamine failed at all times up to 24 hours after surgery to reduce the frequency and severity of sore throat. In other study that was conducted by Honma et al. [14] on 527 patients showed that the use of lidocaine 8% spray on patients' pharynx and larynx 10 minutes before intubation significantly reduced postoperative sore throat. In a review study that was conducted by Lam et al. [15] on 19 trials in which the intra cuff lidocaine versus air or saline was compared in patients receiving endotracheal tube intubation general anesthesia. Investigating the outcome of 1566 patients, it found that the use of both alkalinized and non-alkalinized lidocaine tube can significantly (p<0.05) decrease postoperative sore throat, coughing, hoarseness, agitation and dysphonia. But in this study the use of single-dose pregabalin could not reduce sore throat after intubation. In placebo-controlled clinical trial conducted by Thang et al. [16], 42 patients undergoing laparoscopy, single dose of intravenous diclofenac was studied in the prevention of sore throat after extubated. There was no significant difference (P value respectively 0.361, 0.678, and 862) between the A and B groups after 2, 6, and 18 hours. In this study the highest incidence of throat pain was 76.7% in the group A and 56.7% in the group B 2 hours after surgery.

The lowest incidence of throat pain was 13.3% in the group A and 20% in the group B 24 hours after surgery. Zhao et al. [17] in a systematic review and meta-analysis study on 480 patients, showed that prophylactic use of intravenous dexamethasone before surgery reduces the sore throat significantly 1 hour and 24 hours after extubation. This method could also reduce hoarseness 1 hour after extubation, but was not successful 24 hours after extubation. A study done by Safavi et al. [18] showed reduced the frequency and severity of sore throat, at all times up to 24 hours after surgery, simultaneous use of ketamine gargle with intravenous dexamethasone is more effective than using any of these drugs alone. The use of these two drugs together (gargling of ketamine and intravenous dexamethasone) reduces the frequency and severity of hoarseness at all times up to 24 hours after extubation rather than the use of saline. Ansari et al. [19] showed that dexamethasone and magnesium sulfate inside the endotracheal tube cuff has no significant effect on decreasing incidence of sore throat after tracheal intubation, but found that the severity of sore throat is significantly less (P<0.032) after receiving the endotracheal tube cuff dexamethasone compared to control group and the group receiving magnesium sulfate into the endotracheal tube cuff in the morning after surgery. Ansari et al. [19] had suggested that if these results with larger population were confirmed, injection of dexamethasone into the endotracheal tube cuff can be used as an effective way to reduce the severity of sore throat after intubation. Thus, it can be used as an alternative manner to intravenous administration of dexamethasone in patients who do not receive IV corticosteroids. Maruyama et al. [20] revealed that the use of oral clonidine does not decrease sore throat after intubation immediately and one day after surgery. Park et al. [5] showed that prophylactic use of 0.2mg / kg intravenous dexamethasone can decrease

frequency and severity of sore throat and hoarseness 1 hour and 24 hours after extubation in patients in whom the (Double lumen endotracheal tube) DLT were used. In this study frequency of sore throat and hoarseness 24 hours after extubation was 27 and 15 percent respectively.

Conclusion

The results of this study show that administration of pregabalin one hour prior to anesthesia and intubation decreased the incidence and severity of sore throat in the group A, although this reduction was not statistically significant between the two groups(P=0.45), also in this study any adverse effect of pregabalin was not observed.

Suggestions: Larger population may provide significant difference ($p<0.05$) between the two groups. Meanwhile, due to the half-life of several hours of pregabalin using more and multiple doses may have better results.

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