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Research Article

Comparative Study of the Prophylactic Effect of Intravenous or Gargling Dexamethasone in Reducing Postextubation Sore Throat and Cough

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ABSTRACT

Background: Sore throat, cough and hoarseness after tracheal extubation are common complications after surgery. Due to the proven effect of dexamethasone on reducing these complications, in this study, we compared the prophylactic effect of intravenous dexamethasone and dexamethasone gargle on sore throat and cough after extubation.

Methods: In this clinical trial study, 96 patients between the ages of 18-64 years who underwent elective surgery and intubation under general anesthesia were randomly divided into three groups, respectively, the first group received 6 mg dexamethasone gargle. The second group received 6 mg intravenous dexamethasone and the third group received normal saline. The frequency of cough and sore throat were assessed and compared in these three groups.

Results: There was no significant difference between the three groups based on hemodynamic variables and demographic data (P> 0.05). The frequency of cough in the first (1.54± 2.82) and second (1.57±2.73) groups was less than the third group (1.79±3.14), but this difference was not statistically significant (P>0.66). The mean severity of sore throat in the second group and then in the first group was lower at the time of entry into recovery and 2 hours after surgery, than the third group. (P <0.005) Also, the mean severity of sore throat in the second group and then the first group in 24 hours after surgery was significantly lower than the third group. (P <0.005).

Conclusion: Prophylactic single-dose intravenous dexamethasone is more effective than dexamethasone gargle in reducing sore throat due to endotracheal intubation. Also, gargling and intravenous injection of dexamethasone, both are effective in reducing postoperative cough without any side effects after extubation.

The incidence of cough after general anesthesia is about 15-94%. This condition can be associated with dangerous complications such as hypertension, cardiac dysrhythmias, myocardial ischemia, surgical site bleeding, bronchospasm, increased intraocular pressure, and increased intracranial pressure [1-2]. During cough, intraocular pressure can rise to 30 to 40 mm Hg and cause complications such as loss of vitreous during cataract surgery. Cough is the eighth complication after surgery [3-4].

Sore throat is another common complication of anesthesia after endotracheal intubation and its prevalence is between 6-90% and sometimes more than 90%. This incidence depends on the degree of trauma caused by laryngoscopy and the type of endotracheal tube [5]. The cause of this complication (sore throat) is damage to the throat, larynx or trachea [6]. Sore throat is more common in women and usually lasts up to 24 to 72 hours after the endotracheal tube is removed. In some cases, the sore throat is so severe that it may become the patient's main complaint in the postoperative stage and may even overshadow the patient's main problem [7]. Various factors such as female gender, history of smoking, lung diseases, nausea after surgery [8],

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endotracheal tube size, cuff pressure, time and amount of manipulations required to implant endotracheal incision are effective in the occurrence of postoperative sore throat [9]. Despite efforts to reduce the frequency and severity of postoperative sore throat, sore throat and hoarseness are still common postoperative problems [10-11].

Different pharmacological and non-pharmacological methods have been suggested to reduce these side effects. Use of small-sized endotracheal tube endings endotracheal intubation after complete muscle relaxation, minimization of pressure inside the cuff and removal of the endotracheal tube when the endotracheal tube cuff is completely emptied by non-pharmacological means in reducing postoperative sore throat [12-13]. Medications include gargling with azolenesulfate or lidocaine, aspirin and ketamine [11, 14-15], using a steroid gel [9] and injecting, gargling or inhaling fluticasone propionate (a steroid) [16-19]. However, each of these techniques has its own limitations [20].

Since part of the etiology of postoperative cough is due to irritation and inflammation of the mucous membranes of the airways caused by the endotracheal tube, it seems reasonable to consider a method to anesthetize the mucosa in contact with the endotracheal tube, and tolerate it [21].

Dexamethasone is a potent glucocorticoid with anti-inflammatory and analgesic effects that has prophyl tactic effects on postoperative nausea and vomiting, and its effect on the treatment of sore throat has been reported. [19, 22-27]. Recent studies have shown that dexamethasone is effective in reducing postoperative cough and sore throat.

According to a study by Bagchi et al. prophylactic intravenous dexamethasone in a dose of 0.2 mg/kg can reduce the incidence of postoperative sore throat at 1 hour post-extubation by around 30%, with the efficacy being around 60%. They showed that the use of intravenous dexamethasone can be effective up to 60% in reducing postoperative sore throat till one hour after extubation [28].

Other study findings showed a decrease in the severity of post extubation sore throat in groups who gargled 0.05% dexamethasone solution before surgery compared with those in which a 0.05% dexamethasone-impregnated endotracheal tube was used [19]. Also, Thomas et al. reported that preoperative administration of dexamethasone 8 mg IV reduces the incidence and severity of postoperative sore throat in patients receiving general anesthesia with endotracheal intubation [17].

Moreover, in a study by Gomar and his colleagues, they showed a reduction in cough, sore throat and postoperative hoarseness in patients using intravenous dexamethasone compared to patients using normal saline as a placebo. In this study, the effectiveness of 0.2 mg / kg intravenous dexamethasone was greater than the dose of 0.1 mg / kg in reducing complications [29].

In this case, different and contradictory studies have also been reported. For example, Ruangsin and his colleagues, reported that intravenous dexamethasone had no significant effect on reducing postoperative sore throat. [30] Also, in a study at Kurdistan University of Medical Sciences, they concluded that intravenous administration of dexamethasone before endotracheal intubation does not prevent sore throat, cough and hoarseness in the postoperative stage [7]. Since many studies have been performed on the effect of intravenous dexamethasone and gargling dexamethasone on sore throat and cough due to endotracheal intubation, but the effect of these two methods has not been compared, it was decided to investigate and compare these two methods.

Methods

This double-blind clinical trial study was performed on 96 adult patients aged 18-64 years, who were candidate for elective surgery in Alzahra and Kashani hospitals affiliated to Isfahan University of Medical Sciences Iran from 2018 to 2019 after our Institutional Ethics Committee approval and written informed consent. All patients were placed in one of the following groups using random blocks.

Group 1: In this group, the anesthesia technician, without knowing the type of solution, asks the patient to gargle 6 mg of dexamethasone in 30 cc of normal saline for 30 seconds, 5 minutes before induction of anesthesia. Then patients received 6 cc of normal saline intravenously after induction of anesthesia, before tracheal intubation.

Group 2: In this group, again the anesthesia technician, without knowing the type of solution, asks the patient to gargle 30 cc of normal saline for 30 seconds, 5 minutes before the induction of anesthesia. Patients then received 6 mg of intravenous dexamethasone after induction of anesthesia, before intubation.

Group 3: Placebo group, in this group, the anesthesia technician, without knowing the type of solution, asks the patient to gargle 30 cc of normal saline for 30 seconds, 5 minutes before the induction of anesthesia. Patients then receive 6 cc of normal saline intravenously after induction of anesthesia, before intubation.

No premedication was given on the day of surgery. All patients received standard monitoring. Pre-oxygenation, induction of anesthesia was done with intravenous fentanyl 1-2 micg / kg, atracurium 0.5 mg / kg, and thiopental sodium 5-6 mg / kg, and the maintenance of anesthesia were performed with isoflurane adjusted to MAC, 50% N2O gas mixture in O2 and 0.1 mg / kg morphine.

All patients were intubated with PVC cuffed endotracheal tube (high volume, low pressure cuff) made in Iran with an internal diameter of 7, 7.5 or 8 mm according to the patient's size. The cuff pressure was maintained at 20 CmH2O by using a special manometer.

The sore throat visual analogue scale (VAS) represents a simple instrument, using a 10 Cm linear scale where patient can indicate severity of their sore throat between the two extremes: zero is no sore throat while 10 Cm is the worst sore throat imaginable. Patients should be specifically told what time period is being monitored. In this study the intensity of sore throat was measured by using VAS and by the patient her/himself at 0, 2 and 24 hours after entering the recovery room. Cough frequency can be assessed objectively with cough frequency monitors.

Before induction of anesthesia, patients were asked to record the times of cough till 24 hours after surgery. Laryngoscopy grading was done according to the Cormack–Lehane classification, which is a grading system commonly used to describe laryngeal view during direct laryngoscopy. Most of the glottis opening can be seen with grade 1. In grade 2, only the posterior portions of the glottis or only arytenoid cartilages are visible. In grade 3, only the epiglottis but no portion of the glottis is visible, whereas in grade 4, neither the glottis nor the epiglottises can be seen.

Duration of laryngoscopy, surgery and anesthesia were measured and recorded. Duration of laryngoscopy was defined as the time from insertion of laryngoscope blade into mouth to getting the best view of glottis and duration of intubation was defined as the time from insertion of insertion of laryngoscope into mouth to obtaining three capnography waveforms after intubation. The duration of surgery was defined as the time interval from skin incision to closure of the wound in minutes, and the duration of anesthesia was defined as the time interval from the induction of anesthesia to the recovery of consciousness.

All side effects of dexamethasone, such as headache, dizziness, irritability, nausea, vomiting was asked and recorded, 24 hours after surgery. Hemodynamic changes including systolic and diastolic blood pressure and heart rate at before anesthesia, 3 and 15 minutes after endotracheal intubation, and 3 minutes after extubation were measured and recorded. In this study, all pharmacological interventions were performed by a blinded member of the research team, and the measurements and data collection by an anesthesiologist who was not aware of intervention method.

Statistical analysis

The sample size according to the level of reliability and test power was equal to 0.95 and 0.80 and as a result $z1-\alpha 2$ and $z1-\beta$ from the normal distribution table are equal to 1.96 and 0.84 respectively, and ES, the size of the Cohen effect was considered equal to 0.7 in this study. Therefore, the sample size was considered 32 patients in each group. After collecting data into SPSS statistical software version 20, Chi Square and one-way ANOVA tests were used to compare groups. Repeated Measure ANOVA test was also used to determine data changes at different times. Also, P less than 0.05 were considered as a significant relationship.

Results

In this study, patients were divided into three equal groups, first gargle dexamethasone group (14 men and 18 women), second intravenous dexamethasone group (18 men and 14 women) and third control group (17 men and 15 women). There was no significant difference between groups based on demographic data such as age and sex (P> 0.05). Also, there was no significant difference between the groups based on systolic, diastolic blood pressure and heart rate at, before anesthesia, 3 and 15 minutes after endotracheal intubation, and 3 minutes after extubation (P> 0.05). In addition, there was no significant difference between groups based on duration of anesthesia, duration of intubation, duration of surgery, duration of laryngoscopy and laryngoscopy grading. (P> 0.05) (Table 1) During the 24 hours after surgery, the frequency of cough in the first and then the second group was less than the control group, but these differences were not statistically significant (P> 0.05). The severity of sore throat (VAS) in the intravenous dexamethasone group was significantly lower than the other groups in recovery, at 2 and 24 hours after surgery (P <0.005) (Table 2). No drug side effects were observed in any of the groups.

Table 1- Patient characteristics, hemodynamic variables, anesthesia and surgical data

Variables		Group 1 (n = 32)	Group 2 (n = 32)	Group 3 (n = 32)	P value
Gender	Male	14 (%43.18)	18 (56.3%)	17 (53.1%)	0.58
	Female	18 (%56.3)	14 (43.8%)	15 (46.9%)	
Age (year)		38.64±13.1	35.21±10.11	33.75±12.01	0.67
	Before Anesthesia	125.96 ±15.73	119.64±22.30	116.38±21.19	0.316
	3 min. after intubation	123.8±21.09	128.58±18.86	118.48±13.94	0.9

Systolic Blood Pressure (mmHg)	15 min. after intubation	127.92±24.82	121.13±22.20	110.46±19.87	0-12
	3 min. after extubation	125.18 ±20.28	114.27±20.30	108.74±18.69	0.2
Diastolic Blood Pressure (mmHg)	Before Anesthesia	83.17±12.95	74.37±17.91	74.96±11.93	0.44
	3 min. after intubation	79.53±18.53	81.87±1599	77.25±16.21	0.69
	15 min. after intubation	77.32±13.06	76.34±13.63	69.81±18.54	0.64
	3 min. after extubation	83.03±12.34	61.53±15.75	57.87±13.50	0.3
Heart Rate (n/min)	Before Anesthesia	90.18±14.38	81.53±18.01	80.37±15.75	0.47
	3 min. after intubation	90.54±12.61	90.50±19.20	85.68±17.16	0.34
	15 min. after intubation	90.00±13.65	86.81±18.75	84.75±18.05	0.78
	3 min. after extubation	89.2±13.41	86.34±18.47	84.28±18.21	0.49
Duration of Anesthesia		101.07±15.54	97.32±14.11	95.35±12.62	0.26
Duration of Intubation		90±15.15	88.93±15.66	85.71±14.05	0.14
Duration of surgery		62.67±15.9	61.25±16.98	52.5±11.98	0.08
Duration of Laryngoscopy		42.85±20.65	45±21.9	38.5±20.72	0.43
Laryngoscopy Grade		2.71±0.71	2.64±0.87	2.67±0.82	0.95

Data are expressed as mean ±SD, number of patients or percent

Table 2- Frequency of cough and severity of sore throat

Variables		**Group 1 n= 32**	**Group 2 n= 32**	**Group 3 n= 32**	**P value**
Frequency of coughs during 24 hours after surgery		2.82±1.54	2.73±1.57	3.14±1.79	0.66
severity of sore throat (VAS)	At Recovery	2.5±2	1.01±0.25	3.39±2.79	0.004
	After 2 hours	2.16±1.43	1.54±1.53	3.87±1.85	0.002
	After 24 hours	1.96±1.32	0.71±0.23	2.17±2	0.002

Data are expressed as mean ±SD

Discussion

Tracheal intubation in most patients under general anesthesia causes sore throat and cough in the postoperative period.

In this study we compared the prophylactic effect of intravenous or gargling dexamethasone on post extubation sore throat and cough in patients receiving general anesthesia. We found that intravenous dexamethasone is significantly effective in lowering the severity of postextubation sore throat, and gargling dexamethasone solution is more effective in lowering the incidence of cough than intravenous injection, although this effect was not statistically significant.

In our study, none of these two methods had any effect on hemodynamic variables, laryngoscopy, intubation and duration of anesthesia and surgery (P> 0.05) (Table 1).

We used the same analgesics for all patients in three groups, and we confirmed that the severity of postoperative pain and the dose of analgesics used during the study period were not different between the groups, thus excluding potential distraction effects. Therefore, the differences in the severity scores of post-operative sore throat were attributable only to the difference in the mode of dexamethasone administration. In our study, Intravenous dexamethasone significantly reduced sore throat caused by endotracheal intubation compared to dexamethasone gargling in recovery, 2 and 24 hours after surgery (P <0.05) (Table 2).

Park et al. showed that the prophylactic use of 0.2 mg/kg of dexamethasone intravenously significantly decreased the incidence and severity of sore throat and hoarseness at 1 and 24 h after tracheal extubation of a double-lumen endobronchial tube [4]. Other study showed that Intravenous injection of 10 mg of dexamethasone was more effective in reducing the severity of post-operative sore throat when administered before tracheal intubation compared with after tracheal intubation [31]. In addition, Thomas et al. investigated the effects of preoperatively administered dexamethasone on post-operative sore throat and concluded that prophylactic intravenous dexamethasone (8 mg) reduces the incidence and severity of post-operative sore throat following tracheal intubation [17]. The findings of our study are in line with these studies. This alignment may be due to the potential mechanism that is presumably based on the anti-inflammatory activity of dexamethasone. The pathology of postoperative sore throat involves irritation to the mucosa and cuff-induced pressure on the mucosa as well as a subsequent aseptic inflammatory process.

But in a study by Ruangsin et al, it was reported that intravenous dexamethasone had no significant effect on reducing postoperative sore throat. This contradicting result may be explained from the mechanism of injury and pathophysiological viewpoints. Many confounding factors can affect the postoperative sore throat such as the different types of surgical procedure, and anesthetic protocol, as well as the contributing factors, and the preventive measures. Therefore, the insignificant

prevalence of postoperative sore throat was attributed that the prophylactic effectiveness of dexamethasone in reducing the postoperative sore throat was not verified [30].

Corticosteroids such as dexamethasone generally reduce edema by inhibition of leukocyte migration as well as the migration of plasma components, and stop the swelling of cells beyond a certain extent by increasing the stability of cellular membranes. This effect may be increased when dexamethasone is administered before laryngeal trauma. Furthermore, these drugs inhibit hydrolysis around cells, hamper the release of lysozymes from granulocytes and phagocytes, and also hinder fibrosis by blocking the proliferation of fibroblasts [19].

We also found that the number of coughs was more reduced by gargling dexamethasone than intravenous dexamethasone, but this difference was not significant. Our finding was similar to the finding of Bagchi, et al. who reported that the incidence of cough was lower at most points of observation, but it was not statistically significant when analysed [30]. Dexamethasone gargle is presumed to produce immediate effects (within minutes) directly on the upper respiratory tract, especially on the pharyngeal and laryngeal mucosa. Thus, this effect may be due to the pharmacological actions of dexamethasone gargle, through direct contact with the tracheal mucosa [19].

Dexamethasone is the strongest corticosteroid available with a half-life of 36-72 hours, which is used in the clinic for respiratory symptoms after intubation, therefore is able to reduce sore throat and cough caused by endotracheal intubation.

Long-term use of corticosteroids can have side effects such as intolerance to sugar, delayed wound healing, and increased susceptibility to infections, adrenal suppression, gastrointestinal ulcers, electrolyte imbalance and vascular necrosis of the joints. But in this study we did not see any side effects from taking a single dose of dexamethasone.

The limitation of our study was that we did not use fiber optic bronchoscope to assess the amount of tissue damage and we did not follow up the patients beyond 24 hours, as the process of acute inflammation usually peaks by 24 hours.

Conclusion

Prophylactic single dose intravenous dexamethasone is more effective in reducing sore throat due to endotracheal intubation than dexamethasone gargle. And, gargling dexamethasone solution is more effective in lowering the incidence of cough than intravenous injection, although this effect is not statistically significant.

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