RESEARCH ARTICLE

The Relation between Ketamine Spraying on the Endotracheal Tube Cuff and Reduced Postoperative Sore Throat, Cough and Hoarseness in Parturient Patients

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Background: Tracheal intubation is used in general anesthesia and often leads to traumatization of the airway mucosa. These complications can cause postoperative morbidity. This study was designed to determine the effect of ketamine spraying on the endotracheal tube cuff on sore throat, cough, and hoarseness during the first 24 hours of the postoperative period.

Methods: 120 healthy women with term singleton pregnancy scheduled for elective term cesarean delivery under general anesthesia were enrolled. Patients were randomized into two equal groups. 1 ml (50 mg) ketamine was sprayed on the endotracheal tube cuff in group K as a study group and 1 ml normal saline was sprayed on the endotracheal tube cuff in group N as a control group. The patients were interviewed for sore throat, cough, and hoarseness at 1, 6 and 24 hours after general anesthesia.

Results: In group K, no patient reported sore throat, cough and hoarseness in the first hours after surgery. However at the same time in group N the incidence of these symptoms was significantly higher than group K. The incidence of combined moderate and severe sore throat, cough and hoarseness was significantly lower in group K compared with group N, not only in 6 hours after surgery (1.67%, 0, 0 in group K vs 13.34%, 18.34%, 16.68% in group N, $p<0.05$) but also 24 hours after operation (1.67%, 0, 0 in group K vs13.3%, 16.6%, 11.67% in group N, $p<0.05$).

Conclusion: Ketamine spraying on the endotracheal tube cuff reduces the incidence of sore throat, hoarseness and cough in patients undergoing operation under general anesthesia.

Keywords: ketamine; general anesthesia; sore throat

Tracheal intubation is used in general anesthesia and often leads to traumatization of the airway mucosa. This leads to postoperative sore throat, hoarseness and cough. The prevalence of these was reported 21% -65% [1]. These complications can cause distress for patients [2], and affect patient satisfaction. Accordingly, treatment and prevention management to reduce prevalence of postoperative sore throat (POST) are recommended [3]. Ketamine acts on multiple receptors including the N-methyl-D-aspartic acid (NMDA) receptors, opioid receptors and monoaminergic receptors [4]. Ketamine is the most potent of NMDA antagonist. It binds to the NMDA receptors inhibits the NMDA receptor mediated central sensitization of nervous system [5-6]. The anti-inflammatory and antinociceptive properties of ketamine suggest that it may have a potential role in reducing POST [7-8].We set out to determine the effect of ketamine spraying on the endotracheal tube cuff on sore throat, cough and hoarseness during the first 24 hours of the postoperative period.

Methods

This double-blind randomized controlled clinical trial study was approved by Institutional Ethics Committee of Tehran University of Medical Sciences of Iran, and Iranian registration of clinical trial with the number of IRCT201109101951N2 in June 24, 2013. Written informed consent was obtained from all subjects. Due to study power of 90% and alpha of 5%, one hundred and twenty term singleton pregnant women with the American Society of Anesthesiology (ASA) physical status I or II, who were scheduled for elective cesarean delivery under general anesthesia from December 2012 to April 2013, were enrolled in this study. The most common choice in our hospital is spinal anesthesia but backache is the major cause for our patients refusing spinal anesthesia. So in our study, general anesthesia was administered to pregnant women based on their request.

Exclusion criteria included a history of recent respiratory tract infection or sore throat, asthma, Mallampati grade>2, recent NSAID medication, known allergies to study drug,

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heart rate greater than 100/min, weight>115 kg, diabetes mellitus, pregnancy-induced hypertension, patients receiving steroid therapy, and those who required more than one attempt at intubation. Participants were randomly divided into the two following groups with the help of a computer-generated table of random numbers.

In the ketamine (K) group, 1ml (50 mg) ketamine (Rotexmedica, Trittau, Germany) was sprayed from a distance of 15 cm on the endotracheal tube (ET) cuff. In the normal saline (N) group: 1 ml normal saline was sprayed from a distance of 15 cm on the ET Cuff. At the induction of anesthesia, the ET cuff was sprayed with ketamine or normal saline by a nurse anesthetist blinded to the treatment. We used standard monitoring including pulse oximetry, blood pressure, electrocardiogram and end-tidal carbon dioxide. Uterine displacement was achieved by titling the operating table to the left. An intravenous catheter (18-gauge) was inserted and started infusion of ringer solution. All patients were premedicated with 0.5 mg atropine just before induction. After administration of 100% oxygen at 5 L/min for 4 minutes, rapid sequence induction with cricoid pressure was used. The induction agents were thiopental 5 mg/kg and succinylcholine 1.5 mg/kg. The trachea was intubated with a soft seal cuffed sterile polyvinyl chloride endotracheal tube with a standard cuff (Supa Medical Device, Tehran, Iran) and an internal diameter of 7 mm. Tracheal intubation was performed by the same anesthetist. Immediately after intubation, tracheal tube cuff was filled with the minimal volume of air required to prevent an audible leak with peak airway at 20 cmH2o. General anesthesia was maintained with a mixture of 50% nitrous oxide and 0.8 minimum alveolar concentration of isoflurane. Paralysis was maintained by atracurium. After delivery we used 2 µg/kg fentanyl and 0.02 mg/kg midazolam and 10 IU oxytocin IV in all cases. At the end of surgery, the trachea was extubated when the patient was awake and following commands and neuromuscular blockade was fully reversed. All patients received oxygen by a facemask after surgery. The patients were interviewed by a blinded investigator for postoperative sore throat, cough, and hoarseness at 1and 6 and 24 hours after surgery, using the questionnaire based on the scoring system in (Table 1) [2]. Statistical analysis was performed using SPSS version 16.Statistical significance for differences was analyzed using the t test and $\chi 2$ test as appropriate. $P<0.05$ was considered statistically significant.

Results

The basal characteristics of patients such as age, body mass index (BMI) and duration of surgery and anesthesia were similar between the two groups (Table 2). The total incidence of sore throat, hoarseness and cough was significantly lower in group K compared with group N at all time points ($p<0.05$) (Table 3). The analysis of the results showed that in group N the incidence of combined moderate and severe sore throat in the first 6 and 24 hours after surgery was significantly higher than group K. In the first hour after surgery in group N, 4 (6.67%) patients complained of moderate cough and 6 (10%) patients had combined moderate and severe hoarseness. In group N, symptoms remained not only at 6 hours after surgery (18.34% for cough, 16.68% for hoarseness) but also 24 hours after surgery (16.68% for cough, 11.67% for hoarseness). However no patients in group K reported moderate and severe cough and hoarseness during the first 24 hours after surgery. Apgar scores were greater than 8 in both groups. In all patients umbilical artery PH was more than 7.15, and none of them had psychomimetic effects.

Table 1- Scoring system for sore throat, cough and hoarseness

Score	Sign
Sore throat	
0	No sore throat
1	Mild (less than what is seen in common cold)
2	Moderate (like what is seen in common cold)
3	Severe (more than what is seen in common cold)
Cough	
0	No cough
1	Mild (less than what is seen in common cold)
2	Moderate (like what is seen in common cold)
3	Severe (more than what is seen in common cold)
Hoarseness	
0	No Hoarseness
1	Mild (no hoarseness in the time of interview but had it previously)
2	Moderately (only is felt by the patient)
3	Severe (recognizable in the time of interview)

Table 2- The comparison of preoperative characteristics between two groups

	Ketamine group	Control group	P value
Parameter	**(n = 60)**	**(n = 60)**	
Age (yrs)	28.35 ± 4.17	26.70 ± 5.26	0.06
Height (cm)	161.97± 4.08	161.35 ± 4.95	0.46
Weight (kg)	79.59 ± 9.86	76.39 ± 12.44	0.12
BMI (kg/m2)	30.34 ± 3.17	29.28 ± 4.24	0.13
Operation Time (min)	47.40 ± 14.05	45.52 ± 8.81	0.38
Anesthesia Time (min)	61.12 ± 13.36	59.12 ± 10.22	0.36
Grade of laryngeal exposure			
I	27 (45%)	30(50%)	
II	32 (53.33%)	29 (48.33%)	0.59
III	1 (1.67%)	1 (1.67%)	

Table 3- The comparison of the grade of complications after 1, 6 and 24 hours of surgery

	After 1 Hour			After 6 Hours			After 24 Hours		
	Case	**Control**	**P value**	**Case**	**Control**	**P value**	**Case**	**Control**	**P value**
Sore Throat									
1	5 (8.33)	15 (25)		6 (10)	16(26.67)		4 (6.67)	14(23.34)	
2	0 (0)	3 (5)		1 (1.67)	6 (10)		1 (1.67)	6 (10)	
3	0 (0)	1 (1.67)		0	2 (3.34)		0 (0)	2 (3.34)	
			0.012			0.004			0.003
Cough									
1	1 (1.67)	7(11.67)		10 (16.67)	8 (13.34)		9 (15)	10(16.67)	
2	0 (0)	4 (6.67)		0	8 (13.34)		0 (0)	8 (13.34)	
3	0 (0)	0 (0)		0	3 (5)		0 (0)	2 (3.34)	
			0.009			0.007			0.01
Hoarseness									
1	1 (1.67)	13(21.67)		7(11.67)	21 (35)		6 (10)	20 (33.34)	
2	0 (0)	5 (8.34)		0	5 (8.34)		0 (0)	4 (6.67)	
3	0 (0)	1 (1.67)		0	5 (8.34)		0 (0)	3 (5)	
			<0.0001			<0.0001			<0.0001

Discussion

In the present study preoperative ketamine spraying on the endotracheal tube cuff reduced the incidence and severity of sore throat, hoarseness and cough compared to normal saline spraying during the first 24 hours of the postoperative period. Many factors contribute to postoperative sore throat such as age, gender, size and intra cuff pressure, type of surgery, anesthesia technique, use of succinylcholine and the gynecological procedure [9-11].

In this study there was no significant difference between contributing factors like age, body mass index and duration of surgery and anesthesia between the two groups. Although the main reason for postoperative sore throat is not clear and the postoperative sore throat may occur in patients without tracheal intubation [3], it seems that local irritation and inflammation of the lower airway is a reason of postoperative sore throat, hoarseness and cough [2].

Since, many NMDA receptors are located in the nervous system and in the peripheral nerves [12-13], blocking NMDA receptors such as ketamine, can make pre-emptive analgesia [14] or alter inflammation [15]. Glutamate is stored in neurotransmitter vesicles in nociceptive free nerve ending and following noxious stimulation, it is released into peripheral tissue. Katamine is an excitatory amino acid antagonist which acts to decrease the stimulation of receptors for excitatory amino acids primarily glutamate. The anti inflammatory properties of ketamine spraying may be the reason for decreasing sore throat in the present study [16]. However a peripheral and central action following systemic absorption cannot be excluded. Some studies have shown that gargling with ketamine or use of nebulized ketamine reduce the prevalence of sore throat for 24 hour after surgery [7-8,17]. Also, clinical studies reported that using topical ketamine produce analgesia in case studies with neuropathic and cancer pain [18-19]. In another study Zhu indicated that nebulized ketamine inhalation suppressed allergen-mediated airway hyperreactivity, airway inflammation and airway inflammatory cell infiltration into the brown- Norway rats [15]. Ketamine has been used systemically in sub-anesthetic doses (0.5 to 1mg/kg) during vaginal delivery and also used in cesarean section for an incomplete neuraxial blockade [20]. However in doses greater than 2mg/kg, it may be associated with maternal complications (psychomimetic effects and increased uterine tone) and fetal complications (low Apgar score and abnormalities) [21-22]. In our study, the Apgar scores were similar in both groups and were greater than 8.The umbilical artery PH was higher than 7.15 in all cases. Also none of the patients had psychomimetic effects. The total dose of ketamine administered in this study was 50mg. Body weights were 70-85 kg. If the entire dose was absorbed and distributed systemically, this would lead to doses of 0.62-0.67mg/kg, which is in the sub-anesthetic range. So it seems these effects observed represent a local effect of ketamine in the air ways. A limitation of our study was the use of atropine for decreasing secretions following ketamine administration. We did not adjust the intracuff pressure during operation. Further studies are suggested to compare ketamine with other drugs including steroids or local anesthetics for reducing postoperative sore throat. In conclusion, ketamine spraying on endotracheal tube cuff reduces the incidence of sore throat, hoarseness and cough in patients undergoing operation under general anesthesia.

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