ORIGINAL ARTICLE

Comparison of Ketamine Gargles with Placebo for reducing Postoperative Sore throat

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ABSTRACT

Aim: To compare effectiveness of ketamine gargles with placebo among patients undergoing surgery under general anesthesia.

Methods: This Randomized controlled trial was carried out in the Department of General Surgery, Nishtar Hospital, Multan from July 2013 to January 2014. Sixty patients undergoing endotracheal intuabtion for general anesthesia were selected and divided in two equal groups; group A who received ketamine gargles and group B who received saline gargles as placebo. Both groups were compared for efficacy (no sore throat) at 24 hours. Data was collected on a specially designed Proforma.

Results: The efficacy was labeled as yes in group A in 26(86.7%) patients while in group B in 16 (53.3%) patients. The results were statiscally significant (p-value <0.05).

Conclusions: The efficacy of ketamine gargles is high as compared to placebo. So, ketamine gargles are recommended as a premedication for attenuation of POST.

Keywords: Ketamine gargles; postoperative sore throat; placebo; efficacy

INTRODUCTION

Now days, a variety of surgical procedures are carried out under general anesthesia. Most of the times, laryngoscopy and endotracheal intubation is mandatory for management of air way during anesthesia[1]. Laryngoscopy and intubation almost always causes mechanical stimulation to the epipharynx, laryngopharynx and the tracheobronchial tree which eventually leads to increased reflex sympathetic activities[2]. This resulting increased sympatho-adrenal activity normally causes hypertension, tachycardia or myocardial stress leading to ischemia or infarction. [3] These stress responses caused by intubation maneuvers and anesthetic drugs are noticed and documented in many studies across the globe[4,5,6].

Postoperative sore throat (POST) is a common adverse event after general anesthesia. Typically, the incidence of POST is highest in patients who are tracheal intubated; however, POST also occurs when a laryngeal mask airway (LMA) is used[7]. POST was recently ranked by American anesthesiologists as the eighth most important problem of current clinical anesthesiology. The reported incidence of POST varies from 21 to 65%[8].

Postoperative sore throat can lead to dissatisfaction and discomfort after surgery and can delay a patient's return to normal routine activities. Many factors can contribute to postoperative sore throat and the incidence has been found to vary with the method of airway management[9]. Airway Instrumentation and the number of intubation attempts increase the incidence and severity of the postoperative sore throat. Other factors such as young, female, overweight and procedures where there is neck manipulation like thyroid surgeries have a higher incidence[10].

Numerous non pharmacological and pharmacological measures have been used for attenuating postoperative sore throat, cough, and hoarseness of voice with variable success. Among the non-pharmacological methods are smaller sized endotracheal tubes, lubricating the endotracheal tube with water soluble jelly, careful airway instrumentation, and intubation after full relaxation, minimizing intra-cuff pressure, gentle oro-pharyngeal suctioning, and extubation when the tracheal tube cuff is fully deflated. Numerous pharmacological methods have been tried like, aspirin gargles, gargling with azulene sulphonate, and beclo-methasone inhalation, and spraying the endotracheal cuff with benzydamine hydrochloride[11,12].

Although local-anesthetic jelly can limit potential damage to the tracheal mucosa by suppressing bucking on the tracheal tube, its ability to prevent postoperative sore throat is inconclusive since it does not possess any intrinsic anti-inflammatory properties[13].

The minimal alveolar concentration (MAC) value for endotracheal intuabtion is about 30% higher than MAC value for surgical incision, so relatively deep level of anesthesia must be established to attenuate these responses. Such patients may not tolerate this depth of anesthesia, so the drugs that tend to block these responses to airway instrumentation should be used[14].

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The ionotropic glutamate receptors N-methyl-D-aspartate (NMDA), α-amino-3-hdroxyl-5-methyl-4 isoxazol-epropionic acid, and the kainate receptors are found in the central nervous system as well as the peripheral nerves. Behavioral studies indicated that activation of these receptors results in nociceptive behaviors and contribute to inflammatory pain. Peripherally administered NMDA receptor antagonists are involved with anti-nociception[15].

There is an increasing amount of experimental data showing that NMDA receptors are found not only in the central nervous system (CNS) but also in the peripheral nerves. Moreover, experimental studies point out that peripherally administered NMDA receptor antagonists (i.e. ketamine) are involved with antinociception and anti-inflammatory cascade[8]. NMDA-receptor antagonists act at different levels of inflammation, interacting with inflammatory cells recruitment, cytokines production, and inflammatory mediator regulation. The resultant effect of these interactions confers that ketamine has an anti-proinflammatory effect by limiting exacerbation of systemic inflammation without affecting local healing processes[16].

The intravenous anesthetic, ketamine (K) was first used in humans in 1965 and is still applied in various clinical settings. K has many pharmacological properties, including analgesic, anesthetic, and sympathomimetic effects. Studies have shown that K attenuate symptoms of endotoxemia in a lipopolysaccharide (LPS)-induced rat model of sepsis, by reducing Nuclear Factor (NF)-beta(B) activity and tumour necrosis factor (TNF)-alpha production[17]. It has also been shown to play a protective role against lung injury, via its anti-inflammatory properties and decreasing the expression of inducible nitric oxide synthase (iNOS), which has been implicated in endotoxin-induced tissue injury. Studies into the nasal, oral, and rectal administration of K have suggested that local use of this drug is both effective and plausible. K, a NMDA receptor antagonist is involved in anti-nociception and anti-inflammatory cascade[18].

In a study conducted by Rudra A et al in Kolkata India, in 2009, consisting of 40 patients demonstrated that gargling with ketamine significantly attenuated POST, only 5 (25%) patients from the ketamine group suffered from POST at 24 hours post-operatively with no drug-related side effects[19].

Furthermore, a study was carried out by Shrestha SK et al[20] in Nepal, during the year 2010, consisting of 40 patients (20 in control group and 20 in ketamine group). Group C patients were asked to gargle with 30 ml drinking water for 30 seconds and Group K patients, were asked to gargle with ketamine 50 mg in drinking water 30 ml for 30 seconds, 5 minutes before induction of anesthesia. This study showed that only 3(15%) patients from the ketamine group suffered from POST at 24 hours post-operatively whereas, in the control group; 10(50%) patients had POST at 24 hours[20].

The objective of this was to compare effectiveness of ketamine gargles with placebo among patients undergoing surgery under general anesthesia.

MATERIAL AND METHOD

This Randomized controlled trial was carried out in the Department of General Surgery, Nishtar Hospital, Multan from July 2013 to January 2014. Sixty patients undergoing endotracheal intuabtion for general anesthesia were selected and divided in two equal groups; group A who received ketamine gargles and group B who received saline gargles as placebo. Both groups were compared for efficacy (no sore throat) at 24 hours. Data was collected on a specially designed Proforma.

RESULTS

In group A, there were 20(66.7%) male patient, and 10(33.3%) female patients. In group B, there were 22(73.3%) male patients and 8(26.7%) female patients. The patients were also distributed according to presence of sore throat. In group A, 4(13.3%) patients suffered from sore throat, while 26(86.7%) patients did not suffer from sore throat. In group B, 14 (46.7%) patients suffered from sore throat while 16 (53.3%) patients did not suffer from sore throat. On comparison between the two groups, the difference between the two groups was statistically significant ($p<0.05$). In group A, the efficacy was labeled as yes in 26(86.7%) patients and no in 4 (13.3%) patients. In group B, the efficacy was labeled as yes in 16 (53.3%) patients while no in 14 (46.7%) patients. On comparison between the two groups, the difference between the two groups was statistically significant ($p<0.05$).

The mean age of the patients in group A was 29.80 $\pm$ 6.20 years [range 20 – 50] and in group-B 28.52 $\pm$ 5.97 years [range 20 – 40]. (Table-1)

In group A, score 0 sore throat was seen in 26 (86.7%) patients, score 1 sore throat in 4 (13.3%) patients while none of the patients had score 3 or 4 sore throat. In group B, 16 (53.3%) patients had sore throat severity score 0, 10 (33.3%) patients had severity score 1, 2 (6.7%) patients had severity score 2 and 2 (6.7%) patients had severity score 3. On comparison among these scores, the difference was statistically significant ($p<0.05$). (Table-2)

In the age group 20 2- 25 years, 5 (16.7%) patients in group A and 7 (23.3%) patients in group B had efficacy labeled as yes. On comparison, there was no statistically significant difference between these age groups (p > 0.05). (Table-3)

Among males, 18 (60%) patients in group A and 12 (40%) patients and among females, 8 (26.7%) patients in group A and 16 (53.3%) patients in group B had efficacy labeled as yes. Statistically, the difference between the two gender groups was not significant (p >0.05). (Table-4)

Table 1: Age distribution (n=60)

Age (years)	Group A	Group B
20-25	5(16.7%)	8(26.7%)
26-30	6(20%)	7(23.3%)
31-35	516.7%)	8(26.7%)
36-40	723.7%)	6(20%)
41-45	4(13.3%)	1(3.3%)
46-50	3(10%)	-
Mean±SD	29.80±6.20	28.52±5.97
Range	20-50	20-50

P value: 0.885

Table 2: Comparison of severity of sore throat between two groups (n=60)

Severity of sore throat	Group A	Group B
Score-0	26(86.7%)	16(53.3%)
Score-1	04(13.3%)	10(33.3%)
Score-2	-	2(6.7%)
Score-3	-	2(6.7%)
41-45	4(13.3%)	1(3.3%)
46.50	3(10%)	-

P value: 0.001

Table 3: Stratification of effect modifier (sex) with efficacy in two groups (n=60)

Age (years)	Group-A	Group-B
20–25	5 (16.7%)	7(23.3%)
26–30	6(20%)	3(10%)
31–35	5(16.7%)	4(13.3%)
36–40	6(20%)	2(6.7%)
41–45	3(10%)	0
46–50	1(3.3%)	0
Total	26(86.7%)	16(53.3%)

P value: 0.375

Table 4: Stratification of effect modifier (age) with efficacy in two groups (n=60)

Gender	Group-A	Group-B
Male	18 (60)	12 (40)
Female	8 (26.7)	4 (13.3)
Total	26 (86.7)	16 (53.3)

P value: 0.794

DISCUSSION

Laryngoscopy and intubation of trachea often stimulate the pharyngeal mucosa and causes sore throat, which is unpleasant and leads to dissatisfaction of the patients. This study was conducted to compare the efficacy of ketamine gargles with placebo among 60 patients in a tertiary care unit. The results of this study were in favor of using ketamine gargles by showing a higher efficacy with ketamine gargles (86.6%) than with placebo (53.3%) (p<0,05).

Previously some other studies were also conducted in order to determine the efficacy of ketamine gargles in prevention of postoperative sore throat.

Ketamine plays a protective role against lung injuries, by means of its anti-inflammatory properties. It has shown to attenuate the symptoms of endotoxemia in animal models.

Canbay et al, conducted a prospective, randomized, controlled, single blinded study in 2008 that examined the effects of a ketamine gargle on POST[8]. Forty six patients in their study were divided into two groups, one that gargled with ketamine and others with saline. At 24th hour, they found that incidence of POST was 60.8% among those who had gargled with saline and 30% among those who gargled with ketamine. So, they found a better efficacy of ketamine in order to prevent the POST.

In 2009, Rudra et al [19] designed a prospective placebo controlled single blinded study among patients undergoing abdominal and pelvic surgery. They found that incidence of POST at 24 hours interval after ketamine gargles was25% which was lower as compared to saline gargles i.e. 60%. Similar to our study, they also found a higher efficacy of ketamine gargles over placebo.

In 2010, Shresta et al, designed a prospective comparative trial consisting of 40 patients undergoing through abodominal and orthopaedic surgery under general anesthesia[20]. The patients were divided in two equal groups receiving either drinking water or ketamine gargles. Like our study, they found a higher frequency of patients with no sore throat with ketamine gargle group as compared to that of saline group (85% versus 50%). They concluded that ketamine gargles are more useful as compared to saline gargles for prevention of POST.

Rajkumar G et al, conducted a double blind randomized controlled trial, assigning 90 adult patients of age 18 – 60 years undergoing elective abdominal surgeries under general anesthesia[21]. The patients were divided in two equal groups of 45 each. The patients in one groups received ketamine gargles while others had gargles with saline. Both of the two groups were compared for developing post operative sore throat. It was found that at 24th hour interval, there was no difference in frequency of sore throat. They observed that frequency of sore throat in patients with ketamine gargles was 18% and in

patients with saline gargles was also 18%. So, they concluded that both ketamine and saline were equally good in prevention of POST.

Ketamine gargles is a simple, inexpensive and effective method of prevention of POST. This can be simply carried out in preoperative ward very easily before any surgical procedure is carried out. However, there is need to carry on further studies which could determine the levels of systemic absorbtion of ketamine and compare the sided effects.

In our study, majority of patients (86.7%) in ketamine gargles had severity score 0 i.e. no sore throat, while in placebo group 53.3% patients had score 0 severity of sore throat. In study by Canbay, et al, [8] ketamine group patients had severity score 0 in 70% patients, while in 39% patients in saline gargle group. Like our study, none of the patients in their study had any patient of severity score more than 2 with ketamine gargles. Rudra et al, also showed that majority of patients in ketamine gargle group i.e. 75% had severity score 0 while in placebo group, they had 40% patients with score 0[19]. Shresta et al, also showed that majority of patients in ketamine gargle group i.e. 85% had severity score 0 while in placebo group, they had 50% patients with score 0[20].

CONCLUSION

Ketamine gargles are more effective in prevention of the post operative sore throat as compared to placebo. So, the use of ketamine gargles can be used as a routine before any surgery to be carried out in general anesthesia.

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