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Research Article

Effect of tramadol gargle on postoperative sore throat: A double blinded randomized placebo controlled study



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KEYWORDS

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Abstract *Background:* Postoperative sore throat is an undesirable complaint after general anesthesia with laryngeal mask airway. Tramadol is a synthetic codeine analogue with NMDA receptor antagonist and local anesthetic effects. We compared tramadol gargle to placebo given 5 min before surgery on attenuating postoperative sore throat for 24 postoperative hours.

Method: In a prospective randomized double blind study, fifty patients of ASA I and II, undergoing elective moderate urological surgery under general anesthesia using laryngeal mask airway were allocated into two groups (25 patients each); all patients were asked to gargle for 1 min with 30 ml apple juice containing tramadol 2 mg/kg in group (T), and nothing in group (P) 5 min before surgery. The incidence and the severity of postoperative sore throat were graded at 2, 6, 12, and 24 h after surgery using a four-point scale.

Result: Incidence and severity of postoperative sore throat were significantly less in tramadol treated group compared to placebo group at 2, 6, 12, and 24 h ($p < 0.05$).

Conclusion: Preoperative gargling with tramadol reduced the incidence and severity of POST compared to placebo group in patients undergoing elective moderate urological surgery, during general anesthesia with laryngeal mask airway for up to 24 h postoperatively.

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1. Introduction

Postoperative sore throat (POST) is considered the 8th most undesirable postoperative complaint after general anesthesia [1], with variability in incidences ranging from 14.4% to 50% after tracheal intubation and 5.8% to 34% after laryngeal mask airway (LMA) insertion [2].

Several methods have been used to decrease POST including non-pharmacological methods such as smaller-sized endotracheal tubes, minimizing intracuff pressure, lubrication of

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the endotracheal tube with water-soluble jelly, gentle airway instrumentation and suctioning [3], and pharmacological methods such as beclomethasone inhalation [4], betamethasone gel application over the endotracheal tube [5], benzydamine hydrochloride or lidocaine spray to the endotracheal tube [6].

It has been found that NMDA (N-methyl-D-aspartate) receptor antagonists when peripherally administered have analgesic and anti-inflammatory effects in experimental study [7] and were effective in reducing POST (ketamine and magnesium) [8–11].

Tramadol hydrochloride is a synthetic analogue of codeine, it is a μ opioid receptors agonist, it inhibits reuptake of monoamines (noradrenaline and serotonin), and it is a NMDA receptor antagonist and has local anesthetic effect [12].

We hypothesized that preoperative tramadol gargle would be effective in reducing sore throat because of its NMDA receptors' antagonist effect and its local anesthetic effect. Therefore, this study was aimed to study the efficacy of tramadol gargle compared to placebo given 5 min before surgery on attenuating POST for 24 h after surgery, when POST was caused by LMA in patients undergoing elective moderate urological surgery.

2. Method

After approval of the local ethical committee, an informed written consent was obtained from 50 patients of American Society of Anesthesiology (ASA) physical status I or II, age ranging between 18 and 50 years old, planned for elective moderate urological surgery (as ureteroscopy, transurethral resection of bladder tumor, hydrocelectomy, varicocelectomy) under general anesthesia with LMA in Dar Alshifa hospital (State of Kuwait) from September 2012 to April 2013.

Patients were excluded from the study if they were smokers or had a history of preoperative sore throat, recent upper or lower respiratory tract infection, allergies to the studied drugs, or morbidly obese (BMI > 35).

Sedative premedication drugs were not given to the patients. After arrival to the operation theater, the patients were shifted to anesthesia preparation room where they were randomly allocated into two equally divided groups (25 patients each) by using the closed envelop technique. In order to maintain the blind nature of the study, the studied drugs were prepared by the anesthesia technician unaware of the study drugs according to the instructions written in a sealed envelope.

- *Group (T)* (Tramadol group): patients were asked to gargle for 1 min with 30 ml apple juice containing Tramadol hydrochloride (Tramal, Grünenthal, Germany) 2 mg/kg using the same dose used in the study of Akbay et al. [13].
- *Group (P)* (Placebo group): patients were asked to gargle for 1 min with 30 ml apple juice only.

After 5 min the patients were shifted to the operation room where the monitors including electrocardiogram, pulse oximetry, end tidal CO₂, noninvasive blood pressure and skin temperature probe were attached.

Anesthesia was induced with intravenous fentanyl 1–2 μ g/kg, propofol 2–3 mg/kg followed by insertion of laryngeal mask airway (LMA) using the appropriate size according to

patients' weight with inflation of its cuff with air to prevent an audible leak with maintenance of the cuff pressure between 50 and 60 cm H₂O using handheld pressure gauge (Teleflex medical, Rusch, Germany) which was connected to the pilot balloon of the LMA. Anesthesia was maintained with sevoflurane 2–3 vol% in 50/50 O₂/air with spontaneous ventilation. At the end of the surgery, sevoflurane was discontinued and oxygen 100% was administered. After gentle oral suction, LMA was removed after deflating the cuff and the patients were shifted to the recovery room.

The following parameters were recorded by anesthesia nurse blinded to the patients' group.

- (1) The incidence of POST (the number of patients developed sore throat), and the severity of postoperative sore throat using a four-point scale (Table 1) at 2, 6, 12, and 24 h.
- (2) Postoperative side effects of the used drugs during the recovery time:
 - (a) *Nausea and vomiting* was assessed by a 3-point ordinal scale [14]; (0 = none, 1 = nausea, and 2 = vomiting), 4 mg IV ondansetron was used to treat vomiting.
 - (b) *Sedation* was evaluated on a scale of 0–4 [14]; (0 = fully awake, 1 = slight drowsiness, 2 = sleepy but easily aroused, 3 = fully asleep but arousable and 4 = fully asleep, not arousable).

3. Statistical analysis

The sample size of 25 patients in each group was calculated based on the previous studies that found that the incidence of postoperative sore throat was 65% and providing that tramadol will decrease the incidence of POST by 50% with the α -error level was fixed at 0.05 and the power was set at 80% using the program of Biostatics version 3.01.

Data were presented as means (SD) or number (percentage). Numerical data were analyzed by using one way analysis of variance (ANOVA). Nonparametric data were analyzed by using the Kruskal–Wallis and Mann–Whitney *U* tests. A value of $p < 0.05$ was considered significant. All statistical analysis was performed using the program of Biostatics version 3.01.

4. Results

Fifty patients were enrolled into the two groups of the present study (25 in each group) including 32 males and 18 females. There were no significant differences between the two groups regarding age, sex, ASA status, weight, and operation time (Table 2).

Table 1 Four-point scale [8].

1. No sore throat
2. Mild sore throat (complains of sore throat only on asking)
3. Moderate sore throat (complains of sore throat on his or her own)
4. Severe sore throat (change of voice or hoarseness, associated with throat pain)

Incidence of postoperative sore throat (regardless of its severity) was significantly lower in tramadol treated group compared to placebo group at 2, 6, 12, and 24 h ($p < 0.05$), (Fig. 1).

Regarding the severity of postoperative sore throat, it was significantly lower ($p < 0.05$) in tramadol group compared to placebo group at different times of measurements, (Tables 3–6) as follows:

- At 2 h: mild degree of sore throat was shown in 1 patient (4%) in tramadol group and 5 patients (20%) in placebo group; moderate degree of sore throat was shown only in placebo group; 3 patients (12%).
- At 6 h: 2 patients (8%) in tramadol group show mild degree of sore throat, and 5 patients (20%) in placebo group; moderate degree of sore throat was shown only in placebo group; 3 patients (12%).

Table 2 Patient characteristics and operation time. [Data represented as mean (SD) or number].

Variables	Group (T) (n = 25)	Group (P) (n = 25)
Age (years)	45 (14)	42 (12)
Sex (male/female)	15/10	17/8
ASA (I/II)	22/3	19/6
Weight (kg)	78 (7)	81 (6)
Operation time (min)	52 (7)	51 (8)

Group T: tramadol group, Group P: placebo group.
No significant differences between the studied groups.

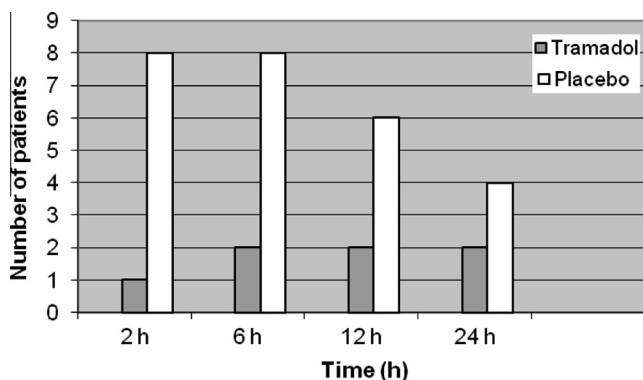


Figure 1 Incidence of postoperative sore throat. [Data presented as number of patients].

Table 3 Severity of postoperative sore throat at 2 h postoperative. [Data presented as number (percentage)].

	Group (T) (n = 25)	Group (P) (n = 25)
Mild	1 (4%)*	5 (20%)
Moderate	0 (0%)*	3 (12%)
Severe	0 (0%)	0 (0%)

Group T: tramadol group, Group P: placebo group.
* Significant difference ($p < 0.05$) compared to group P.

Table 4 Severity of postoperative sore throat, at 6 h postoperative. [Data presented as number (percentage)].

	Group (T) (n = 25)	Group (P) (n = 25)
Mild	2 (8%)*	5 (20%)
Moderate	0 (0%)*	3 (12%)
Severe	0 (0%)	0 (0%)

Group T: tramadol group, Group P: placebo group.

* Significant difference ($p < 0.05$) compared to group P.

Table 5 Severity of postoperative sore throat, at 12 h postoperative. [Data presented as number (percentage)].

	Group (T) (n = 25)	Group (P) (n = 25)
Mild	2 (8%)*	4 (16%)
Moderate	0 (0%)*	2 (8%)
Severe	0 (0%)	0 (0%)

Group T: tramadol group, Group P: placebo group.

* Significant difference ($p < 0.05$) compared to group P.

Table 6 Severity of postoperative sore throat, at 24 h postoperative. [Data presented as number (percentage)].

	Group (T) (n = 25)	Group (P) (n = 25)
Mild	2 (8%)*	4 (16%)
Moderate	0 (0%)	0 (0%)
Severe	0 (0%)	0 (0%)

Group T: tramadol group, Group P: placebo group.

* Significant difference ($p < 0.05$) compared to group P.

- At 12 h: mild degree of sore throat was shown in 2 patients (8%) in tramadol group and 4 patients (16%) in placebo group; moderate degree of sore throat was shown only in placebo group; 2 patients (8%).
- At 24 h: 2 patients (8%) in tramadol group and 4 patients (16%) in placebo group showed mild degree of sore throat. Moderate or severe degree of sore throat was not shown in any patient in the two groups.

No side effects (nausea, vomiting and sedation) were recorded in any patient in the two studied groups.

5. Discussion

This study showed that preoperative gargling with tramadol was effective in reducing the incidence and severity of postoperative sore throat compared with the placebo group in patients undergoing elective moderate urological surgery during general anesthesia with laryngeal mask airway for up to 24 h postoperatively.

The postoperative sore throat (POST) related to LMA might be caused by pharyngeal irritation with aseptic inflammation, edema, congestion, and pain [8]. It is suggested that NMDA antagonists attenuated the incidence and severity of POST because of their analgesic and anti-inflammatory effects [7].

To our knowledge, there were no reports about the effect of tramadol on POST; therefore, we used the studies of the other NMDA antagonists.

In line with the present study results, the study done by Canbay et al. [8] and the study done by Shrestha et al. [9] who found that preoperative gargling with ketamine 40 mg or 50 mg respectively reduced the incidence and severity of POST after endotracheal intubation. This could be explained by Zhu et al. who found that locally administered ketamine inhibits the inflammatory response as NMDA receptors are present in the CNS and peripheral nerves [7].

Another NMDA antagonist, magnesium sulfate, has anti-inflammatory effect and decreases the inflammatory mediators as histamine and leukotriens [15] and it was found to be effective in reducing the incidence and severity of POST in the study done by Gupta et al. [10], who found that preoperative magnesium nebulization reduced the incidence and severity of POST. Also the study done by Hale et al. [11] who showed that preoperative magnesium lozenge reduced the incidence and severity of POST.

In addition to its NMDA antagonistic effect, another mechanism of action of tramadol could be involved in the explanation of its reducing effect of POST, is its local anesthetic effect was evidenced in several studies; Akbay et al. showed that topical 5% tramadol 2 mg/kg applied to the tonsillar fossa provides good analgesia after tonsillectomy [13], Tekelioglu et al. concluded that topically applied tramadol and ketamine to tonsillar fossa for 5 min after tonsillectomy reduced postoperative pain [16], Gercek et al. concluded that subcutaneous tramadol injection provides good analgesia and anti-inflammatory effects [17], Ugur et al. showed that peritonsillar tramadol injection reduced intraoperative and postoperative analgesic requirements for tonsillectomy [18], Kargi et al. found that 5% tramadol (2 mg/kg) injection provides good local anesthetic effect as effective as 2% prilocaine during circumcision [19], Kaki and Al Marakbi concluded that postoperative wound infiltration with tramadol decreased analgesic requirements after herniorrhaphy [14], Kargi et al. showed that local infiltration with 5% tramadol was similar to 2% lidocaine in tendon repair surgery of the hand [20], and Jabalameli et al. found that wound infiltration with tramadol or pethidine after cesarean section provides good analgesia and decreases postoperative morphine requirements compared with bupivacaine [21]. The local anesthetic effect of tramadol can be explained by a mechanism similar to that of local anesthetics by blocking the voltage dependent Na⁺ channels similar to lidocaine and K⁺ channels more than lidocaine [22].

No postoperative systemic side effects were recorded in the groups of the present study. In line with these results comes the study done by Demiran et al., who found that nausea, vomiting and sedation were not recorded with wound infiltration with tramadol [23].

We concluded that preoperative gargling with tramadol reduced the incidence and severity of POST compared to placebo group in patients undergoing elective moderate urological surgery, during general anesthesia with laryngeal mask airway for up to 24 h postoperatively with no systemic side effects.

Conflict of Interest

There were no conflicts during the study.

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