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ORIGINAL ARTICLE

Comparison of Siccoral® spray, Stomatovis® gargle, and Strefen® lozenges on postoperative sore throat

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Abstract
Purpose Postoperative sore throat (POST) is a frequent complication caused by mucosal trauma to the pharyngeal, laryngeal, and tracheal airway after endotracheal intubation. We compared the effectiveness of Siccoral, Strefen, and Stomatovis treatments in alleviating POST.
Methods This prospective, randomized, single-blinded, controlled trial compares the incidence of POST with Strefen lozenges, Siccoral spray, or Stomatovis gargle. Three hundred and twenty American Society of Anesthesiologists class I–III patients undergoing elective genitourinary surgery under general orotracheal anesthesia were randomly allocated to four groups of 80 patients each. In the postoperative awakening unit and during related services, POST was evaluated by a blinded anesthesiologist at 0, 1, 6, and 24 h post extubation.
Results The highest incidence of POST occured at 0 and 1 h post extubation in all groups ($P = 0.002 \times 10^{-7}$, $P = 0.004 \times 10^{-6}$, respectively). A significantly lower incidence of POST was observed in Strefen and Siccoral groups at 0 and 1 h compared to Control group (Strefen: $P = 0.004 \times 10^{-2}$, $P = 0.007 \times 10^{-4}$; Siccoral: $P = 0.003 \times 10^{-8}$, $P = 0.007 \times 10^{-5}$, respectively). A significantly lower incidence of POST was observed with Siccoral treatment at 0 h post extubation ($P = 0.002$ vs. Strefen treatment). Although POST incidence was not significantly different between the Stomatovis and Control groups, it was lower in the Stomatovis group at 0 and 1 h ($P = 0.026$ and 0.013, respectively). The incidence of POST was similar in all groups at 6 and 24 h post extubation ($P = 0.141$ and 0.426, respectively).
Conclusion Siccoral and Strefen can be effective in relieving POST in the early hours after extubation.

Keywords Intubation tracheal · Complications · Postoperative sore throat · Pharmacological method · Siccarol · Strefen · Stomatovis

Introduction

Postoperative sore throat (POST) is an uncomfortable, distressing sequela reported in 21–65 % of cases after tracheal intubation [1–3]. The etiology of POST is multifactorial: the size of the tracheal tube, type of the cuff, movement of the endotracheal tube during surgery, and excessive pharyngeal suctioning might cause localized trauma and inflammation of the pharyngeal mucosa [2]. One of the important causative factors of POST is general anesthesia using dry cool anesthetic gases, which decrease the humidity and temperature of the ciliary mucosal epithelium of the lower respiratory tract. The anesthetic dry gases also induce inflammation, which inhibits the normal function of these cells [4].

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Several pharmacological and nonpharmacological methods have been reported for the attenuation of POST, such as lubricating the endotracheal tube cuff, inhaling beclomethasone, and gargling with benzydamine hydrochloride [1].

There are several convenient drugs for the care of the mouth and throat. Stomatovis mouthwash is useful for prevention of symptoms associated with stomatitis and gingivitis and helps with lubrication of the oral cavity. Strefen, a sugar-based lozenge formulation containing flurbiprofen, was developed to provide soothing topical effects in addition to pain relief [5]. Siccoral, containing sea salt and glycerine, moisturizes the mouth and throat mucosa with an osmotic effect, providing saliva-like oral viscosity. This study hypothesized that these drugs could alleviate POST with different mechanisms of action on the mucosal surfaces of the airway. The aim of this study is to compare the effectiveness of Siccoral, Strefen, and Stomatovis treatments in alleviating POST.

Methods

Institutional Ethics Committee approval and written informed consent (Ref. no. 11, 16/11/2012) were obtained, and the study was registered in ANZCTR (ACTRN12613000477729). Three hundred and twenty American Society of Anesthesiologists (ASA) class I–III patients, 18–80 years of age, undergoing elective genitourinary surgery under general orotracheal anesthesia were randomly allocated to four groups of 80 patients each. The exclusion criteria included patients having sore throat and asthma, allergies to study drugs, recent use of nonsteroidal antiinflammatory drugs (NSAID) medication, upper respiratory tract infections, Mallampati grade >2, a known surgical duration of >240 min, use of nasogastric tube, one or more unsuccessful attempts at intubation, and a history of steroid therapy. The study was conducted between January and April 2013 at Dışkapı Yıldırım Beyazıt Research and Training Hospital.

Patients were randomized into the following four groups by a computer-generated random number table: Strefen (STF), Siccoral (SCO), Stomatovis (STM), and Control (C) groups. Patients allocated to these groups received STF oral lozenges 45 min before induction of anesthesia; or received four puffs of SCO spray into the oropharyngeal cavity 30 s before induction of anesthesia; or gargled 15–20 ml STM for at least 60 s before induction of anesthesia; or received no additional treatment (C) (Table 1). Becuse of drug taste and drug administration techniques, patients could not be blinded.

All patients were premedicated with 0.01–0.03 mg/kg i.m. midazolam, 30 min preoperatively. Single-use polyvinly chloride endotracheal tubes (Bıçakçılar®, İstanbul, Turkey), having low-pressure, high-volume, soft-seal cuffs of size 8.0–9.0 and 7.0–7.5 mm internal diameter, were used for male and female patients, respectively. After connecting to standard monitors, anesthesia was induced with fentanyl (2 μg/kg), propofol (2 mg/kg), and atracurium (0.5 mg/kg). After achieving maximum neuromuscular blockade by train-of-four stimulation (TOF) (TOF Watch SX; Organon, Dublin, Ireland), an experienced anesthesiologist who was blinded to group allocation performed tracheal intubations without applying cricoid pressure. For sufficient neuromuscular blocade, a TOF ratio <10 % was used. The cuff was inflated until no air leak could be heard with peak airway pressure at 20 cm H_2O. Cuff pressure was maintained between 18 and 22 cm H_2O using a handheld pressure gauge (Endotest; Rüsch, Kernen, Germany).

Table 1 Content of the three drugs

Strefen lozanges	Flurbiprofen 8.75 mg, sucrose, glucose syrup, honey, Macrogol 300, lemon flavor, potassium hydroxide, Levomenthol (Drossapharm, Basel, Switzerland)
Siccoral spray	10 mg sea salt 1 %, glyserol, patent blue, methyl paraben, prophyl paraben, purified water (Drossapharm, Basel, Switzerland)
Stomatovis gargle	Purified water, xylitol, marshmallow mucilage, vegetable glycerol, dipotassium glycyrrhizinate, phosphoglucan, carboximethyl beta-glucan, sodium bicarbonate, chlorobutanol, PVM/MA, sodium hydroxymethyl glycinate, PEG-40 hydrogenated castor oil, acesulfame K, flavoring, green color (E102, E131, E514) (Pomezia, Roma, Italy)

Anesthesia was maintained with sevoflurane in 33 % oxygen, and an i.v. bolus of atracurium was repeated intermittently to maintain one or two twitches on TOF stimulation of the ulnar nerve. Remifentanil i.v. infusion was initiated in all the patients at a dose of 0.1–0.2 μg/kg/min. All patients received i.v. acetaminofen (1,000 mg) before extubation for postoperative surgical pain.

At the end of surgery, residual neuromuscular block was antagonized with atropine (0.02 mg/kg) and neostigmine (0.05 mg/kg). Nasogastric tubes were not inserted in any patients. To avoid tissue trauma and to confirm complete clearance of secretions, oral suctioning was performed just before extubation and under direct vision. When the TOF ratio was >70 % and the patient was fully awake, patients were extubated.

Outcome measures

POST was evaluated by an anesthesiologist who was blinded to the group allocations at 0 h (within 20 min) in the postoperative awakening unit, and at 1, 6, and 24 h

during related postoperative services. At the time of the first evaluation, patients with a Ramsey Sedation Score [6] of 2 (cooperative, oriented, and tranquil) or 3 (responding to commands only) were included.

The severity of POST was graded on a 4-point scale as follows: 0, no throat pain; 1, mild throat pain (complaint of sore throat only on questioning); 2, moderate throat pain (complaint of sore throat without direct questioning); or 3, severe throat pain (change of voice associated with throat pain) [1–3].

Sample size estimation was performed using NCSS and PASS 2000 (NCSS LLC; NCSS, Kaysville, Utah, USA) software. A total sample size of at least 300 (75 per group) cases was required to detect at least a 23.8 % difference between any of two groups with a power of 90 % at the 5 % significance level. The difference of 23.8 % was taken from published literature [7]. We decided to enroll 80 cases in each group to ensure a sufficient sample size in the case of subject withdrawal or incomplete/missing data.

Statistical analysis

Data analysis was performed using SPSS for Windows, version 11.5 (SPSS, Chicago, IL, USA). The Shapiro–Wilk test was used to determine whether the discrete data were normally distributed. The Levene test was used for the evaluation of homogeneity of variances. Metric discrete variables are shown as mean ± standard deviation (SD) and number of cases and percentages used for nominal data. Mean age differences among groups were analyzed using one-way analysis of variance (ANOVA); the Kruskal–Wallis test was applied for comparisons of surgery duration. The Mann–Whitney *U* test was used to determine whether associations between duration of operation and sore throat were statistically significant. Nominal data were analyzed by Pearson's chi square test. A *P* value less than 0.05 was considered statistically significant. All possible multiple comparisons (the Bonferroni correction) were applied to minimize type I error. A *P* value less than 0.0125 was considered statistically significant for the Bonferroni correction.

Results

No patients were excluded from analysis. Patient characteristics, duration of surgery, and remifentanyl consumption were comparable between the groups ($P = 0.114$, 0.991, 0.258, and 0.183, respectively) (Table 2).

The highest incidence of POST occured at 0 and 1 h after extubation in all groups ($P = 0.002 \times 10^{-7}$, 0.004×10^{-6}, respectively). There was a significantly lower incidence of POST in STF and SCO groups at 0 and 1 h compared to C group (C vs. STF: at 0 h, $P = 0.004 \times 10^{-2}$, and at 1 h, $P = 0.007 \times 10^{-4}$; C vs SCO: at 0 h, $P = 0.003 \times 10^{-8}$, and at 1 h, $P = 0.007 \times 10^{-5}$). A significantly lower incidence of POST was observed in the SCO group at 0 h compared to the STF group ($P = 0.002$). Although POST incidence was not significantly different between the STM

Table 2 Patient characteristics and total remifentanyl consumption of groups

Groups ($n = 80$)	Age (years)	Gender (M/F)	Duration of surgery (h)	Total remifentanyl consumption (μg)
Control	61.3 ± 12.3	72/8	1.6 ± 0.6	801.4 ± 267.8
Strefen	56.5 ± 13.8	72/8	1.7 ± 1.0	797.6 ± 429.5
Siccoral	60.0 ± 12.1	73/7	1.5 ± 0.8	722.3 ± 360.4
Stomatovis	60.2 ± 13.0	72/8	1.5 ± 0.6	758.3 ± 269.4
P	0.114	0.991	0.258	0.183

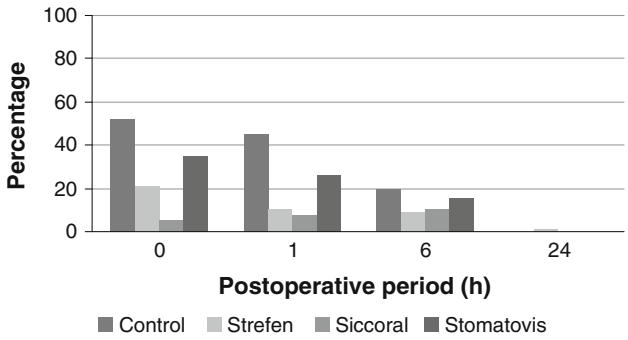

Fig. 1 Incidence of postoperative sore throat (POST) among groups

Table 3 Duration of surgery and total remifentanyl consumption in relationship to postoperative sore throat (POST) incidence at 0, 1, and 6 h

	Duration of surgery (h)	Total remifentanyl consumption (μg)
0 h (20 min)		
POST (−) ($n = 229$)	1.5 ± 0.8	741.4 ± 347.7
POST(+) ($n = 91$)	1.7 ± 0.7	841.6 ± 304.5
P	0.005	0.005
1 h		
POST (−) ($n = 249$)	1.6 ± 0.8	759.5 ± 358.4
POST (+) ($n = 71$)	1.6 ± 0.6	806.4 ± 255.8
P	0.109	0.061
6 h		
POST (−) ($n = 277$)	1.6 ± 0.8	776.7 ± 347.6
POST (+) ($n = 43$)	1.5 ± 0.6	725.8 ± 272.5
P	0.573	0.514

and C groups, it seems to be lower in the STM group at 0 and 1 h ($P = 0.026$ and 0.013, respectively). The incidence of POST was similar in all groups at 6 and 24 h post extubation ($P = 0.141$ and 0.426, respectively) (Fig. 1).

Operation duration seems to affect the incidence of POST. Independent of treatment, POST incidence is higher at 0 h postoperatively in longer-duration operations with higher remifentanyl consumption ($P = 0.005$; Table 3). As there is no POST score greater than 1, we analyzed the absence or presence of POST.

Discussion

We found that the incidence and severity of POST in patients undergoing genitourinal surgery during general orotracheal anesthesia with endotracheal intubation was significantly less at early postoperative periods by preoperative spraying of SCO into the oral cavity or administration of STF lozenges.

POST has been rated by patients as the eighth most undesirable outcome in the postoperative period [1–3]. There are numerous studies of various approaches for reducing POST, including the use of i.v. dexamethasone, inhaled fluticasone, applying lidocaine or betamethasone gel over the tracheal tube, and spraying the tube cuff with benzydamine or lidocaine [2, 7–9]. Topical steroids can cause local mucosal infection, and 10 % or 2 % lidocaine solution containing ethanol polyethylene glycol 400 could cause tracheal mucosa damage [2, 7]. Benzocaine also increased the risk of pulmonary aspiration by releasing the gag reflex and allowing regurgitation [10]. In this study, we used different medications, often used by ear, nose, and throat (ENT) surgeons, that are cheap, easily administered, and associated with rare side effects.

In our study, we used SCO with an effective time of about 4 h. SCO contains sea salt and glycerol, and with osmotic activity, humidifies and cleanses the mucous membranes of the throat and mouth and exerts a positive effect on the healing process in damaged epithelial mucosa [11]. The incidence of POST has been reported to be as high as 3.3 %, even in patients using a face mask [12]. Jung et al. showed that active humidification of inspired gases reduces the incidence and severity of sore throat after surgery [4]. We also suggest that preventing dehydration of mucosal epithelium and regenerating the barrier function are the most important factors in alleviating POST. Schaller [11] demonstrated that SCO can be an effective treatment in xerostomia and pharyngitis sicca, as they observed an 80 % therapeutic success in the mouth and throat and with regard to irritation of the mucosa [11]. Also, Fluhr et al. [13] showed an increase in epidermal hydration by glycerol in xerosis and atopic dermatitis diseases. In our study, administration of SCO, because of its mechanism of action, was found to be more effective than the other drugs.

The finding that SCO is most effective at reducing POST suggests that the most important factor for sore throat may be the maintenance of the osmotic, hygroscopic, and barrier functions of the mucosal epithelium. SCO is also relatively inexpensive, is available without a prescription, and is a well-established medication that has been used for years.

Our study has shown that STF, which includes flurbiprofen, a propionic acid derivative of NSAID, which has potent antiinflammatory effects in addition to antipyretic and analgesic activity, had similarly low pain scores to SCO in the early postoperative (1-h) period than the other groups. Strepsils lozenges and lozenges containing dexpanthenol have similar effects in reducing sore throat [14, 15]. Throat lozenges with active medicines have a stronger effect in the throat because of the longer presence of this medicine in the mouth; the extended interaction with the mucosal lining allows the medicine to bind to the target tissues [16]. In our study, STF from lozenges reached a peak concentration at 30–40 min, with an elimination half life of 3–6 h and reduced POST at 1 h after extubation.

STM exerts lubricating, moisturizing and reepithelializing, and antiinflammatory effects on the oral cavity. It is administered on mucosal surfaces three times a day. Our patients gargled it directly before intubation so that the operation time would be within the duration of action. Gargling STM did not significantly reduce POST relative to the control treatment, which may be explained by the fact that gargles are only able to deliver active ingredients to the anterior oral cavity, not to the palatine tonsils or the pharynx. Also, gargles are expelled from the mouth after 30 s, leaving little behind when compared to lozenge medicinal forms [17].

Independent of treatment modality, patients with a longer surgical duration demonstrated a higher incidence of POST at 0 h postoperatively, with higher total remifentanyl consumption, which is most likely the result of increased duration of inflammation and irritation of the respiratory mucosa caused by cool, dry gases.

The lack of records of coughing and bucking at the time of extubation is a limitation of this study and prevents testing the correlation between the incidence of POST and the frequency of coughing and bucking.

In conclusion, SCO and STF were found to be effective in relieving POST during the early postextubation period.

References

1. Canbay O, Celebi N, Sahin A, Celiker V, Ozgen S, Aypar U. Ketamine gargle for attenuating post-operative sore throat. Br J Anaesth. 2008;100:490–3.
2. Sumathi PA, Shenoy T, Ambareesha M, Krishna HM. Controlled comparison between betamethasone gel and lidocaine jelly applied over tracheal tube to reduce post-operative sore throat, cough, and hoarseness of voice. Br J Anaesth. 2008;100:215–8.
3. Agarwal A, Nath SS, Goswami D, Gupta D, Dhiraaj S, Singh PK. An evaluation of the efficacy of aspirin and benzydamine hydrochloride gargle for attenuating post-operative sore throat: a prospective, randomized, single-blind study. Anesth Analg. 2006;103:1001–3.
4. Jung TH, Rho JH, Hwang JH, Lee JH, Cha SC, Woo SC. The effect of the humidifier on sore throat and cough after thyroidectomy. Korean J Anesthesiol. 2011;61:470–4.
5. Russo M, Bloch M, de Looze F, Morris C, Shephard A. Flurbiprofen microgranules for relief of sore throat: a randomised, double-blind trial. Br J Gen Pract. 2013;63:149–55.
6. Ramsay MA, Savege TM, Simpson BR, Goodwin R. Controlled sedation with alphaxalone-alphadolone. Br Med J. 1974;22:656–9.
7. Hung NK, Wu CT, Chan SM, Lu CH, Yuan-Shiou H, Yeh CC, Lee MS, Cherng CH. Effect on post-operative sore throat of spraying the endotracheal tube cuff with benzydamine hydrochloride, 10% lidocaine and 2% lidocaine. Anesth Analg. 2010;111:882–6.
8. Tazeh-Kand NF, Eslami B, Mohammadian K. Inhaled fluticasone propionate reduces post-operative sore throat, cough, and hoarseness. Anesth Analg. 2010;111:895–8.
9. Thomas S, Beevi S. Dexamethasone reduces the severity of post-operative sore throat. Can J Anaesth. 2007;54:897–901.
10. Chrubasik S, Beime B, Magora F. Efficacy of a benzocaine lozenge in the treatment of uncomplicated sore throat. Eur Arch Otorhinolaryngol. 2012;269:571–7.
11. Schaller H. Efficacy of Siccoral solution in xerostomia and pharyngitis sicca. Ther Woche. 2003;11:1–4.
12. Higgins PP, Chung F, Mezei G. Post-operative sore throat after ambulatory surgery. Br J Anaesth. 2002;88:582–4.
13. Fluhr JW, Darlenski R, Surber C. Glycerol and the skin: holistic approach to its origin and functions. Br J Dermatol. 2008;159:23–34.
14. Ebneshahidi A, Mohseni M. Strepsils® tablets reduce sore throat and hoarseness after tracheal intubation. Anesth Analg. 2010;111:892–4.
15. Gulhas N, Canpolat H, Cicek M, Yologlu S, Togal T, Durmus M, Ozcan Ersoy M. Dexpanthenol pastille and benzydamine hydrochloride spray for the prevention of post-operative sore throat. Acta Anaesthesiol Scand. 2007;51:239–43.
16. McNally D, Shephard A, Field E. Randomised, double-blind, placebo-controlled study of a single dose of an amylmetacresol/2,4-dichlorobenzyl alcohol plus lidocaine lozenge or a hexylresorcinol lozenge for the treatment of acute sore throat due to upper respiratory tract infection. J Pharm Pharm Sci. 2012;15(2):281–94.
17. Limb M, Connor A, Pickford M, Church A, Mamman R, Reader S, Shephard A, Aspley S, Goulder MA. Scintigraphy can be used to compare delivery of sore throat formulations. Int J Clin Pract. 2009;63:606–12.