

EFFECT OF PREOPERATIVE LICORICE
LOZENGES ON INCIDENCE OF POSTEXTUBATION
COUGH AND SORE THROAT IN SMOKERS
UNDERGOING GENERAL ANESTHESIA
AND ENDOTRACHEAL INTUBATION

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Abstract

Introduction: Post-Operative Sore Throat (POST) is an undesirable side effect of endotracheal intubation. Pharmacological and non-pharmacological measures have been utilized for minimizing the morbidity caused by POST. We have tested whether medicated lozenges of Licorice provides efficacy in decreasing POST in smokers presenting for surgery under general anesthesia with endotracheal intubation.

Methods: 100 patients, 20 - 65 years, American Society of Anaesthesiologists (ASA) physical status Grade I & II, of either sex, with history of smoking, and posted for elective surgical procedure lasting more than one hour and requiring general anesthesia with endotracheal intubation were included and randomly divided into two groups (n= 50) to receive Licorice lozenges (Group A) and Sugar Candy (Group B). The patients were assessed for cough, sore throat and hoarseness of voice immediately after extubation and then at 30 min, 12 hrs and 24 hrs after extubation utilizing scoring system of Harding and McVey.

Results: Overall incidence of postextubation cough was less in Group A (12patients, 24%) compared to Group B (26 patients,52%) (p= 0.002). Magnitude of sore throat (Grades 0/1/2/3) was seen in 48/2/0/0 patients (Group A) and 46/4/0/0 (Group B) at extubation (p= 0.40) and 34/16/0/0 (Group A) and 28/20/2/0 (Group B) at 30 min (p= 0.17). At 12 and 24 hours, the magnitudes of sore throats were 24/25/1/0 (Group A) & 12/38/0/0 (Group B) (p=0.02) and 26/23/1/0 (Group A) & 15/35/0/0 (Group B) (p= 0.03) respectively.

Conclusion: Use of licorice lozenges is efficacious for reducing the distressing complaint of POST in postoperative period among smokers.

Key words: POST, lozenges, Licorice.

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Introduction

The symptoms of postoperative pharyngeal dryness, throat pain, uncoordinated / inability / pain on swallowing associated with cough and hoarseness of voice is commonly termed as Postoperative Sore Throat (POST)¹. Tracheal intubation has been found to be the foremost cause of POST² with an incidence of 21- 65%^{3,4}. Chronic smoking is associated with inflammation of tracheal mucosa secondary to effects of substances in cigarette smoke, leading to increased respiratory problems in perioperative period. These patients have an increased incidence of POST⁵. Various techniques have been utilized to decrease the incidence of POST. Use of licorice gargles 5 minutes before induction of anaesthesia are effective in decreasing the incidence of POST by 50%⁶. Lozenges of licorice are available for management of sore throat associated with pharyngitis due to varied causes in traditional Indian medicine. Such lozenge contains a lower dosage of licorice and has been found efficacious for management of pharyngitis.

In this study, we evaluated the effectiveness of low dose licorice lozenges for decreasing the incidence of POST in smokers undergoing surgery under general anesthesia and endotracheal intubation.

Methods

This randomized placebo controlled study was conducted between March 2012 and August 2012 at Himalayan Institute of Medical Sciences. Institution Ethical Committee review was obtained and written informed consent of patients were taken. 100 patients, of either sex, 20-65 years of age, American Society of Anesthesiologists(ASA) physical grade I and II, posted for elective surgical procedures lasting more than one hour, and requiring general anesthesia and endotracheal intubation were included. Exclusion criteria included surgeries lasting less than one hour, anticipated difficult intubation, Mallampatti Grade III and IV, pregnancy, Body Mass Index > 30 kg/m², surgeries requiring insertion of Ryles' tube, throat packing or rapid sequence intubation, history of upper respiratory tract infection, gastroesophageal reflux disease, asthma and significant cardiovascular disease.

The patients were divided into 2 groups by sealed envelope technique to receive Licorice lozenges

(Sualin; Hamdard Pharma, India) (Group A) and Sugar Candy (Dabur India Limited) (Group B). All patients were asked to refrain from smoking for 48 hrs prior to surgery and were asked to suck (and not chew) the lozenges as per group allotment, 30 minutes prior to expected induction of anesthesia. Before shifting to operating room (OR), it was ensured that any leftover lozenges was not present in oral cavity. In the OR after establishing intravenous (i.v.) access, standard monitoring electrocardiogram (ECG), non - invasive blood pressure (NIBP) and pulse oximetry (SpO₂) were attached. Induction of anaesthesia was achieved with injection (inj.) fentanyl 2 mcg/kg and inj. propofol 2 mg/kg till loss of verbal contact. Ease of mask ventilation was confirmed and neuromuscular blockade was achieved with inj. vecuronium 0.1mg/kg. Patients were ventilated with 66% nitrous oxide in oxygen and isoflurane for 3 minutes. Endotracheal intubation was completed using size 3 Macintosh curved blade and a high volume low pressure cuffed endotracheal tube (Portex, Smiths Medical International Limited, UK) of size 7-7.5 for females and 8-8.5 for males. The tube size selection was at the discretion of single anaesthesiologist with an experience of > 5 years. Duration of laryngoscopy and number of attempts for intubation was noted. The cuff of endotracheal tube was filled with air to maintain cuff pressure ≤ 25 mm of Hg as assessed periodically in the intraoperative period utilizing Portex Cuff Manometer (Smiths Medical International Limited, Germany).

Anesthesia was maintained with 66% nitrous oxide in oxygen, isoflurane, intermittent boluses of inj. vecuronium and inj. fentanyl. Last dose of opioids was administered at least 30 minutes prior to expected extubation and inj. Diclofenac Sodium 75 mg (Dynapar AQ, Troikka Limited, India) in 100 ml normal saline was administered 20 min prior to expected extubation. Isoflurane was switched off 10 minutes prior to extubation. Neuromuscular paralysis was reversed with inj. Neostigmine(0.05 mg/kg) and inj. Glycopyrrolate(0.01 mg/kg). With resumption of spontaneous respiration, nitrous oxide was switched off and patients were made to breath spontaneously with 100 % oxygen. Gentle oral suction was done once and patients were extubated. Care was taken to avoid bucking on endotracheal tube and too harsh or repeated suctioning was not allowed. The patients

were assessed for cough, sore throat and hoarseness of voice at extubation, 30 min, 12 hrs and 24 hrs post-anesthesia by framing the questions in the local dialect and language of the patients,utilizing the scoring system of Harding and McVey (Table 1)⁷.

Table 1
Scoring system of Harding and McVey

Sore throat	
	Score
No sore throat at any time since the operation	0
Minimal sore throat (Complains of sore throat only on asking)	1
Moderate sore throat (Complains of sore throat on his / her own)	2
Severe sore throat (Complains of throat pain)	3
Cough	
	Score
No cough at any time since the operation	0
Minimal cough or scratchy throat (Light or single episode of cough)	1
Moderate cough (more than one episode of non-sustained cough)	2
Severe cough (Sustained and repetitive cough with head lift)	3
Hoarseness	
	Score
No evidence of hoarseness at any time since the operation	0
No evidence of hoarseness at the time of interview	1
Hoarseness at the time of interview noted by patient only	2
Hoarseness that is easily noted at the time of interview	3

Sample size was calculated on the basis of previous studies⁶. Presuming the reduction in incidence of POST by 50%, α error of 5% and power of 80%, 46 patients were needed in each group. So, 50 patients were selected in each group. Statistical analysis was performed using SPSS version 19 (SPSS

Software, IBM Corporation Amrok, New York). Results are presented as mean \pm standard deviation (SD) for parametric data and as percentage (%) for non-parametric data. Analysis of variance (ANOVA) was used to analyze the continuous data while non-parametric data was compared by using Chi-square test (χ^2). Mann - Whitney test was applied to compare the independent groups considering mean of sum of ranks. p value of < 0.05 was considered significant.

Results

The patients in both groups were comparable in their demographic profile (Table 2). Intubation characteristics such as duration of laryngoscopy (DOL), number of intubation attempts, duration of surgery (DOS) and duration of anaesthesia (DOA) were also comparable (Table 3).

Table 2
DEMOGRAPHIC PROFILE

Criteria	Group A	Group B	p value
Number (n)	50	50	--
Male: Female	45:5	46:4	0.12
ASA I/II	46 / 4	41 / 9	0.46
Age(yr) (Mean \pm SD)	39.48 \pm 11.15	41.60 \pm 14.63	0.87
Range of Age (yr)	20 – 65	20 - 65	--
Weight (kg) (Mean \pm SD)	57.20 \pm 11.65	61.08 \pm 9.86	0.12
Range of Weight (kg)	40 – 80	45 - 85	--

12 patients (24%) in Group A and 26 patients (52%) in Group B had cough of grade 1 at extubation ($p=0.002$). Only 1 patient in Group B complained of cough at 12 hrs and 24 hrs postoperatively ($p > 0.05$) (Table 4).

Table 3
INTUBATION CHARACTERSTICS

Criteria	Group A	Group B	p value
DOL (sec) (Mean \pm SD)	11.00 \pm 3.64	10.56 \pm 3.11	0.68
No. of Attempts (1 / 2)	44 / 6	45 / 5	0.44
DOA (min) (Mean \pm SD)	149.00 \pm 51.67	156.00 \pm 62.825	0.70
DOS (min) (Mean \pm SD)	125.60 \pm 50.24	131.80 \pm 61.60	0.69

DOL: duration of laryngoscopy; DOA: duration of anesthesia; DOS: duration of surgery

Table 4
COUGH IN SMOKERS

Cough		At Extubation				At 30 Min				At 12 Hrs				At 24 Hrs			
		Scores				Scores				Scores				Scores			
		0	1	2	3	0	1	2	3	0	1	2	3	0	1	2	3
Group A	n	38	12	0	0	50	0	0	0	50	0	0	0	50	0	0	0
	%	76	24	0	0	100	0	0	0	100	0	0	0	100	0	0	0
Group B	n	23	26	1	0	50	0	0	0	49	1	0	0	49	1	0	0
	%	46	52	2	0	100	0	0	0	98	2	0	0	98	2	0	0
p value*		0.002				1.00				0.31				0.31			

* Mann-Whitney test

Complaint of sore throat was present at all times with the lowest, incidence being at extubation and at 30 min postoperatively ($p > 0.05$). At 12 hrs, scores of 0/1/2 were present in 24 (48%), 25 (50%), 1(2%) (Group A) and in 12 (24%), 38 (76%), 0 (0%) (Group B) ($p = 0.02$). Scores at 24 hrs were 26 (52%), 23 (46%), 1 (2%) (Group A) and 15 (30%), 35(70%), 0 (0%) (Group B) ($p = 0.03$). There was an overall reduction in severity of sore throat in group A except for 1 patient who complained of persistent sore throat of Score 2 up to 24 hours (Table 5).

None of the patients complained of hoarseness of voice at any time of observation.

Discussion

Our study demonstrated that preoperative use of licorice lozenges is effective in decreasing the incidence of postextubation cough and sore throat. This study differs from previous reports of effectiveness of licorice in the following ways: dosage, formulation and time of administration.

Agrawal et al in their study have utilized a dosage of 0.5 g as gargle 5 minutes prior to intubation⁶. Similarly Sessler et al have also demonstrated effectiveness of licorice gargle for attenuation of POST. In contrast, we have utilized lozenges of licorice which contained only 97mg of licorice. Secondly, the time of administration was 30 minutes prior to intubation compared to 5 minutes in other studies. Only two studies are available in literature showing the effectiveness of lozenges for decreasing the incidence of POST: one utilizing Strepsils lozenges⁸ and other being magnesium lozenges⁹. To our knowledge, our study is probably the only study where effectiveness of lozenges of licorice is evaluated for decreasing the incidence of POST. We evaluated the incidence of sore throat utilizing the scale as derived by Harding and McVey which is a more subjective assessment of the symptomology while the majority of the other studies have utilized VAS as the tool for measuring POST. The etiology of POST is multifactorial with incidences ranging from 0-50%^{10,11,12,13,14} to as high as 100%^{15,16,17,18,19, 20}. The method and type of airway instrumentation is the single most influential factor in development of pharyngeal complication²¹. Patient related factors such as female

Table 5
SORE THROAT IN SMOKERS

Sore Throat		At Extubation				At 30 Min				At 12 Hrs				At 24 Hrs			
		Scores				Scores				Scores				Scores			
		0	1	2	3	0	1	2	3	0	1	2	3	0	1	2	3
Group A	n	48	2	0	0	34	16	0	0	24	25	1	0	26	23	1	0
	%	96	4	0	0	68	32	0	0	48	50	2	0	52	46	2	0
Group B	n	46	4	0	0	28	20	2	0	12	38	0	0	15	35	0	0
	%	92	8	0	0	56	40	4	0	24	76	0	0	30	70	0	0
p value*		0.40				0.17				0.02				0.03			

sex, younger age groups, gynecological surgeries, use of succinylcholine for intubation, history of smoking or lung disease all predispose to POST^{2,14}.

Smokers develop laryngeal epithelial inflammation, metaplasia and dysplasia due to chronic irritation by substances in cigarette smoke. This impairs laryngeal integrity and function causing greater exposure of subepithelial airway receptors to stimuli²². Erskine et al evaluated airway reflexivity to chemical and mechanical stimulations. Tracheal intubation results in stretch stimulation of trachea leading to respiratory complications²³.

Various pharmacological and non – pharmacological modalities are utilized to decrease the incidence of POST. Use of smaller size tube, avoidance of nitrous oxide, maintaining intracuff pressure <25 mm of Hg, careful instrumentation and intubation after full neuromuscular blockade have all been found to prevent POST²⁴. Similarly use of lubricants, gargles or medications in preoperative period have also been found to decrease the incidence of POST.

Licorice is extracted from the plant *Glycyrrhiza glabra* Linn and has been used in traditional medicine worldwide for the treatment of ailments of respiratory tract, digestive tract, hepatitis and cancer. Licorice consists of a number of active ingredients such as glycyrrhizin, glycyrrhizic acid, liquilitin, liquiritigenin, and hispaglabridins²⁵. Anti-inflammatory and antiallergic properties are due to glycyrrhizin²⁶. while glycyrrhizic acid decreases the inflammatory process by inhibiting cyclooxygenase activity, prostaglandin formation, and inhibition of platelet aggregation²⁷. Liquilitin and liquiritigenin have peripheral and central antitussive properties²⁸. Glabridin has significant antioxidant and ulcer-healing properties which might be helpful in minimizing the extent of ischemic injury to the pharyngeal and tracheal

mucosa and expedite their healing²⁹.

Side effects of the use of licorice have been reported. Prolonged use is associated with pseudoaldosteronism^{30,31} hypertension^{32,33} and hyperkalemia^{34,35}. Liquorice extract and glycyrrhizin have also been reported to induce changes in Cytochrome P450 linked activities resulting in accelerated metabolism of co-administered drugs and adverse effects due to change in cytochrome profiles such as toxicity/ cytotoxicity³⁶. In the current study, no side effects were reported as a once and low dose of licorice was used in the study group.

Shortcomings of our study were the absence of patients' blinding as patients were able to recognize the taste of these commonly available lozenges. Also, we didn't assess the incidence of POST at other shorter times post operatively (e.g. 4-8 hours) Another shortcoming was not categorizing the patients according to the number of pack years of smoking. Does this influence the incidence and severity of POST needs to be further studied? Moreover relation between type of surgery and intraoperative position of patient with the incidence of POST was also not taken into consideration.

A further study investigating use of licorice lozenges for prevention of POST in surgeries requiring Ryles tube insertion, pharyngeal packing, surgeries in positions other than supine, LMA insertion, intubation by anesthesiology residents could give an idea of its further effectiveness in different clinical situations and conditions.

Conclusion

Incidence of post intubation cough and sore throat can be decreased with the preoperative use of one licorice lozenge. This low dose serves as an effective, cost limited and ready to use method for decreasing the distressing symptoms of POST.

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