

To Study the Effect of Preoperative Licorice Lozenges on Incidence of Postoperative Sore Throat in Patients Undergoing Laparoscopic Cholecystectomy under General Anaesthesia

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Abstract:

Background: Postoperative sore throat (POST) is one of the most reported complications after general anaesthesia with an incidence of as high as 60%, which may impact patient satisfaction and increase the cost of treatment. Different pharmacological and non-pharmacological measures to attenuate POST has variable success rates. "Licorice" derived from the root of Glycyrrhiza gabra has history of use in medicine due to its anti-inflammatory and antitussive properties. Use of licorice gargles 5 minutes before induction of anaesthesia are effective in decreasing the incidence of POST by 50%, according to previous available literature. This study was performed to evaluate the effectiveness of licorice lozenges on the incidence of post operative sore throat in patients undergoing elective laparoscopic cholecystectomy under General anaesthesia.

Methods: After obtaining ethical committee clearance and patient consent, 92 patients posted for elective laparoscopic cholecystectomy under general anaesthesia were divided into 2 groups of 46 each. Group A (n=46) received Licorice lozenges (43.24mg) orally and Group B (n=46) received sugar candy 30 minute before the induction of general anaesthesia. Patients were assessed for sore throat, hoarseness of voice and cough at extubation, at 30 min, 12 hrs and 24 hrs post-extubation utilizing the scoring system of Harding and McVey.

Incidence of Sorethroat: At 12hrs postop, 76.1% of patients in Group B had minimal sore throat when compared to 50% of patients in Group A. The distribution was found to be statistically significant (P = 0.017).

At 24hrs postop, 69.6% of patients in Group B had minimal sore throat when compared to 43.5% of patients in Group A. The distribution was found to be statistically significant (P = 0.02).

Incidence of Cough: Post Extubation, 50% of patients in Group B had cough when compared to 26.1% of patients in Group A. This distribution was found to be statistically significant (P = 0.03).

Conclusion: Preinduction gargling of licorice lozenge decreased the occurrence of sorethroat and cough and preoperative use of licorice lozenges appears to be simple favourable way to prevent sorethroat postoperatively.

Keywords: Licorice, Postoperative Sore Throat, General Anaesthesia.

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Introduction

The symptoms of postoperative pharyngeal dryness, throat pain, pain on swallowing associated with cough and hoarseness of voice is commonly termed as Postoperative Sore Throat (POST). Tracheal intubation has been found to be the foremost cause of POST with an incidence of 21- 65%.[1]

The etiology of POST is complex and multiple mechanisms may contribute including airway trauma and irritation with mucosal injury and inflammation, prolonged ischemia of the mucosa

caused by mechanical pressure, regurgitation of the gastric contents, placement of a gastric tube, etc.[2]

Pharmacological measures for attenuating postoperative sore throats include inhalation of beclomethasone or fluticasone propionate; gargling with azulene sulfonate, aspirin, or ketamine; gargling or spraying benzydamine hydrochloride on the endotracheal cuff; IV dexamethasone; oral clonidine; topical or systemic lidocaine; and ingestion of strepsils tablets.

Nonpharmacological methods for preventing an intubation-related sore throat include using smaller-sized endotracheal tubes, lubricating the endotracheal tube with water-soluble jelly, careful airway instrumentation, intubation after full relaxation, gentle oropharyngeal suctioning, minimizing cuff pressure and extubation with a fully deflated tracheal tube cuff.[3]

Licorice" derived from the root of *Glycyrrhiza glabra* has history of use in medicine due to its anti-inflammatory and antitussive properties. Licorice contains anti-inflammatory ingredients, such as glycyrrhizin, glycyrrhizic acid, and glabridins. Glycyrrhizin has anti-inflammatory properties. Glycyrrhizic acid inhibits cyclooxygenase activity and prostaglandin formation, thereby impeding the inflammatory process. Glabridins have an ulcer-healing effect, which may accelerate the healing process of pharyngeal and tracheal mucosal injuries due to intubation and endotracheal tube cuff inflation.[4]

Use of licorice gargles 5 minutes before induction of anaesthesia are effective in decreasing the incidence of POST by 50%, according to previous available literature.[5]

This study was performed to evaluate the effectiveness of licorice lozenges on the incidence of post operative sore throat in patients undergoing elective laparoscopic cholecystectomy under General anaesthesia.

Materials and Methods

This prospective comparative double-blind study was conducted after obtaining ethical committee clearance and written informed consent. A total of 92 (n=46 in each group) patients scheduled for elective laparoscopic cholecystectomy under general anaesthesia were randomised in 2 groups using computer generated sampling after obtaining written informed consent.

Patients aged 18-60 years, with ASA Physical status I and II posted for elective laparoscopic cholecystectomy lasting more than one hour and requiring general anaesthesia and endotracheal intubation were included in the study. Patients with anticipated difficult intubation/Difficult airway, Body Mass Index > 30 kg/m², smokers, surgeries requiring insertion of Ryles' tube, throat packing or rapid sequence intubation, patients with history of upper respiratory tract infection, gastroesophageal reflux disease, asthma and significant cardiovascular disease, patients requiring multiple attempts of intubation were excluded from the study.

After a detailed pre-anaesthetic evaluation patients fulfilling the above inclusion criteria were explained

in detail about the anaesthetic procedure, surgery, and the study protocol. Special emphasis given on baseline ECG ensuring patients have normal sinus rhythm with no rate or rhythm abnormality.

A written informed consent was obtained and the patients willing to participate in the study were kept nil per orally 8 hour a before the surgery. On arrival to the preoperative room, 18 Gauge Intravenous line was secured and patients were started on Intravenous fluid Ringer Lactate 8-10ml/kg at 75-100ml/hr. Inj Pantoprazole 40mg was given as premedication as slow IV.

Patients were allocated to either the two groups: GROUP A (received Licorice Lozenges Dose-43.24mg orally), GROUP B (received sugar candy). All patients were asked to suck (and not chew) the lozenges as per group allotment 30 minutes prior to expected induction of anaesthesia. Patients were shifted to the operative room. Non-Invasive Blood Pressure, pulse oximeter, ECG were connected. Baseline systolic and diastolic blood pressure, Mean Arterial Pressure, Heart Rate, oxygen saturation was recorded. Standard institutional protocol for General Anaesthesia was followed. Inj Glycopyrrolate 0.04 mg/kg IV, Inj Midazolam 0.05 mg/kg IV and Inj Fentanyl 2mcg/kg IV was given. Patient was induced with Inj Propofol 2mg/kg IV and Inj Vecuronium 0.1mg/kg IV. A gentle laryngoscopy was performed using Macintosh 3 or 4 blade. A sterile single lumen cuffed polyvinylchloride (PVC) endotracheal tube with an inner diameter of 7mm in females and 8mm in males was used for tracheal intubation. Duration of laryngoscopy and number of attempts for intubation was noted. Heart rate, Systolic and diastolic blood pressure, Mean arterial pressure, oxygen saturation was monitored throughout the surgery. Anaesthesia was maintained by 50% oxygen, 50% nitrous oxide, isoflurane 1 Minimum Alveolar Concentration and muscle relaxation by Inj Vecuronium 0.01mg/kg IV in regular bolus doses. 30 minutes before the end of surgery Inj Ondansetron 0.12 mg/kg IV was given along with Inj Diclofenac 75mg in 100mL of normal saline IV slowly over 15-20 minutes.

Once surgery was completed, oropharynx gently suctioned and reversal of neuromuscular blockade was given (Inj Neostigmine 0.05mg/kg IV and Inj Glycopyrrolate 0.01mg/kg IV). After the extubation criteria were met and after gentle thorough suction and cuff deflated, patient was extubated and shifted to postanaesthesia care unit.

Patients were assessed for sore throat, hoarseness of voice and cough at extubation, 30 min, 12 hrs and 24 hrs post-anaesthesia utilizing the scoring system of Harding and McVey.

<i>Scoring system of Harding and McVey</i>	
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

Statistical Analysis

The data was analyzed using SPSS for Windows [SPSS version 26.0, IBM Corp., Armonk, NY]. Continuous data and categorical data were compared between the groups using unpaired t-tests and Chi-squared tests. Results were presented using tables and graphs. The level of significance was set at $P < 0.05$.

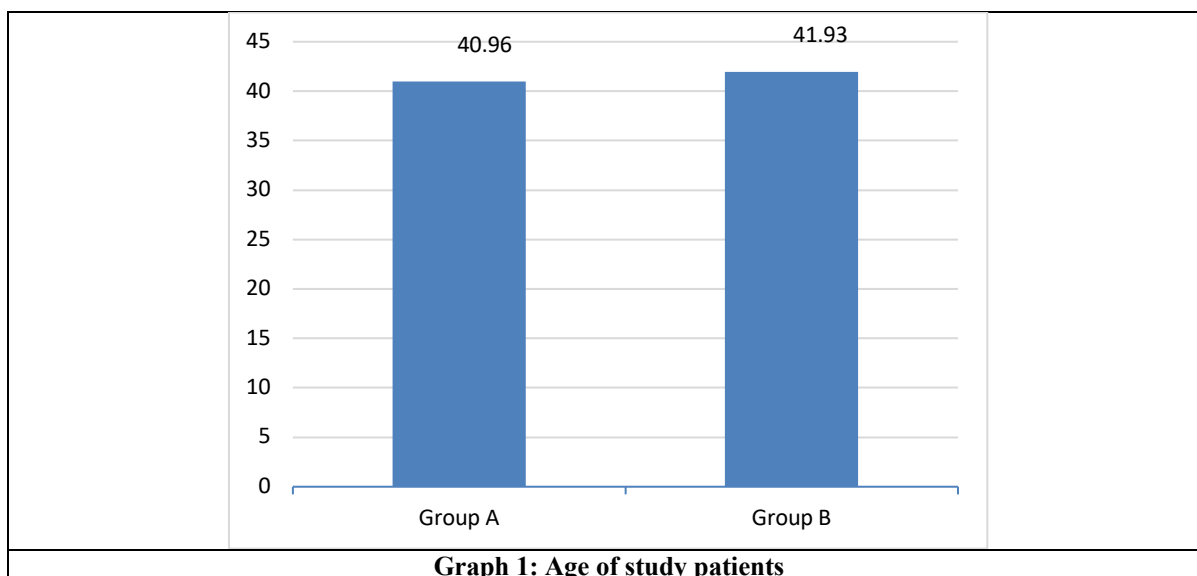
Results

The present study had 92 patients with 46 in each study group. The demographic parameters are

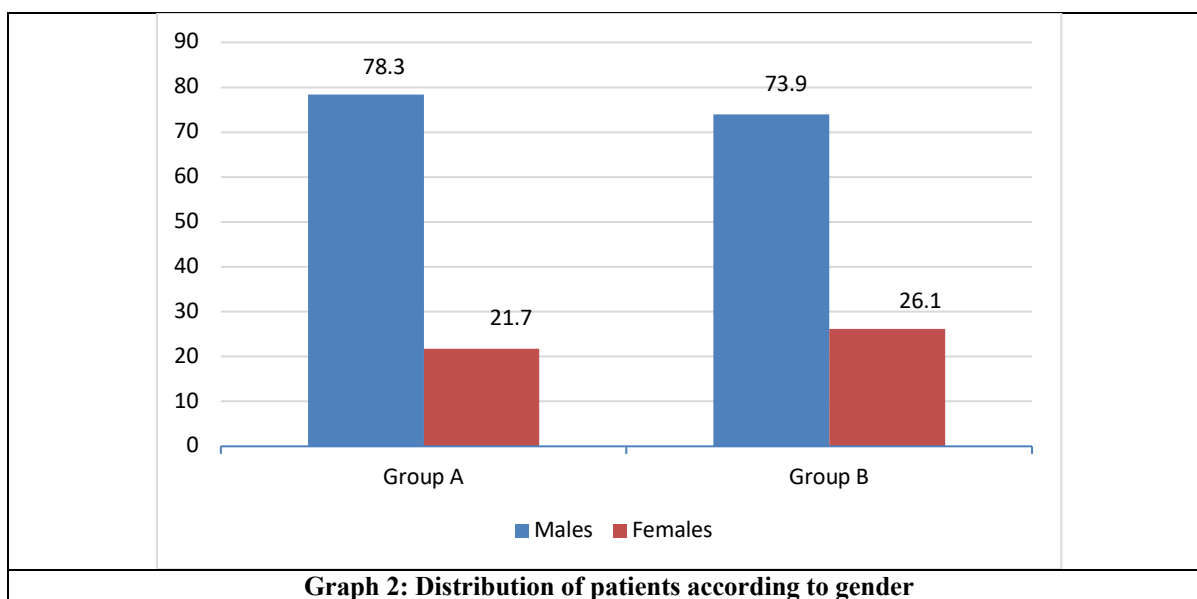
described in table-1 and table 2 and both the groups were comparable with respect to age and gender.

Table-3 represents the incidence of sorethroat in both the groups and shows that there is a statistically significant decrease in the incidence of sorethroat at 12hrs and 24hrs postextubation in the licorice group.

Table-4 represents the incidence of cough in both the groups and shows that there is a statistically significant decrease in the incidence of cough postextubation in the licorice group.

**Table 1: Comparison of mean age of patients between the groups**

	Number	Mean	SD	t	P value
Group A	46	40.96	10.2	-0.51	P = 0.61
Group B	46	41.93	8.01		NS

**Table 2: Comparison of the distribution of patients according to gender**

	Group A	Group B	Total	P value
Gender	N (%)	N (%)	N	
Males	36 (78.3)	34 (73.9)	70	P = 0.807
Females	10 (21.7)	12 (26.1)	22	
Total	46 (100)	46 (100)	92	NS

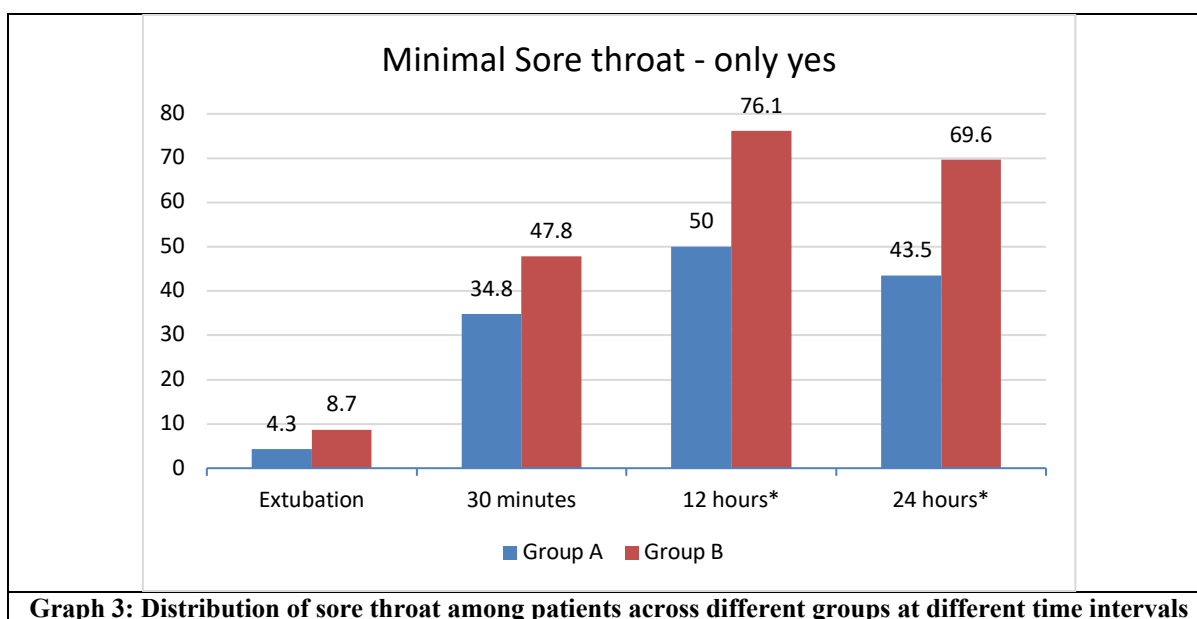
N-number; %-percentage; NS-not significant using chi-square test

Sore throat

Table 3: Distribution of sore throat among patients across different groups at different time intervals

Sore throat		Group A N (%)	Group B N (%)	Total N	P value
Extubation	None	44 (95.7)	42 (91.3)	86	P = 0.39 (NS)
	Minimal sore throat	2 (4.3)	4 (8.7)	6	
30 minutes	None	30 (65.2)	24 (44.4)	54	P = 0.2 (NS)
	Minimal sore throat	16 (34.8)	22 (47.8)	38	
12 hours	None	23 (50)	11 (23.9)	34	P = 0.017*
	Minimal sore throat	23 (50)	35 (76.1)	58	
24 hours	None	26 (56.5)	14 (30.4)	40	P = 0.02*
	Minimal sore throat	20 (43.5)	32 (69.6)	52	

N-number; %-percentage; NS-not significant and statistically significant *P < 0.05 using the Chi-square test



At Extubation: It was found that 8.7% of patients in Group B had minimal sore throat when compared to 4.3% of patients in Group A. The distribution was not statistically significant (P = 0.39).

At 30 minutes: It was found that 47.8% of patients in Group B had minimal sore throat when compared to 34.8% of patients in Group A. The distribution was not statistically significant (P = 0.2).

At 12 hours: It was found that 76.1% of patients in Group B had minimal sore throat when compared to 50% of patients in Group A. A greater percentage of

patients in Group B had sore throats when compared to Group A. The distribution was found to be statistically significant (P = 0.017).

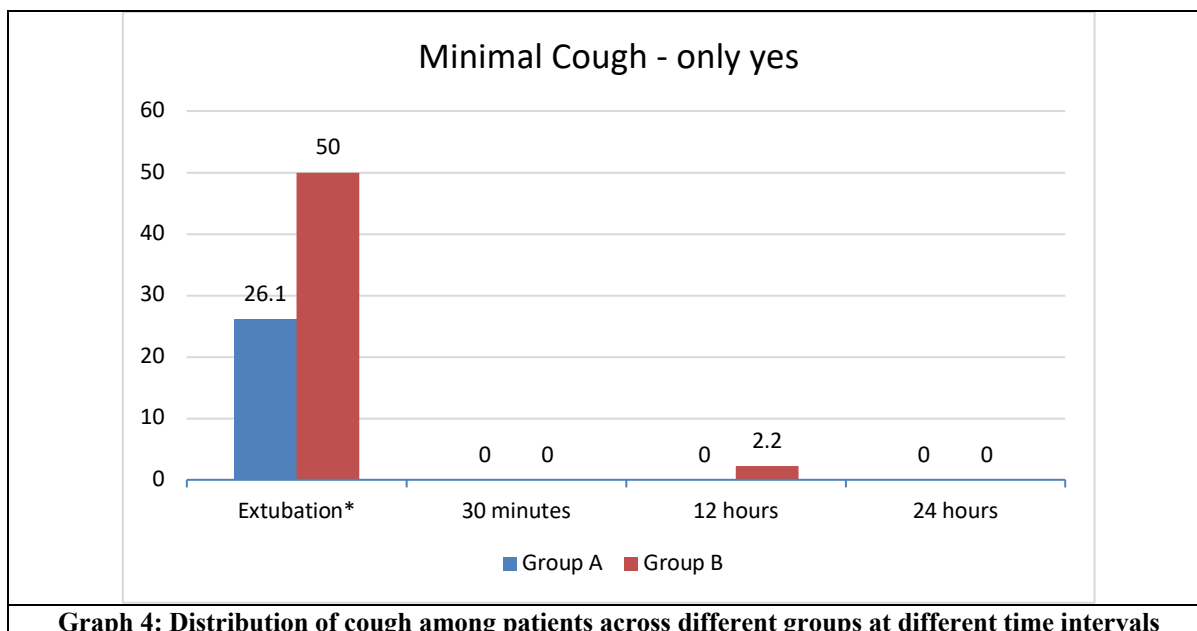
At 24 hours: It was found that 69.6% of patients in Group B had minimal sore throat when compared to 43.5% of patients in Group A. A greater percentage of patients in Group B had sore throats when compared to Group A. The distribution was found to be statistically significant (P = 0.02).

Cough

Table 4: Distribution of cough among patients across different groups at different time intervals

Cough		Group A N (%)	Group B N (%)	Total N	P value
Extubation	None	34 (73.9)	23 (50)	57	P = 0.03*
	Minimal Cough	12 (26.1)	23 (50)	35	
30 minutes	None	46 (100)	46 (100)	0	-
	Minimal Cough	0	0	0	
12 hours	None	46 (100)	45 (97.8)	91	P = 0.99 (NS)
	Minimal Cough	0	1 (2.2)	1	
24 hours	None	46 (100)	46 (100)	0	-
	Minimal Cough	0	0	0	

N-number; %-percentage; NS-not significant using the Chi-square test



Graph 4: Distribution of cough among patients across different groups at different time intervals

Extubation: It was found that 50% of patients in Group B had cough when compared to 26.1% of patients in Group A. This distribution was found to be statistically significant ($P = 0.03$).

After 30 minutes: It was found that 2.2% of patients in Group B had minimal cough and none of the

patients in Group A had any cough. The distribution was not statistically significant ($P = 0.99$).

Hoarseness of voice: It was found that none of the patients in either group had any hoarseness of voice.

Table 5: Distribution of patients according to hoarseness of voice

Hoarseness		Group A N (%)	Group B N (%)	Total N	P value
Extubation	None	46 (100)	46 (100)	92	-
	Hoarseness of voice	0	0	0	
30 minutes	None	46 (100)	46 (100)	92	-
	Hoarseness of voice	0	0	0	
12 hours	None	46 (100)	46 (100)	92	-
	Hoarseness of voice	0	0	0	
24 hours	None	46 (100)	46 (100)	92	-
	Hoarseness of voice	0	0	0	

Discussion

The present study is aimed at the use of licorice lozenges preoperatively and its efficacy in reducing Postoperative sore throat.

Post extubation sorethroat is a common postoperative ailment accounting to 14% to 90% of incidence attributed to variation in the experience, skill of the anaesthesiologist along with other contributing factors like excessive cuff pressure and type of surgery.

In our study consisting of 92 patients, 46 patients received Licorice lozenges and 46 patients received sugar candy 30minutes before induction of general anaesthesia. The incidence of sorethroat was decreased at 12hrs and 24hrs postextubation in the Licorice group and the incidence of cough was decreased postextubation in the Licorice group.

This was in accordance with the findings of Gupta D et al who conducted a study in 2013 and demonstrated that preoperative use of licorice lozenges is effective in decreasing the incidence of postextubation cough and sore throat.

Agrawal et al in 2009, conducted a study to evaluate the efficacy of licorice gargle for attenuating POST. They utilized a dosage of 0.5 g licorice used as gargle 5 minutes prior to intubation. They concluded that Licorice gargle performed 5 min before anesthesia is effective in attenuating the incidence and severity of POST.[5]

Similarly, Sessler et al in 2013, conducted a study to evaluate the effect of preoperative gargling with licorice solution on postoperative sore throat and postextubation coughing in patients intubated with double-lumen tubes and concluded that licorice

gargle decreased the incidence of postoperative sore throat.[3]

Kuriyama A et al in 2018, conducted a study to evaluate the efficacy and safety of topical licorice for preventing postoperative sore throat in adults undergoing tracheal intubation for general anesthesia. The study concluded that preoperative topical application of licorice reduced incidence of POST and was effective than nonanalgesic methods for preventing postoperative sore throat.[4]

Our findings indicate that patients who received licorice lozenges preoperatively experienced a significantly lower incidence of 43.5% to 50% POST as compared to those who received sugar candies.

This aligns with previous studies suggesting anti-inflammatory, analgesic and soothing properties of licorice attributed to mainly GLYCYRRHIZIN, which is known to reduce inflammation and irritation in mucosal tissues.

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, glabridin, and hispaglabridins. Anti-inflammatory and antiallergic properties are due to glycyrrhizin.[6] while glycyrrhizic acid decreases the inflammatory process by inhibiting cyclooxygenase activity, prostaglandin formation, and inhibition of platelet aggregation.[7] Liquilitin and liquiritigenin have peripheral and central antitussive properties.[8] Glabridin has significant antioxidant and ulcer-healing properties which might be helpful in minimizing the extent of ischemic injury to the pharyngeal and trachea mucosa and expedite their healing[9]. Side effects of the use of licorice have been reported. Prolonged use is associated with pseudoaldosteronism[10] hypertension[11] and hyperkalemia.[12] Licorice 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/cytotoxicity.[13] In the current study, no side effects were reported as a single low dose of licorice was used in the study group.

Also, one of the strengths of this study are it is a double-blind placebo-controlled study, which eliminates potential BIAS and enhances the VALIDITY of the result.

Conclusion

Licorice lozenges prove to be a safe and effective intervention with no significant adverse effects reported. Therefore, licorice lozenges may be a beneficial adjunct in the management of postoperative sore throat, improving patient comfort and reducing reliance on analgesics post-surgery.

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