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Original Article

Anaesthesia Section

Evaluation of Preventive Effect of Zinc Lozenge on Sore Throat after Placement of ProSeal Laryngeal Mask Airway: A Randomised Controlled Study

RAJMALA JAISWAL[1], PRIYANKA AGGARWAL[2], DEEPIKA[3], MONICA CHHIKARA[4], MANOJ KATEWA[5], TEYIESITO YANO[6]

ABSTRACT

Introduction: Postoperative Sore Throat (POST) is a known complication after general anaesthesia with an endotracheal tube (14.4% to 50%) and less so with Supraglottic Airway (SGA) devices (5.8% to 34%). Various modalities and drugs can decrease POST. Zinc possesses anti-inflammatory and antioxidant properties and is utilised in oral mucositis and xerostomia.

Aim: To evaluate the effect of preoperative administration of a zinc lozenge on POST after the removal of the Proseal Laryngeal Mask Airway (PLMA).

Materials and Methods: In this randomised, double-blinded controlled study was conducted at the Department of Anaesthesia at Pt. BD Sharma PGIMS, Rohtak, Haryana, India, over a period of five months from August 2020 to December 2020. 100 patients aged 18-60 years of either sex belonging to American Association of Anesthesiologists (ASA) I and II undergoing elective surgery under general anaesthesia with PLMA placement were randomly allocated into two groups to receive a 40 mg zinc lozenge (Group-I) or placebo (Group-II) and were asked to chew it 30 minutes preoperatively. Patients with upper respiratory tract infections, at risk of aspiration, or with anticipated difficult intubation were excluded from the study. The incidence and severity of POST were assessed on a 4-point scale (0-3) at 30 minutes, 2, 4, and 24 hours postoperatively. The primary outcome of the study was the incidence of POST at four hours postoperatively, and the secondary outcome was the severity of POST at 30 minutes, two hours, and 24 hours postoperatively. Statistical analysis was conducted using Statistical Package for Social Sciences (SPSS) version 20.0 (IBM SPSS Statistics Inc., Chicago, Illinois, USA) Windows software programme. The Chi-square test and unpaired t-test were used for statistical analysis.

Results: The mean age in Group-I was 38.6±12.32 years and in Group-II was 37.90±14.84 years (p-value 0.79). Data regarding the distribution of patients according to sex were comparable with a p-value of 0.31. There was a significantly lower incidence of POST in Group-I (zinc group) than in Group-II (placebo group) at four hours with a p-value of 0.004.

Conclusion: The present study has shown that the preoperative administration of a 40 mg zinc lozenge effectively reduces the incidence and severity of POST in the postoperative period, peaking at four hours after general anaesthesia. Zinc lozenges are easy, convenient, non invasive, and successfully prevent POST.

Keywords: Intubation, Postoperative sore throat, Supraglottic

INTRODUCTION

The POST is an uncomfortable and distressing consequence of tracheal intubation due to the irritation of local tissues in the pharynx and larynx. It is caused by local tissue trauma leading to inflammation, can last for 2-3 days, and may result in patient dissatisfaction, discomfort after surgery, and a delay in the patient's return to normal activities [1]. The incidence of POST with an endotracheal tube ranges from 14.4% to 50% and is lower with SGA devices, ranging from 5.8% to 34% [2]. A sore throat is classified as "mild" if it lasts for one or two days without accompanying loss of voice, hoarseness, or stridor, and "severe" if it is accompanied by loss of voice, hoarseness, or stridor, or lasts for three days or more [2].

Various methods have been attempted in the past to reduce POST, such as using a smaller size endotracheal tube, maintaining low cuff pressure [3], using beclomethasone inhalation, applying betamethasone gel, using benzydamine hydrochloride, and using lignocaine spray [4-6]. N-methyl-D-aspartate (NMDA) receptor antagonists like ketamine and magnesium, which have analgesic and anti-inflammatory effects, have also been shown to reduce POST [7-9]. Preoperative zinc and magnesium lozenges can reduce POST [10,11], and a single dose of a 40 mg zinc lozenge administered 30 minutes preoperatively is effective in reducing both the incidence of POST in the immediate postoperative period [12].

Zinc lozenges have been used to reduce the incidence of POST following endotracheal intubation. Through an internet literature search (like PubMed and Google Scholar), we did not find any published study that demonstrates the preventive use of zinc for reducing POST after SGA device placement. The present study aimed to evaluate the effect of preoperative administration of a zinc lozenge on POST after the removal of the PLMA.

MATERIALS AND METHODS

This randomised, double-blinded controlled study was conducted at the Department of Anaesthesia at Pt. BD Sharma PGIMS, Rohtak, Haryana, India, over a period of five months from August 2020 to December 2020. Ethical clearance was obtained from the Institutional Ethical Committee (IEC/Th/19/Anst13). Informed written consent was obtained from all the patients. This trial was registered, and the Clinical Trials Registry-India (CTRI) number is CTRI/2020/07/026513.

Sample size calculation: A total of 100 patients were enrolled in the present study based on the sample size calculation derived from a study by Farhang B et al., where the incidence of POST in the control group was 29% and 7% in the study group [12]. Therefore, a sample size of 47 patients per group provided an 80% power to detect a significant difference between any two groups at an alpha level of 0.05.

The formula for calculated sample size is given below:

$$n=\frac{\{z_{1-\alpha/2}.\sqrt{2P(1-P)}+z_{1-\beta}.\sqrt{\{P_1(1-P_1)+P_2(1-P_2)\}}\}^2}{(P1-P2)^2}$$

$$n=\frac{\{1.96*0.543+0.842*0.521\}^2}{(0.22)^2}$$

=2.2597/0.0484

=46.68

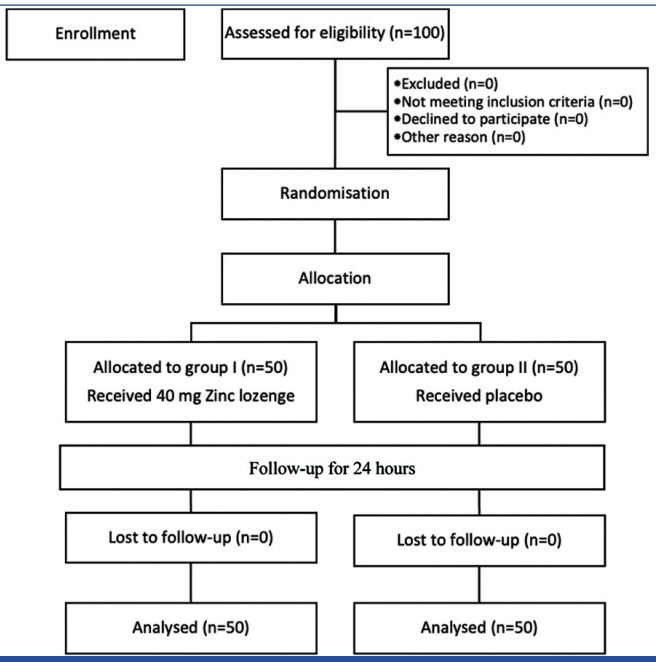
Where, Zα/2 is the critical value of the normal distribution at α/2 (e.g., for a confidence level of 95%, α is 0.05 and the critical value is 1.96), Zβ is the critical value of the normal distribution at β (e.g., for a power of 80%, β is 0.2 and the critical value is 0.842), and p1 and p2 are the expected sample proportions of the two groups.

Inclusion criteria: One hundred patients aged 18 to 60 years, ASA I and II, who underwent elective surgery under general anaesthesia in the supine position with the placement of a PLMA size 3.0 or 4.0 were enrolled.

Exclusion criteria: Patients with an active infection within the oral cavity and those at an increased risk of aspiration (such as those with a full stomach, morbidly obese patients, obstetric patients, and those with upper gastrointestinal dysfunction) were excluded from the study.

Study Procedure

Randomisation was done using a computer-generated randomisation table [Table/Fig-1], and patients were divided into two groups. Group-I (n=50) received a 40 mg zinc lozenge [12], while Group-II (n=50) received a placebo prepared by the pharmacist at the study institution. The placebo was identical in colour, appearance, smell, and taste to the zinc lozenge but had no pharmaceutical activity. The lozenges were administered by a fellow colleague, and patients were instructed to completely dissolve them by sucking orally 30 minutes prior to surgery. Patients, the individual administering the lozenge, and the investigator were all blinded to the group allocation. None of the patients received sedative medication.



[Table/Fig-1]: Consolidated Standards of Reporting Trials (CONSORT) diagram.

Upon arrival in the operating theatre, standard monitors for heart rate, Electrocardiogram (ECG), pulse oximetry (SpO_2), and Non invasive Arterial Blood Pressure (NIBP) were attached for monitoring vital signs. Ringer lactate solution was started after securing an intravenous line. After preoxygenation with 100% oxygen for three minutes, anaesthesia induction was performed with glycopyrrolate (0.005 mg/kg), fentanyl (2 μg/kg), and thiopentone (5 mg/kg). The patient's ability to mask ventilate was assessed before administering a neuromuscular blocking agent. Vecuronium (0.1 mg/kg) was administered as the neuromuscular blocking agent. Anaesthesia was maintained with either sevoflurane or isoflurane with 50% nitrous oxide in oxygen, and then the appropriate size PLMA was placed and the cuff inflated. Neostigmine and glycopyrrolate were given to reverse any residual neuromuscular block at the beginning of skin closure. After completion of surgery and emergence from general anaesthesia, the patient was extubated and monitored for nausea and vomiting before being transferred to the Post-anaesthesia Care Unit (PACU). In the PACU, the patient received tramadol 50-100 mg every eight hours for postoperative pain relief. The incidence of POST was determined by asking patients about the presence or absence of throat soreness at 30 minutes in the PACU. Patients were then transferred to the ward and observed for POST at two hours, four hours, and 24 hours, as well as for any nausea, vomiting, and managed accordingly.

Patients were assessed for the incidence and severity of POST using a standardised scale ranging from 0 to 3: 0 for no sore throat, 1 for mild discomfort (complained only upon questioning), 2 for moderate sore throat (complained on their own), and 3 for severe sore throat (change in voice, hoarseness, and throat pain) [12,13]. This evaluation was conducted at 30 minutes, two hours, four hours, and 24 hours postsurgery, with the assessment at four hours being the primary outcome of the study. No treatment was provided for grades 0 and 1, while patients with grades 2 and 3 were advised to use oral aspirin (acetylsalicylic acid) gargles every six hours.

STATISTICAL ANALYSIS

After the data was coded, it was entered into a Microsoft excel spreadsheet. Data analysis was performed using SPSS version 20 (IBM SPSS Statistics Inc., Chicago, Illinois, USA) Windows software programme. The unpaired t-test was used for quantitative data to compare two independent groups, while the Chi-square test was used for qualitative data when comparing two or more than two groups. The level of significance was set at $p \leq 0.05$.

RESULTS

One hundred patients were enrolled for the study in the preoperative area, and none were excluded. They were then randomised into two groups: Group-I received a 40 mg zinc lozenge, and Group-II received a placebo. Both groups were assessed postoperatively for sore throat at various time intervals, and no patient was lost to follow-up. The data was analysed.

The mean age and gender were comparable between the two groups with p-values of 0.79 and 0.31, respectively. The number of attempts taken for the placement of the PLMA and the presence or absence of blood after the removal of the PLMA did not show any significant differences. Patient satisfaction was 100% in both groups, and the data for the duration of surgery was also comparable [Table/Fig-2].

Variables	Group-I	Group-II	p-value
Age (in years)	38.6±12.322	37.90±14.840	0.79
Gender (Male/Female)	25/25	20/30	0.31
Patients with size of PLMA (3/4)	22/28	27/23	0.31
Number of attempts in placement of PLMA (1/2)	45/5	48/2	0.24
Presence or absence of blood following removal of PLMA (Present/absent)	2/48	0/50	0.15
Patient satisfaction Yes/No	50/0	50/0	Not applicable
Duration of surgery (minutes)	101.38±19.603	106.20±16.369	0.18

[Table/Fig-2]: Patient demographics, size of PLMA used absence or presence of blood after removal of LMA, patient satisfaction, duration of surgery.
Unpaired t-test-age and duration of surgery
Chi-square test- gender, size of PLMA, no of attempts, absence or presence of blood on PLMA and patient satisfaction

Evaluation time	Group-I				Group-II				p-value
	0	1	2	3	0	1	2	3	
30 minutes	50 (100%)	0	0	0	45 (90%)	5 (10%)	0	0	0.02
2 hours	50 (100%)	0	0	0	41 (82%)	8 (16%)	1 (2%)	0	0.007
4 hours	50 (100%)	0	0	0	40 (80%)	8 (16%)	2 (4%)	0	0.004
24 hours	50 (100%)	0	0	0	50 (100%)	0	0	0	Data not comparable

[Table/Fig-3]: Incidence and grading of sore throat at different time intervals postoperatively. Chi-square test was used for analysis.

At 30 minutes, two hours, and four hours, there was a statistically significant difference between the two groups. In Group-II, the incidence of sore throat was higher with p-values of 0.02 at 30 minutes, 0.007 at two hours, and 0.004 at four hours. At 24 hours postoperatively, none of the patients had a sore throat in both groups [Table/Fig-3].

No other significant side-effects, like nausea or vomiting, were observed in either of the groups.

DISCUSSION

The POST is due to pharyngeal, laryngeal, or tracheal irritation, leading to inflammation of local tissues. Multiple treatments have been recommended for POST, and recently, zinc lozenges have been used to reduce the incidence of POST [12]. Studies have shown that following epithelial injury, endogenous zinc is released, which may lead to the activation of intracellular signaling pathways associated with wound healing. The topical application of zinc may enhance the formation of barriers and have anti-inflammatory effects [13,14]. Polprezinc (PZ) is a zinc-containing molecule that has been used in the treatment of gastric ulcers and oral mucositis associated with radiochemotherapy. It inhibits the induction of Tumour Necrosis Factor-α (TNF–α) as well as the cellular signalling of TNF–α [15-18].

In the current study, patients were allocated into two groups to receive either a placebo or a 40 mg zinc lozenge 30 minutes preoperatively. They were instructed to completely dissolve it by sucking. The incidence and severity of POST were assessed at 30 minutes, two hours, four hours, and 24 hours post-extubation. The primary outcome was the incidence of POST at four hours.

Both groups were comparable in terms of age, gender distribution, size of the PLMA used, the presence or absence of blood on the PLMA after removal, the number of attempts taken, patient satisfaction, and the duration of surgery. The mean age in Group-I was 38.6±12.32 years, and in Group-II, it was 37.90±14.84 years, with a p-value of 0.79, which was statistically not significant. The distribution of sex was also comparable in both groups, with a p-value of 0.31. The mean duration of surgery in Group-I was 101.38±19.60 minutes, and in Group-II, it was 106.20±16.36 minutes, with a p-value of 0.18, which was statistically not significant.

The overall incidence of POST was reduced in the zinc group compared to the placebo group. The maximum reduction was observed at four hours in the zinc group (Group-I) with a statistically significant p-value of 0.004. Farhang B and Grondin L studied the effect of zinc lozenges on POST in patients undergoing the placement of an endotracheal tube. Patients were randomly assigned to two groups: the control group received a placebo, and the zinc group received 40 mg zinc lozenges 30 minutes preoperatively. Patients were assessed for the incidence and severity of POST (using a 4-point scale from 0-3) at 0, two, four, and 24 hours postoperatively. At four hours, the zinc group had a significantly lower incidence of POST at 7% compared to the control group at 29% (p=0.046). The incidence of POST at 0 hours was 0% in the zinc group and 24% in the control group (p=0.004) [12]. Sarkar T and Mandal T also studied the effect of zinc tablets on the prevention of sore throat and found a significantly lower incidence of POST in the zinc group compared to the placebo group. At four hours postoperatively, there was a significantly lower incidence of POST in the zinc group at 6.8% compared to the control group at 31.8%, with a p-value of 0.003 [13].

The reduction in the incidence of POST in the zinc group is most likely due to the prevention of cytokine release, a decrease in radical oxygen species, and subsequent decrease in Cyclooxygenase-2 (COX-2) and prostaglandin E2 release [19]. Zinc is a chemical element with an oxidation state of +2 and is involved in various physiological processes such as immune system modulation, growth and tissue repair, and acts as an anti-inflammatory agent. It has also been shown to be an effective antioxidant by protecting sulfhydryl groups against oxidation and inhibiting the production of reactive oxygen species by transition metals [20].

In the present study, the severity of sore throat was found to be lower in the zinc group compared to the placebo group. In Group-II (placebo group), at 30 minutes, 10% of patients developed mild sore throat; at two hours, 16% had mild sore throat and 2% had moderate sore throat; and at four hours, 16% had mild sore throat and 4% had moderate sore throat. At 24 hours, no patient developed sore throat. The data was comparable between the two groups, and the difference was found to be statistically significant with a p-value of 0.004 at four hours. The present study's findings were similar to those of the study conducted by Farhang B and Grondin L [12], where the severity of POST was significantly lower in the zinc group (p=0.004) [12].

It was concluded that the oral intake of a 40 mg zinc lozenge 30 minutes preoperatively is effective in reducing the incidence of POST in the first four hours and the severity of POST in the immediate postoperative period. Sarkar T and Mandal T also showed in their study that the incidence and severity of POST were significantly lower in the zinc group than the control group, with p-values of 0.003 and 0.001, respectively, at four hours and 0 minutes [13]. It was concluded that the prophylactic administration of a 40 mg dispersible zinc tablet before surgery reduces the incidence and severity of POST in the immediate postoperative period. Our study was very similar to their study in preventing sore throat after using zinc lozenges, except that we used PLMA in the present study.

Limitation(s)

The limitation of the present study was that it was not multicentric. The authors recommendation for future studies is to use a larger sample size, study the exact dosage, timing, and frequency of administration of zinc lozenges, and explore different preparations. It would also be beneficial to compare different SGAs, as well as compare different drugs such as zinc, magnesium, antioxidants like vitamin C, vitamin D, vitamin E, and other anti-inflammatory agents.

CONCLUSION(S)

The prophylactic administration of a 40 mg zinc lozenge 30 minutes before surgery effectively reduces the incidence and severity of POST in the first four hours after extubation, with a significant reduction at four hours. This could be beneficial for preventing POST in patients undergoing general anaesthesia, whether with an endotracheal tube or supraglottic devices. Proper management of POST will enhance patient satisfaction and improve the overall anaesthesia experience.

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PARTICULARS OF CONTRIBUTORS:
1. Senior Professor, Department of Anaesthesia, Pt. BD Sharma PGIMS, Rohtak, Haryana, India.
2. Senior Resident, Department of Anaesthesia, Pt. BD Sharma PGIMS, Rohtak, Haryana, India.
3. Associate Professor, Department of Anaesthesia, Pt. BD Sharma PGIMS, Rohtak, Haryana, India.
4. Associate Professor, Department of Anaesthesia, Pt. BD Sharma PGIMS, Rohtak, Haryana, India.
5. Senior Resident, Department of Anaesthesia, Pt. BD Sharma PGIMS, Rohtak, Haryana, India.
6. Senior Resident, Department of Anaesthesia, Pt. BD Sharma PGIMS, Rohtak, Haryana, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Monica Chhikara,
Flat No. 27, Spring Cottage Apartment, Raj Garden, Rohtak-124001, Haryana, India.
E-mail: chhikara.monica@gmail.com

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