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Original Article

# The Effect of Flurbiprofen on Postoperative Sore Throat and Hoarseness After LMA-ProSeal Insertion: A Randomised, Clinical Trial

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Abstract

**Objective:** We hypothesized that flurbiprofen lozenges reduce the ProSeal laryngeal mask airway (LMA) related symptoms of Post Operative Sore Throat (POST), hoarseness and dysphagia compared to placebo lozenges.

**Methods:** Eighty American Society of Anesthesiologists (ASA) I–II patients undergoing general anaesthesia with LMA were included in this prospective, randomized, placebo-controlled clinical and single centre (university hospital) study. Group F received an 8.75 mg flurbiprofen lozenge (Strefen®) and Group P received a placebo lozenge 45 minutes before the induction of anaesthesia. Postoperative sore throat, hoarseness and dysphagia were evaluated 30 minutes after removal of the LMA in the recovery room and then at 4, 12 and 24 h after surgery using a 4-point scale. Data were analysed using Student's t test, and Fisher's exact and Mann-Whitney U tests. A p value of <0.05 was considered statistically significant.

**Results:** The 8.75 mg flurbiprofen lozenges reduced the severity of early (30 mins) POST and dysphagia. The severity of dysphagia at 4 h and hoarseness at 12 h were also significantly reduced in Group F. There were no significant differences betweeen the groups regarding incidence of sore throat, dysphagia and hoarseness throughout the study period.

**Conclusion:** Preoperative flurbiprofen lozenges reduce the severity of early postoperative sore throat and dysphagia.

**Key Words:** Laryngeal mask airway, flurbiprofen, sore throat

## Introduction

Postoperative sore throat (POST) is an unpleasant side effect of general anaesthesia (1-6). Although it seems to be a trivial adverse effect, especially with the addition of hoarseness and dysphagia, it may negatively affect patient comfort and lead to postoperative morbidity (7). Even though POST frequently occurs after endotracheal intubation, some patients may also suffer from sore throat after laryngeal mask airway (LMA) insertion (1). The incidence of sore throat has been shown to range between 5.8% and 34% when LMA is used (2-5).

Recommended interventions to reduce this adverse effect involve avoiding the physical trauma caused by LMA insertion and the use of various topical or systemic drugs. No drug is commonly accepted to prevent this adverse effect in clinical practice (6). One of the alleged solutions to the aforementioned symptoms may be the soothing effect of a lozenge of flurbiprofen (8).

Flurbiprofen (Strefen®) is a propionic acid derivative NSAID with potent anti-inflammatory effects in addition to its antipyretic, analgesic and soothing topical effects (8, 9). It has proved to be an efficient and safe medicine to treat conditions like rheumatoid arthritis, osteoarthritis and other musculoskeletal disorders (8), and is also used for oral hygiene as a mouthwash and toothpaste (10). Flurbiprofen 8.75 mg lozenge is a commonly used medicine for sore throat, and is effective during upper airway inflammatory disease (8).

In this placebo-controlled study, we planned to evaluate the effect of flurbiprofen lozenges on POST, hoarseness, and dysphagia symptoms of patients in whom a ProSeal LMA was inserted during general anaesthesia.

## Methods

Following approval by the ethics committee of Yeditepe University Hospital (25.02.2011/No: 074) and written informed consent, 80 ASA I, II patients (18-65 years of age) undergoing elective orthopaedic, gynaecologic, general surgical and

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urologic procedures under general anaesthesia were enrolled in this randomized, double-blind, single-centre clinical study between February 2011 and December 2011.

Patients undergoing general anaesthesia with LMA were included in this study. Patients with a history of NSAID-induced allergy, sore throat, hoarseness or dysphagia, or gastro-oesophageal reflux were excluded from the study. Patients who had symptoms of hoarseness or a history of dysphagia during preoperative evaluation were excluded. A body mass index >30, current NSAID use, potential difficult airway management, active respiratory tract infection, pregnancy and lactation were also considered as exclusion criteria. More than one LMA insertion attempt was also considered as an exclusion criterion.

Patients were randomly assigned to the flurbiprofen (Group F; n=40) or placebo (Group P; n=40) groups. The participants were randomised and allocated into groups using computerised random numbers (Excel; Microsoft, Redmond, Washington, USA) by an anaesthesiologist not participating in the trial. A nurse blinded to the groups gave lozenges 45 minutes before the induction of anaesthesia. Flurbiprofen (Strefen® honey and lemon lozenge, Slough, Berkshire, UK) contains the active ingredients of flurbiprofen 8.75 mg, sucrose, glucose syrup, honey, macrogol 300, lemon flavour, potassium hydroxide, levomenthol and 2.5 g carbohydrate. The placebo tablets, identical to the study drug and prepared by the Yeditepe University Faculty of Pharmacy (Istanbul, Turkey), contained sugar, glucose, lemon flavour and citric acid.

After premedication with 0.04 mg $kg^{-1}$ intravenous midazolam, all patients were transferred to the operating room. Anaesthesia was induced with iv propofol 2-2.5 mg $kg^{-1}$, iv fentanyl 1.5 mcg $kg^{-1}$. The LMA cuff was fully deflated and then lubricated with saline on the posterior aspect in preparation. The LMA was inserted after the patient lost consciousness and eyelash reflex. The LMA size was chosen according to the gender and weight of the patient: size 3 (>50 kg) or size 4 (≤50 kg) for women; size 4 (<70 kg) or size 5 (≥70 kg) for men (11). LMA cuff pressure was adjusted to less than 44 mmHg (12). Cuff pressure was monitored using a pressure monitoring transducer (VBM, Germany). LMA was inserted using the index finger insertion technique by the same experienced anaesthesiologist in all patients. LMA insertion success was confirmed with chest expansion, capnography and airway pressure traces. Anaesthesia was maintained with sevoflurane in a 40% oxygen-air mixture and remifentanil infusion 0.1-0.2 mcg $kg^{-1}$ $min^{-1}$. Mechanical ventilation with an initial tidal volume of 8 mL $kg^{-1}$ and respiratory frequency of 12 breaths $min^{-1}$ was used to maintain normocapnia. Pain control was provided with 0.5 mg $kg^{-1}$ iv pethidine, given 30 minutes before the end of the operation. LMA was removed when spontaneous ventilation was adequate and patients were able to follow verbal commands.

Postoperative sore throat (POST), hoarseness, and dysphagia were evaluated when the patient's Ramsay Sedation Score (13) was 2 (cooperative, oriented and tranquil). This problem was evaluated 30 minutes after LMA removal in the recovery room and then at 4, 12 and 24 h after surgery by a nurse blinded to the study.

For evaluation of preoperative dysphagia, hoarseness and sore throat, the patients were asked if they were having any difficulty when eating and swallowing, whether they had a dry harsh voice, and whether they had any throat pain. The severity of sore throat was graded as follows: 1: no sore throat, 2: minimal, 3: moderate, 4: severe; for dysphagia the grading was: 1: no dysphagia, 2: minimal, 3: moderate, 4: severe; and for hoarseness: 1: no hoarseness, 2: slight hoarseness, 3: severe hoarseness, 4: cannot speak because of hoarseness.

**Statistical analysis**

Data are given as the mean (±SD) and median, as appropriate. Since a 40% decrease in the incidence of postoperative sore throat is clinically important, sample size determination was performed with chi-square analysis (Statistical software Gpower 3.0) to detect a 40% decrease in the incidence of sore throat (from 34% to 20%). A type I error of 0.05 ($\alpha$=0.05) and a power of 80% (1-$\beta$=0.20) revealed that a total patient number of 75 was required. Five patients were added for possible losses and 80 patients completed the study. Statistical analyses were performed with Student's t test, and the Fisher's exact and Mann-Whitney U tests were used for nominal and/or categorical variables. A p value of <0.05 was considered statistically significant.

## Results

Eighty patients were found to be eligible to enrol in the study. Figure 1 shows the flowchart of the study.

The demographics, operative data and surgical positions of the patients were similar in the two groups (Table 1).

There were no significant differences between groups regarding the incidence of sore throat, dysphagia and hoarseness throughout the study (Table 2).

Comparison of the severity scores revealed that the median severity scores of early (30 min) POST (0 vs. 0.2; p<0.05) and dysphagia (0 vs. 0.2; p<0.05) were significantly higher in group P than group F. Likewise, the median severity score of dysphagia at 4 hours (0 vs.1; p<0.05) and hoarseness at 12 hours (0 vs.1; p<0.05) was significantly higher in the placebo group than the flurbiprofen group (Table 3).

None of the patients complained about the taste of the lozenges.

## Discussion

This study has shown that a single preoperative dose of flurbiprofen lozenges (8.75 mg) effectively reduced the severity, but not the incidence of early postoperative sore throat and dysphagia related to LMA use when compared to placebo.

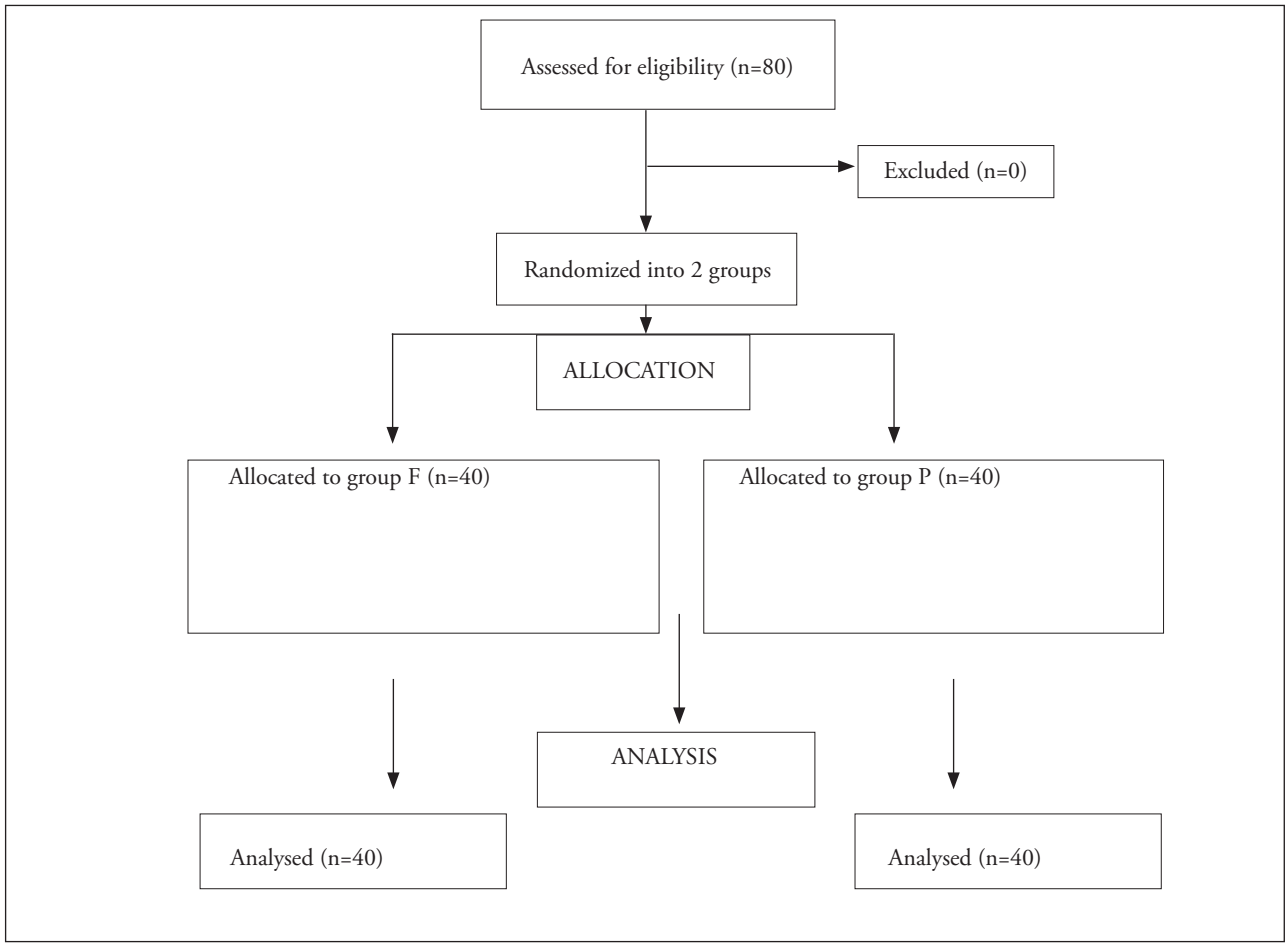


Figure 1. Flow chart

Table 1. Patients' demographic data

| | Group F n=40 | Group P n=40 | p |
|---|---|---|---|
| Age (years)* | 41±15 | 41±13 | ns |
| Gender (male/female) | 22/18 | 19/21 | ns |
| Weight (kg)* | 76±10 | 72±9.6 | ns |
| Anaesthesia time (mins)* | 47±19 | 41±15 | ns |
| Position | | | |
| Supine | 15 | 14 | ns |
| Lithotomy | 25 | 26 | ns |

*Data are presented as mean (SD).
There were no significant differences in demographic data between groups.
Abbreviations: Group F: flurbiprofen, Group P: placebo, ns: not significant

Postoperative sore throat (POST) occurs at a rate of between 5.8% and 34%, when a laryngeal mask airway (LMA) is used (2-5). LMA-induced pharyngolaryngeal complications (POST, hoarseness, dysphagia) are related to the insertion technique, number of insertion attempts, LMA size, duration of anaesthesia and surgical position (11, 14-16). Studies have shown that the use of lubricants to facilitate insertion and cuff pressure control does not reduce the incidence of sore throat (2).

Several studies have been performed to prevent or treat POST related to LMA. Kati et al. (17) reported the effectiveness of benzydamine hydrochloride spray application to the pharynx to prevent POST caused by LMA. However, lidocaine 2% used as a lubricant to avoid POST after LMA insertion was found to be ineffective (18). Nowadays, sugar-based lozenge formulations are popular for their immediate demulcent effects. Flurbiprofen 8.75 mg lozenge effectively treats subjective and objective symptoms of sore throat related to upper respiratory system infection (8). The effective dose range of flurbiprofen to treat sore throat related to inflammation of the upper airway is 5.0 mg to 12.5 mg (9). To our knowledge, there are no studies evaluating the effects of prophylactic flurbiprofen on postoperative pharyngeal complications after LMA use.

In our study, the severity of early POST and dysphagia was reduced with preoperative use of flurbiprofen following LMA insertion. A study with topical benzydamine showed that the drug significantly reduced sore throat symptoms related to LMA insertion. This study evaluated only sore throat symptoms until 4 hours postoperatively. Furthermore, the authors reported that the patients complained about the taste of the drug (17). In our study, patient satisfaction regarding the taste of the lozenges was good.

Another study showed that flurbiprofen lozenges reduced sore throat symptoms due to upper respiratory tract infection

Table 2. Comparison of the groups according to the side-effects related to LMA

| | | Group F (n=40) | Group P (n=40) | p |
|---|---|---|---|---|
| 30 mins postoperatively | Sore throat | 4 | 8 | 0.3 |
| | Dysphagia | 5 | 8 | 0.5 |
| | Hoarseness | 5 | 11 | 0.1 |
| 4 h postoperatively | Sore throat | 1 | 2 | 1 |
| | Dysphagia | 0 | 4 | 0.1 |
| | Hoarseness | 1 | 5 | 0.2 |
| 12 h postoperatively | Sore throat | 2 | 2 | 1 |
| | Dysphagia | 1 | 3 | 0.6 |
| | Hoarseness | 0 | 4 | 0.1 |
| 24 h postoperatively | Sore throat | 3 | 3 | 1 |
| | Dysphagia | 1 | 3 | 0.6 |
| | Hoarseness | 0 | 1 | 1 |

Data are given as the number of the patients with symptoms.
Abbreviations: Group F: flurbiprofen, Group P: placebo.

Table 3. Comparison of the severity scores

| | | Group F (n=40) | Group P (n=40) | p |
|---|---|---|---|---|
| 30 mins postoperatively | Sore throat | 0 (0-1) | 0 (0-2) | 0.026 |
| | Dysphagia | 0 (0-1) | 0 (0-2) | 0.02 |
| | Hoarseness | 0 (0-2) | 0 (0-2) | ns |
| 4 h postoperatively | Sore throat | 0 (0-2) | 0 (0-1) | ns |
| | Dysphagia | 0 (0-0) | 1 (0-1) | 0.04 |
| | Hoarseness | 0 (0-1) | 0 (0-1) | ns |
| 12 h postoperatively | Sore throat | 0 (0-1) | 0 (0-1) | ns |
| | Dysphagia | 0 (0-1) | 0 (0-1) | ns |
| | Hoarseness | 0 (0-0) | 1 (0-1) | 0.04 |
| 24 h postoperatively | Sore throat | 0 (0-2) | 0 (0-1) | ns |
| | Dysphagia | 0 (0-1) | 0 (0-2) | ns |
| | Hoarseness | 0 (0-0) | 0 (0-1) | ns |

Data are shown as median (range)
Abbreviations: Group F: flurbiprofen, Group P: placebo, ns: not significant

for at least 4 hours (8). In our study the severity of sore throat symptoms decreased significantly only during the 30 minutes after taking the drug. This is probably related to the pharmacokinetics of the lozenges or to the trauma in addition to the inflammation during LMA insertion. Therefore, repeated doses of flurbiprofen may be recommended to extend the pain-free period. Spontaneous elimination of the symptoms in both groups at 4 hours may be explained by the nature of the LMA-related POST. The severity of early dysphagia was also reduced by flurbiprofen lozenge. The severity of hoarseness was significantly reduced at 12 hours compared to placebo. These findings might be related to the better anti-inflammatory efficacy of flurbiprofen than its analgesic effects.

This study did not evaluate the effects of timing and repetition of flurbiprofen usage after surgery. Perioperative pethidine use for analgesia may have affected the results of our study. Decreasing the target POST incidence to 5% instead of 10% would have yielded a different outcome.

## Conclusion

A single preoperative dose of flurbiprofen lozenge seems to be effective in reducing the severity of early symptoms of sore throat, and dysphagia related to LMA use. Further studies are required to evaluate the effect of flurbiprofen lozenges on POST incidence and severity using different doses and dosing regimens.

**Ethics Committee Approval:** Ethics committee approval was received for this study from the ethics committee of Yeditepe University Hospital.

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

**Peer-review:** Externally peer-reviewed.

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