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Long-lasting relief of throat symptoms (throat pain and swollen throat) and throat function (ability to swallow) with flurbiprofen 8.75 mg lozenge

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INTRODUCTION

- Sore throat is a symptom of pharyngeal inflammation[1,2]
- The majority of cases of sore throat are caused by a self-limiting viral infection;[3,4] however, it is one of the most common reasons for visits to primary care[5,6]
- Patients reporting to primary care often seek treatments which will provide long-lasting relief from symptoms such as throat pain (a "sore throat"), a "swollen throat", and difficulty swallowing (a throat function)[7,8]
- A sugar-based, flavored lozenge containing flurbiprofen 8.75 mg was developed to provide the immediate physical soothing properties of the lozenge vehicle and the analgesic properties of the non-steroidal anti-inflammatory drug, flurbiprofen[9,10]
- To investigate the duration of action of flurbiprofen 8.75 mg lozenge on common sore throat symptoms, we conducted a randomized, double-blind, placebo-controlled study in patients with painful pharyngitis

METHODS

Study design

- Randomized, double-blind, placebo-controlled, single-center study (ClinicalTrials.gov identifier: NCT01049334)

Study population

- Male and female adults (≥18 years) with acute sore throat with onset ≤4 days prior to randomization
- Patient characteristics included:
  - Moderate-to-severe pain on the Throat Pain Scale (TPS)
  - The presence of three throat symptoms associated with pharyngitis rated on 100-mm visual analog scales (Figure 1)[11]
    - Sore throat pain (≥66 mm on the Sore Throat Pain Intensity Scale [STPIS])
    - Difficulty swallowing (≥50 mm on the Difficulty Swallowing Scale [DSS])
    - Swollen throat (≥33 mm on the Swollen Throat Scale [SwoTS])
  - Physical findings of pharyngitis (a score of ≥5 on the Tonsillo-Pharyngitis Assessment [TPA], a 21-point index of seven features of tonsillo-pharyngitis each rated on a 0–3 categorical scale) (Table 1)[12]
  - Pharyngeal inflammation rated using the Practitioner's Assessment of Pharyngeal Inflammation (PAIN: categorical scale indicating the severity of pharyngeal inflammation: none, mild, moderate, severe)

Figure 1. (A) STPIS used to assess sore throat pain, (B) DSS used to assess difficulty swallowing and (C) SwoTS used to assess sensation of swollen throat

A. The patient was instructed to swallow and:
"Place a line on the scale that best characterizes the severity of your sore throat *now*"

NO PAIN ——— SEVERE PAIN

B. The patient was instructed to swallow and:
"Place a line on the scale that best characterizes how difficult it is to swallow *now*"

NOT DIFFICULT ——— VERY DIFFICULT

C. The patient was instructed to swallow and:
"Place a line on the scale that best characterizes how swollen your throat feels *now*"

NOT SWOLLEN ——— VERY SWOLLEN

Table 1. Tonsillo-Pharyngitis Assessment (TPA)

Item	0 Points	1 Point	2 Points	3 Points
Oral temperature	≤98.6ºF	98.7–98.9ºF	99.0–99.9ºF	≥100.0ºF
Oropharyngeal color	Normal/ pink	Slightly red	Red	Beefy red
Size of tonsils	Normal/ absent	Slightly enlarged	Moderately enlarged	Much enlarged
Number of oropharyngeal enanthems (vesicles, petechiae or exudates)	None	Few	Several	Many
Largest size of anterior cervical lymph nodes	Normal	Slightly enlarged	Moderately enlarged	Much enlarged
Number of anterior cervical lymph nodes	Normal	Slightly increased	Moderately increased	Greatly increased
Maximum tenderness of some anterior cervical lymph nodes	Not tender	Slightly tender	Moderately tender	Very tender

Study medications

- Patients were randomly assigned to suck one sugar-based, flavored flurbiprofen or placebo lozenge
- Rescue medication (acetaminophen 650 mg) was allowed, if required

Study assessments

- Patients rated sore throat pain (on the STPIS), difficulty swallowing (on the DSS), and swollen throat (on the SwoTS) at baseline and at regular intervals over 6 hours post-dose
- Any adverse events (AEs) occurring throughout the study were also recorded

Statistical analysis

- Baseline comparisons were performed using the chi-square test for gender, the Wilcoxon Rank-Sum test for duration of sore throat, and an independent t-test for age, STPIS, DSS, SwoTS, and TPA
- Efficacy endpoints included:
  - Time-weighted summed pain intensity difference (SPID) from 0–6 hours ($SPID_6$)
  - Time-weighted summed difference in difficulty swallowing from 0–6 hours (DSS_6)
  - Time-weighted summed difference in swollen throat from 0–6 hours ($SwoTS_6$)
- Efficacy was calculated using least square (LS) means from an analysis of variance (ANOVA) mixed model, with treatment as the fixed effect and the relevant baseline as the covariate. This was used to compare time-weighted summed differences between treatments for each endpoint
- For patients who re-dosed within 6 hours or took rescue medication, their values were set to baseline
- AEs were analyzed using chi-square test
- Two-sided statistical tests were performed with significance determined at the 5% significance level
  - All analyses were performed using SAS Version 9.2

RESULTS

Patient population

- 204 patients with moderate/severe sore throat pain, swollen throat, and difficulty swallowing were randomized 1:1 (n=102 for each treatment)
- Mean age was 19.8 years, 57.4% of the patients were female
- Treatment groups were well balanced in terms of demographic and clinical baseline characteristics (Table 2)

Table 2. Baseline demographics and characteristics

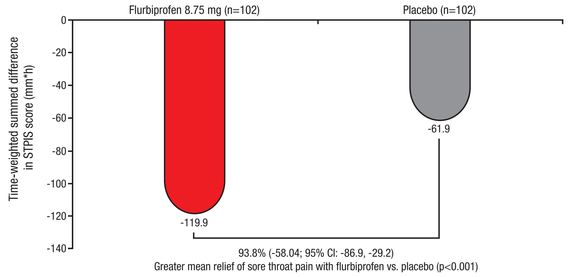
	Flurbiprofen 8.75 mg (n=102)	Placebo (n=102)	Overall (N=204)
Sex, % female	52.9	61.8	57.4
Age, mean (SD), years	19.8 (1.48)	19.8 (1.47)	19.8 (1.47)
STPIS, mean (SD), mm	78.8 (8.56)	80.5 (7.92)	79.7 (8.27)
DSS, mean (SD), mm	76.9 (12.41)	76.3 (11.04)	76.6 (11.72)
SwoTS, mean (SD), mm	76.6 (13.98)	79.0 (12.05)	77.8 (13.07)
TPS, %			
Moderate pain	56.9	53.9	55.4
Severe pain	43.1	46.1	44.6
TPA, mean (SD)	9.7 (2.63)	10.1 (2.90)	9.9 (2.77)
PAIN, %			
Mild inflammation	32.4	33.3	32.8
Moderate inflammation	56.9	52.0	54.4
Severe inflammation	10.8	14.7	12.7
Days with sore throat (%)			
1	13.7	16.7	15.2
2	41.2	42.2	41.7
3	29.4	29.4	29.4
4	15.7	11.8	13.7

DSS, Difficulty Swallowing Scale; PAIN, Practitioner's Assessment of Pain; SD, standard deviation; STPIS, Sore Throat Pain Intensity Scale; SwoTS, Swollen Throat Scale; TPA, Tonsillo-Pharyngitis Assessment; TPS, Throat Pain Scale

Efficacy

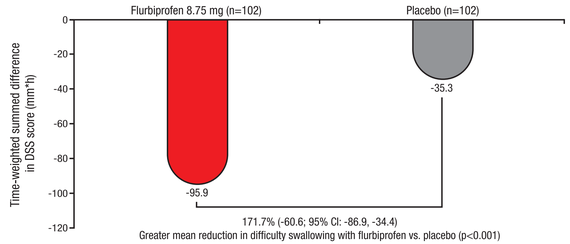
- Over the 6-hour period, patients taking flurbiprofen 8.75 mg lozenge experienced significantly greater relief of each of the three patient-reported outcomes compared with patients taking placebo (all p<0.001)
  - 93.8% greater reduction in sore throat pain (Figure 2)
  - 171.1% greater reduction in difficulty swallowing (Figure 3)
  - 105.5% greater reduction in swollen throat (Figure 4)

Figure 2. Time-weighted summed pain intensity difference from 0–6 hours ($SPID_6$)



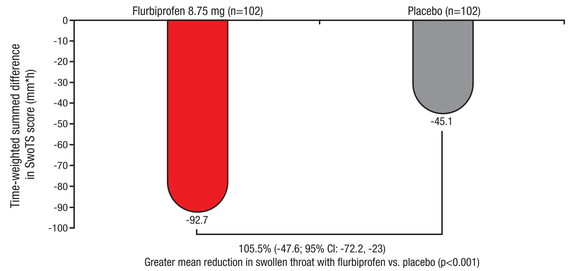
CI, confidence interval; STPIS, Sore Throat Pain Intensity Scale

Figure 3. Time-weighted summed difference in difficulty swallowing from 0–6 hours (DSS_6)



CI, confidence interval; DSS, Difficulty Swallowing Scale

Figure 4. Time-weighted summed difference in swollen throat from 0–6 hours ($SwoTS_6$)



CI, confidence interval; SwoTS, Swollen Throat Scale

Safety

- There were no serious AEs reported during the study
- The occurrence of AEs was similar between treatment groups
  - Reported by 22 patients (10.8%), including 11 patients from each treatment group
- 9 patients in the flurbiprofen 8.75 mg lozenge group experienced an AE possibly related to the study drug
- Most AEs were mild and self-limiting

DISCUSSION

- The results of this study demonstrate that flurbiprofen 8.75 mg lozenge provides significant relief of sore throat pain, difficulty swallowing, and the sensation of a swollen throat compared with placebo for up to 6 hours (all p<0.001) in adults with acute sore throat
- There were no serious AEs or clinical sequelae

CONCLUSION

- One flurbiprofen 8.75 mg lozenge provides long-lasting relief of different sore throat symptoms (throat pain, swollen throat, and difficulty swallowing)

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