Efficacy of Sucralfate in the Postoperative Management of Uvulopalatopharyngoplasty

A Double-blind, Randomized, Controlled Study

Prakash Zodpe, MS; Jae Gu Cho, MD; Hee Joon Kang, MD; Soon Jae Hwang, MD; Heung-Man Lee, MD

Objective: To evaluate the effectiveness of sucralfate in influencing throat pain, otalgia, analgesic requirement, bleeding, mucosal recovery, and incidence of postoperative bleeding in patients undergoing uvulopalatopharyngoplasty.

Design: A prospective double-blind randomized study.

Setting: University-affiliated tertiary referral hospital.

Participants: Eighty adult patients with obstructive sleep apnea syndrome requiring uvulopalatopharyngoplasty were recruited and randomly allocated into either a sucralfate treatment group or a control group.

Interventions: All patients underwent uvulopalatopharyngoplasty. Patients enrolled in the sucralfate group (n=40) were instructed to gargle the sucralfate suspension and then to swallow. Patients enrolled in the control group (n=40) were instructed to gargle placebo suspension at the same doses and schedule.

Main Outcome Measures: Postoperative throat pain, otalgia, amount of analgesic required, degree of strength (defined as patients' general well-being and return to regular daily activities), percentage of mucosal covering, and postoperative bleeding.

Results: Throat pain and otalgia occurred significantly less often in sucralfate group, with less analgesic requirement and with rapid mucosal healing and early return to regular daily activities. There was no significant difference in episodes of postoperative bleeding between the 2 groups (P=.37).

Conclusions: Although sucralfate therapy may not provide complete analgesia after uvulopalatopharyngoplasty, it may reduce the amount of analgesic required, thus preventing dose-related adverse effects from the analgesic agent. It can also significantly reduce the total number of days needed to return to normal daily activities (P=.41).


UVULOPALATOFPARYNGO-

plasty (UPPP) is still the most commonly performed surgical procedure for the treatment of obstructive sleep apnea syndrome (OSAS). When UPPP was first described by Fujita et al1 in 1981, it represented a major surgical advance in the management of OSAS. Kamami2 introduced laser-assisted uvulopalatoplasty in 1990. Pain, which is caused by irritation of the nerve endings, inflammation, and pharyngeal muscle spasm, is a major complication of UPPP and continues until mucosal recovery is complete. In UPPP, patients often complain of discomforting otalgia.

Sucralfate, which is a basic amino salt of sucrose octasulfate, has been used for decades in the treatment of peptic ulcer disease. It is believed to provide a protective coating because it has a tendency to bind exposed protein of damaged cells. Also, there is evidence that sucralfate promotes local production of prostaglandin E2, thus increasing blood flow, mucous production, mitotic activity, and surface migration of cells. Sucralfate may act in the same manner after UPPP, protecting the raw surfaces of the superior constrictor and palatine muscles and preventing muscle spasm and irritation of open nerve endings. Also, because sucralfate binds with growth factors and has angiogenic effects, it promotes mucosal healing and early restoration of daily activities.

The present study was designed to evaluate the effectiveness of sucralfate in the management of postoperative throat pain and otalgia and to compare the severity of postoperative pain, consumption of analgesics, mucosal recovery, postoperative bleeding, and degree of strength between a control group and a sucralfate-treated group. We hypothesized that if a coating that is similar to the peptic ulcer
Anesthesiologists; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CPAP, continuous positive airway pressure.

**Table 1. Criteria for Uvulopalatopharyngoplasty**

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
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<tbody>
<tr>
<td>Snoring complaint with social disturbance for more than 1 year</td>
<td>BMI ≥32 and AHI ≥10</td>
</tr>
<tr>
<td>Failure to tolerate or refusal of therapy with CPAP</td>
<td>Failure to tolerate or refusal of therapy with CPAP</td>
</tr>
<tr>
<td>No upper airway obstruction besides velopharynx, at rest and during Muller maneuver</td>
<td>BMI ≥32</td>
</tr>
<tr>
<td>ASA classification ≤II</td>
<td>Marked mandibular micrognathia or retrognathia</td>
</tr>
<tr>
<td>Moderate or severe narrowing of tongue base</td>
<td>ASA classification ≥III</td>
</tr>
</tbody>
</table>

Abbreviations: AHI, apnea-hypopnea index; ASA, American Society of Anesthesiologists; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CPAP, continuous positive airway pressure.

Eighty patients who underwent UPPP at Korea University College of Medicine, Seoul, South Korea, from January 2004 to December 2004 were randomized into 2 groups. The sucralfate treatment group consisted of 37 men and 3 women with a mean age of 48.7 years and a mean body mass index (calculated as weight in kilograms divided by height in meters squared) of 28.3. The control group was composed of 35 men and 5 women with a mean age of 49.2 years and a mean body mass index of 27.9. All patients underwent preoperative polysomnography and an upper airway examination, which included nasopharyngolaryngoscopy. The mean apnea-hypopnea index was 13.3 in the sucralfate group and 12.8 in the control group. The apnea index was 3.9 and 6.2 in the sucralfate and control groups, respectively. The inclusion and exclusion criteria used for UPPP at our institution are listed in Table 1.

The study was fully approved by the local ethics committee of Korea University College of Medicine. Patients gave informed consent for the trial before surgery. The randomization was computer generated in blocks of one. The random number allocation, surgery, and data collection were performed by a different person to reduce the chances of bias. All analyses were prospectively planned and were performed on study completers (intention-to-treat basis). There were no withdrawals or dropouts.

Electrocautery is used to resect the tonsils and a wedge of soft palate on each side of the uvula and then to resect and recreate the uvula itself. Elimination of the pharyngeal redundant folds is achieved by approximation of the muscular tissue of the tonsillar fossa and the soft palate with interrupted 2-0 polyglactin sutures. The mucosal flap edges can then be loosely approximated, without undermining, using 3-0 vicryl sutures.

Postoperative instructions included cold and soft food during the first 3 days after surgery, warm and soft food during the next 3 days, and a normal diet afterward. Both the sucralfate group and the control group were given 500 mg of amoxicillin sodium suspension every 8 hours for 7 days, 20 mg of intravenous piroxicam every 12 hours on the operative day, and 200-mg ibuprofen tablets when needed (maximum, 4 tablets per day). Sucralfate was prepared as an oral suspension (1 pack of Ulcermin, which contains 1 g of sucralfate, was dissolved in 60 mL of water). Patients enrolled in the sucralfate group were instructed to gargle the sucralfate suspension gently for 5 minutes and then to swallow. The suspension was given 2 hours after the operation and then every 6 hours during the next 6 days. Patients enrolled in the control group were instructed to gargle placebo suspension, which was similar in appearance to the sucralfate suspension and was given at the same doses and schedule.

Patients were examined and scored clinically on the day of the operation and once a day for the next 6 days. Throat pain, otalgia, amount of analgesic, degree of strength, percentage of mucosal coverage, and postoperative bleeding were the clinical parameters. The degree of strength was defined as general well-being and return to regular daily activities. Throat pain, otalgia, or both were estimated by the patients themselves using a visual analog scale based on a linear scale from 0 to 7, with 0 representing an absence of pain and 7 maximal pain. The remaining parameters were evaluated and recorded daily according to a numerical scoring system developed in our department (Table 2). Patients in the sucralfate group were questioned regarding the possible adverse effects of sucralfate, and any adverse effect, if present, was noted.

The statistical analysis was performed with repeated-measures analysis and the χ² test. P<.05 was considered significant.

**RESULTS**

Eighty patients, 40 in each group, received the intended treatment and completed the study protocol as planned without any participant withdrawal. There was no significant difference in terms of age, sex, body mass index, or polysomnographic data between the 2 groups. The overall tolerance of sucralfate was excellent, and there were no adverse effects. Table 3 shows a summary of the results in both groups, with mean scores and P values.

The severity of throat pain (according to our scale) was significantly reduced in the sucralfate group, showing statistical significance (P=.02) between the 2 groups on the third to the sixth postoperative day. There was no significant difference in the severity of throat pain between the 2 groups on the operative day or on the first and second postoperative days. The sucralfate group had less otalgia than the control group in the entire follow-up period, and the difference between the groups was statistically significant (P=.04).

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**Table 1. Scoring System**

<table>
<thead>
<tr>
<th>Analgesic requirement</th>
<th>Degree of strength</th>
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<tbody>
<tr>
<td>0—No analgesic required</td>
<td>1—Patient felt well</td>
</tr>
<tr>
<td>1—1 tablet per day</td>
<td>2—Patient felt moderately well</td>
</tr>
<tr>
<td>2—2 tablets per day</td>
<td>3—Patient felt weakness</td>
</tr>
<tr>
<td>3—3 tablets per day</td>
<td>Mucosal coverage</td>
</tr>
<tr>
<td>4—4 tablets per day</td>
<td>0—Complete healing</td>
</tr>
<tr>
<td></td>
<td>1—1%-25% bare mucosa</td>
</tr>
<tr>
<td></td>
<td>2—26%-50% bare mucosa</td>
</tr>
<tr>
<td></td>
<td>3—51%-75% bare mucosa</td>
</tr>
<tr>
<td></td>
<td>4—76%-100% bare mucosa</td>
</tr>
</tbody>
</table>

**Table 2. Criteria for Uvulopalatopharyngoplasty**
The analgesic requirement is accepted as an objective measurement of pain. Although the sucralfate group required less analgesic than the control group in the entire follow-up period, the difference between the groups was statistically significant up to the third postoperative day.

The difference in degree of strength, which is defined as general well-being and return to regular daily activities, was significant from the fourth postoperative day onward.

The mucosal coverage of the postoperative wound was found to be more rapid in the sucralfate group than in the control group. The difference between the groups was significant from the fourth postoperative day onward (Figure). One patient in the sucralfate group and 3 patients in the control group had late postoperative bleeding. The difference was not statistically significant ($P = .76$).

Table 3. Summary of Results

<table>
<thead>
<tr>
<th>Postoperative Day</th>
<th>Throat Pain</th>
<th>Otolgia</th>
<th>Degree of Strength</th>
<th>Mucosal Coverage</th>
<th>Analgesic Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean Scores</td>
<td>$P$ Value</td>
<td>Mean Scores</td>
<td>$P$ Value</td>
<td>Mean Scores</td>
</tr>
<tr>
<td>0</td>
<td>6.0</td>
<td>.07</td>
<td>4.3</td>
<td>.02</td>
<td>3.0</td>
</tr>
<tr>
<td>1</td>
<td>5.8</td>
<td>.09</td>
<td>4.0</td>
<td>.03</td>
<td>3.0</td>
</tr>
<tr>
<td>2</td>
<td>5.3</td>
<td>.06</td>
<td>3.8</td>
<td>.02</td>
<td>2.8</td>
</tr>
<tr>
<td>3</td>
<td>4.5</td>
<td>.03</td>
<td>3.3</td>
<td>.04</td>
<td>2.3</td>
</tr>
<tr>
<td>4</td>
<td>4.3</td>
<td>.03</td>
<td>3.0</td>
<td>.04</td>
<td>1.8</td>
</tr>
<tr>
<td>5</td>
<td>4.0</td>
<td>.02</td>
<td>2.8</td>
<td>.04</td>
<td>1.5</td>
</tr>
<tr>
<td>6</td>
<td>3.5</td>
<td>.02</td>
<td>2.5</td>
<td>.04</td>
<td>1.5</td>
</tr>
</tbody>
</table>

Abbreviations: C, control group; S, sucralfate group.

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Uvulopalatopharyngoplasty is the most common, and in many situations the only, surgical procedure performed by most otolaryngologists for the treatment of snoring and some cases of mild OSAS. It opens the airway at the level of the palate and reduces vibratory tissue of the palate and uvula.

Pain after UPPP is one of the most important symptoms of postoperative morbidity. The pain, which is usually severe, is mainly located in the throat and ears and continues until mucosal recovery is complete. It is most probably caused by irritation of open nerve endings, pharyngeal and palatal muscle spasms, and inflammation. Pain during chewing and swallowing may interfere with oral intake, and reduced oral intake may cause more muscle spasm. Oral flora may increase, causing inflammation and infection in the throat and more pain in advance of infection. Chewing and swallowing may decrease the pain by releasing muscle spasm, decreasing oral flora, and hence decreasing inflammation and infection. Infection of the tonsillar fossae is the most common cause of secondary postoperative bleeding. Some authors have reported that electrocauterization for dissection or hemostasis causes more pain than cold dissection and suture ligation.

Analgesics must be administered judiciously after UPPP. There is some evidence to suggest that anesthetic and narcotic agents increase the tendency for upper airway collapse; these agents also impair normal arousal mechanisms and may therefore worsen the severity of OSAS. Nonsteroidal anti-inflammatory agents such as paracetamol, ibuprofen, and aspirin have also effectively been used to reduce postoperative pain; however, the antiplatelet activity of aspirin and other nonsteroidal anti-inflammatory agents could theoretically result in bleeding. Benzylamine hydrochloride spray, a local anti-inflammatory and analgesic agent, has been used to control posttonsillectomy pain. Steroids, because of their anti-inflammatory effects, may reduce postoperative inflammation and pain. Despite the use of many medications, pain is one of the most important complications of UPPP. A drug that has few or no adverse effects, does not increase postoperative bleeding, and provides complete postoperative analgesia, or at least reduces the...
amount of analgesic used, is still needed to reduce the complications related to analgesia.

Sucralfate, which is a basic amino salt of sucrose octasulfate, has a unique mechanism of action. It is said to have a cytoprotective effect and to increase mucosal renewal by stimulating prostaglandin E synthesis.7 The negatively charged polyanions of sucralfate form polyvalent bonds with the positively charged mucoproteins of the damaged mucosa, so the drug adheres to mucoproteins at the ulcer site, forming a protective coating. The absorption of 1 dose of sucralfate is only approximately 2% to 5%. The drug acts locally at the ulcer site, and its effect lasts for 5 hours. However, physicians should take into account that sucralfate decreases the absorption of cimetidine, ranitidine, theophylline, tetracycline, quinolones, phenytoin, digoxine, quinidine, and fat-soluble vitamins.

Adverse reactions of sucralfate include dizziness, drowsiness, vertigo, constipation (most common), diarrhea, nausea, dry mouth, gastric discomfort, indigestion, rash, pruritus, back pain, and allergy (rare). Its use should be discontinued if abdominal pain or allergy develops.8 Because only 2% to 5% is absorbed through the gastrointestinal tract, the incidence of adverse effects and drug interactions is very low.

Although sucralfate is mainly an antiulcer drug, it has been used for alleviating posttonsillectomy pain,3 for treating recurrent aphthous stomatitis9 and chronic venous stasis ulcer,10 and for preventing stomatitis induced by cancer chemotherapy.11 The results have been moderate to encouraging. Kyrmizakis et al12 conducted a block-randomized, single-blind clinical study on 28 patients who underwent laser-assisted uvulopalatoplasty and reported that the 14 patients in the sucralfate group had significantly less postoperative pain than the 14 patients in the placebo group. Sucralfate significantly lowered the need for analgesic drug use as well as the total number of days the patients required “to almost reach their normal diet quantity.”12

Our study of 80 patients was intended to examine the effect of sucralfate on post-UPPP throat pain and otalgia. We also wanted to examine sucralfate's effects on postoperative analgesic requirement, mucosal covering, bleeding, and total number of days needed to return to normal daily activities. Patients who used sucralfate had significantly less throat pain than the control group from the third postoperative day onward. Analgesic activity of sucralfate during the postoperative period promotes recovery and makes oral intake less difficult. In the present study, the patients in the sucralfate group had significantly less otalgia than those in the control group during the entire postoperative follow-up period and they took less analgesics. The mucosal coverage of the tonsillar fossae and the palatal ulcers was more rapid in the patients in the sucralfate group and they felt well before those in the control group. However, there was no significant difference in episodes of bleeding between the 2 groups (P = .65). No patient in the sucralfate group complained of adverse effects such as abdominal pain, constipation, diarrhea, nausea, dizziness, or rash.

In conclusion, our study adds to the evidence suggesting that sucralfate is safe and provides good analgesia after UPPP. Moreover, our findings indicate that sucralfate promotes rapid mucosal healing and early restoration of normal activity. Although sucralfate may not provide complete analgesia, it may reduce the amount of the analgesics required and prevent the dose-related adverse effects that can be caused by analgesic agents.

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Author Contributions: Dr Lee had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Zodpe and Lee. Acquisition of data: Zodpe, Cho, and Kang. Analysis and interpretation of data: Zodpe and Cho. Drafting of the manuscript: Zodpe, Cho, and Hwang. Critical revision of the manuscript for important intellectual content: Zodpe, Kang, and Lee. Statistical analysis: Cho and Hwang. Obtained funding: Hwang and Lee. Administrative, technical, and material support: Cho and Hwang. Study supervision: Lee.

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