

A randomized controlled study evaluating medical treatment versus surgical treatment in addition to medical treatment of nasal polyposis

Ebba Hedén Blomqvist, MD,^a Lars Lundblad, MD, PhD,^a Anders Änggård, MD, PhD,^a Per-Olle Haraldsson, MD, PhD,^a and Pär Stjärne, MD, PhD^b *Stockholm, Sweden*

Background: Controlled prospective studies are needed to determine whether surgical treatment in fact has an effect additive to that of medical treatment of nasal polyposis.

Objective: We sought to compare the effect of medical treatment versus combined surgical and medical treatment on olfaction, polyp score, and symptoms in nasal polyposis.

Methods: Thirty-two patients with nasal polyposis and symmetrical nasal airways were randomized to unilateral endoscopic sinus surgery after pretreatment with oral prednisolone for 10 days and local nasal budesonide bilaterally for 1 month. Postoperatively, patients were given local nasal steroids (budesonide). Patients were evaluated with nasal endoscopy, symptom scores, and olfactory thresholds. They were followed for 12 months.

Results: The sense of smell was improved by the combination of local and oral steroids. Surgery had no additional effect. Symptom scores improved significantly with medical treatment alone, but surgery had additional beneficial effects on nasal obstruction and secretion. After surgery, the polyp score decreased significantly on the operated side but remained the same on the unoperated side. Twenty-five percent of the patients were willing to undergo an operation also on the unoperated side at the end of the study.

Conclusions: Medical treatment seems to be sufficient to treat most symptoms of nasal polyposis. When hyposmia is the primary symptom, no additional benefit seems to be gained from surgical treatment. If nasal obstruction is the main problem after steroid treatment, surgical treatment is indicated. Selection of those who will benefit from surgery should be based on the patient's symptoms and not on the examiner's polyp score. (*J Allergy Clin Immunol* 2001;107:224-8.)

Key words: Nasal polyposis, olfaction, sinus surgery, medical treatment, surgical treatment, corticosteroids, scoring, staging, endoscopy, symptoms

Nasal polyposis, a common inflammatory condition seen in 1% to 2% of the adult population in Europe,¹ does not appear to be a disease per se but rather the result or expression of underlying mucosal pathology. Its cause is not yet fully understood.²⁻⁴ However, nasal polyposis is often associated with intrinsic asthma and aspirin/non-steroidal anti-inflammatory drug intolerance. The condition may seriously affect the quality of life.⁵ Many patients have a reduced sense of smell, nasal obstruction, secretion, and sometimes headache and a feeling of pressure over their sinuses. Moreover, the nasal polyps may obliterate the sinus ostia and predispose for infections in the sinuses.

The treatment of nasal polyposis is debated. Surgical or medical treatment or both have been recommended as the treatment of choice. The rationale for surgery of the ostiomeatal complex was first advocated by Messerklinger.⁶ In the last decade, a number of studies have reported good results after endoscopic sinus surgery (eg, marked improvement of nasal blockage)⁷ in nasal polyposis. However, according to the "Position statement on nasal polyps,"⁸ medical treatment should be used for at least 1 month before surgery is contemplated in patients with typical nasal polyposis because some studies have indicated that in those patients who respond to medical treatment, no additional treatment is necessary. Thus Lildholdt et al⁹ compared a single intramuscular depot injection of betamethasone with that of snare polypectomy, followed by a maintenance dose of topical nasal beclomethasone dipropionate for 1 year. The improvement was found to be similar in the medically and surgically treated groups. In a 3-phase trial in 126 patients with bilateral nasal polyposis, the same author reported the results of the first double-blind phase,¹⁰ in which they compared the effects of budesonide nasal Turbuhaler, 400 or 800 µg/d, and placebo for 1 month. The treatment was successful in 82% of patients treated with budesonide powder versus 43% in the placebo group.

Thus there is a dearth for controlled prospective studies to determine whether surgical treatment in fact has an effect additive to that of medical treatment. The aim of this study was to compare the effect of medical treatment with that of combined surgical and medical treatment of nasal polyposis, regarding olfaction, nasal symptoms, and polyp score.

From ^athe Department of Otorhinolaryngology, Karolinska Hospital, Stockholm; and ^bthe Department of Otorhinolaryngology, Huddinge Hospital, Stockholm.

Supported by Vårdalstiftelsen, Astra Zeneca, and the Karolinska Institute. Received for publication June 8, 2000; revised September 20, 2000; accepted for publication September 29, 2000.

Reprint requests: Ebba Hedén Blomqvist, MD, Department of Otorhinolaryngology, Karolinska Hospital, 171 76 Stockholm, Sweden.

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0091-6749/2001 \$35.00 + 0 1/81/112124

doi:10.1067/mai.2001.112124

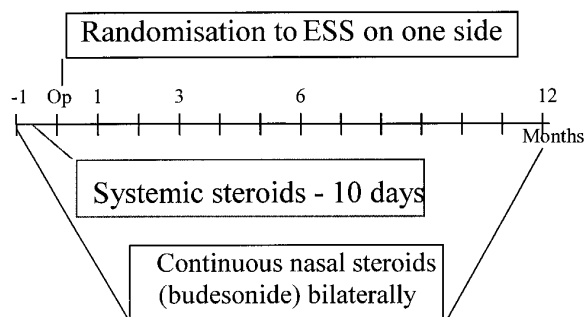


FIG 1. Schematic presentation of study procedure. ESS, Endoscopic sinus surgery.

METHODS

Inclusion and exclusion

Thirty-two consecutive patients (17 men and 15 women) with nasal polyposis recruited from the Outpatient Clinic of the Department of Otorhinolaryngology, Karolinska Hospital, were included. The subjects were 22 to 64 years old (median, 48 years) at the time of surgery. Regarding nasal anatomy and extent of nasal polyposis, they all had symmetrical nasal airways, as judged by endoscopy and anterior rhinoscopy. On the first visit, the polyp score was not allowed to differ by more than 1 point between the nasal cavities or be less than 1 on either side (Table I). All subjects who had a history of nasal surgery, severe systemic disease (eg, diabetes), or smoking more than 20 cigarettes daily were excluded.

Procedure

A schematic representation of the procedure is shown in Fig 1. The patients were first treated with oral prednisolone for the first 10 days (40 mg daily for 3 days, followed by a reduction of 5 mg daily) supplemented with nasal budesonide bilaterally (Rhinocort Turbuhaler, 400 µg/d) for 1 month. The patients were then randomized to surgery on the right or left side. The operation was followed by administration of nasal budesonide bilaterally (Rhinocort Turbuhaler, 400 µg/d) for 1 year postoperatively. Patients were processed from December 1994 through May 1997. The operations were performed by the 4 senior authors. The study was approved by the local ethics committee at the Karolinska hospital.

Evaluation

A schematic presentation of the study evaluation is shown in Fig 2. The patients were evaluated with nasal endoscopy and symptom scores by using the visual analogue scale graded from 0 (no symptoms) to 10 cm (maximum severity of symptoms) before treatment, before surgery, and 1, 3, 6, and 12 months after surgery. Polyp scores (Table I) were evaluated by using nasal endoscopy after application of local anesthesia and a decongestant (Nafazolin hydrochloride and Lidocaine hydrochloride, 0.02% and 3.4%). Olfactory thresholds were determined with the butanol test before treatment, preoperatively, and 3 and 12 months postoperatively.

At the end of the study, all patients were asked if they wanted to undergo an operation on the unoperated side.

Olfactory thresholds

The olfactory threshold test, described by the Connecticut Chemosensory Clinical Research Center, uses aqueous dilutions of 1-butanol (n-butyl alcohol) as the odorant. The highest concentration (4%) in deionized water is called dilution step 0, and then the solution is diluted by successive factors of 3 to step 13. The test

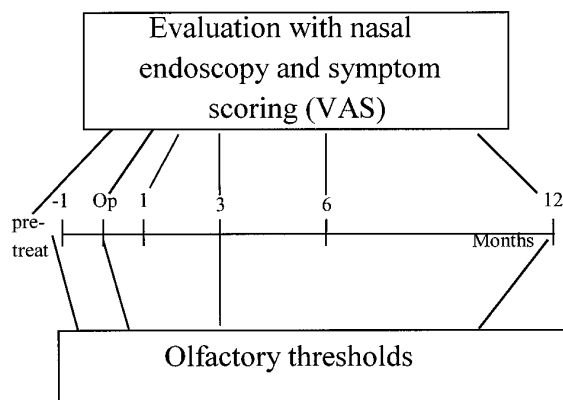


FIG 2. Schematic presentation of study evaluation. VAS, Visual analogue scale.

TABLE I. Polyp scoring

Polyps were scored (0-3) according to endoscopic appearance:

- 0: No polyposis
- 1: Mild polyposis (small polyps not reaching the upper edge of the inferior turbinate)
- 2: Moderate polyposis (medium polyps between the upper and lower edges of the inferior turbinate)
- 3: Severe polyposis (large polyps reaching the lower edge of the inferior turbinate, polyps from posterior ethmoidal sinuses, or both)

solutions were presented in squeezable polyethylene bottles. Olfactory thresholds were considered normal at a dilution threshold of 8.0.¹¹ Testing began with a low concentration of butanol dilution and a blank. The subject had to decide which smelled the strongest. If the answer was wrong, the concentration was increased; if the answer was correct, the subject was given a bottle containing a solution with the same concentration and a blank. Five correct answers in a row were regarded as the olfactory threshold. Each nostril was tested separately, and the other nostril was occluded.

Surgery

Endoscopic sinus surgery was performed after achievement of general anesthesia. Local anesthesia with Lidocaine hydrochloride, 10 mg/mL, and epinephrine, 5 µg/mL, was also used to minimize bleeding and improve visualization. The extent of the surgery was determined by the disease but always included uncinectomy, anterior ethmoidectomy, and exploration of the posterior ethmoids. If the posterior cells were involved, surgery was continued posteriorly with posterior ethmoidectomy and in some cases with sphenoidotomy. The ostium to the maxillary sinus was enlarged, and diseased mucosa from the frontonasal recess was removed. If there was a pneumatized concha bullosa (when the middle turbinate was pneumatized), the lateral mucosa and bone were usually removed to decompress the ostiomeatal complex. Care was taken to preserve an intact mucosa.

Statistical analysis

The Wilcoxon signed rank test was used for the statistical analysis. A *P* value of less than .05 was considered significant. In the figures results are presented as mean values.

Drugs

We used budesonide (Rhinocort Turbuhaler) and prednisolone (Prednisolone).

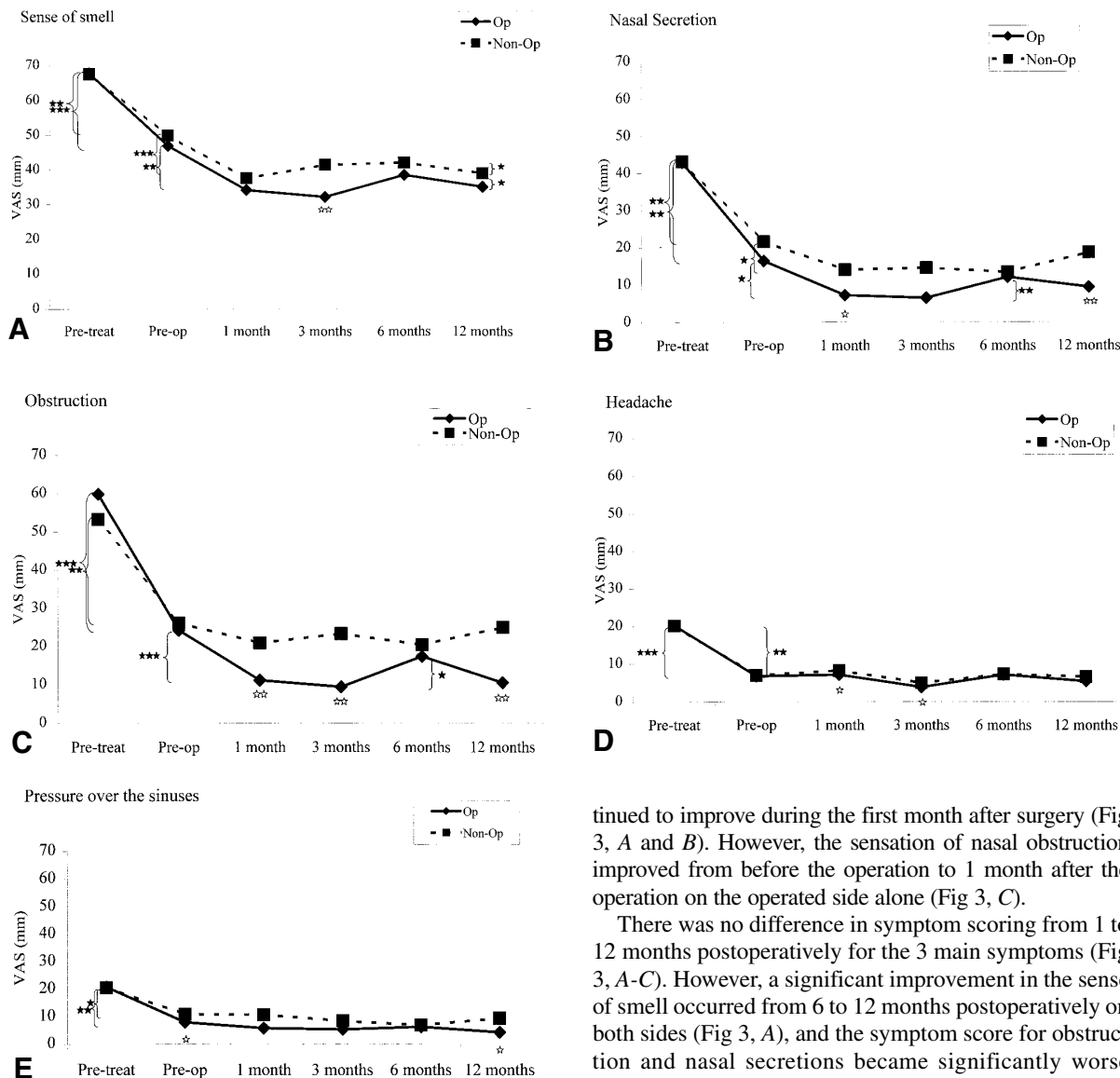


FIG 3. Data are presented as means. Filled stars, Significant differences within the group (one star, $P < .05$; two stars, $P < .01$; three stars, $P < .001$); open stars, significant differences between the groups. **A**, Symptom score of sense of smell; **B**, symptom score of nasal secretion; **C**, symptom score of nasal obstruction; **D**, symptom score of headache; **E**, symptom score of pressure over the sinuses. Op, Operative; VAS, visual analogue scale.

RESULTS

Symptom scores

Reduced sense of smell, nasal obstruction, and nasal secretion were common symptoms, but only a few patients complained of headache or a feeling of pressure over their sinuses. Before treatment, no significant difference in the scores for the 5 symptoms was found between the operated and unoperated sides. All of these nasal symptoms improved significantly during the first month of treatment with the combination of oral and local steroids (Fig 3, A-E). The sense of smell and nasal secretions on both sides con-

tinued to improve during the first month after surgery (Fig 3, A and B). However, the sensation of nasal obstruction improved from before the operation to 1 month after the operation on the operated side alone (Fig 3, C).

There was no difference in symptom scoring from 1 to 12 months postoperatively for the 3 main symptoms (Fig 3, A-C). However, a significant improvement in the sense of smell occurred from 6 to 12 months postoperatively on both sides (Fig 3, A), and the symptom score for obstruction and nasal secretions became significantly worse from 3 to 6 months after surgery on the operated side (Fig 3, B and C). Apart from these differences, no other changes in the symptom scores were noted after the examination 1 month after surgery.

One year after surgery, patients noted no significant difference in the sense of smell between the 2 sides. However, surgery had improved the sensation of nasal obstruction, nasal secretions, and pressure over the sinuses (Fig 3, A-C and E).

All patients were offered an operation of the unoperated side at the end of the study. Twenty-five percent of the patients requested additional surgery because of remaining problems.

Polyp score

Endoscopically evaluated polyp scores are illustrated in Fig 4. Before treatment or preoperatively, no significant difference was found in the polyp scores between the operated and unoperated sides. Preoperative treatment resulted in a significant reduction in the polyp score. After

surgery, the polyp score was significantly lower on the operated side than on the unoperated side in all of the postoperative checkups. No significant change in polyp score was noted on the unoperated side after surgery.

Olfactory thresholds (butanol test)

Olfactory thresholds are illustrated in Fig 5. No significant difference was found in the olfactory thresholds between the operated and unoperated sides on any visit. A significant improvement in olfaction occurred after the first month of combined treatment with oral and nasal steroids, but no additional significant change was noted during the follow-up period.

DISCUSSION

In this study we have designed a method for randomized controlled evaluation of medical treatment versus surgical treatment in addition to medical treatment of nasal polyposis. We found that surgical treatment does not have any additional effect on hyposmia but reduces nasal obstruction, even after a previous combined oral and nasal steroid treatment. We also found disparity between the objective findings by using the polyp score and the symptom score.

In clinical rhinologic research there is a need for randomized controlled prospective studies to compare the effects of various types of treatment. One obstacle in performing such studies is the difficulty in finding a well-matched control group. Regarding nasal polyposis, the 2 major problems are that there are many different factors contributing to the cause and that there are problems with staging of the disease. A control group should preferably be matched for age, sex, social habits, associated diseases, and heredity. To avoid these problems, we designed a study where the patients are used as their own control subjects. This experimental design has previously been used effectively when evaluating the effect of adenoidectomy on otitis media with effusion.¹² This demands strict inclusion criteria and exclusion of patients without symmetrical nasal airways or symmetrical involvement by the disease. When medical or surgical treatment are thought to have the same effect, this design can be recommended for evaluation and research.

An estimate of the severity of nasal polyposis must be based on a good scoring system. Several systems are used, and therefore it is difficult to compare the results of other studies regarding polyp scores. Such systems evaluate the location of the polyps but not always in relation to their size or volume. This may be a problem when scoring is used to evaluate the effects of treatment. With our scoring system, we regarded polyps medial to the middle turbinate as arising from the posterior ethmoidal sinuses. The advantage of this method is that it is a more holistic system for assessing polyps. Involvement of the posterior ethmoids is a more serious disease than involvement of the anterior ethmoids alone. On the other hand, there is a disadvantage with this type of system; if a patient with large polyps from the posterior ethmoidal sinuses is successfully treated with corticosteroids and the polyps

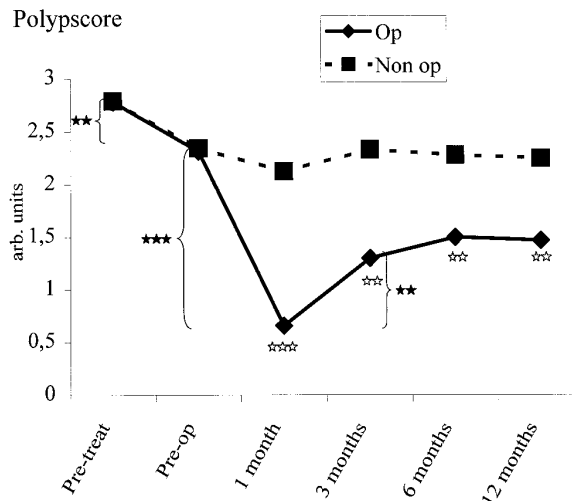


FIG 4. Endoscopically evaluated polyp score. Op, Operative.

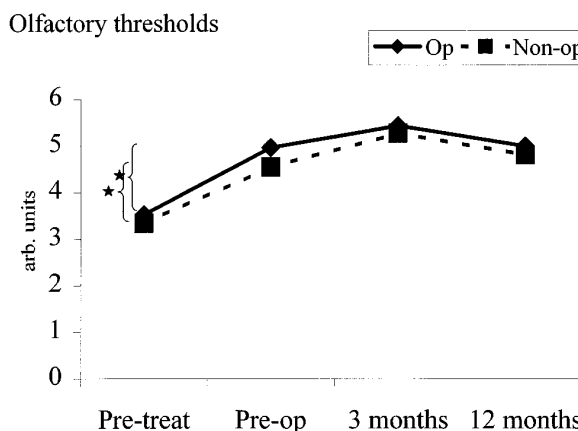


FIG 5. Olfactory thresholds determined with butanol test. Op, Operative.

decrease in size and symptoms improve, the score will not change as long as there are remnants of polyps from the posterior ethmoidal sinuses. At the International Conference on Sinus Disease: Terminology, Staging and Therapy held in July 1993,¹³ an international scoring system for nasal polyposis was proposed. With this system, a polyp score of 0 indicated absence of polyps, 1 indicated presence of polyps confined to the middle meatus, and 2 indicated presence of polyps beyond the middle meatus. This system had not been reported when we designed our study. However, we prefer our scoring system because it includes involvement of the posterior ethmoidal sinuses as a sign of more extensive disease (Table I). In a recent study¹⁴ in which several methods for endoscopic staging of nasal polyposis were evaluated, the score system with 3 steps only showed poorer correlation in repeated measurements than a 4-step system.

In several other studies, the authors do not decongest the nasal mucosa before endoscopy. However, we consider it essential to distinguish between polyps from the posterior and anterior ethmoidal sinuses. To do this in a painless way, local anesthesia and decongestion are necessary.

We do not believe that this had any major effect on our results, but it shows that most of the patients included in this study had a severe disease, including the posterior ethmoidal sinuses. This might explain the need for complementary surgery for some (25%) of our patients. In the study of Lildholdt et al,⁹ results from medical and surgical treatment were considered alike, although surgery was limited to removal of the visible polyps. However, the severity of nasal polyposis in that study is not clearly defined because nasal endoscopy was not performed.

Nasal polyposis can induce severe symptoms, and a recent study shows that it impairs the quality of life even more than perennial allergic rhinitis.⁵ The severity of nasal polyp disease has generally been correlated to the degree of nasal obstruction. A major finding of this study is the result of the subjective scoring, where the patients scored the reduced sense of smell as the major complaint. According to our own data from quality-of-life studies on olfaction (unpublished data), olfactory dysfunction severely affects the quality of life. Therefore treatment of olfactory disorders should have a high priority.

Mott et al¹⁵ studied patients with olfactory dysfunction and nasal and sinus disease (defined as sinusitis, rhinitis, and/or polyposis) and found that three fourths (74%) had complete loss of olfactory function (anosmia) and one fourth (26%) had partial loss (hyposmia). Several potentially surgically correctable causes of chemosensory dysfunction, including nasal polyposis, have been identified.¹⁶ Improvement in olfaction after sinus surgery has been reported by Hosemann et al¹⁷ in 78%, Downey et al¹⁸ in 52%, and Shin et al¹⁹ in 68%. However, in these studies the importance of simultaneous medical treatment is not clear. Several studies have shown that steroids alone can improve olfaction in nasal and sinus disease.²⁰⁻²³

In this study the patients reported the reduced sense of smell as one of the worst symptoms associated with nasal polyposis. We found no additional effect of surgery on the sense of smell or olfactory thresholds. One question is whether this is due to the extent of surgery performed. Our understanding is that mucosal inflammation is more important for olfaction than volume changes in the nasal cavity induced by the presence of polyps. Moreover, recent data indicate that olfactory impairment in IgE-mediated nasal allergy has a higher correlation to the degree of inflammation, as measured by eosinophil cationic protein, than nasal volume flow, as measured by anterior rhinomanometry.^{24,25} A reduced sense of smell, as measured with the olfactory threshold test, also correlates better with increased nasal secretions than reduced nasal volume, as measured by acoustic rhinometry.²⁶ Therefore it seems rational that patients with nasal polyposis inflammation must be treated primarily.

In conclusion, we have found that surgical treatment does not have any additional effect on hyposmia to combined oral and nasal steroid treatment. If an objective method for evaluation of patients is necessary, olfactory thresholds seem to be better than the polyp score. Surgery significantly reduces the polyp score, and its effect is long lasting, but in our study the polyp score

showed no relation to the symptom score. This suggests that selection of those who benefit from surgery can be based on the patient's symptoms and not on the degree of polyposis scored by the examiner, at least not with the present scoring system. Our data suggest that surgical treatment of nasal polyposis reduces nasal obstruction, even after combined oral and nasal steroid treatment.

REFERENCES

- Hosemann W, Gode U, Wagner W. Epidemiology, pathophysiology of nasal polyposis, and spectrum of endonasal sinus surgery. *Am J Otolaryngol* 1994;15:85-98.
- Stammberger H. Surgical treatment of nasal polyps: past, present, and future. *Allergy* 1999;54(Suppl 53):7-11.
- Tos M. Early stages of polyp formation. Providence (RI): OceanSide Publications, Inc; 1997.
- Bernstein JM. The immunohistopathology and pathophysiology of nasal polyps (the differential diagnosis of nasal polyposis). Providence (RI): OceanSide Publications, Inc; 1997.
- Radenne F, Lamblin C, Vandezande LM, et al. Quality of life in nasal polyposis. *J Allergy Clin Immunol* 1999;104:79-84.
- Stammberger H, Posawetz W. Functional endoscopic sinus surgery. Concept, indications and results of the Messerklinger technique. *Eur Arch Otorhinolaryngol* 1990;247:63-76.
- Lund VJ, MacKay IS. Outcome assessment of endoscopic sinus surgery. *J R Soc Med* 1994;87:70-2.
- Lildholdt T. Position statement on nasal polyps. *Rhinology* 1994;32:126.
- Lildholdt T, Fogstrup J, Gammelgaard N, Kortholm B, Ulsoe C. Surgical versus medical treatment of nasal polyps. *Acta Otolaryngol* 1988;105:140-3.
- Lildholdt T, Rundercrantz H, Lindqvist N. Efficacy of topical corticosteroid powder for nasal polyps: a double-blind, placebo-controlled study of budesonide. *Clin Otolaryngol* 1995;20:26-30.
- Cain WS, Gent JF, Goodspeed RB, Leonard G. Evaluation of olfactory dysfunction in the Connecticut Chemosensory Clinical Research Center. *Laryngoscope* 1988;98:83-8.
- Maw AR, Herod F. Otoloscopic, impedance, and audiometric findings in glue ear treated by adenoidectomy and tonsillectomy. A prospective randomised study. *Lancet* 1986;1:1399-402.
- Lund VJ, Kennedy DW. Quantification for staging sinusitis. International conference on sinus disease: Terminology, Staging and Therapy. *Ann Otol Rhinol Laryngol Suppl* 1995;104:17-21.
- Johansson L, Akerlund A, Holmberg K, Melen I, Stierna P, Bende M. Evaluation of methods for endoscopic staging of nasal polyposis. *Acta Otolaryngol* 2000;120:72-6.
- Mott AE, Cain WS, Lafreniere D, Leonard G, Gent JF, Frank ME. Topical corticosteroid treatment of anosmia associated with nasal and sinus disease. *Arch Otolaryngol Head Neck Surg* 1997;123:367-72.
- Jafek BW, Hill DP. Surgical management of chemosensory disorders. *Ear Nose Throat J* 1989;68:398, 400, 402-4.
- Hosemann W, Goertzen W, Wohlleben R, Wolf S, Wigand ME. Olfaction after endoscopic endonasal ethmoidectomy. *Am J Rhinol* 1993;7:11-5.
- Downey LL, Jacobs JB, Lebowitz RA. Anosmia and chronic sinus disease. *Otolaryngol Head Neck Surg* 1996;115:24-8.
- Shin SH, Park JY, Sohn JH. Clinical value of olfactory function tests after endoscopic sinus surgery; a short-term result. *Am J Rhinol* 1999;13:63-6.
- Goodspeed RB, Gent JF, Catalanotto FA, Cain WS, Zaganiski RT. Corticosteroids in olfactory dysfunction. In: Meiselman HS, Rivlin RS, eds. Clinical measurement of taste and smell. New York: Macmillan; 1986. p. 514-8.
- Jafek BW, Moran DT, Eller PM, Rowley JCD, Jafek TB. Steroid-dependent anosmia. *Arch Otolaryngol Head Neck Surg* 1987;113:547-9.
- Mott AE. Topical corticosteroid therapy for nasal polyposis. In: Getchell TV, Doty RL, Bartoshuk LM, Snow JB, eds. Smell and taste in health and disease. New York: Raven press; 1991. p. 553-72.
- Scott AE. Caution urged in treating 'steroid-dependent anosmia' [letter]. *Arch Otolaryngol Head Neck Surg* 1989;115:109-10.
- Klimek L. Sense of smell in allergic rhinitis. *Pneumologie* 1998;52:196-202.
- Klimek L, Eggers G. Olfactory dysfunction in allergic rhinitis is related to nasal eosinophilic inflammation. *J Allergy Clin Immunol* 1997;100:158-64.
- Hinrikssdottir I, Murphy C, Bende M. Olfactory threshold after nasal allergen challenge. *ORL J Otorhinolaryngol Relat Spec* 1997;59:36-8.