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Chronic Rhinosinusitis-Related Smell Loss: Medical And Surgical Treatment Efficacy

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Abstract

Chronic rhinosinusitis (CRS) is an inflammatory disorder of the nasal cavities and paranasal sinuses. Olfactory dysfunction is a common manifestation of CRS and one of its cardinal diagnostic features. A decreased sense of smell can have a profound impact on a CRS patient's quality of life and overall wellbeing. The treatment of CRS-associated olfactory dysfunction includes a wide range of medical interventions, including anti-inflammatory and antibiotic medications, and surgical interventions, including endoscopic sinus and nasal surgery. The evidence and treatment efficacy for these interventions is quite varied. This review provides a summary of the efficacy of the medical and surgical therapeutic options for CRS-associated olfactory dysfunction.

Keywords

Olfaction; smell loss; hyposmia; anosmia; chronic rhinosinusitis; olfactory dysfunction; endoscopic sinus surgery

INTRODUCTION

Chronic rhinosinusitis (CRS) is an inflammatory disorder of the nasal cavities and paranasal sinuses lasting 12 weeks or longer, and the clinical diagnosis requires a constellation of both objective and subjective findings. While inflammation may be identified objectively by endoscopy or radiography, the symptomology is complex and varies widely among CRS

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Compliance with Ethics Guidelines

Human and Animal Rights and Informed Consent

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Conflict of Interest

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patients. In general, practice guidelines concur that two or more cardinal symptoms must be present for the diagnosis of CRS: nasal airway obstruction, facial or periorbital pain or pressure, mucopurulent drainage, and decreased sense of smell.^{1–3} These symptoms and their impact on patients' quality of life and overall state of health vary in degree and frequency among CRS patients.

Olfactory dysfunction has been reported to occur in approximately 60–80% of patients who suffer from CRS.⁴ The etiology of CRS-associated smell loss is multifactorial and likely occurs by a combination of localized inflammation of the olfactory mucosa and mechanical obstruction of the olfactory cleft from either mucosal edema or structural abnormalities (Figure 1).^{1,4–11}

It is critical that physicians recognize the impact that olfactory dysfunction may have on patients' quality of life. Clinicians assessing CRS patients frequently inquire about the ability to appreciate the smell and taste of food; however, subjective surveys of patients suffering from smell loss have revealed that olfactory dysfunction is associated with a multitude of psychosocial issues that often go unnoticed by their physicians. Large surveys of people with olfactory dysfunction have revealed that as many as 85% of patients have had exposure to dangers such as rotten food and hazardous fumes, over half of patients suffer from emotional difficulties and isolation, and over half of patients feel that their smell dysfunction affects their interpersonal relationships, including sex life for some.^{12,13} Almost half of patients report an increase in the feeling of vulnerability as a result of their decreased sense of smell, and this emotion may be well-founded: some investigators have proposed that olfactory dysfunction among the aging is responsible for the disproportionate number of elderly who die in accidental gas poisonings and explosions each year.^{13,14} Olfactory dysfunction may also be associated with poorer diet quality and nutrition, with subsequent systemic health effects.¹⁵ Additionally, decreased sense of smell has been demonstrated to be an independent risk factor for mental health disorders and an overall reduced quality of life.^{16,17}

Olfactory dysfunction in CRS is associated with worse objective metrics, including endoscopy and overall computed tomography scores, in addition to radiographic opacification of the olfactory cleft specifically.^{18–20} However, in CRS patients who already demonstrate a decreased quality of life, it appears that olfactory dysfunction does not have an additional negative additive effect.²¹ Among patients with CRS, those with nasal polyposis, eosinophilia, asthma, smoking, and increased age are more likely to demonstrate decreased olfactory function.^{7,22,23}

The treatment of CRS-associated olfactory dysfunction includes a wide range of medical and surgical therapies with variable efficacy. Several clinical trials have examined the outcome of various interventions on olfactory outcomes. Subjective olfactory outcomes are evaluated by survey responses of symptom scores, visual analog scales, or the Questionnaire of Olfactory Disorders (QOD).²⁴ Objective olfactory tests measure identification, discrimination, or threshold. Commonly utilized tests include the Smell Identification Test (SIT), Butanol Threshold test (BTT) and the Sniffin' Sticks Test (SST) (Table 1).

MEDICAL TREATMENT

Oral Corticosteroids

Several randomized clinical trials have examined the impact of oral steroids on subjective olfactory outcomes.^{25–33} A meta-analysis by Banglawala et al. in 2014 pooled four of these studies.^{4,25–28} Each of the four studies individually, and their meta-analysis, found that a course of oral steroids leads to a statistically significant improvement in subjective olfaction compared to placebo. One of these studies also identified a significant improvement in objective olfactory function from oral steroids alone versus placebo.²⁸

Several other studies have similarly found that oral steroids lead to a statistically significant improvement in subjective olfactory function over placebo.^{29,31,33} One placebo-controlled study did not identify an improvement in smell function, although this study combined oral steroids with surgical therapy and was not designed to assess the effect of oral steroids alone on subjective olfactory outcomes.³²

Overall, oral steroids have demonstrated efficacy in the treatment of CRS-associated smell loss for both subjective and objective outcome measures. In these studies, the formulation and dosage of oral corticosteroids varied, and the duration of oral steroid therapy was generally less than 3 weeks. No significant adverse events from the short courses of oral steroids were reported in these trials. However, it should be noted that in general the duration of follow-up and demonstrated efficacy of oral steroids is one year or less in these trials, and therefore the long-term efficacy of oral steroids in the treatment of CRS-associated smell loss is unclear.

Topical Corticosteroids

Twelve placebo-controlled trials have examined the effect of topical nasal steroids alone on CRS-associated olfactory dysfunction, with heterogeneous results. Of these twelve, nine studies found that topical nasal steroid therapy significantly improves subjective olfactory outcome measures compared to placebo.^{34–42} Three studies did not demonstrate any significant benefit of topical nasal steroids over placebo for subjective olfactory outcomes.^{43–45} Interestingly, several of these studies contained subgroups who were administered various formulations, doses, and frequencies of topical nasal steroids, and none found any dose-dependent changes in subjective outcomes.^{34–36,38,41,43,45}

Three placebo-controlled trials of topical nasal steroids alone have evaluated objective olfactory outcomes. Two of the three studies found no significant improvement by any objective metric.^{39,44} The third study found significant improvement in only one of the two experimental groups, and only by one of the two objective metrics used in the analysis.⁴⁵

Five of these studies of topical nasal steroids examined both subjective and objective outcome measures. Interestingly, concordance was not always present. The experimental group of one study showed subjective improvement in response to topical steroids over placebo, but no objective improvement.³⁹ A subgroup of another study experienced no significant subjective improvement despite evidence of objective improvement.⁴⁵ This

discrepancy between subjective and objective olfactory metrics has been previously described in patients without chronic sinusitis.⁴⁶

The evidence supporting topical nasal steroids alone in the treatment of CRS-associated olfactory dysfunction is less compelling than the evidence for oral steroids. However, no investigators report significant adverse events in response to topical therapy, and several studies have demonstrated subjective olfactory improvement. The low incidence of systemic side effects makes topical steroids an attractive long-term treatment option.

Combined Oral and Topical Corticosteroids

There have been no trials of oral steroids plus topical steroids versus oral placebo plus topical placebo. However, one trial by Vaidyanathan et al. compared oral steroids followed by topical steroids to oral placebo followed by topical steroids.²⁸ As mentioned above, this study did demonstrate an improvement in both subjective and objective olfactory function during the initial oral steroid versus placebo phase of the study, but no significant subjective or objective improvement was identified at the conclusion of the combined oral and topical steroid trial. A subsequent trial by Alobid et al., however, did identify a statistically significant objective improvement in olfactory function from combined oral and topical steroids.²⁵ Various other studies have examined the role of combined oral and topical steroids, generally administered as a short course of oral steroids followed by weeks to months of topical nasal steroid spray, on subjective olfactory outcomes, with mixed results.^{25,27,29,47}

There is inadequate data to support the use of a specific combined oral and topical steroid regimen to treat CRS-associated olfactory dysfunction. However, the compelling data of oral steroids for CRS-associated smell loss, combined with the mixed efficacy yet favorable safety profile of topical steroid therapy, together suggest that patients with CRS-associated smell loss are likely to experience subjective olfactory improvement and possibly also objective olfactory improvement from combined oral and topical steroid therapy.

Other Medical Therapies

A variety of other medical therapies have been studied in the setting of CRS-associated smell loss. Three placebo-controlled trials of oral antibiotics, one with doxycycline, one with azithromycin, and one with roxithromycin, failed to demonstrate an improvement in subjective or objective olfaction.^{33,48,49} One placebo-controlled trial of topical amphotericin for CRS with polyposis failed to demonstrate an improvement in subjective olfaction.⁵⁰ And one placebo-controlled trial of the immunomodulatory drug omalizumab also failed to demonstrate a significant improvement in subjective or objective olfactory outcomes.⁵¹

It should be noted that many medical therapies discussed above, including oral steroids, topical steroids, oral antibiotics, and others, have demonstrated efficacy for many subjective and objective features of CRS apart from their effect on olfaction. Furthermore, many trials of medical therapy for CRS have demonstrated clinical efficacy by validated symptom outcome measures, but without reporting changes in olfactory metrics specifically.

SURGICAL TREATMENT

Several studies have examined the effect of surgery for CRS on olfactory outcomes. The studies are limited for several reasons. They generally do not specifically define the surgical procedures performed, and the surgeries in these studies are performed for CRS and not specifically for the isolated symptom of decreased olfaction. Additionally, there have been no randomized studies of surgical versus non-surgical therapy, or surgery versus sham surgery, for a defined group of CRS patients or a defined level of CRS-associated olfactory dysfunction. Furthermore, there is wide heterogeneity in the method of assessment of subjective and objective olfaction, the duration of follow-up, the concurrent perioperative and postoperative systemic and topical medical therapy, and the design of such studies. Nevertheless, the data from several studies is instructive regarding the efficacy of ESS on olfactory function.

Ling et al. evaluated the incidence and severity of CRS symptoms in patients undergoing ESS and their response to surgical therapy.⁵² The authors found a significant improvement in subjective olfactory outcomes through a follow-up of one year. Soler et al. subsequently evaluated prospectively the efficacy of ESS on the primary CRS symptoms including nasal airway obstruction, fatigue, headache, decreased sense of smell, nasal drainage, and facial pressure.⁶ The investigators demonstrated statistically significant and clinically meaningful improvement as a result of ESS for all of the symptoms except headache. The improvement in sense of smell remained significant throughout a follow-up period of 18 months post-operatively. Ehnhage et al. examined olfaction in asthma patients specifically, who are at increased risk of olfactory dysfunction, and also demonstrated objective improvement in olfactory function in response to ESS.⁵³

Some studies have attempted to predict the response of olfactory function to ESS. A prospective multi-institutional study by Litvack et al. demonstrated that the degree of preoperative objective olfactory dysfunction impacts the response to surgical therapy.²² In this prospective cohort study, olfaction was evaluated using the Smell Identification Test (SIT), a 40-question test of objective olfactory function. The study demonstrated that objective olfactory impairment improved significantly in patients with preoperative anosmia after ESS sustained through 12-month follow-up, but not in patients with preoperative hyposmia. Specifically, anosmic patients' mean SIT score increased from 9.7 to 21.7 at 12 months follow-up, whereas hyposmic patients' mean SIT score changed only from 28.8 to 29.5. This finding was confirmed by another prospective surgical trial demonstrating that worse olfactory function preoperatively corresponded to a greater improvement in olfaction in response to surgery.⁵⁴ Some investigators have identified polyposis as an important predictor of olfactory response to ESS.^{55,56} One study proposed that patients' wound healing status as assessed by postoperative endoscopy predicts their improvement in olfactory function after ESS.⁵⁷ Yet another study by Jiang et al. failed to demonstrate any improvement at all in subjective or objective olfactory outcome measures in response to ESS.⁵ It should also be noted that iatrogenic hyposmia or anosmia is a potential, albeit very rare, complication of sinonasal surgery.

A systematic review of symptom-specific outcomes in response to surgical therapy was performed in 2009 by Chester et al.⁵⁸ The investigators grouped studies that evaluated olfaction by different methods, but found overall a statistically significant improvement in olfaction in response to ESS.

MEDICAL VERSUS SURGICAL TREATMENT

A prospective multi-institutional study by DeConde et al. in 2014 compared the effectiveness of medical and surgical therapy on olfaction in CRS.⁵⁹ In this trial, olfaction was evaluated using the Brief Smell Identification Test (B-SIT), a validated 12-item “scratch-‘n’-sniff” test. All patients enrolled were considered candidates for ESS; one-fifth of the patients elected continued medical therapy and four-fifths elected surgical therapy. Patients with normosmia before therapy remained normosmic after therapy. The patients in both the surgical and the medical cohorts experienced statistically significant improvement in subjective and objective olfactory metrics by a similar degree. The patients with baseline olfactory dysfunction who underwent medical therapy had an improvement in average B-SIT score from 4.4 to 6.7, and the patients with baseline olfactory dysfunction who underwent surgical therapy had an improvement in average B-SIT score from 4.7 to 6.8. The only identified risk factor for failure to improve subjectively or objectively was a history of prior sinus surgery. Of note, subsequent study by the same investigators demonstrated that all of the cardinal symptoms of CRS other than olfaction respond better to surgery than medical management.⁶⁰

CONCLUSION

Olfactory dysfunction is a common symptom of chronic rhinosinusitis, affecting over 60% of patients with CRS. Both inflammatory and structural factors are believed to contribute to smell loss. Decreased olfaction significantly impacts CRS patients’ quality of life, resulting in emotional and psychosocial sequelae. Furthermore, there is evidence that decreased olfaction may impair the ability of a patient to respond to environmental hazards. It is therefore incumbent upon the clinician to assess this symptom and consider therapeutic interventions for patients with chronic rhinosinusitis. The study of olfaction in response to various medical and surgical therapies has been complicated by significant heterogeneity in patient population, intervention, study design, and method of olfaction assessment. Various medical therapies have been explored in clinical trials, including topical corticosteroids, oral corticosteroids, topical antibiotics, oral antibiotics, and systemic immunomodulation, among others. Surgical interventions including endoscopic sinonasal surgery have also been evaluated in the treatment of smell loss. While the efficacy of these interventions varies across studies, there is evidence to support the use of oral steroid therapy, topical steroid therapy, and ESS in the treatment of CRS with olfactory dysfunction. The clinician treating patients with chronic rhinosinusitis should become familiar with the evidence for the management options of olfactory dysfunction.

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Figure 1.
Sinonasal polyposis completely obstructing the olfactory cleft.

Table 1

Evaluation Methods of Olfactory Function

Evaluation Methods of Olfactory Function	
Subjective	Objective
Symptom scores (e.g. SNOT-22)	Smell Identification Test (SIT)
Visual Analog Scales (VAS)	Butanol Threshold Test (BTT)
Questionnaire of Olfactory Disorders (QOD)	Sniffin' Sticks Test (SST)