

Medical therapy and smell dysfunction

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Abstract. *Medical therapy and smell dysfunction.* Olfactory dysfunction is deemed to be a significant contributor to poor quality of life in different nasal inflammatory conditions like common cold, allergic rhinitis, and acute and chronic rhinosinusitis with and without nasal polyps (NP). The mechanism underlying olfactory impairment in inflammatory sinonasal disease relates to either the obstruction of the olfactory cleft due to congestion of the nasal mucosa, the presence of secretions or polyps inside the nasal cavity, or to dysfunction of the sensory mucosa of the olfactory bulb resulting from local inflammation. The reduction of smell capacity in nasal inflammatory conditions may have an acute or gradual onset, often with resolution of smell dysfunction after adequate medical treatment or surgery. In contrast to the well documented effects of surgery for rhinosinusitis on smell dysfunction, the available information about the effects of medical treatment is limited. Most studies have looked at corticosteroids, evaluating the restoration of olfactory capacity as a primary or secondary study outcome parameter. Both nasal and systemic corticosteroids have a beneficial effect on olfactory dysfunction, with systemic treatment being the most powerful. This review aims to provide an overview of current knowledge about medical treatment for rhinosinusitis and its effects on smell.

Introduction

Olfactory symptoms like reduced smell capacity – hyposmia – or total loss of smell – anosmia – may be presenting symptoms of sinonasal diseases. Inflammatory disorders constitute the primary cause of acquired smell dysfunction.¹ As the olfactory cleft is located in the upper part of the nasal fossa, which is reached by approximately 15% of the inspired air, any sinonasal inflammation with congestion, secretions and/or polyp formation may impede the normal transduction of inspired air to the olfactory neuro-epithelium. Frequent acquired rhinological diseases that impair olfactory function are allergic/non-allergic rhinitis, atrophic rhinitis, chronic rhinosinusitis with and without nasal polyps and some tumoral lesions located in the nasal fossa and/or in the sinuses.

Common characteristics of inflammatory sinonasal smell dysfunction are a gradual decline in olfactory function or fluctuations in olfactory function, low percentages of qualitative olfactory problems (parosmia, phantosmia) and higher retro-olfactory performance than with others causes of olfactory disorders. The slow onset of olfactory loss in sinonasal diseases means that patients are often unaware of, and not disturbed by, the olfactory impairment, and it also facilitates the retro-olfactory routes of sensory stimulation because of the impaired orthonasal route.

The medical treatment of inflammatory sinonasal diseases should aim to alleviate the smell disorder in parallel with the restoration of other nasal functions, primarily nasal congestion, secretions and NP size. This review provides an overview of

smell impairment associated with different sinonasal inflammatory diseases and the effects of medical treatment on smell dysfunction.

Allergic, non-allergic and atrophic rhinitis

Smell dysfunction is not considered to be a cardinal symptom of rhinitis.² However, hyposmia may be associated with allergic and non-allergic rhinitis (Table 1). Psychophysical olfactory testing of rhinitis patients reveals lower scores in allergic and non-allergic rhinitis patients than controls.³⁻¹⁰ For example, olfactory thresholds for phenylethyl alcohol are significantly higher in allergic patients than in controls: 23% of allergic patients have smell loss.⁶ Interestingly, smell loss does not correlate with nasal resistance in the patient group, suggesting that factors other than nasal congestion

Table 1

Sinonasal diseases with estimated incidences of smell problems, type of smell disorder, clinical course and treatment of choice

	Incidence of smell symptoms	Olfactory dysfunction	Characteristics	Treatment
CRS -NP	20-30%	Hyposmia >anosmia	Fluctuation	Corticosteroids
CRS+NP	70-90%	Hyposmia = anosmia	Fluctuation	Corticosteroids
Allergic rhinitis	15-20%	Hyposmia	Fluctuation	Corticosteroids and antihistamines
Atrophic rhinitis	60-80%	Hyposmia = cacosmia	Persistent	No recommended treatment

play an aetiological role in hyposmia. Olfactory function has been shown to fall off after allergen challenge in allergic patients, with no link to the decrease in nasal patency.¹⁰ Interactions between the olfactory and the trigeminal system also take place in patients with allergic rhinitis. Electrophysiological studies have demonstrated higher trigeminal sensitivity in allergic rhinitis patients after exposure to the allergen.¹¹ Olfactory performance in patients with non-allergic rhinitis is even worse than in allergic rhinitis.^{9,12} As the mechanisms underlying non-allergic rhinitis are most often unknown, one can only speculate about the aetiological link between this nasal condition and smell dysfunction.

In addition to allergic and non-allergic rhinitis, patients with atrophic rhinitis may present with olfactory dysfunction. Atrophy of the nasal mucosa may be secondary to over-resection of nasal mucosa or turbinates or secondary to bacterial colonisation. In spite of the limited presence or even absence of mucosa at the inferior turbinate, there are paradoxical symptoms of nasal obstruction. This phenomenon can be explained by the fact that those patients do not feel the

inspired air passing through their nasal fossa due to the lack of trigeminal function and/or nasal obstruction caused by turbulence in inspired air. Acute viral-related rhinitis or rhinosinusitis, adenoidal hypertrophy and rhinitis medicamentosa are also medical conditions associated with olfactory disturbances of varying severity. Patients with rhinitis still have better olfactory performance than patients with rhinosinusitis.⁷

Chronic rhinosinusitis

Alongside nasal obstruction, secretions and headache, smell dysfunction is a key symptom of rhinosinusitis¹ (Table 1). Traditionally, olfactory deficits in chronic rhinosinusitis (CRS) are considered to be the result of inflammation and decreased airflow with impaired access to the olfactory cleft. Indeed, medical anti-inflammatory treatment increases both nasal patency as well as olfactory capacity. However, biopsies from the olfactory neuroepithelium in CRS patients reveal inflammation and apoptotic pathological changes that include the receptor organ.¹³ Moreover, olfactory dysfunction has been related to inflammatory mediators,⁸ indicating that blockage of

the olfactory pathways alone may not be the only factor resulting in smell disorder and explaining the smell symptoms in the subgroup of patients with patent nasal passages.

Patients with NP are at increased risk of both hyposmia and anosmia.¹ Smell dysfunction is one of the most important symptoms of NP. It is progressive in nature and is related to the stage of the disease.¹⁴ The progressive pattern of smell dysfunction in NP leads to habituation and may explain the underestimation of smell dysfunction by patients with NP.¹⁴ Smell and taste are often both reduced in NP. Taste sensation includes the activation of gustatory, trigeminal and olfactory components. However, a large number of NP patients with subjective loss of smell have no taste problem. This observation can be explained by the higher percentage of retronasal olfactory function in patients with NP, which is more related to taste than ortho-nasal olfaction.¹⁵

Medical treatment

By contrast with the significant impact on quality of life caused by smell disorders and the frequent nature of the condition,¹⁶ only

limited studies have been conducted dealing with the recovery of olfactory dysfunction as a primary or secondary outcome in sinonasal disease. Clinical trials of medical treatment for smell disorders have primarily dealt with the effects of nasal and oral corticosteroid treatment, whereas no properly conducted studies have been performed on antihistamines, anti-leukotrienes, antibiotics and other drugs for the alleviation of smell disorder in allergic, non-allergic, and atrophic rhinitis, or in chronic rhinosinusitis with/without NP.

Table 2 provides an overview of the studies dealing with nasal and oral steroid treatment and the effects on smell disorder.

* Nasal steroids and olfaction

The major class molecules given for sinonasal-related olfactory dysfunction are corticoids. Nasal or topical corticoids currently available on the market are beclomethasone, budesonide, furoate mometasone, propionate fluticasone, furoate fluticasone. Nasal steroids are recommended as first-line treatment for allergic

rhinitis, non-allergic rhinitis, rhinitis medicamentosa and chronic rhinosinusitis with/without NP. They are highly effective, providing relief for most of the symptoms, including smell disorder, with a rapid onset of action (6 hours) and a cumulative effect after several days of use. Although improvement in olfaction is often possible, it is frequently transient and incomplete.

* Oral steroids and olfaction

Oral corticoids are potent anti-inflammatory molecules that

Table 2

Summary of studies of the clinical efficacy of corticosteroids for smell dysfunction

References	Treatment	Diagnosis	Effect on smell	Remarks
17	Oral prednisone	Nasal polyposis	Increased	Reversal after 10 days
18	Combination of anti-inflammatory and surgery	Inflammatory disease in the nose and paranasal sinuses	Increased	Temporary relief
19	Topical Betamethasone	Allergic rhinitis	Slight increase	One of the first studies with olfactory tests
20	Topical Flunisolide	Inflammatory disease of the paranasal sinuses	Moderate increase	Head-down forward position of nasal corticoid
4	Topical Mometasone Furoate	Seasonal allergic rhinitis	Slight increase	Independently of the nasal airflow increase
5	Topical Fluticasone Propionate	Chronic rhinosinusitis and post-infectious olfactory loss	No effect	
21	Topical Budesonide	Nasal polyposis	Slight increase	
22	Oral corticoid	Different aetiologies	Slight increase	For patients with inflammatory disease
23	Oral and topical	Different aetiologies	Oral more effective than topical	Oral corticoid as a diagnostic tool for conductive olfactory loss
24	Topical Beclomethasone	Chronic rhinosinusitis	Moderate increase	Post-operative period
25	Topical Budesonide	Chronic rhinosinusitis	No effect	Comparison of two dosages
26	Topical Mometasone Furoate	Chronic rhinosinusitis with polyp	Increase of smell function	Better effect when twice daily
27	Topical Mometasone Furoate	Chronic rhinosinusitis with polyp	No effect after four months	Effect on nasal obstruction
28	Topical Fluticasone Propionate	Chronic rhinosinusitis with polyp	Increase of smell function	With nasal drop

improve the olfactory function by direct and indirect effects. Several studies have been conducted in patients with CRS with or without NP on sinonasal-related olfactory dysfunction. These studies are listed in Table 2 with a summary of their efficacy for smell acuity. Heilmann *et al.*³ conducted an interesting study that confirms much current knowledge about the efficacy of corticoids for olfactory loss. They compared the local and systemic administration of corticosteroids in a cohort of patients with olfactory loss due to sinonasal disease but also in idiopathic and post-infectious olfactory loss. Nasal steroid treatment was less beneficial than systemic treatment. There was no prediction of response to therapy in terms of the duration of the disease, patient sex or age, or the presence of parosmia. Olfactory function improved in the three groups of patients treated with oral corticosteroids. Adverse systemic effects need to be taken into account when prescribing oral corticosteroids and avoided if possible. Repeated administration of a short course of oral corticoids is an alternative for prolonged use, and may prevent significant side-effects.

Conclusion

Several chronic inflammatory conditions of the upper airways are associated with smell dysfunction. Olfactory dysfunction in sinonasal-related disease is probably a mixed problem, with varying degrees of conductive and sensory problems in individual patients.

Corticosteroids represent the standard treatment for olfactory disorders related to inflammatory sinonasal disease. Topical corti-

coids have the advantage of being a local therapy with limited side-effects but efficacy is usually lower than with oral corticosteroids. Oral corticosteroids should be reserved for those patients in whom nasal steroids fail, or for whom this treatment is used as a diagnostic tool.

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