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# Assessment of taste functions in allergic rhinitis patients undergoing allergen-specific immunotherapy

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## Abstract

**Background** We evaluated taste functions of patients with perennial allergic rhinitis (AR) before and after allergen-specific immunotherapy (AIT).

**Methods** The study was designed as a prospective clinical study in our tertiary care hospital. Patients ($n=21$) who were diagnosed with perennial AR on the basis of physical examination, skin prick test of at least 3* for HDM allergen and treated with AIT were enrolled in this study. A control group ($n=21$) was selected from patients who were given intranasal steroids (INS) for perennial AR. Both groups had self-reported hyposmia and subjective loss of the sense of taste before treatment. Taste strips (Burghart, Wedel, Germany) were used for the taste identification scores before and after 6 months treatment.

**Results** A total of 42 subjects were included, with a mean age of $24.1 \pm 7.9$ years (range 15–43 years). Overall, the AIT group showed more of an improvement of taste function, observed in the total average test scores, compared to the INS group ($p<0.05$), but no change was detected between the groups before treatment. No difference was found for the bitter taste scores between the study groups ($p=0.053$).

**Conclusion** Subcutaneous allergen immunotherapy resulted in more of an improvement in taste function than intranasal steroids. Further studies are needed.

**Keywords** Perennial allergic rhinitis · Taste · Allergen-specific immunotherapy · Olfaction · Taste strips

## Abbreviations

| | |
|---|---|
| AR | Allergic rhinitis |
| QOL | Quality of life |
| OFC | Orbitofrontal cortex |
| SCIT | Subcutaneous immunotherapy |
| AIT | Allergen-specific immunotherapy |
| INS | Intranasal steroid |

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## Introduction

Allergic rhinitis (AR), a chronic inflammatory disorder of the nasal mucosa, affects approximately 20% of the world's population. Seasonal AR is most often caused by outdoor allergens, such as pollens or molds and is intermittent, perennial AR is mostly caused by indoor allergens such as house dust mites and molds [1, 2]. AR often causes olfactory dysfunction, with 54% of AR patients complaining of a decreased sense of smell [1]. In addition to the characteristic symptoms of the disease (sneezing, nasal obstruction, rhinorrhoea, and pruritus), other atypical and less common symptoms may affect a patient's quality of life (QOL), including halitosis, fatigue, malaise, irritability, and taste disorders [2, 3]. Problems with olfaction in AR have been researched extensively [1, 4, 5], whereas taste dysfunction in AR population has received less attention.

The etiology of olfactory dysfunction in AR patients involves more than physical inhibition of the delivery of odor molecules to the olfactory mucosa in the skull base [6]. In AR patients, hyposmia also arises from inflammatory dysfunction of the neuroepithelium with reduced signaling, inflammatory hypersecretion, and mucosal destruction [1, 2]. The prevalence of hyposmia ranged from 88 to 95% in patients in with moderate/severe perennial AR patients [1, 7, 8]. According to Landis et al. [9], long-term olfactory impairment lowers taste function. Little is known as to how taste function is affected by changes to olfactory function.

It is generally recognized that olfactory stimuli contribute a significant proportion of the experience of flavor [10]. Smell and taste are closely related chemical senses, there is also increasing understanding of the neural basis of this smell-taste integration [11]. Although olfactory and gustatory fibers are not found together at any peripheral anatomical site (e.g., tongue or olfactory cleft), it is likely that they are brought together in the central nervous system to form a representation of flavor. Neuroimaging studies of olfaction and gustationare beginning to isolate regions responsible for smell-taste integration ie flavor.

Presentation of a tastant or an odorant produces overlapping activation in regions of the insula and operculum, the orbitofrontal cortex (OFC) and the anterior cingulate cortex [11–15]. These same regions are also sensitive to somatosensory stimulation of the oral cavity by the trigeminal nerve [13, 15]. Rolls et al. [16] found that in the OFC, of 112 single neurons which responded to taste, olfactory and visual stimuli, many were unimodal (taste 34%, olfactory 13%, visual 21%), and in close proximity to each other. Some of the single neurons showed convergence, responding to taste and visual inputs (13%), taste and olfactory inputs (13%), or olfactory and visual inputs (5%). As a consequence, these three senses frequently interact, are functionally linked [17–19] and a change in one sense impacts on the other senses. Concomitant co-activation of the visual, trigeminal mediated somatosensory, the gustatory, and the olfactory systems are also utilized in daily life activities such as eating, breathing or drinking makes them often work simultaneously [17, 18].

Treatments for AR include lifestyle changes to decrease allergen exposure, oral or topical H1-antihistamines, intranasal or systemic glucocorticoids, leukotriene antagonists, cromolyns, decongestants, anticholinergics, and allergen-specific immunotherapy (AIT) [20, 21]. In AIT, tolerance to a certain allergen is induced by administering gradually increasing doses to the patient [20], and is continued for at least 3 years—which some patients find difficult. The success rate of this treatment is comparable to medical treatment and adherence rates to therapy range from 23 to 55% [22, 23]. Immunotherapy is commonly used and is the only treatment for AR that is potentially curative by inducing immunological tolerance to allergens [24, 25].

Although taste dysfunction is commonly reported in AR patients [2, 3], at present, no studies have measured the changes in taste function in AR patients undergoing AIT treatment. The accuracy of focused taste questions in discerning taste dysfunction is unknown. In most patients, self-reported gustatory function is not reliably correlated with psychophysical test results due to a combination of factors like the relatively low prevalence of taste deficits in the general population and the tendency of patients to confuse loss of olfaction-related flavor sensations with taste-bud mediated deficits [26]. Evaluation of patients with taste complaints is difficult without standardized quantitative methods of assessment with either psychophysical tests or electrogustometry. In the present study, the psychophysical technique for measuring taste function is based on strips ("Taste Strips"; Burghart, Wedel, Germany) made from filter paper which are soaked with different taste solutions (four concentrations each for sweet, sour, salty and bitter) and then dried [27]. Taste Strips are used in clinics as a diagnostic tool to quantitatively evaluate the sense of taste. Our study aims to quantitatively evaluate the effects of subcutaneous AIT on taste function in perennial AR patients.

## Materials and methods

### Volunteers and study design

We conducted a prospective case–control clinical study. All investigations were performed in accordance with the Declaration of Helsinki on biomedical studies involving human subjects. The Ethics Committee of our institution approved the study, and signed informed consent was obtained from

all patients. This study included 42 perennial AR patients managed in our otolaryngology clinic. Inclusion criteria were: perennial AR symptoms for at least 2 years due to HDM according to ARIA guideline [28], a positive skin prick test of at least 3* for HDM allergen with a commercial solution (ALK, Copenhagen, Denmark), in addition to having both self-reported subjective loss of the sense of taste and hyposmia for at least 2 years. Patients were also evaluated for severity of symptoms following the ARIA guideline, and only moderate/severe perennial AR patients were included. A detailed otorhinolaryngologic examination, including an endoscopic evaluation of the nasal cavity and nasopharyngeal structures, was performed prior to the study. 21 patients who were treated with subcutaneous immunotherapy for house dust mites (HDM) were enrolled and designated as the study group (AIT group). The control group was selected from patients treated with intranasal steroids (INS group) ($n = 21$). For homogeneity, patients were given the same intranasal steroid (fluticasone furoate) in two sprays into both nasal cavities, 200 micrograms in each nostril once or twice a day, continuously for 6 months. Subcutaneous immunotherapy was given to patients with a diagnosis of AR based on history, physical examination, skin prick test of at least 3* for HDM allergen and patient consent to AIT. Only subcutaneous (not sublingual or oral) AIT treatment was used to standardize the study. Exclusion criteria were as follows: any contraindication for subcutaneous AIT; additional anatomic or systemic disease that decreased olfactory function such as chronic sinusitis, nasal polyposis, clinically significant nasal septal deviation, presence of anatomic or systemic disease that decreases taste function such as chronic kidney disease, middle ear disease and so on; any mental or motor conditions that would inhibit taste testing; and patients taking beta blocker or antihypertensive drugs or any drugs known to alter taste function [29]. The AIT group did not use any AR medication including intranasal steroid and antihistaminic during the study. Taste Strips were used for the taste test in both groups before starting the treatment and after the 6 months after treatment.

### Taste function evaluation

Both the cohorts underwent taste function evaluation with the taste strips before and after treatment to assess objectively their subjective loss of the sense of taste. One hour prior to testing, the patients were asked not to eat or drink anything except water, not to smoke, and not to brush their teeth. Taste strips are filter paper strips 8 cm long, with a tip area of 2 $cm^2$ impregnated with one of four basic taste (sweet, sour, salty and bitter) substances at one of four concentrations of each [27]. The following substances and concentrations were used for the taste strips: sweet, 0.4, 0.2, 0.1, and 0.05 g sucrose/mL; sour, 0.3, 0.165, 0.09, and 0.05 g citric acid/mL; salty, 0.25, 0.1, 0.04, and 0.016 g sodium chloride/mL; and bitter, 0.006, 0.0024, 0.0009, and 0.0004 g quinine hydrochloride/mL. Distilled water was used as the solvent. The taste solutions were prepared freshly at regular intervals. The strips were placed on the left or right side of the anterior third of the extended tongue, resulting in a total of 32 trials. Before the administration of a strip, the participant was asked to rinse his or her mouth with water. The tastes were presented in increasing concentrations and the taste qualities in a randomized fashion at each of the four concentrations, alternating the side of presentation. With their tongue still extended, patients had to identify the taste from a list of four descriptors: sweet, sour, salty, and bitter (multiple forced choice). To estimate overall taste function, the number of correctly identified tastes per side was summed to obtain a ''taste identification score'' [27]. The mean score of the left and right sides was used in the statistical analysis of each taste. The whole testing procedure for the four taste substances typically required 20 min for lateralized (right and left side separately) testing. One study found a score of 19 or higher as normogeusic [30] whilst another suggested a score of 26 or higher [31].

In parallel with the testing procedure, patients were requested to indicate whether their taste sensitivity had changed over of the course of treatment. The answer options were (1) taste sensitivity remained unchanged; (2) taste sensitivity improved compared with pretreatment; and (3) taste sensitivity is reduced compared with pretreatment.

### Statistical analysis

Data analyses were performed with SPSS 21.0 software (SPSS Inc, Chicago, Illinois). Data are presented as mean ± standard deviation for continuous variables and as the number of cases for the categorical data. Differences between the groups were analyzed by the $t$ test or Mann–Whitney $U$ test, as appropriate. Correlation analyses were also performed using Spearman statistics where appropriate. The Wilcoxon signed rank test was used to compare numerical variables. Comparative analysis between groups was performed using the $\chi^2$ test. All analyses were performed using two-tailed tests with significance at the $p < 0.05$ level.

## Results

### Demographics

No differences in sex, smoking status or age were detected between the immunotherapy (AIT) and control (INS) groups. Table 1 shows the descriptive statistics of the patient groups.

**Table 1** Patient demographics

| | Treatment | | | | *p* |
|---|---|---|---|---|---|
| | INS | | AIT | | |
| | Mean ± SD | Min–Max | Mean ± SD | Min–Max | |
| Age | 23.7 ± 8.1 | 15–43 | 24.2 ± 7.0 | 16–41 | 0.734 |
| | *n* | % | *N* | % | |
| Gender | | | | | |
| Male | 11 | 55.0 | 11 | 55.0 | 1.000 |
| Female | 9 | 45.0 | 9 | 45.0 | |
| Smoke | 5 | 25.0 | 4 | 20.0 | 1.000 |

*INS* intranasal steroid, *AIT* allergen-specific immunotherapy, *SD* standard deviation

## Pretreatment taste scores

Total taste function expressed as taste identification scores before treatment were 20.5 ± 3.1 in the AIT group and 21.1 ± 2.8 for the INS groups ($p > 0.05$). No significant difference in taste function, (sweet, sour, bitter and salty) between the two groups were detected before treatment ($p = 0.863$, $p = 0.590$, $p = 0.606$, $p = 0.548$; respectively) (Table 2).

## Post-treatment taste scores

Total taste identification scores were 28.8 ± 1.9 in the AIT group and 25.9 ± 2.4 points for the INS group. Overall, the AIT group showed more of an improvement of taste, observed in the total average test scores, compared to the INS group ($p < 0.05$). The sweet, sour and salty taste scores increased significantly in the AIT group compared with the INS control group ($p = 0.004$, 0.03 and 0.013, respectively). No difference was found for the bitter taste scores between the study groups ($p = 0.053$) (Table 2) (Fig. 1). At the 6th

**Table 2** Results of taste identification scores before and after treatment of the two groups

| | Treatment | | | | | | *p* |
|---|---|---|---|---|---|---|---|
| | INS | | | IT | | | |
| | Mean ± SD | Min–Max | Median | Ort. ± SD | Mean ± SD | Median | |
| Sweet (before) | 4.8 ± 0.8 | 4–6 | 5 | 4.8 ± 0.9 | 3–6 | 5 | 0.863 |
| Sweet (after) | 6.2 ± 0.9 | 5–8 | 6 | 7.0 ± 0.7 | 6–8 | 7 | 0.004 |
| Δ | 1.35 ± 0.67 | 0–2 | 1 | 2.20 ± 0.70 | 1–4 | 2 | 0.001 |
| *p* | < 0.001 | | | < 0.001 | | | |
| Sour (before) | 5.2 ± 1.1 | 4–8 | 5 | 5.1 ± 1.1 | 4–8 | 5 | 0.590 |
| Sour (after) | 6.4 ± 0.9 | 5–8 | 6 | 7.2 ± 0.7 | 6–8 | 7 | 0.003 |
| Δ | 1.15 ± 0.59 | 0–2 | 1 | 2.15 ± 0.88 | 0–3 | 2 | < 0.001 |
| *p* | < 0.001 | | | < 0.001 | | | |
| Bitter (before) | 5.9 ± 1.2 | 4–8 | 6 | 5.7 ± 1.2 | 4–7 | 6 | 0.606 |
| Bitter (after) | 6.9 ± 1.0 | 5–8 | 7 | 7.5 ± 0.8 | 6–8 | 8 | 0.053 |
| Δ | 0.95 ± 0.51 | 0–2 | 1 | 1.80 ± 0.83 | 1–4 | 2 | < 0.001 |
| *p* | < 0.001 | | | < 0.001 | | | |
| Salty (before) | 5.2 ± 0.9 | 4–7 | 5 | 5.1 ± 1.0 | 4–7 | 5 | 0.548 |
| Salty (after) | 6.6 ± 0.8 | 5–8 | 6.5 | 7.2 ± 0.8 | 6–8 | 7 | 0.013 |
| Δ | 1.35 ± 0.81 | 0–3 | 1 | 2.15 ± 0.99 | 0–3 | 2 | 0.006 |
| *p* | < 0.001 | | | < 0.001 | | | |
| Total (before) | 21.1 ± 2,8 | 16–25 | 22 | 20.5 ± 3.1 | 16–25 | 20.5 | 0.558 |
| Total (after) | 25.9 ± 2.4 | 22–29 | 26 | 28.8 ± 1.9 | 26–32 | 28.5 | < 0.001 |
| Δ | 4.80 ± 1.44 | 2–8 | 5 | 8.30 ± 2.23 | 4–12 | 8 | < 0.001 |
| *p* | < 0.001 | | | < 0.001 | | | |

*INS* intranasal steroid, *AIT* allergen-specific immunotherapy, *SD* standard deviation

month of treatment, all of the 42 patients claimed superior taste sensitivity.

## Discussion

Our study demonstrates that treatment of AR with nasal steroids or AIT improves taste scores. And that allergen-specific immunotherapy was significantly better in improving sweet, sour and salty taste performance in AR patients compared to intranasal steroids. Bitter taste scores did not benefit from this effect. No study investigating the effects of subcutaneous AIT or sublingual AIT on taste dysfunction in AR patients has been previously reported to our knowledge.

AR is a cause of olfactory dysfunction. Rydzewski et al. revealed that the incidence of taste disorders in allergic rhinitis patients to be 30.7%, with no positive correlations between the thresholds of taste and smell among the individuals examined [2]. We found that taste function was decreased in all parameters in patients with AR.

Somatosensory and central neural interactions are known to play a major role in the association of the olfactory and taste function. In patients who suddenly lose one chemical sense (e.g., olfaction), this missing afferent information would also lead to a decreased chemosensory integration with lowered overall performances in the remaining chemical senses (e.g., trigeminal function) confirmed on patient studies [32, 33]. As the nose has no gustatory innervation and the tongue no olfactory innervation, decreases in taste function after acquired olfactory impairment is thought to be due to central nervous changes. This might explain why olfactory dysfunction can lead to decrease taste perception as in our study findings.

Intranasal steroid treatment may improve olfaction in AR patients [34]. Intranasal steroids decrease the number of eosinophils in the nasal mucosa, which is thought to directly decrease inflammation and edema in the nasal mucosa, thereby improving the delivery of air and odor molecules to the olfactory fissure [32]. Although intranasal steroids are first line medical treatment for allergic rhinitis and included in most international guidelines [35]; they are not disease-modifying, and symptoms recur shortly after they are discontinued, they must be taken life long. AIT, on the other hand, is disease-modifying and can induce long-term tolerance after 3–5 years of therapy [36, 37]. Immunotherapy also confers beneficial clinical effects by modulating immunoglobulin levels [20]. In several studies, AIT in house dust mite-related allergic rhinitis showed significantly reduced symptoms and medication use [38–40]. Immunotherapy down-regulates the allergic response in an allergen-specific manner by a variety of mechanisms still being elucidated.

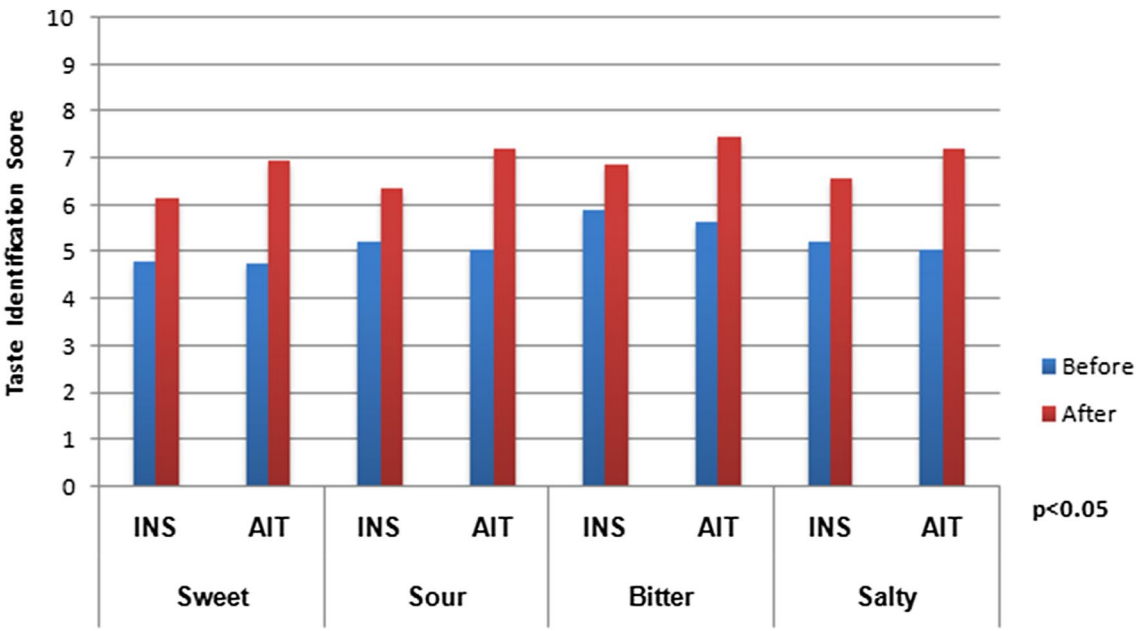


**Fig. 1** Taste strip results of the study groups

A limitation of the current study was the small sample size. Only 42 patients were included in the study because of the specific subcutaneous AIT indication criteria, inconvenience of the treatment for the patient, low patient compliance, high cost, potential risks, and voluntary nature of the study. The relatively small sample size may explain the statistical insignificance of the improvements in some parameters.

The taste strip test has resulted in a series of publications [27, 41–43] and was proven reliable concerning the investigation of gustatory testing before and after an intervention [44, 45], the subjective and qualitative method of the test can make the results of the study open to debate without any normative range. In their study based on a high number of tested healthy subjects ($n = 548$), Landis et al. [30] proposed that women with a score of 19 and higher can be regarded as normogeusic, while this score is 17 in men. Pingel et al. [31], in their study consisting 944 healthy patients, using liquid taste solutions which is an another test based on the chemical stimuli, found that a total score of 26 and higher can be regarded as normogeusic in the same percentile and similar age group (10th percentile, 16–35 years). However, at present, there is no existing standardized validated taste score in the literature. Electrogustometry [46] is an alternative method of taste assessment that results in repeatable quantitative measures (dB). Correlation between taste strip test and electrogustometry results is unproven at present. The advantage of the taste strip test compared electrogustometry is that it is a simple bed side psychophysical test by means of chemicals rather than electrical stimulation.

## Conclusion

Treatment of allergic rhinitis with intranasal steroids or subcutaneous allergen immunotherapy treatment can improve taste function. Our study demonstrated this effect and showed that, subcutaneous allergen immunotherapy resulted in more of an improvement in taste than intranasal steroids. This is the first study to investigate the effects of subcutaneous AIT on taste function. Studies with larger populations are needed to confirm our preliminary results.

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## Compliance with ethical standards

**Conflict of interest** All of the authors declare that they have no conflict of interest.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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