OLFACTORY FUNCTION IN CHRONIC RHINITIS SUBTYPES: ANY DIFFERENCES?

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ABSTRACT

Introduction*: Olfactory dysfunction is a common problem in rhinological disease, but it has been few evaluated among patients with different chronic rhinitis subtypes. The aim of this study was to assess olfactory function in patients with allergic rhinitis (AR), non-allergic rhinitis (NAR) and mixed rhinitis (MR).*

Materials and methods*: A total of 122 patients with AR, NAR, and MR were included in the study. Sniffin' Sticks test was applied to all groups. The study groups were compared in terms of odor scores and an association between olfactory dysfunction and rhinitis grading, according to ARIA (Allergic Rhinitis and its Impact on Asthma) criteria, was also investigated.*

Results*: A significant difference was observed between NAR patients and the two other study groups with respect to all odor scores. TDI (Threshold, Discrimination, Identification) score, for overall olfactory function, resulted significantly lower in NAR patients than that in the other two groups (P=0.038). Conversely, no significant difference was observed between patients with AR and MR. Consistent with ARIA classification, NAR patients suffered mostly from persistent symptoms, whereas, AR patients generally suffered by intermittent symptoms, as well as MR patients, but this last with a significative higher presence of patients with persistent symptoms, when compared to AR group (P<0.05). A significative association was also observed between lower TDI scores and presence of persistent rhinitis symptomatology (P<0.001).*

Conclusions*: Impaired olfaction is a feature more evident in NAR patients when compared to the other rhinitis subtype and it was much more affected by longer duration of rhinitis symptomatology rather than severity.*

Keywords*: Olfaction disorders, Rhinitis, Allergic, Rhinitis, Vasomotor.*

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Introduction

Allergic rhinitis (AR) is a common inflammatory disease with a relevant impact on the quality of life affecting between 10 and 25% of the worldwide general population[1].

Although AR is the most common form, it has significant overlap in clinical symptomatology with non-allergic rhinitis (NAR)[2]. This last does not involve an IgE-mediated inflammation of the nose with histamine release caused by airborne allergens as AR but is thought to be characterized by sensory nerve dysregulation or autonomic dysfunction in the nose[3]. Frequently, NAR occurs in tandem with AR and presents as mixed rhinitis (MR). Recent surveys suggest that mixed rhinitis (MR), is a specific rhinitis subtype that may represent between 50 and 70% of all AR patients[4]. Olfactory dysfunction has been reported to be a frequent symptom in patients with AR and NAR[5,6].

Although the mechanism remains unclear, it is likely due to both a mechanical component (ie, blockage of the nasal airways through mucosal congestion) and an inflammatory component[7].

The olfactory sensation is one of the most important sensory perceptions in humans because it detects dangerous substances (e.g., gas leak) and facilitates flavor and taste sensation[8]. Olfactory dysfunction may emerge in several situations other than rhinitis, such as in upper respiratory tract infections, sinonasal diseases, laryngopharyngeal reflux, aging and head trauma[5,9,10]. Smell dysfunction can worsen patients' quality of life and can lead to depression in some patients[11]. The frequency of olfactory dysfunction in adults with allergic rhinitis is 20-40%[12], in population-based studies, the frequency is 19%[13].

Although relatively large numbers of patients suffer from these rhinitis subtypes, few studies examining olfactory function in such kind of patients. Therefore we performed a prospective study to assess the impact of AR, NAR, and MR on the sense of smell in a group of adult patients with chronic rhinitis and to characterize olfactory dysfunction on the basis of ARIA (Allergic Rhinitis and its Impact on Asthma) duration and severity criteria.

Materials and methods

Patients aged 18-60 years who presented symptoms of chronic rhinitis were recruited from January 2017 to October 2017 at the ENT Unit Acireale. Investigations were performed according to the Declaration of Helsinki on Biomedical Studies Involving Human Subjects. The study design was approved by the local ethics committee. All subjects were informed about the procedures and aims of the study and provided written informed consent. Patients were excluded if they had history of asthma symptoms or evidence of asthma according to a pulmonary function test, those who have other causes of nasal obstruction, e.g., nasal polyp, nasal tumor, and/or sensorineural olfactory disorder, e.g., post- head trauma, dementia, Alzheimer's disease, multiple sclerosis, or congenital disorders. Patients who had undergone nasal surgery or who were receiving symptomatic medication in the 2 weeks before examination were also excluded from the study. Patients underwent a detailed evaluation of medical history and an otorhinolaryngological examination using nasal endoscopy.

Rhinitis diagnosis, as well as, classification and severity grading were performed based upon the Allergic Rhinitis and its Impact on Asthma (ARIA) criteria such as intermittent (mild or moderate-severe) or persistent (mild or moderate-severe) rhinitis[14]. Patients were categorized as having AR or NAR based on history, clinical signs[15] and results from the skin prick test (SPT), according to a procedure previously described[2].

Patients with MR were defined as having symptoms correlating with positive SPT results in addition to symptoms triggered by nonallergic stimuli[16]. Olfactory function was evaluated by an otorhinolaryngologist, blinded to results of SPT, using the Sniffin' Sticks test (Burghart Messtechnik GmbH, Wedel, Germany) consisting of a threshold, a discrimination and an identification test[17]. For odor presentation, the cap of the pen was removed by the investigator for approximately 3 s and the odorized tip was placed approximately 2 cm in front of the subject's nostrils. All olfactory tests were performed birhinally and according to a procedure described previously[18].

The n-Butanol threshold test was assessed using a single-staircase, three alternative and it was defined as the mean of the last four of seven staircase reversals. Scores between 1 and 16 were possible. The score for discrimination was the sum of correctly discriminated triplets of pens presented in randomized order. Odor identification score was the sum, ranging from 0 to 16, of correct answers given by subjects for the identification of 16 different odorants by means of 4 given possibilities for each pen.

Statistical analysis

Data were analyzed by using the Statistical Package for Social Sciences program (SPSS for Windows 20.0 Chicago, USA). Groups were compared using an independent t-test for normally distributed quantitative data. Data not showing normal distribution were analyzed using the Mann-Whitney U-test and Kruskal-Wallis test. Pearson's chi-squared test was used for the analysis of categorical data. For non-normally distributed data, the correlation between the variables was analyzed with Spearman correlation analysis. Results were presented as frequency, mean ± standard deviation and median (min-max).

$P<0.05$ was considered as significant difference.

Results

A total of 122 patients (60 men and 62 women; mean age 38.10 ± 2.84) were included in this study. Of these, 50 were diagnosed as having AR, 40 had NAR, the remainder 32 had MR. There was no statistically significant difference with respect to age or gender among groups (P>0.05).

On the basis of ARIA classification, 44 % of patients with AR had mild intermittent symptoms followed by moderate to severe intermittent symptoms (36 %). The most frequent forms of NAR were either mild persistent (35%) or moderate/severe persistent (30%). Patients with MR suffered from intermittent symptoms in most cases, but with a higher presence of patients with persistent symptoms, when compared to AR group. In addition, there was a significant difference among all ARIA groups for the proportion of AR, NAR, and MR as shown in table 1.

Characteristics	Allergic rhinitis N=50	Non-allergic rhinitis N=40	Mixed rhinitis N=32	Overall N = 122	*P value*
Age, in years					
Mean ± SD	38.74 ± 3.11	37.67 ± 2.45	37.88 ± 2.97	38.10 ± 2.84	0.116
Median	39	38	38	38	-
Range	18-60	19-58	18-59	18-60	-
Gender, n(%)					
Male	26 (52.0)	19 (47.5)	15 (46.9)	60 (49.2)	0.177
Female	24 (48.0)	21 (52.5)	17 (53.1)	62 (50.8)	
ARIA classification, n(%)					
Mild intermittent	22 (44.0)^{A}	8 (20.0)^{B}	12 (37.5)^{A}	40 (32.8)	0.026*
Moderate/Severe intermittent	18 (36.0)^{A}	6 (15.0)^{B}	9 (28.1)^{A}	29 (23.8)	0.046*
Mild persistent	8 (16.0)^{A}	14 (35.0)^{B}	6 (18.8)^{A}	32 (26.2)	0.031*
Moderate/Severe persistent	2 (4.0)^{A}	12 (30.0)^{B}	5 (15.6)^{C}	21 (17.2)	0.019*

Table 1: Demographic and clinical characteristics of the patients included in the study (N=122).
SD: standard deviation; ARIA: Allergic Rhinitis and its Impact on Asthma
**P < 0.05. Note: There is no difference between the groups with the same superscript letter.*

The AR, NAR, and MR groups were compared in terms of odor scores, and a statistically significant difference was observed between them (OI score, P=0.036, OD score, P=0.041, and TO score, P=0.043) with lower scores in NAR group when compared to the other two groups.

The TDI score for overall olfactory function resulted in 25.85 ± 2.18 for the AR group, 20.08 ± 2.08 for the NAR group and 23.61 ± 2.01 for the MR group. Also, there was a significant difference (P=0.038) with a lower score in the NAR group as in the subtests when compared to the other two study groups (Table 2).

Characteristics	Allergic rhinitis N=50	Non-allergic rhinitis N=40	Mixed rhinitis N=32	*P value*
OI Score	8.34 ± 2.17^{A}	6.37 ± 2.17^{B}	7.85 ± 2.03^{A}	0.036*
OD Score	8.92 ± 2.41^{A}	6.95 ± 2.05^{B}	7.94 ± 2.05^{A}	0.041*
TO Score	8.59 ± 1.97^{A}	6.76 ± 2.01^{B}	7.82 ± 1.95^{A}	0.043*
TDI Score	25.85 ± 2.18^{A}	20.08 ± 2.08^{B}	23.61 ± 2.01^{A}	0.038*

Table 2: Comparison of the odor scores between the study groups.
OI: Odor Identification; OD: odor discrimination; TO: threshold odor; TDI: theshold discrimination, identification
**P < 0.05. Note: There is no difference between the groups with the same superscript letter.*

Changes in odor score were significantly related to severity and frequency of rhinitis. There was a significantly higher frequency of both hyposmia and anosmia, according to the TDI score, in patients in the mild persistent group (P<0.001) and in the moderate/severe persistent group (P<0.001). On the contrary, no significant change in TDI score was observed in moderate/severe intermittent group of patients (P=0.104) (Table 3).

Characteristics	Normosmia (TDI > 30.5)	Hyposmia (TDI 30.5 - 16.5)	Anosmia (TDI < 16.5)	*P value*
Mild intermittent, n (%)	8 (6.6)^{A}	8 (6.6)^{A}	0 (0)^{B}	0.009*
Moderate/Severe intermittent, n (%)	7 (5.7)	10 (8.2)	7 (5.7)	0.104
Mild persistent, n (%)	3 (2.5)^{A}	24 (19.7)^{B}	7 (5.7)^{C}	< 0.001*
Moderate/Severe persistent, n (%)	0 (0)^{A}	37 (30.3)^{B}	11 (9.0)^{C}	< 0.001*

Table 3: Comparison of TDI scores among the ARIA groups.
TDI: theshold discrimination, identification
**P < 0.05. Note: There is no difference between the groups with the same superscript letter.*

Discussion

Although the pathogenesis of olfactory dysfunction in rhinitis patients is not fully understood, two potential mechanisms may be involved: conductive and sensorineural mechanisms.

Allergic or non-allergic inflammation can induce mucosal hypertrophy and swelling, resulting in blocking of the transportation of odor particles to the olfactory epithelium. Olfactory receptor neurons can be irreversibly damaged by inflammatory mediators or oxidative free radicals, which may be released by allergic inflammatory cells. Reduction of the olfactory receptor neurons and displacement of the olfactory neuroepithelium by respiratory epithelium culminate in sensorineural loss of smell[19,20].

Few studies have investigated olfactory function in patients with chronic rhinitis subtypes.

This is the first study to use the Sniffin' Sticks test battery for evaluation of olfactory function in patients with AR, NAR, and MR, moreover we classify the patients using the ARIA classification, comparing odor score among the ARIA groups.

Our study results revealed more persistent symptoms and lower scores in the olfactory function for patients with NAR when compared to MR or AR groups, in which prevail intermittent rhinitis subtype and a less severe olfactory dysfunction has been reported. This is in contrast to a previous finding, where through the use of an automated olfactometer, was reported that there was no difference identified in olfactory threshold responses among patients with AR, NAR, and MR[21].

Trying to explain our results we can say that given the higher frequency of hyposmia and anosmia in patients with persistent rhinitis and being most of these patients belonging to NAR group, the difference of olfactory dysfunction among the three rhinitis subtypes is probably due to the long-standing non-allergic inflammation in NAR patients, rather than immediate allergic reaction. Thus, NAR patients may have a more prolonged mucosal inflammation compared with AR or MR patients. This chronic inflammation may reduce the flow of information from the olfactory receptor cells to the brain, thereby provoking impairment in the olfactory identification, as shown by some studies where it has been hypothesized that patients with NAR have abnormalities in their olfactory transduction pathway, leading to pathologic changes in the olfactory mucosa[22-24,5].

Only a few studies have reported a more severe olfactory loss in patients with NAR than that in patients with AR, this is probably due to the inclusion of heterogeneous NAR groups that included rhinosinusitis and polyposis cases[5,25,26], which were excluded from our study.

Other studies reported that decreased olfaction in those with NAR was age-dependent, reporting that aging is one of the most important factors negatively affecting olfactory function in patients with rhinitis[5]. However, there are also studies in the literature reporting no relationship between age and olfactory dysfunction in rhinitis patients[27-29].

We did not investigate a possible correlation between the age and odor scores in our study and this is a limitation of our study. Further analysis regarding a possible effect of age on olfactory function is required to better elucidate this issue.

Conclusions

Anyway, some conclusions can be drawn from this study. A significant difference in olfaction function were found between different rhinitis subtype groups, with a more severe olfactory loss in patients with NAR when compared to patients with AR or MR, indicating that impaired olfaction is a feature quite evident in NAR patients and assuming that the frequency and duration of rhinitis symptoms rather than severity negatively affecting olfactory function. Additional investigations with more clinical tools are needed to explore and better elucidate the underlying mechanisms of olfactory dysfunction in patients with chronic rhinitis.

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