Current perspectives

Olfaction in allergic rhinitis: A systematic review

Boris A. Stuck, MD,[a] and Thomas Hummel, MD[b] *Essen and Dresden, Germany*

Olfactory dysfunction is a key symptom in patients with allergic rhinitis (AR). Despite the implications for quality of life, relatively few articles have tested olfactory function in their investigations. The current systematic review aimed to investigate the following 2 questions: (1) What does AR do to human olfaction? (2) How effective is the treatment of AR in restoring the sense of smell? A comprehensive literature search was performed, and human studies of any design were included. A total of 420 articles were identified, and 36 articles were considered relevant. Data indicate that the frequency of olfactory dysfunction increases with the duration of the disorder, and most studies report a frequency in the range of 20% to 40%. Although olfactory dysfunction does not appear to be very severe in patients with AR, its presence seems to increase with the severity of the disease. There is very limited evidence that antihistamines improve olfactory function. In addition, there is limited evidence that topical steroids improve the sense of smell, especially in patients with seasonal AR. This is also the case for specific immunotherapy. However, many questions remain unanswered because randomized controlled trials are infrequent and only a few studies rely on quantitative measurement of olfactory function. (J Allergy Clin Immunol 2015;■■■:■■■-■■■.)

Key words: *Allergy, rhinitis, smell, olfaction, hyposmia, anosmia*

Olfactory dysfunction is a key symptom in patients with allergic rhinitis (AR). It is likely due to both a mechanical component (ie, blockage of the nasal airways through mucosal congestion) and an inflammatory component[1,2]; see Doty and Mishra[3] for a review. In addition, olfactory function is a key contributor to quality of life; its loss is accompanied by the decreased enjoyment of food and drink, a decrease in social competence, and an increased risk for other factors, including food poisoning.[4,5] Although relatively large numbers of patients have AR and as a consequence, could exhibit olfactory dysfunction, there remains a lack of studies examining olfactory function in AR-related investigations.

Abbreviations used

AR:	Allergic rhinitis
Mesh:	Medical subject heading
OD:	Odor discrimination
OI:	Odor identification
OT:	Odor threshold
RCT:	Randomized controlled trial
Tiab:	Title/abstract
UPSIT:	University of Pennsylvania Smell Identification Test
VAS:	Visual analog scale

Although instruments that measure olfactory dysfunction have been developed and are commercially available (eg, Doty et al[6] and Hummel et al[7]), most studies report qualitative ratings by patients. This limits the quality of the data, with most patients typically having trouble rating their olfactory function[8] because nasal patency and olfactory function are often difficult to distinguish. Therefore throughout this article a distinction will be made between "rated" olfactory function and assessment of olfactory function by using quantitative methods ("measured" olfactory function), including tests for odor thresholds (OTs) or odor identification (OI). If not otherwise specified, rated olfactory function will be discussed because this has been more widely administered in comparison with measured olfactory function.

The present structured review aimed to investigate the following 2 questions: (1) What does AR do to human olfaction? (2) How effective is the treatment of AR in reducing olfactory dysfunction?

METHODS

A comprehensive literature search was performed in August 2014 with the help of a professional librarian specialized in medical database reviews. All human studies published in English or German were included. The search strategy was adjusted to the database in use and was specified as follows (Medical subject heading [Mesh]/mh, title/abstract [tiab], title [ti], and abstract [ab]):

PubMed (no date restriction): ("Rhinitis, Allergic, Perennial" [Mesh] or "Rhinitis, Allergic, Seasonal" [Mesh] or Allergic rhiniti* [tiab] or Nasal allerg* [tiab] or Nose allerg* [tiab] or Pollen allerg* [tiab] or Pollinosis [tiab] or Pollinoses [tiab] or Hay fever [tiab] or hayfever [tiab]) AND ("Olfaction Disorders" [Mesh] or "Olfactory Mucosa" [Mesh] or "Smell" [Mesh] or olfact* [tiab] or odor* [tiab] or smell [tiab] or taste [tiab] or Cacosmia* [tiab] or Dysosmia* [tiab] or Paraosmia* [tiab] or Anosmia* [tiab] or Hyposmia* [tiab]) AND (English [lang] or German [lang]) NOT (animals [Mesh] not humans [Mesh]).

Web of Science Core Collection (since 1987, limits: English or German): TS = (["Allergic rhiniti*" or "Nasal allerg*" or "Nose allerg*" or "Pollen allerg*" or "Pollinosis" or "Pollinoses" or "Hay fever" or "Hayfever"] AND ["olfact*" or "odor*" or "smell" or "taste" or "Cacosmia*" or "Dysosmia*" or "Paraosmia*" or "Anosmia*" or "Hyposmia*"]).

The Cochrane Library (no date restriction): ([mh "Rhinitis, Allergic, Perennial"] or [mh "Rhinitis, Allergic, Seasonal"] or ["Allergic rhiniti*" or

From [a]the Department of Otorhinolaryngology, Head and Neck Surgery, University Hospital Essen, and [b]the Smell and Taste Clinic, Department of Otorhinolaryngology, Head and Neck Surgery, TU Dresden.

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Corresponding author: Boris A. Stuck, MD, Department of Otorhinolaryngology, Head and Neck Surgery, University Hospital Essen, Hufelandstrasse 55, 45147 Essen, Germany. E-mail: boris.stuck@uk-essen.de.

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"Nasal allerg*" or "Nose allerg*" or "Pollen allerg*" or "Pollinosis" or "Pollinoses" or "Hay fever" or "Hayfever"]: ti,ab) AND ([mh "Olfaction Disorders"] or [mh "Olfactory Mucosa"] or [mh "Smell"] or "olfact*" or "odor*" or "smell" or "taste" or "Cacosmia*" or "Dysosmia*" or "Paraosmia*" or "Anosmia*" or "Hyposmia*": ti,ab).

Study design was not an exclusion factor. The initial electronic search was conducted by a medical librarian, as stated above, and the results were screened independently by the 2 authors of this review based on title, abstract, and key words, if available. Articles were considered relevant if one of the 2 authors rated them accordingly. Relevant articles were then evaluated based on the full-text version independently by the 2 authors. Again, articles were considered relevant if one of the 2 authors rated them accordingly based on the full-text version.

RESULTS

Search results

After eliminating duplicate findings, 420 articles were identified by using the search criteria described above. In the initial evaluation 74 articles were considered relevant for this review, leading to exclusion of 346 articles based on the title, abstract, and key words. After evaluation of the full-text version, 38 articles were additionally excluded. The 38 articles were excluded as follows. Seven articles were meeting abstracts,[9-15] and 1 was published in French.[16] Four articles investigating different therapeutic approaches did not address olfactory function as an outcome parameter but only mentioned smell or taste under potential adverse events.[17-20] Six articles included patients with AR and non-AR and did not provide a separate analysis for the subgroup of patients with AR.[21-26] Two articles were excluded because they only assessed the immediate effects of an allergic challenge, therefore providing little clinical information.[27,28] One article consisted of a meeting abstract of work in progress without sufficient data.[29] In addition, 1 search result was incomplete but turned out to be a duplicate finding, whereas 5 review articles did not provide new data with regard to olfactory function in patients with AR.[3,30-33] The data from 1 article[34] were included in a later publication, and the latter was used for this review. One article was only a case report,[35] another was an animal study,[36] and 6 others did not report data that would have been useful for this review.[37-42]

Lastly, 2 review articles that were initially considered relevant were not included in the analysis. One of the articles addressed medical treatment of olfactory dysfunction resulting from various underlying pathologies,[43] and the other article reviewed olfactory function in a different form of rhinitis.[44] Neither articles provided relevant data or articles not already identified in the current initial literature search.

After the aforementioned exclusions, 36 articles were selected for final analysis (Fig 1).

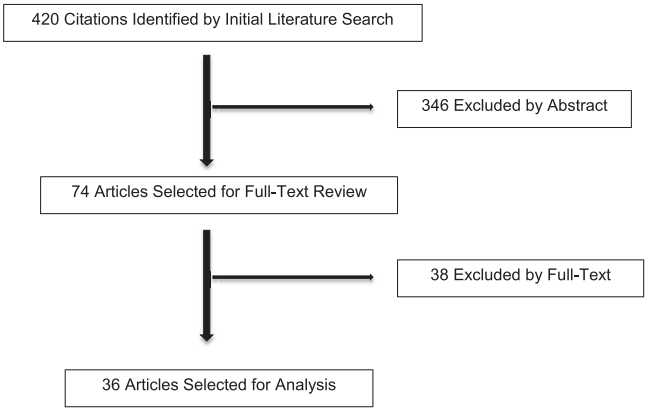

FIG 1. Flowchart showing search results for the systematic review.

EFFECT OF AR ON OLFACTION

Numerous studies indicate that olfaction is affected by inflammatory causes[1,2]; see Doty and Mishra[3] for a review. The frequency and severity of olfactory dysfunction in patients with AR were examined. In the present review the term olfactory dysfunction is used to describe a reduced sense of smell based on patient self-report or quantitative measures. The terms hyposmia and anosmia are restricted to corresponding results of quantitative tests. The most frequently used quantitative tests mentioned in this review are characterized in Table I.[6,7,45-47]

What is the frequency of olfactory dysfunction in patients with AR?

A study by Cowart et al[48] indicated that in 91 patients with AR, 23% exhibited "measured" smell loss. Binder et al[49] showed that 92 (31%) of 293 patients with self-reported symptoms for a period of less than 10 years reported smell impairment. In comparison, 56 (43%) of 130 patients from the same study with allergic symptoms for more than 10 years exhibited olfactory dysfunction. These data indicate that the frequency of olfactory dysfunction increases with the duration of the disorder, although there are no concrete longitudinal data available.

Meltzer et al[50] observed that OTs were within the normal range in 90% of 121 patients with seasonal AR. Chaiyasate et al[51] found that 36% of 434 patients with AR reported smell dysfunction, Di Lorenzo et al[52] found that 24% of 1017 patients with AR reported olfactory dysfunction, and Jareoncharsri et al[53] observed that 11% of 83 patients with AR reported a disturbance in their sense of smell. In a larger sample (n = 770) Binder et al[49] found that 41% of patients with perennial AR and 26% of patients with seasonal AR reported smell dysfunction. Guss et al[54] showed, although in a much smaller group of patients with AR, that 48% of 31 patients had measured olfactory dysfunction. Work by Sivam et al[55] showed that measured olfactory function was normal in 2 of 16, mild-to-moderate dysfunctional in 12 of 16, and anosmic in 2 of 16 patients during the allergy season. Altogether, the data suggest that, depending on the group studied, olfactory dysfunction could occur with a frequency ranging from 10% to 88% (mode range, 20% to 40%). The wide range might be explained by differences in study design, definition, and assessment of olfactory dysfunction and the type of AR studied (see below).

How severe is olfactory dysfunction in patients with AR?

Guilemany et al[56] observed in 49 patients and 60 control subjects that AR had an overall moderate effect on measured olfactory function. Becker et al[57] showed in 72 patients that measured olfactory dysfunction in patients with AR is present but not severe. Additionally, in that study patients with seasonal or persistent AR scored in the normal range on average. Similarly, Olsson et al[58] reported in a study including 10,670 subjects that the prevalence of reduced olfactory function in patients with