The impact of Allergic Rhinitis in clinical practice: An International Survey

D. Passali [1], G.C. Passali[2,3], V. Damiani[4], F.M. Passali[5], C. Cingi[6], S. Di Girolamo[5], G. Ciprandi[7], and International Study Group on Allergic Rhinitis*

[1]International Federation ORL Societies (IFOS) Executive Board members Rome Italy; [2]UOC di Otorinolaringoiatria, Dipartimento Scienze dell'Invecchiamento, Neurologiche, Ortopediche e della testa collo. Fondazione Policlinico Universitario A. Gemelli IRCCS, Roma, Italy; [3]Institute of Otolaryngology, Università Cattolica del Sacro Cuore, Policlinico Agostino Gemelli, Rome, Italy; [4]Medical Deparment, DMG Italy, Pomezia, Italy; [5]Department of Clinical Sciences and Translational Medicine univ Tor Vergata, Rome, Italy; [6]Department of Otorhinolaryngology, Eskisehir Osmangazi University, Eskisehir, Turkey; [7]Consultant allergist, Casa di Cura Villa Montallegro, Genoa, Italy

International Study Group on Allergic Rhinitis: Agius A, Ahluwalia H, Al Abri A, Alho OP, Bachert C, Balaji N, Balsevicius T, Baudoin T, Benghalem A, Bhattarai H, Boci B, Bunnang C, Carvajal JD, Charalambous M, Chen L, Cuilty Siller C, Dimov P, Din MF, Douglas RG, Durham SR, Eloy P, Erdenechuluun B, Felippu Neto A, Fliss DM, Gendeh S, Gerlinger I, Golusinski W, Hadi U, Hasbellaoui M, Heinichen J, Huizing EH, Jenko K, Kamel R, Kawauchi H, Kennedy D, Kern E, Kiesling Calderon V, Kopacheva Barsova G, Landis BN, Lopatin A, Lubbe D, Marakyna-Kibak L, Matuba KMD, Melendez A, Mesbahi A, Metsmaa M, Mladina R, Mosges R, Nassir TH, Negm HMA, Nguyen Thi ND, Nyembue DT, Onerci TM, Pais Clemente M, Papavassiliou AG, Patil NP, Perdomo Flores EA, Plzak J, Rahman HA, Rhee CS, Rodriguez HA, Sacks R, Salaverry F, Sandul A, Sarafoleanu CC, Sarandeses Garcia A, Shukuryan AK, Sicak M, Siguror K, Silva Chacon F, Stankovic M, Stierna LEP, Stott C, Tariq Rafi SM, Talishinskiy A, Tarafder KH, Tong M, Tulebayev RK, Vicente GM, Von Buchwald C, Wagener M, Wang DY, Wardani RS, Yeh TH, Zabolotnyi D.

Abstract Allergic rhinitis (AR) is a frequent disease caused by an IgE-mediated inflammation of the nose and characterized by typical symptoms. Diagnostic workup is directed to document the production of specific IgE (sensitization). Clinical management aims to relieve symptoms, resolve allergic inflammation, use medications, and potentially induce allergen tolerance, using allergen immunotherapy (AIT). The current survey was conducted in 17 International ear nose throat experts using a questionnaire with 20 questions concerning the practical management of AR patients. It was administered in the 2020 summer. The large majority (94%) of participants use the ARIA classification in clinical practice. On average, subjects with suspected AR represent half of the patients who turn to the ENT experts; 80% have the confirmed diagnosis. Most of the experts use both cutaneous and serum assay to document IgE production. Antihistamines are prescribed in 59% of AR patients, intranasal corticosteroids in 69%, non-adrenergic decongestants in 88%, nasal lavage in 88%, and AIT in 22%. About 68% of AR patients had turbinate hypertrophy, which requires surgery in 62% (mostly surgical decongestion). In conclusion, the current International Survey demonstrated that AR is a common disorder worldwide, the diagnostic workup is mainly based on IgE assessment, and the therapeutic approach is also based on non-pharmacological remedies.

Allergic rhinitis (AR) is a type 2 inflammation of the nasal membrane (1). AR is characterized by symptoms, including nasal itching, sneezing, watery rhinorrhea, and nasal obstruction (2). Nasal obstruction depends on allergic inflammation, whereas itching, sneezing, and runny nose ("irritative

Keywords: Allergic rhinitis, Italy, Survey, general population, questionnaire, on the road

Corresponding Author:
Giorgio Ciprandi
Via P. Boselli 5, 16146 Genoa, Italy
e-mail: gio.cip@libero.it

0393-974X (2020)

symptoms) are histamine-associated symptoms (3). AR may be classified considering the duration of symptoms (seasonal and perennial AR) or their persistency and severity (intermittent and persistent mild or moderate-severe AR) according to the ARIA (allergic rhinitis and its impact on asthma) guidelines, mainly concerning the rhinitis control (4).

The diagnosis of AR is based on the demonstration of the production of allergen-specific IgE and the concordance between allergy testing and history, such as the symptom that occurs after the inhalation of the sensitizing allergen (5). Allergen-specific IgE can be measured by cutaneous and/or serologic tests (6).

The International guidelines proposed pharmacological treatments, mainly concerning antihistamines, intranasal corticosteroids, and allergen-specific immunotherapy (AIT), the only disease-modifier treatment still now (5-7). In particular, antihistamines are most effective on "irritative symptoms" (8), whereas intranasal corticosteroids preferably relieve nasal obstruction (9). AIT aims to restore immunologic tolerance toward the causal allergen (10). However, the practical management of AR patients could vary between countries. Therefore, a Survey evaluated the behavior of a group of International ear nose throat (ENT) experts managing AR patients in clinical practice.

MATERIALS AND METHODS

The current survey was performed using a questionnaire administered and completed in 17 Countries, including Albania, Azerbaijan, Belarus, Croatia, Germany, India, Iran, Iraq, Italy, Japan, Kazakhstan, Macedonia, Malaysia, Mexico, Moldova, Philippines, Romania, and South Chorea. The International Survey was performed, using a questionnaire, in August 2020. The questionnaire included 20 queries, reported in detail in Table I. The analysis of the data was descriptive. Data were expressed as absolute numbers or frequency.

RESULTS

Globally, 17 ENT international experts participated in the survey, equally distributed along with the world. The results are reported in detail in Table I. The large majority (94%) of participants use the ARIA classification in clinical practice. All participants believe that the AR prevalence was increasing in the last year. About 50% of patients referring to ENT clinics have the suspect of AR; in 80.5% of them, the AR diagnosis is confirmed. Skin prick tests and serum IgE assay are performed in most patients (71%). Quality of life is measured in about 80% of ENT clinics. However, only one expert considers nasal cytology in the AR workup. The most prevalent symptoms in AR patients are those "histamine-dependent" (82%), whereas inflammation-dependent complaints affect 71%.

Antihistamines are prescribed in 59% of AR patients, intranasal corticosteroids in 69%, non-adrenergic decongestants in 88%, nasal lavage in 88% (70.5% using hypertonic saline solution and 23.5% isotonic one), and AIT in 22%. The 82% of ENT experts consult an allergist in selected cases, whereas 47% consult a pulmonologist in selected cases. About 68% of AR patients had turbinate hypertrophy, which requires surgery in 62% (mostly surgical decongestion 60% or coblation 40%).

DISCUSSION

Allergic rhinitis is a disease affecting many people. AR is usually classified using the ARIA criteria, such as considering the symptoms' duration and severity. Moreover, its prevalence is unanimously considered increasing. Consistently, the patients with suspected AR represent about half of the people referring to ENT clinics. This outcome is relevant and underlines the social importance of AR in the healthcare scenario. ENT experts are successful in confirming AR diagnosis in most patients. This outcome could depend on professional expertise and proper workup. Namely, 71% of participants consider both cutaneous and serologic assessment of specific IgE. This way allows us to obtain optimal diagnostic performance. Quality of life is a particular aspect that deserves adequate attention in managing AR patients (11). Accordingly, three-quarters of ENT experts consider QoL in AR patients. Instead, nasal cytology is very rarely used in clinical practice.

From a pathophysiological point of view, AR

symptoms may depend on two main pathogenic mechanisms, such as involving mediators, essentially histamine, or cellular pathways of allergic inflammation (12,13). The expert panel believes that histamine-dependent symptoms are preponderant in AR patients, even though inflammation-associated complaints assume an essential remark. Consequently, antihistamines and intranasal corticosteroids are the most commonly prescribed medications as they target AR's pathophysiological events.

Table I. *Questionnaire with answers*

QUESTION	ANSWER
Do you prefer to classify Allergic Rhinitis using the classical definition (Seasonal and Perennial) or the ARIA one (Intermittent and Persistent)?	SAR-PAR 6% ARIA 94%
Do you believe that the prevalence of AR is increasing in the last years?	Yes 100%
Which is the percentage of patients visited in your clinic with suspected AR?	48.5%
Which is the percentage of patients with suspected AR who have the diagnostic confirm of AR?	80.5%
Which method do you prescribe to assess allergen-specific IgE	Skin prick test 29% Both cutaneous and serologic assay 71%
Do you consider nasal cytology in the AR workup?	No 94%
Which are the most relevant symptoms in your patients?	Histamine-dependent (Itching, Sneezing, Watery rhinorrhea) 82% Inflammation-dependent (Nasal Obstruction) 71%
Which is the percentage of your patients treated with oral antihistamines?	59%
Which is the percentage of your patients treated with intranasal corticosteroids?	69%
Which is the percentage of your patients treated with the combination of oral antihistamines plus intranasal corticosteroids?	30%
Which is the percentage of your patients treated with allergen-specific immunotherapy?	22%
Which is the percentage of your patients treated with decongestants?	24%
Do you prescribe non-adrenergic decongestants (e.g., natural compounds, osmotic agents)?	88%
Do you prescribe nasal lavage with a saline solution?	Yes with isotonic saline 23.5% Yes, with hypertonic saline. 70.5% No 12%
Do you consider the assessment of Quality of Life in AR patients?	Yes 76.5%
Do you consult an Allergist?	Never 18% In selected cases, 82%
Do you consult a Pulmonologist?	Never 53% In selected cases, 47%
Which is the percentage of patients with turbinate hypertrophy?	68%
Which is the percentage of patients who need surgery for turbinate hypertrophy?	62%
Which surgical technique do you prefer to treat turbinate hypertrophy?	Surgical decongestion 60% Coblation 40%

Unfortunately, AIT is scarcely used in AR. This fair use could depend on the long duration and costs. Notably, adrenergic decongestants are barely prescribed. The relief provided by adrenergic agents has a short duration, but overall, these agents are also burdened with severe side effects and can easily induce abuse and addiction. For these reasons, non-adrenergic compounds are prevalent in ENT clinics. Many products are available, including a medical device containing glycyrrhetic acid and mannitol. This product exerts both anti-inflammatory effects and osmotic activity and, in randomized clinical trials on adult and paediatric patients with allergic rhinitis, resulted equivalent to mometasone furoate in symptoms relief, with no reported adverse effects (14,15). Also, nasal lavage is a frequent remedy for AR patients. Hypertonic saline solution is preferred to isotonic, probably because the first may also exert decongestant and anti-inflammatory effects (16). Saline irrigation could provide a cheap, safe, and acceptable alternative to intranasal steroids and antihistamines (17). Concerning the consultation with other specialists, allergists are consulted more frequently than pulmonologists. It depends on the allergic nature of the disease.

Turbinate hypertrophy (TH) is very common in AR patients, affecting 68% of patients. TH reflects the intense inflammatory reaction and may be associated with inadequate response to decongestants (18). Namely, it has been proposed that patient non-responder to decongestants should be considered a candidate for surgery, whereas patients responder to decongestants could be initiated for medical therapy (19). Moreover, different surgical techniques are available in clinical practice (20). Interestingly, surgery could be considered the fourth way to treat AR besides prevention, medications, and AIT (21). Surgical decongestion and coblation, such as high frequencies, are the most used (22). In this regard, the panel of experts believes that surgical decongestion is more common than coblation.

The outcomes of the current International survey are consistent with another recent survey (23). In particular, the previous survey provided evidence that the prevalence of AR was between 15%–25%, asthma, sinusitis, conjunctivitis, and nasal polyposis were frequent comorbidities, AIT was prescribed for both perennial and seasonal allergens (32.69%) via sublingual swallow (46.15%) and subcutaneous (32.69%) routes. The most prescribed drugs were intranasal corticosteroids (86.54%) and oral H1-antihistamines (82.69%).

The current survey has some limitations, including the cross-sectional design, the lack of a methodologically correct definition of the questions, and the answers based only on experts' opinions. On the other hand, the strength of this study is based on the worldwide origin of participants. Further issues to be addressed could be the role of biologics in patients with AR and other allergic comorbidities as recently advanced (24). In conclusion, the current International Survey demonstrated that AR is a common disorder worldwide, the diagnostic workup is mainly based on IgE assessment, and the therapeutic approach is also based on non-pharmacological remedies.

REFERENCES

1. Krempski JW, Dant C, Nadeau KC. The origins of allergy from a systems approach. Ann Allergy Asthma Immunol. 2020; S1081-1206.
2. Ciprandi G, Cirillo I, Vizzaccaro A, Milanese M, Tosca MA. Nasal obstruction in patients with seasonal allergic rhinitis: relationships between allergic inflammation and nasal airflow. Int Arch Allergy Immunol 2004; 134:34-40.
3. Ciprandi G, Cirillo I, Klersy C, Marseglia GL, Caimmi D, Vizzaccaro A Nasal obstruction is the key symptom in hay fever patients. Otolaryngol Head Neck Surg. 2005; 133(3):429-35.
4. Valero A, Del Cuvillo A, Navarro AM, Colás C, Sastre J, Mullol J. Validation of the ARIA items to assess allergic rhinitis control (ARIA-C). Allergy. 2020 (in press)..
5. Dykewicz MS, Fineman S. Executive Summary of Joint Task Force Practice Parameters on Diagnosis and Management of Rhinitis. Ann Allergy Asthma Immunol 1998; 81:463-8.
6. Wise SK, Lin SY, Toskala E, Orlandi RR, Akdis CA, Alt JA, et al. International Consensus Statement on Allergy and Rhinology: Allergic Rhinitis. Int Forum

Allergy Rhinol 2018; 8(2):108-352.
7. Bousquet J, Schünemann HJ, Togias A, Bachert C, Erhola M, Hellings PW, et al. Next-generation Allergic Rhinitis and Its Impact on Asthma (ARIA) guidelines for allergic rhinitis based on Grading of Recommendations Assessment, Development and Evaluation (GRADE) and real-world evidence. J Allergy Clin Immunol. 2020; 145(1):70-80.e3.
8. Ciprandi G, Cosentino C, Milanese M, Mondino C, Canonica GW Fexofenadine treatment reduces nasal congestion in allergic rhinitis Allergy 2001; 56:1068-70.
9. Bousquet J, Cezmi A, Jutel M, Bachert C, Klimek L, Agache I, et al. Intranasal corticosteroids in allergic rhinitis in COVID-19 patients: an ARIA-EAACI statement. Allergy 2020 (in press).
10. Kucuksezer UC, Ozdemir C, Cevhertas L, Ogulur I, Akdis M, Akdis CA. Mechanisms of allergen-specific immunotherapy and allergen tolerance. Allergol Int. 2020; S1323-8930.
11. Ciprandi, G, Klersy C, Cirillo I, Marseglia GL. Quality of Life in Allergic Rhinitis: relationship with clinical, immunological, and functional aspects. Clin Exp Allergy 2007; 37(10):1528-35.
12. Berghi NO, Dumitru M, Vrinceanu D, Ciuluvica RC, Simioniuc-Petrescu A, Caragheorgheopol R, Tucureanu C, et al. Relationship between chemokines and T lymphocytes in the context of respiratory allergies (Review). Exp Ther Med. 2020; 20:2352-60.
13. Breiteneder H, Peng YQ, Agache I, Diamant Z, Eiwegger T, Fokkens WJ, et al. Biomarkers for diagnosis and prediction of therapy responses in allergic diseases and asthma. Allergy. 2020 (in press).
14. Mansi N, D'Agostino G, Scirè AS, Morpurgo G, Gregori D, Gulati A, Damiani V. Allergic Rhinitis in Children: A Randomized Clinical Trial Targeted at Symptoms. Indian J Otolaryngol Head Neck Surg. 2014 Dec;66(4):386-93.
15. Gariuc L, Sandul A, Rusu D, Passali D, Bellussi LM, Damiani V, et al. A comparison between mometasone furoate nasal spray and intranasal glycyrrhetic acid in patients with allergic rhinitis: a preliminary study in clinical practice. Acta Biomedica 2020; 91(1-S):65-72.
16. Gutiérrez-Cardona N, Sands P, Roberts G, Lucas JS, Walker W, Salib R, et al. The acceptability and tolerability of nasal douching in children with allergic rhinitis: A systematic review. Int J Pediatr Otorhinolaryngol. 2017; 98:126-135.
17. Head K, Snidvongs K, Glew S, Scadding G, Schilder AG, Philpott C, et al. Saline irrigation for allergic rhinitis. Cochrane Database Syst Rev. 2018; 6(6):CD012597.
18. Ciprandi G, Tosca MA, Gallo F, Passali GC, Ameli F. Turbinate hypertrophy in children with allergic rhinitis: clinical relevance. Acta Biomed. 2020; 91(1-S):43-47.
19. Passali D, Lauriello M, De Filippi A, Bellussi L. Comparative study of most recent surgical techniques for the treatment of the hypertrophy of inferior turbinates. Acta Otorhinolaryngol Ital. 1995; 15(3):219-28.
20. Sommer F, Lindemann J, Scheithauer MO, Hoffmann TK, Veit JA. Nasal turbinate surgery. HNO. 2017; 65(5):443-456.
21. Chhabra N, Houser SM. Surgery for allergic rhinitis. Int Forum Allergy Rhinol. 2014; 4 Suppl 2:S79-83.
22. Passali D, Loglisci M, Politi L, Passali GC, Kern E. Managing turbinate hypertrophy: coblation vs. radiofrequency treatment. Eur Arch Otorhinolaryngol. 2016; 273(6):1449-53.
23. Passali D, Cingi C, Staffa P, Passali F, Muluk NB, Bellussi ML. The International study of the allergic rhinitis survey: outcomes from 4 geographical regions. Asia Pac Allergy 2018; 8(1):e7.
24. Meng Y, Wang C, Zhang L. Advances and novel developments in allergic rhinitis. Allergy 2020 (in press).