

Allergic rhinitis in Italy: epidemiology and definition of most commonly used diagnostic and therapeutic modalities

La rinite allergica in Italia: caratteristiche epidemiologiche e definizione delle modalità diagnostico-terapeutiche più utilizzate

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Parole chiave

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Summary

Allergic rhinitis is classically defined as an IgE-mediated inflammation of nasal mucosa, characterised by nasal obstruction, rhinorrhea, sneezing and nasal itching. It is certainly a high-prevalence disease and an important social and medical problem in many industrialised Countries, affecting about 20% of the general population; moreover, it is diagnosed with increasing frequency, both in adults and children in many developing countries. In view of the high medical and social costs, a correct diagnostic approach to allergic rhinitis is a fundamental need for the otorhinolaryngologist, also considering the severe complications (asthma, rhinosinusitis, rhino-otitis, rhinosinusoidal polyposis) which could develop if this disease is not recognised and adequately treated in its early phases. In order to evaluate not only the present epidemiological characteristics of allergic rhinitis in Italy but also the most commonly used diagnostic and therapeutic approaches in the management of this disease, 145 Italian otorhinolaryngologists were selected to take part in the investigation. Each was invited to complete a questionnaire, divided into 8 different sections, to be answered according to their daily clinical practice. The significance of the results has been compared with those of the international samples comprised in the ARIA Document and in the epidemiologic survey of the Standing Committee on Rhinology and Allergy of the International Federation of Otorhinolaryngological Societies. A critical analysis of these data leads to some interesting epidemiological and therapeutic considerations.

Introduction

Allergic rhinitis (AR) is classically defined as an IgE-mediated inflammation of the nasal mucosa, characterised by one or more of the following symptoms: nasal obstruction, rhinorrhea, sneezing and nasal itching¹

Other symptoms may also be present, such as, for example, cephalalgia, hyposmia and conjunctival symptoms.

Riassunto

La rinite allergica è classicamente definita come una flogosi IgE-mediata della mucosa nasale, caratterizzata da ostruzione nasale, rinorrea, starnutazione e prurito nasale. Essa è sicuramente una patologia ad alta prevalenza ed un importante problema sociale in molte nazioni industrializzate, interessando circa il 20% della popolazione generale; inoltre, essa è sempre più frequentemente diagnosticata in bambini ed adulti in molte Nazioni in via di sviluppo. Alla luce del suo alto costo medico e sociale, un corretto approccio diagnostico alla rinite allergica è una esigenza fondamentale per l'otorinolaringoiatra, anche in considerazione delle temibili complicanze (asma, rinosinusiti, rino-otiti, poliposi rinosinusale) che possono insorgere se questa patologia non viene riconosciuta ed adeguatamente trattata nelle fasi iniziali. Al fine di valutare le attuali caratteristiche epidemiologiche della rinite allergica nel nostro Paese e le modalità diagnostiche e terapeutiche più utilizzate per il management di questa patologia, abbiamo selezionato 145 otorinolaringoiatri, operanti sul territorio italiano. Ad essi abbiamo amministrato un questionario, suddiviso in 8 sezioni tematiche, a cui rispondere in base alla loro esperienza clinica quotidiana. La significatività dei nostri risultati è stata inoltre comparata con quella delle casistiche internazionali incluse nel documento ARIA e nell'indagine epidemiologica effettuata dallo Standing Committee on Rhinology and Allergy dell'IFOS (International Federation of Otorhinolaryngological Societies). L'analisi critica dei nostri dati conduce ad alcune interessanti considerazioni epidemiologiche e terapeutiche.

AR is a high prevalence disease and a relevant social problem in many industrialised Countries, affecting about 20% of the general population²; moreover, it is increasingly diagnosed in children and adults in many developing Countries³.

Based upon the duration of the symptoms and the mode of exposure to allergens, AR is classically defined as non-seasonal (perennial) and seasonal⁴. Perennial AR is mainly caused by exposure to dust mites or animal danders, while the seasonal type is

more frequently related to pollen allergens, such as Graminaceae, Parietaria, ambrosia, olive-tree, cypress, etc.

A recent WHO document entitled "Allergic Rhinitis and its impact on Asthma" (ARIA)⁵, has, in part, modified this classification; in particular, the Document suggests that the old terms "seasonal" and "non-seasonal" should be replaced by the terms "intermittent" (< 4 days a week or < 4 weeks) and "persistent" (> 4 days a week or > 4 weeks).

Leaving aside problems related to terminology, AR is still one of the most widespread chronic inflammatory diseases in the world.

In the European Community, for example, the incidence of AR ranges between 11% and 20% of the adult population in most countries^{6,7}, with the exception of Belgium and Russia where percentages are lower (5-8%)⁸.

The incidence in Latin America is comparable to European data, with the exception of Mexico and Bolivia, where about half the population is affected by allergic nasal disease⁹.

Also in Asia and Oceania, the incidence of the disease is extremely high; an epidemiological evaluation of the situation in Africa is not feasible since the data collected are not reliable¹⁰.

It is not surprising, then, that the management of this disease results in an annual expenditure of about 1.9 billion US Dollars in USA and of 1.5-2 billion Euro in the European Community¹¹.

Due to these high social costs, a correct diagnostic approach to AR is essential for the otorhinolaryngologist, also bearing in mind the risk of severe complications (asthma, rhinosinusitis, rhino-otitis, rhinosinusal polyposis) that could develop if the disease is not recognised and appropriately treated, in the early phases.

In the light of these considerations, it is, in our opinion, mandatory: 1. to improve both our diagnostic and therapeutic skills in the management of AR; 2. to analyse the recent epidemiological modifications in this disease (and possible complications) in Italy, and 3. to define the state of the art of the most commonly used diagnostic and therapeutic instruments available, in daily clinical practice.

Materials and Methods

To evaluate the current epidemiological features of AR in Italy and the most common diagnostic and therapeutic approaches used in the management of this disease, 145 Italian otorhinolaryngologists were selected to take part in the investigation. Each received a quiz-type (or open-ended answer) questionnaire, divided into 8 different sections, which

they had to answer, according to their daily clinical practice.

The various sections of the questionnaire focused on: evaluation of the percent distribution of AR prevalence in the out-patient population of each one of them (Section 1); evaluation of the allergens most frequently responsible for the disease (Section 2); diagnostic approach used to evaluate allergic sensitivity (Section 3); definition of the changes in the incidence of the disease over the last ten years (Section 4) and on the causes that could have triggered these changes (Section 5). Colleagues were also asked to define the demographic characteristics of their allergic out-patient population (Section 6) and the therapeutic approaches most commonly used by them in the management of AR of those classified as efficacious in the treatment of AR referred to in the ARIA⁵ Document (Section 7). Finally, the last section of the questionnaire aimed to evaluate the frequency of onset of complications (specifically asthma, rhinosinusitis, rhino-otitis, rhinosinusal polyposis) of AR (Section 8).

A statistical analysis was made of the data obtained, comparing the specific probability according to each class of data and the definition of the specific confidence intervals; significance of the results were then compared with those of the international samples, presented in the ARIA Document⁵ and with the epidemiological research made by the Standing Committee on Rhinology and Allergy of the International Federation of Otorhinolaryngological Societies (IFOS)¹⁰.

Results

From an analysis of the 145 questionnaires, a variable number of answers were considered reliable for evaluation, depending on the specific Section under examination.

Thus the analysis is reported of the results of all 145 questionnaires referring to Sections 3, 4, 5, 7 and 8, of 116 questionnaires for Section 1 and of 126 questionnaires for Section 6.

The present report, does not include the results referring to Section 2 of the questionnaire, on account of the non-homogeneity and non-reliability of the data obtained. The data not included in the analysis have been discarded exclusively due to the lacunae (and sometime total absence) of these data.

The most relevant results emerging from this epidemiological analysis are summarised in Figures 1-5 and Tables I, II.

As far as concerns the evaluation of the epidemiological evolution of AR in Italy (Fig. 1), according to 137 of the 145 taking part in the study, the

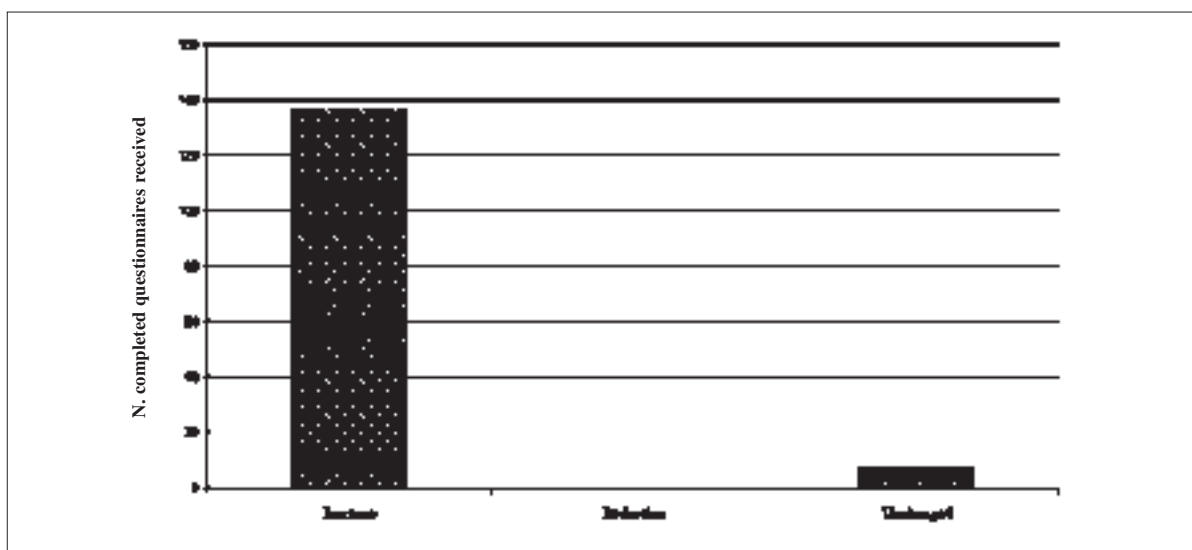


Fig. 1. Epidemiologic evolution of allergic rhinitis in Italy.

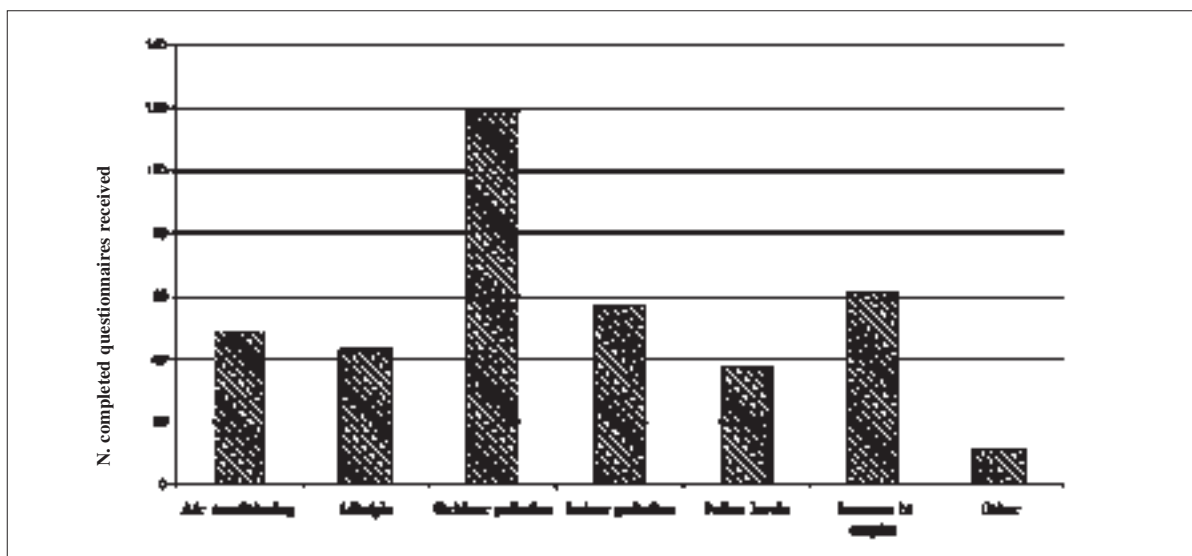


Fig. 2. Causes of increased prevalence of allergic rhinitis.

prevalence of this disease had steadily risen over the last 10 years whilst the remaining 8 evaluated this phenomenon as stationary; none reported the prevalence of AR as decreasing.

From an analysis of the different percentages reported of seasonal or perennial type of AR, in relation to the out-patient population (Fig. 3), the latter seems to be the most frequent type, even if the frequency differences between the two groups failed to reach statistical significance ($p > 0.5$). Prevalence of the perennial forms over the seasonal types was observed not only in South America but also in Asiatic Countries³

⁹. With regard to the demographic and social characteristics of AR, in our sample (Table I), there does not appear to be any difference in frequency between males and females.

The age class most affected is that between 12 and 30 years ($p < 0.005$) representing $>75\%$ of the allergic population in 21 centres, and $\geq 50\%$ of the population in 73; moreover, almost their entire activity, in 3 of the ENT specialists, referred to patients in this age class.

The overall probability of a patient presenting AR belonging to this age-class is $37.9 \pm 6.6\%$.

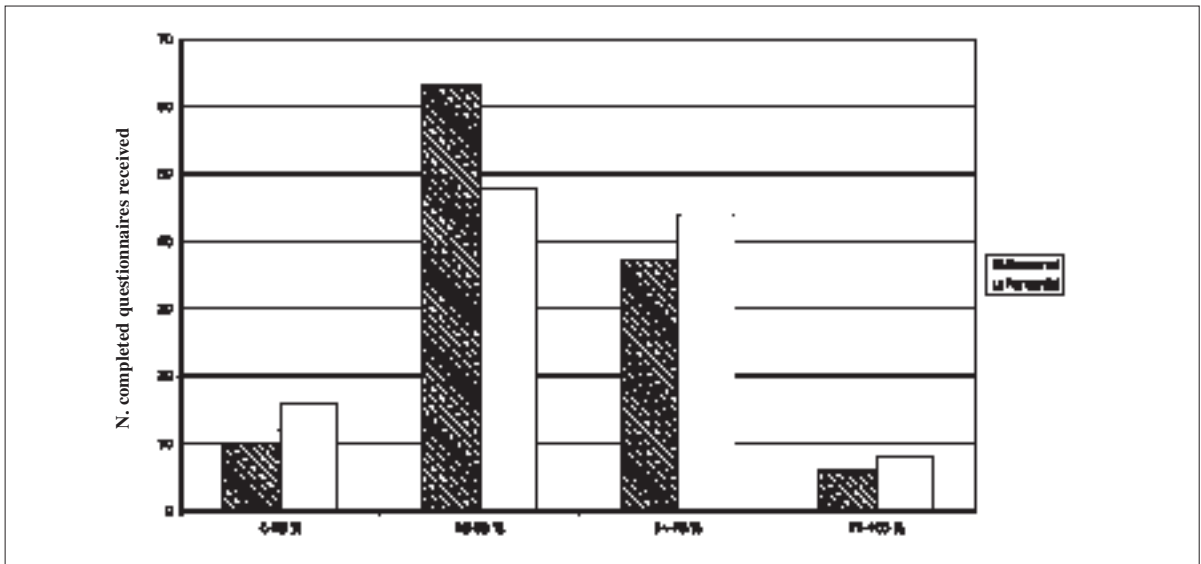


Fig. 3. Prevalence of allergic rhinitis.

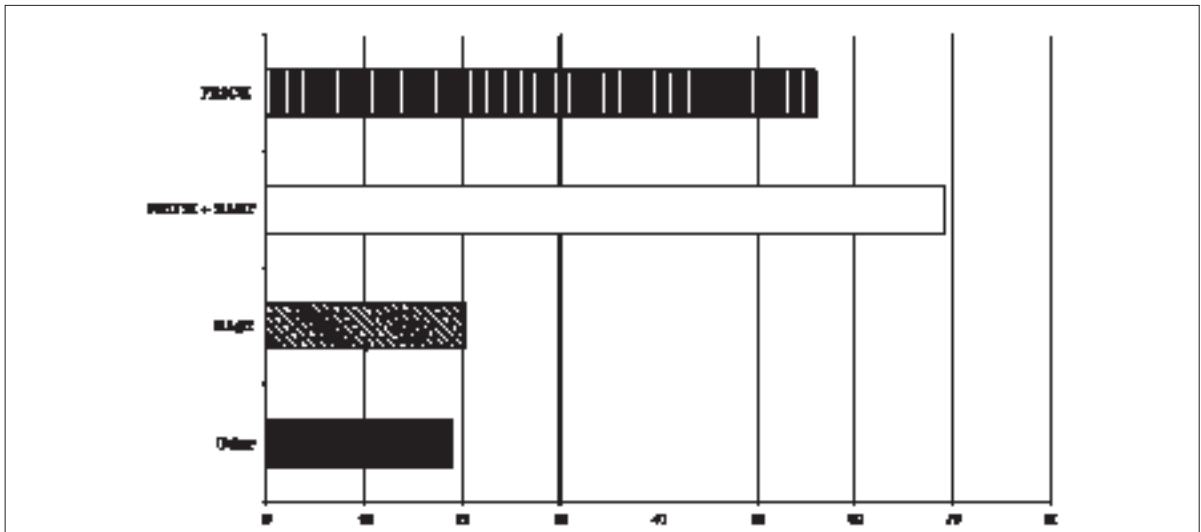


Fig. 4. Diagnostic approach.

The second age-group, according to order of frequency, ranges between 31 and 60 years, accounting for 75% or 50% of the clinical activity of, respectively, 8 and 55 of the specialists taking part. Reports in the literature, and, in particular, the international epidemiological surveys comprised in the ARIA Document of the WHO⁵, confirm these epidemiological results. Focusing attention on population stratification, in relation to the residence, the presence of this disease is

evenly distributed throughout the country, the centre of the city and the suburban zone of the city, albeit with a statistically consistent prevalence in the latter class with respect to the other two ($p < 0.05$). Moreover, from an analysis of this sample, it seems that as far as concerns social class, AR more frequently affects the middle class than the high/low classes, with a statistically significant difference ($p < 0.05$). In our opinion, this finding depends on the larger

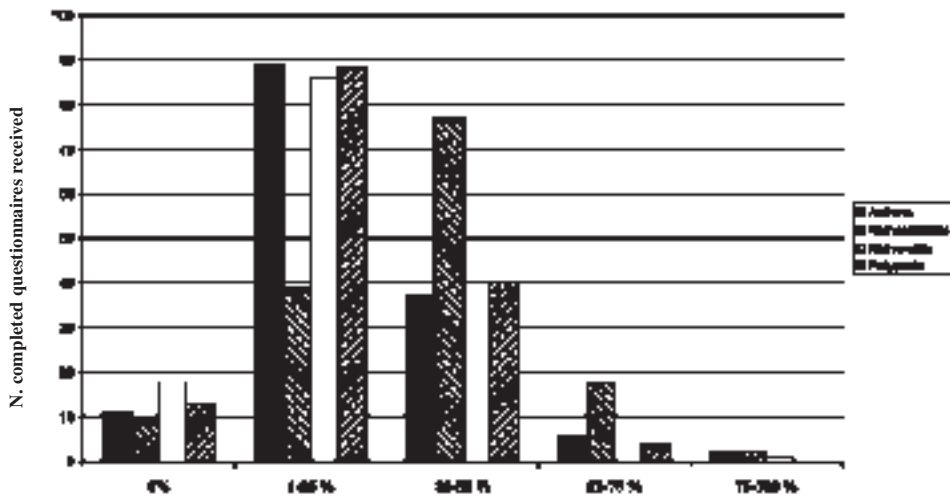


Fig. 5. Frequency of complications.

Table I. Epidemiologic and demographic data.

	0%	1-25%	26-50%	51-75%	76-100%
Sex					
Male	0	2	86	34	1
Female	1	5	82	35	0
Age (years)					
<12	4	74	36	9	
12-30	2	24	73	21	3
31-60	4	56	55	8	
>60	35	82	6		
Residence					
Countryside	16	56	40	9	2
City (centre)	4	21	78	15	5
City (suburbs)	16	19	72	12	4
Social class					
High	16	43	58	5	1
Medium	10	5	74	27	7
Low	13	48	58	4	

size of the sample referring to the first social class considered i.e., middle class, more than on an effective epidemiological difference.

In the present sample, AR was complicated by onset of asthma in <25% of cases in 89 infirmaries-centres and in $\leq 50\%$ of the cases in 37.

The frequency of rhinosinusal polyposis onset thus obtained can be overlapped to the previous one: the disease resulted in complications in 1-25% of the

cases in 88 centres and in 26-50% in the other 40. The most frequent complication observed, in these AR patients, was onset of rhinosinusitis: 39 specialists of those interviewed, indeed, reported a frequency of onset of 26-50% while 18 reported an onset frequency of 51-75% (Fig. 5).

Data reported by the ENT specialists, concerning medical treatment, the type and frequency of use, are shown in Table II.

Table II. Treatment (frequency of use).

Treatment	>70%	30-70%	<30%	<10%	Never
Avoiding allergens	54	33	29	16	13
Systemic antihistamines	59	65	13	7	1
Topical antihistamines	13	47	25	38	22
Chromones	4	17	32	40	52
Systemic corticosteroids	4	23	49	50	19
Topic corticosteroids	60	58	16	8	3
Systemic immunotherapy	14	38	42	30	21
Local immunotherapy	3	7	33	40	62
Nasal decongestants	17	27	42	32	27
Others	6	1	7	5	126

Discussion

Critical analysis of the present data leads to some interesting epidemiological and therapeutic considerations.

AR is constantly increasing in Italy, in all age-classes.

This finding is confirmed in the international literature; the ISAAC Study (International Study of Asthma and Allergies in Childhood)¹², involving 155 centres in 56 Countries, the results of which were reported in the ARIA Document showed, in fact, that the overall prevalence of AR (limited to the 13-14-year-old age class increased from 2% to 39% ($p < 0.05$).

Moreover, Linneberg et al., in a recent study (also included in the ARIA Document), has shown that the prevalence of AR in Denmark, in young adults (aged 15-41), increased from 25% to 32% during the 1990-1998 period ($p < 0.05$)¹³.

Finally, another large epidemiological investigation carried out by the Standing Committee on Rhinology and Allergy of the IFOS, involving 41 Countries, over the 1993-1996 period, led to comparable conclusions¹⁰.

The reasons for this increased prevalence are due, in the opinion of the Colleagues interviewed, to the increase in atmospheric pollution (outdoor) and to the number of atopic subjects; moreover, an important contribution to the increase in this disease would appear to depend on the more widespread use of air-conditioning, on the bad habits in lifestyle and on the increase in indoor pollution (Fig. 2).

The epidemiological survey of the IFOS Standing Committee on Rhinology and Allergy confirms that causal factors, also identified in the Italian population, play an important role in the genesis of the pathology even in other geographic contexts; added to these factors is the impact of global warming on the annual pollen count¹⁰.

Other interesting considerations emerge from the definitions of the diagnostic methodology most frequently adopted by those interviewed to confirm the suspected allergic sensitisation (Fig. 4): in 56 centres, it is routine practice to use only allergy skin tests (PRICK test), in 20, a second level test is used, such as the serum specific IgEs (RAST), while in 69 an association of both tests is preferred, for safety and diagnostic reasons.

Moreover, of those interviewed, 19 reported that other diagnostic methods were associated with the PRICK or RAST test, such as the nasal provocation test (NPT), eosinophil count or the degranulation test for mastocytes.

The general awareness is evident, in our opinion, within the medical sample interviewed, of the need for early and timely diagnosis of this important disease, also in the light of the severe complications that may ensue. Awareness of the absolute need to commence treatment in the early phases of the natural course of the disease is recognised in the wider use of many integrated diagnostic techniques, aimed at increasing a more accurate clinical picture.

Examining the frequency of onset of complications, it is worthwhile stressing that, in the present sample, the total overall probability of allergic patients developing asthma is $21.5 \pm 3.4\%$.

This result is confirmed also by the ARIA document: Leynaert et al., in fact, showed that AR represents an independent risk factor for the development of asthmatic disorders ($p < 0.001$). In patients presenting AR studied here, the prevalence of this complication was approximately 20%¹⁴: thus, in relation to the percent risk of developing this complication, there is no statistically significant difference between Leynaert's survey and findings in the present report ($p = 1$).

Finally, focusing on the therapeutic protocols most frequently adopted by those interviewed (Table II), of interest is the "therapy" of the avoiding allergens, which is useful since it allows the operator to eliminate the

cause without the need of drugs. This therapy is used as a first approach by 54 centres in 70% of the patients, while 33 centres use it in 30 to 70% of cases. Systemic antihistamines are widely used, being prescribed very frequently (about 70% of patients) by 59 of those interviewed and frequently (30-70% of patients) by 65.

On the contrary, topical antihistamines have not been widely accepted; in fact, even if 47 of those interviewed prescribe them frequently (30-70% of patients), this category of drugs is never prescribed in 22 centres or seldom prescribed (<10% of patients) in 38 centres.

Chromones are an even less widely prescribed, if compared to topical antihistamines. In fact they are never prescribed in 52 centres; moreover, another 40 colleagues refer to prescribing them in <10% of their patients.

It is now proven that corticosteroids modify the mechanisms of allergic inflammation in many ways. Specifically, they can inhibit or reduce the release of lysosomal enzymes, inhibit the proliferation and migration of inflammatory cells, inhibit the synthesis of the arachidonic acid by-products (prostaglandins, thromboxanes, leukotrienes), reduce capillary and cellular permeability.

Moreover, corticosteroids can inhibit or reduce IgE production, blocking the allergic reactions at onset¹⁵.

In agreement with data in the literature, the doctors interviewed referred to wide use of this kind of drug, especially formulations for local use; these drugs have the advantage of inducing, with the same local rhinosinusual effectiveness, scanty or null systemic side-effects if compared to systemic diffusion formulations.

Specifically, 60 of those interviewed reported to prescribe topical corticosteroids in >70% of their patients while 58 prescribe this drug in 30-70% of cases.

At present, there is only one treatment regimen for AR that can be defined as aetiological: specific hyposensitising immunotherapy. It consists in giving progressively increasing doses of the allergen to which the patient is sensitised.

A recent meta-analysis showed the great efficacy of this therapy in reducing specific symptomatology and interfering with the natural history of the disease and also development of complications¹⁶.

The main limits of this treatment are long duration and applicability in selected categories of patients. Systemic immunotherapy has very frequently been used (>70% of cases) and frequently (30-70% of cases) only by 14 and 38 of those interviewed, respectively; moreover, 21 of these reported never having used this treatment.

Together with systemic administration, the nasal spray formulation or oromucosal absorption formulation have been proposed since the early 1990s. These forms of administration, are to be preferred, nowadays, due not only to the substantial absence of side-effects but also to the optimal compliance on the part of the patients.

Local immunotherapy, recently introduced into clinical practice, is still slow in becoming part of the routine therapeutic protocol used by the majority of the otorhinolaryngologists; in fact, 62 of those interviewed reported that they do not use this form of therapy while another 4 seldom use it (<10%).

Nasal decongestants act by stimulating the α -adren-ergic receptor of the mucosa of the upper airways, which results in vasoconstriction of the vessels of the nasal mucosa; their use should be limited to short periods of treatment, since extended use could lead to paradox congestion¹⁷; in our sample, more than half of those interviewed use this treatment in <30% of cases.

Finally, only 7 of the Colleagues who received the questionnaire reported associating the therapies described here with other treatments such as nasal washes or salt-bromide-iodic inhalation therapy.

In conclusion, this epidemiological survey shows that in Italy AR represents, in accordance with data emerging from similar surveys made in several European and extra-European Countries^{3 5 7-10}, a phenomenon in continuous increase over the last 10 years. Moreover, on account of its evolutionary peculiarities, appropriate diagnostic and therapeutic management are mandatory.

Finally, frequency of the onset of complications of AR in our sample, when compared with the European and International data^{5 10}, can be interpreted as an indirect index of the effectiveness of the therapeutic and diagnostic instruments used by the otorhinolaryngologists interviewed.

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