

Allergic Rhinitis: keys for the clinician

Rinitis Alérgica: claves para el clínico

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Abstract: Allergic rhinitis (AR) and asthma are the most common inflammatory diseases of the airways. According to the review of the literature, there is a prevalence of AR of 10-40% worldwide. AR is defined as a type I allergic disease caused by immunoglobulin E mediated inflammation. The symptoms include nasal congestion, watery rhinorrhea and sneezing. In most cases it is accompanied by ocular symptoms like ocular redness, tearing and itchy eyes. AR can have an influence on the quality of life in patients, for example: sleep disturbances, fatigue, irritability, depression, also affect the attention, learning and memory deficits. The classification of AR is seasonal AR, perennial AR, other classification is by duration of symptoms, like intermittent, persistent, also a severity classification, based on disturbances in quality life, proposed by the Allergic Rhinitis and Its Impact on Asthma (ARIA). The first steps in the diagnosis are the clinical history and physical examination of the patient. Also, the diagnosis can include laboratory tests like skin prick test and the determination of immunoglobulin E levels in serum. In the first line of the treatment there is the no pharmacologic changes in the patient's life, emphasizing the avoidance of contact between the patient and the allergen, and the pharmacological treatment are the second-generation antihistamines, inhaled glucocorticoids and immunotherapy, also alternative treatments can be used like acupuncture, ginger extract and probiotic therapy. Allergic rhinitis represents a limitation in the daily activity of those affected, it affects their quality of life, interferes with their ability to sleep, as well as their life at work and school.

Keywords: Allergic rhinitis, allergen, allergy, IgE, immunoglobulin E.

Resumen: La rinitis alérgica (RA) y el asma son las enfermedades inflamatorias más comunes de las vías respiratorias. De acuerdo a la revisión de la literatura existe una prevalencia de RA del 10-40% en todo el mundo. La RA se define como una enfermedad alérgica de tipo I causada por una inflamación mediada por la inmunoglobulina E. El conjunto de estos síntomas de la RA incluye congestión nasal, rinorrea acuosa y estornudos. En la mayoría de los casos se acompaña de síntomas oculares como el enrojecimiento ocular, lagrimeo y picor de los ojos. La RA puede influir en la calidad de vida de los pacientes, por ejemplo, en las alteraciones del sueño, la fatiga, la irritabilidad, la depresión, también afecta a la atención, el aprendizaje y los pacientes pueden sufrir déficit de memoria. La clasificación de la RA es estacional, perenne, existe una

clasificación por la duración de los síntomas como intermitente, persistente, también existe una clasificación de la gravedad, basada en las perturbaciones en la calidad de vida, propuestas por el Allergic Rhinitis and Its Impact on Asthma (ARIA). El primer paso en el diagnóstico es la historia clínica y la exploración física del paciente. El diagnóstico también puede incluir pruebas de laboratorio como la prueba de punción cutánea y los anticuerpos de inmunoglobulina E en suero. La primera línea de tratamiento son los cambios no farmacológicos en la vida del paciente, haciendo hincapié en evitar el contacto del paciente con el alérgeno, y el tratamiento farmacológico son los antihistamínicos de segunda generación, los glucocorticoides inhalados y la inmunoterapia, también se pueden utilizar tratamientos alternativos, como la acupuntura, el extracto de jengibre y la terapia probiótica. La rinitis alérgica representa una limitación en la actividad diaria de los afectados, desde su calidad de vida, interfiere con la capacidad de dormir, así como en el trabajo y la escuela.

Palabras clave: Rinitis alérgica, alérgeno, alergia, IgE, inmunoglobulina E.

INTRODUCTION

Atopic syndrome is an exaggerated immunoglobulin E - immune response in reaction to an unknown allergen.¹ Allergic rhinitis (AR) and asthma are the most common inflammatory diseases of the airways², and usually persist along the patient's life.³ Both diseases are frequently coexisting, this concept is based on epidemiological studies, physiopathology, symptoms and interactions in the airway are similar⁴, the prevalence of the association between asthma and rhinitis are 15% to 38% and the presence of AR increases the risk for asthma and patients with uncontrolled asthma symptoms.³ According to the review of the literature, there is a prevalence of AR of 10-40% worldwide.^{5,6} Every day, the prevalence of atopic syndromes increases, especially in countries with low-income population.⁶ This literature review is intended to create a guide for the first contact clinician to update, diagnose and treat patients.

DEFINITION

AR is defined as a type I allergic disease of the nasal mucosa, the characteristic symptoms include nasal congestion, watery rhinorrhea and sneezing⁷⁻⁹, when patient is exposed to the allergen¹⁰, caused by an immunoglobulin E mediated inflammation.^{5,10} The terms used for this disease entity include: allergic rhinitis, nasal allergy, nasal hypersensitivity and pollinosis, this last one is a seasonal type of allergic rhinitis, caused by pollen.⁹

CLASSIFICATION

The rhinitis management depends on the type of rhinitis, the classification is suggested by The Allergic Rhinitis and its Impact on Asthma (ARIA), it is classically divided into seasonal AR (SAR) caused mainly by outdoor allergens, mainly pollen; and perennial AR (PAR) due to indoor allergens like dust mites, molds and insects.¹⁰ Another classification is about the type of duration and divide the AR in: intermittent AR

(IAR) characterized by a temporal duration, less than 4 days per week or less than 4 consecutive weeks; and persistent AR (PAR) which symptoms occur for more than 4 consecutive weeks.¹¹ ARIA guidelines proposed a classification for severity (mild and moderate-severe) by the disturbances of quality of life.¹² A classification of sensitization is: monosensitization, only one allergen is causing the allergy and polysensitization in this one, exists 2 or more allergen, this finding can only be made by testing allergy (skin testing or serum Immunoglobulin E).¹⁰ According to a biomarkers classification, AR is divided into four endotypes: 1. Type 1 immune response, the biomarkers are neutrophilia and IFN γ 2. Type 2 immune response, the typical biomarkers are classical cytokines of the T_H2 profile, eosinophils and IgE, 3. Neurogenic rhinitis, biomarkers are neurokinins and substance P and 4. Epithelial dysfunction, having the biomarkers: thymic stroma lymphopoietic, IL-33 and IL-25.¹³

EPIDEMIOLOGY

There are almost 400 million people worldwide affected by AR.¹⁴ The experts estimate a prevalence range between five to twenty two percent of population affected by this disease.¹⁵ The International Study of Asthma and Allergies in Childhood (ISAAC) is a study about the prevalence and severity in atopy syndrome (asthma, rhinitis and eczema). Evaluated by validated questionnaires, this study was realized from 1992 to 1998 then from 2002 to 2003. It evaluated patients of two age groups 6 to 7 years old and 13 to 14 years old. The results present an increase in the prevalence of AR from 1990s to the first years of the first decade of the 21st century in low-income and middle-income countries. It decreased or stabilized in Western Europe.^{14,16} In the systematic review and meta-analysis of 86 cross-sectional studies conducted mainly in Asia and Europe, then America, Africa and Oceania, this study was performed in children and adolescents. The diagnosis of AR was mainly using the ISAAC questionnaire for children and adolescents, then the European Community Respiratory Health Survey (ECRHS) in adults. The study included 291,726 males and 301,781 females. The results were: a prevalence in participants under 11 years old, where the symptoms of rhinitis reported by the parents themselves was 1.27%. These results did not report sex differences. In the age group between 11 and 17 years old, the prevalence of rhinitis symptoms was 0.90%, in three studies in Korea, Iran and Kuwait, it showed a higher prevalence in males, but 15 studies had a strong female predominance in this age group. In adults, patients above 18 years old, there was a prevalence of 0.96% in this case, none of the studies reported a male predominance, just two studies conducted in Korea and Nigeria presented a borderline male predominance. In studies conducted in France and Sweden a female predominance was presented.¹⁷

In the study where the first transnational survey on symptoms was conducted, the impact on quality of life and treatment of nasal allergies in Latin America, a cross-national study performed in Argentina, Brazil, Chile, Colombia, Ecuador, Mexico, Peru and Venezuela included 1088 adults and 457 children and 457 adults. In this study, it was revealed a 7% prevalence of nasal allergies, but only 6.6% had a physician diagnosis of AR in the Latin American survey. In Peru and Venezuela it was reported the highest prevalence and in Argentina it was reported the lowest prevalence. Mexico reported a higher prevalence of seasonal allergies in parents of children and adolescents with nasal allergy, meanwhile Argentina reported the lowest rate.¹⁸

A cross-sectional study was realized in 535 children between 3 and 5 years old in Cuenca, Ecuador. The collected results were of 48% of patients with AR symptoms, but only a small fraction was attributable to atopy, the total prevalence attributable to skin prick test was 7.9%.¹⁹

Another study was a cross-sectional population-based study from 2009 to 2010 in Bogotá, Colombia. The study included 5978 patients, where the prevalence of AR symptoms was 32%, but only 14% had a prevalence in physician diagnosis.²⁰

The local panorama of AR prevalence in Mexico has fluctuations in the prevalence from 5.5% to 47.7%, in studies conducted on Mexican population.²¹

CLINICAL MANIFESTATIONS

Cardinal symptoms include nasal congestion, rhinorrhea, sneezing, nasal itching, cough, although multiple related symptoms may occur.^{7,8} In most cases it is accompanied by ocular symptoms like ocular redness, tearing and itchy eyes.^{22,23} The congestion gets worse in the late summer and early fall.²⁴ The severity of the symptoms determine a disruption of the quality of life, also sleep disturbances like somnolence, falling asleep, and staying asleep, the patient may present fatigue, irritability, depression, it may also affect the attention, learning and the memory.^{25,26} Patients can have excoriations for the persistent congestion, and an increase in the blood flow in the periorbital region can produce allergic pimples.²³ The symptoms depend on the age and the sex of patients, the changes in Immunoglobulin E in different ages, and the sex hormone levels determine a change in the symptoms.²⁵

PHYSIOPATHOLOGY

The nasal cavity is composed by bone and cartilage, divided by septum, and lined with pseudostratified columnar respiratory epithelium. The main function is the regulation of air temperature, humidification and cleansing of the inspired air.^{23,27} Mucus maintains hydration and traps particles, bacteria and virus, and provides an innate immunity.²⁸ The nasal epithelium is the first to have contact with the air in the respiratory tract and the first line of defense against infectious agents, like induce a mechanism of protection and inflammation, like in AR the exposure of allergens relates an interaction with recognition receptors¹⁶, it creates a physical and chemical stimulation. This response of the nervous system includes parasympathetic and sympathetic nerves, this nerves transmit signals to the mucosa and generate an itchy sensation and motor reflexes like sneezing. The stimulation of the nervous system generates an exaggerated response in the nervous and immune systems.²⁹ The immune system starts a IgE-mediated reaction against inhaled allergens and it involves a mucus inflammation driven by type 2 helper T (Th2) cells.^{5,7,30} The IgE synthesized in the mucosa, then enters the blood stream through the lymphatic system³¹, and cysteinyl leukotrienes of the allergen are recognized by antigen-specific IgE receptors on mast cell and basophils, and have an influence on the mucosal inflammation in tissue and nasal symptoms (sneezing and rhinorrhea) and ocular symptoms (itching, redness and watering) mainly caused by the release of histamine, leukotrienes and prostaglandins.^{5,23,32,33} During the next hours, through a complex interaction of mast cells, epithelial cells, dendritic cells, T cells, innate lymphoid cells, eosinophils, and basophils, this due to the release of neuroactive and vasoactive substances like histamine, prostaglandin D2, tryptase and eosinophil cationic protein^{7,32,34} and develop an immediate hypersensitivity¹³. After some hours that the allergen remains in the local tissue, the mucosa is more reactive to this allergen, even with other strong irritants, resulting in tissue edema and the perpetuation of nasal congestion.^{7,32}

DIAGNOSIS

The first steps in the diagnosis are the clinical history and physical examination of the patient, recognize the type of rhinitis (allergic or non-allergic).³ Figure 1. Diagnosis for AR, summarizes the steps to diagnose AR. The interrogatory includes age of onset, duration, frequency, severity, timing during the year, suspected

triggers, pattern of presentation, and progression of the symptoms¹⁰. Also, the past therapeutic and effectiveness, the personal and family history of atopy conditions, especially asthma, AR coexists with asthma in 75 to 100% of the patients⁸. Also asking about potential triggers at home and work like pollen, animals, tobacco smoke, humidity.²² The physical examination includes, especially in children, a growth assessment, since airways problems are associated with growth reduction, the inhaled corticosteroids reduce height at high doses.¹⁶ The presence of conjunctivitis, allergic nasal crease, allergic salute or double creases beneath the eyes or Dennie-Morgan lines, allergic pimples, allergic salute, rubbing of the nose can guide the physician about a case of AR.³⁵ Patients with moderate to severe AR and with uncontrolled symptoms needs a nasal examination, with rhinoscopy where the typical appearance in nasal cavity is swollen pale bluish inferior turbinate edema with copious clear secretions; it is also performed an ear inspection, the otitis media is a comorbidity in children with AR.¹⁶ When the clinical history and physical examination suggest AR, the confirmatory diagnosis is by skin prick test or blood tests to identify specific antigens and vitro of specific IgE antibodies.³⁶ The skin prick test allows to directly observe the reaction of the organism to a specific antigen, as well as activated mast cells and released histamine²⁶, sensitivity ranged from 68% to 100% and specificity ranged from 70% to 91%¹⁶ and can be done safely in the allergy consultation and provides results within 20 minutes³⁵. The main contraindications are an antecedent of anaphylaxis, unstable cardiovascular disease, some medication like antihistamines, tricyclic antidepressant, β -blockers, since they can suppress the test results.²⁶ The component- resolved diagnosis is not recommended as a diagnosis routine, the detection of serum IgE antibodies using a biomarker can be useful to predict morbidities, and persistence in the future.¹⁰ The allergen-specific test also can be useful for immunotherapy and guide the content of the vaccine¹⁶, also advantages of using immunoassays for allergy testing are sensitivity to specific antigens and adverse reactions get eliminated, including anaphylaxis, and the effects on the patient's skin and the patient should not suppress the current medication.²⁶

TREATMENT

Non-Pharmacological treatment

To avoid relevant allergens, like pets, pollen, mounds, and irritants like tobacco smoke.³⁷ Also, dehumidification lower than 50%, as well as the reduction of the exposure to pollen can be reduced by closing windows, the use of high-efficiency particulate air (HEPA) and limited outdoor time in pollen season, also eliminating contact with animals can reduce the symptoms and the incidence of AR.²²

Pharmacological treatment

Intranasal glucocorticoids and intranasal oral antihistamine drugs are the first-line therapies.³⁵ The initial treatment is monotherapy and then a combination pharmacologic therapeutic option for AR⁸. Table 1 shows the pharmacological treatment for AR, it includes the summarized dose, main contraindication for the main medical option.

Glucocorticoids

They are considered the most effective medication class for the treatment of all symptoms related to perennial allergic rhinitis (including nasal congestion) and they provide a more effective relief to symptoms than

oral antihistamines.^{35,38} Glucocorticoids are used for acute and chronic rhinosinusitis with and without nasal polyps, and adenoid hypertrophy with or without middle ear disease, the evidence on intranasal corticosteroids producing greater nasal symptom relief suggests than topical antihistamines even if there are no difference in ocular symptoms, corticosteroid nasal sprays include: beclomethasone dipropionate, budesonide, ciclesonide, flunisolide, fluticasone furoate, fluticasone propionate, triamcinolone acetonide, and mometasone furoate³⁵, the minimum recommended duration of nasal corticosteroid therapy is 12 weeks.⁸

Corticosteroids increase the production of reactive oxygen and reactive nitrogen species; they also reduce the secretion of mucus and the development of inflammatory edema. The process of blocking mucus production is linked to corticosteroids inhibiting the expression of MUC-2 and MUC-5AC genes. Nasal corticosteroids are strong vasoconstrictors, so they reduce edema and effusion; and corticosteroids have no effect on the innate immune response mechanisms, this effect is observed from minute 2 to 20.³⁹

FIGURE 1.
Diagnosis for Allergic Rhinitis.

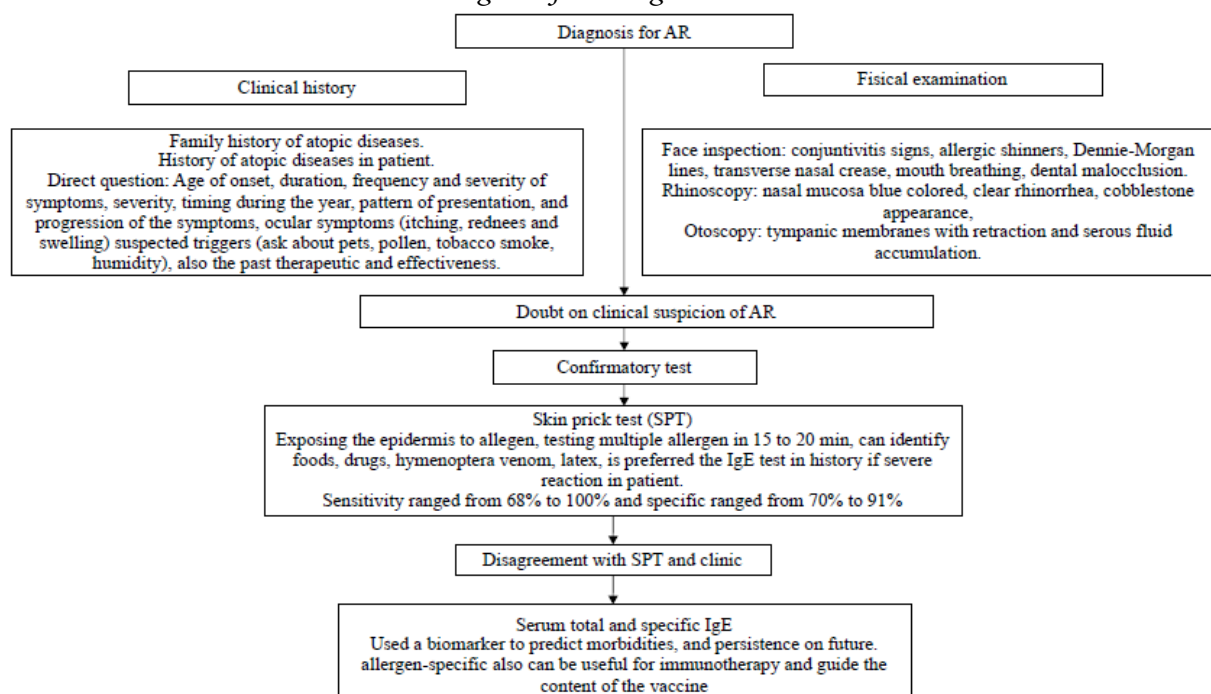


Figure 1. *Diagnosis for Allergic Rhinitis.*^{10,16,22,26,35,36}

10, 16, 22, 26, 35, 36

Antihistamines

The antihistamines are the standard therapy for allergic diseases, first-generation antihistamines are not recommended to treat allergic rhinitis, especially in older patients, because there is a high risk of adverse reactions, like anxiety, confusion, dyskinesia, sedation or sleepiness, arrhythmias, urinary disturbances, constipation, hypotension, memory dysfunction, and problems with kinetic coordination, this caused by the capacity to cross the blood-brain barrier^{5,35}. The sedative properties of H1 antihistamines are caused by inhibition of the functions of central histamine neurons, hydroxyzine (30 mg tablets) significantly prolonged

the break reaction time while driving a car compared, for this reason the second generation antihistamines are preferred.^{39,40}

The second-generation antihistamines have a relatively low rate of passage across the blood–brain barrier, and are minimally sedating or nonsedating; They are highly selective for H1 receptors and do not have anticholinergic effects^{41,42} in this group like fexofenadine (30 mg, 60 mg, 180 mg tablets, oral disintegrating tablet 30 mg, suspension 6 mg/ml), cetirizine, (5 mg and 10 mg tablets, and chewable 5mg tablets, 10 mg, syrup 1 mg/ml), loratadine (10 mg, 60 mg, 180 mg tablets, oral disintegrating 5 mg tablet, 10 mg), levocetirizine (30 mg tablets,

0.5 mg/ml syrup), desloratadine (5 mg tablets, oral disintegrating 5 mg tablet, syrup 0.5 mg/ml), bilastine (20 mg tablets) and ebastine (20 mg tablets), all of this are administrated one a day^{43,44}, the majority of second-generation antihistamines are metabolized by the cytochrome P450 enzyme and interactions with macrolides, antifungals, and calcium antagonists.^{41,42} Their first metabolism is through the liver and thus they are not recommended for patients with significant liver dysfunction; in patients with renal impairment it is recommended to prescribe azelastine, ebastine, desloratadine and cetirizine.³⁵

DECONGESTANTS

Nasal decongestants such as sympathomimetic amine derivatives (phenylephrine) and imidazole derivatives (oxymetazoline), are not a first-line therapy nor used as a monotherapy, particularly for a prolonged, the adverse events, increased arterial hypertension, headache, arousal, prostatism, and aggravation of glaucoma, and urination.³⁵

LEUKOTRIENE RECEPTOR AGONIST

The leukotriene receptor agonists like montelukast (10 mg tablet, 4 mg chewable tablet, 5 mg, oral granules: 4 mg) and zafirlukast (10 mg tablet)⁴³, in the evidence, the combination of this with antihistamines is effective as intranasal corticosteroids, this is recommended when the antihistamine/corticosteroid are not tolerated.²² Montelukast undergoes extensive CYP 3A4 and CYP 2C9 metabolism, the main interaction is with phenobarbital, it can decrease montelukast plasma concentrations by up to 40, also rifampin reduce montelukast concentrations. It has also been found that montelukast can potently inhibit CYP 2C8, for this reason the coadministration of montelukast with repaglinide, rosiglitazone or cerivastatin.^{43,44}

IMMUNOTHERAPY

Allergen immunotherapy is very effective, even for local allergic rhinitis, and the shortcomings of subcutaneous immunotherapy regarding inconvenience and safety are reduced with the introduction of sublingual immunotherapy (SLIT) and intranasal immunotherapy.⁹ This therapy reduces the IgE levels, and block the union between IgE and FcεRI.³⁸ This treatment is the only etiological treatment and it modifies the natural course of AR.⁴⁵

TABLE 1
Pharmacological treatment for Allergic Rhinitis

Loratadine	1 tablet (10 mg) once a day 10 ml (10 mg) once a day	>30 kg: 10 ml (10 mg) once a day. <30 kg: 5 ml (5 mg) once a day.	History of hypersensitivity. anticholinergic Activity that could thicken bronchial secretions, aggravating asthma attacks
Desloratadine	1 tablet (5 mg) once a day	>12 years: 10 ml (5 mg) once a day. 6-11 years: 5 ml (2.5 mg) once a day. 12 months - 5 years: 2.5 ml (1.25 mg) once a day. 6-11 months: 2 ml (1.0 mg) once a day.	History of hypersensitivity. No recommended for children under 6 months.
Fexofenadine	1 tablet (120 mg) once a day.	6-11 years: 1 tablet (30 mg) once a day 2-11 years: 5 ml (30 mg) twice a day.	History of hypersensitivity. No recommended for children under 2 years.
Cetirizine	1 tablet (10 mg) once a day.	More than 6 years: 20 drops (10 mg) or 5-10 ml (5-10 mg) once day. 2-6 years: 2.5 mg twice a day. 1-2 years: 2.5 mg twice a day.	History of hypersensitivity to piperazine derivatives.
Bilastine	1 tablet (20 mg) once a day.	No recommended in children under 12 years.	History of hypersensitivity or under 12 years.
Intranasal corticosteroids			
Beclomethasone	1-2 sprays (50 µg/spray) twice a day.	1-2 sprays (50 µg/spray) twice a day.	History of hypersensitivity, pulmonary tuberculosis, hemostasis disorders.
Budesonide	2 sprays (64 µg/spray) once daily or 1 spray twice a day.	2 sprays (64 µg/spray) once a day or 1 spray twice a day, (do not exceed 256 µg)	History of hypersensitivity.
Ciclesonide	2 sprays (50 µg/spray) once a day.	No recommended in children under 12 years.	History of hypersensitivity.
Fluticasone furoate	2 sprays (27.5 µg/spray) once a day.	1 sprays (27.5 µg/spray) once a day.	History of hypersensitivity.
Fluticasone propionate	2 sprays (50 µg/spray) once a day.	1-2 sprays (50 µg/spray) once a day.	History of hypersensitivity.
Mometasone	2 sprays (50 µg/spray) once a day.	1 sprays (50 µg/spray) once a day.	History of hypersensitivity.
Leukotriene receptor antagonists			
Montelukast	1 tablet (10 mg) once a day.	No recommended in <15 years of age.	History of hypersensitivity.

ALTERNATIVE TREATMENT

In a randomized, double-blind, controlled trial for 3 and 6 weeks, patients with AR were treated with 500 mg of ginger extract compared to those treated with 10 mg loratadine. The efficacy was evaluated from clinical examinations in a total nasal symptom scores (TNSS), cross-sectional area of the nasal cavity with acoustic rhinometry and with the quality of life questionnaire of rhino conjunctivitis. The safety of treatment was measured by blood pressure, blood analysis and history- taking for side effects. The results showed that the groups treated with both ginger extract and loratadine significantly decreased TNSS scores but there was no significant differences between the two groups. This study demonstrated that ginger extract is as good as loratadine in improving nasal symptoms and quality of life of AR patients, but ginger extract is associated with more adverse effects.⁴⁶ A meta-analysis about the efficacy of acupuncture in allergic rhinitis and the evidence of acupuncture treatment for allergic rhinitis in several aspects, including symptom score, drug score, quality of life score, asthma control score, side effects and laboratory examinations such as nasal function test, serum total immunoglobulin (IgE), nasal secretion smear, and so on.^{47,48} Different studies have tested the efficiency of probiotic administration, activating or inhibiting type 1 T-helper cells from the intestinal microbiota, although the results have not been conclusive, the studies, especially those performed in animals, as well as those using probiotic administration versus placebos, seem to be useful in atopic diseases, including allergic rhinitis. Different studies have tested the efficiency of probiotic administration, activating or inhibiting type 1 T-helper cells from the intestinal microbiota, although the results have not been conclusive, the studies, especially those performed in animals, as well as those using probiotic administration versus placebos, seem to be useful in atopic diseases, including allergic rhinitis.⁴⁹

PREVENTION

The attempts to prevent an allergic disease are unsuccessful¹⁶, the polarization in adaptive immune system and stimulated the innate immune, immunological prevention in infants, are focused on producing TH2.³⁹ The diet in the infant can influence the risk of allergies in children, the deficiency of vitamin D, have a direct association with the development of AR.⁴² Studies indicated that prenatal and postnatal probiotics or prebiotics can reduce the AR.¹⁶

FORECAST

AR is a chronic condition that is caused by specific allergens, it is important for patients to try to identify allergens and/or environmental agents that may precipitate their disease, and this reduce the symptoms, and have a beneficial prognosis for the pathology.¹⁶ The symptoms can interfere in the patient's life quality with the ability to sleep, anxiety, depression, fatigue, social interaction, and cognitive dysfunction.⁴²

CONCLUSION

AR is the most common atopic disease according to current epidemiology, so the clinician in contact with patients should consider the most important points of this pathology. Also, it really affects the life quality of patients. The diagnosis ranges from clinical to cabinet tests that can be used by the physician to find the severity of the pathology, as well as the individualization of the treatment. Priority should be given to changes

in the patient's lifestyle, as well as the desired line of treatment, to improve the prognosis and avoid possible complications (mainly asthma) that can have an impact on the patient's quality of life.

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GLOSSARY

AR: Allergic Rhinitis

ARIA: Allergic Rhinitis and its Impact on Asthma ECRHS European Community Respiratory Health Survey FcεRI High-affinity IgE receptor

H₁: Histamine receptor 1.

IAR : Intermittent Allergic Rhinitis

IFNγ 2: Gamma interferon **IgE** Immunoglobulin E **IL-25** Interleukin-25

IL-33: Interleukin-33

ISAAC : International Study of Asthma and Allergies in Childhood

MUC-2: Mucin 2

MUC-5AC: Mucin 5AC

PAR : Perennial Allergic Rhinitis

PAR : Persistent Allergic Rhinitis

SAR: Seasonal Allergic Rhinitis

SLIT : Sublingual immunotherapy

TH2: Lymphocytes helper 2.

TNSS: Total nasal symptom scores