Review

A Review Regarding the Connections between Allergic Rhinitis and Asthma - Epidemiology, Diagnosis and Treatment

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ABSTRACT: Allergic rhinitis is characterized by an acute or chronic inflammation of the nasal mucosa, being frequently associated with other airway conditions such as sinusitis, serous otitis media, nasal polyposis, sleep disorders and asthma in particular. Among the comorbidities of allergic rhinitis it counts asthma, being a risk factor for this disorder, in which, more than 75% of patients develop asthma (either allergic or nonallergic), whereas the patients with allergic rhinitis can be affected up to 40% by asthma. The classic symptoms for allergic rhinitis involves sneezing, nasal mucosal swelling and watery rhinorrhea; whereas the main symptoms which occurred in patients with asthma are wheezing, breathlessness, chest tightness, coughing, fast heartbeat, confusion, exhaustion or dizziness. Avoiding allergens is the first line of treatment for allergic rhinitis, followed by medication and allergen immunotherapy. Due to the strong connection between allergic rhinitis and asthma, one can affirm that the treatment for allergic rhinitis lead to the improvement of asthma symptoms. One can diagnose asthma by recognizing a certain pattern of respiratory symptoms and expiratory airflow restriction, which varies for each patient. In conclusion, accurate identification of the differences between allergic rhinitis and asthma depends on a thorough history, physical examination, and therapeutic treatments. This article provides an overview of the connection between these disorders, as well as of the diagnosis of these conditions and their current management options.

KEYWORDS: *Rhinitis, asthma, allergy, antihistamine, corticosteroids, allergen immunotherapy, desensitization therapy.*

Introduction

Almost half of the world's population suffers from allergic disorders, which are brought on by a confluence of genetic and environmental variables. This decrease in life expectancy has a significant impact on personal, societal, and financial consequences [1].

Between common allergic diseases worldwide, it counts: rhinitis; sinusitis; atopic dermatitis; allergic conjunctivitis and asthma [2].

Rhinitis occurs due to an inflammation of nasal mucosa. Allergies and heightened sensitivity to irritants are some of the factors that contribute to rhinitis (smoke, temperature changes or the overuse of decongestant nasal sprays) [3].

The most frequent allergens for allergic rhinitis are those that can be inhaled, like dust mites, animal dander, and/or pollen. [3,4].

Allergic rhinitis is considered to be the most chronic disease due to the fact that affects approximately 20% of the world population [5].

Allergic rhinitis represent an allergic inflammation of the upper airways, being a very common disease, which affects 5 to 50% of children and 10 to 30% of adults, depending on various factors (e.g. age, sex, social/economic impact, and/or different geographic zones considered) [6,7].

It is a non-fatal disease, but, due to its frequency, can alter the quality of life of patients, meaning, decreases the learning capacity of children and adolescents, as well as the work performances of adults and leads to increased medical costs [8-10].

Generally, can be classified as atopic, idiopathic, nonallergic or infectious heterogeneous disorder, being characterized by the symptoms which occurs after allergen exposure.

10.12865/CHSJ.49.01.01

Theoretically, there are two main types of allergic rhinitis: seasonal (occurring during a specific season) and perennial (occurring throughout the year) [11]; however, there are additional types that can be caused by environmental factors, reflexes, hormonal conditions, pregnancy, oral contraceptives, menstrual cycles, exercise, and occupations as well as chemicals or irritants, gustatory rhinitis, chemical- or irritant-induced, posture reflexes (rhinitis medicamentosa, oral contraceptives, antihyperthensive therapy, aspirin, nonsteroidal anti-inflammatory drugs) [11,12].

Seasonal allergic rhinitis is often associated with conjunctivitis. It appears especially in spring and summer, the major cause being pollen, then hay and grasses. Occupational rhinitis appears as a result of constant exposure to various allergenic substances within the work environment (e.g. solvents, detergents, etc.). The symptoms which may occur are: sneezing, hyper-secretion, airflow limitation and pruritus [13].

Perennial allergic rhinitis lasts throughout the year. It is often associated with asthma type pathology. It is caused by allergens constantly present in the environment: dust mites (presents in mattresses, pillows, carpets, armchairs, etc.), mold spores, feathers, animal dander, etc. The person with perennial allergic rhinitis seems to have a cold all the time. The crisis can start in the morning and can be repeated several times a day.

Asthma represent a chronic inflammatory disease that often affects children and adolescents, being recognized as a serious global health problem. Inflammation of the small airways is a common feature of the disease, which is typically characterized by bronchial inflammation and may be significantly influenced by allergens, irritants, or infections [14].

Via several, distinct paths, the aforementioned factors can either alter the development of asthma or cause acute airway blockage in people who are already afflicted. Infections with respiratory viruses, particularly respiratory syncytial virus and parainfluenza virus, are the main causes of wheezing diseases that signal the start of asthma in infants and some children [14].

Viral infections continue to affect asthma in children and people with established asthma, typically causing lower respiratory tract symptoms and asthma exacerbations. Thus, it has been suggested that some childhood infections may trigger an adequate immunological response, affecting the immune system's development and changing the risk of developing allergies and asthma in the future.

According to epidemiological data, allergic rhinitis is the primary risk factor for asthma, and in general, the majority of asthma patients (>75% of patients) also have allergic rhinitis, even though asthma can impact up to 40% of people with allergic rhinitis [15].

This review will discuss the connections between allergic rhinitis and asthma, as well as the epidemiologic associations between the both diseases. Finally, will be mentioned pharmacologic therapies of the diseases as well as diagnosis methods.

Allergic Rhinitis

Inflammation of the nasal passages, accompanying bacterial and viral upper respiratory tract infections, or structural abnormalities brought on by nasal polyps are all symptoms of allergic rhinitis, a type 1 allergic condition [16].

Depending on its severity, can reduce the quality of life [17].

Due to exposure to nasal allergens, allergic rhinitis is an IgE-mediated type 1 inflammatory disease of the nasal mucosa epithelium. Mature B cells respond by producing specific immunoglobulin E antibodies that bind to receptors on mast cells and basophils, releasing a number of chemical mediators, chemokines, and cytokines [18].

The chemokines, cytokines and chemical mediators are stimulated due to the presence of an antigen in the nasal mucosa and their response are the release of various inflammatory cells, such as activated eosinophils which infiltrate in the nasal mucosa. On the other hand, leukotrienes which are produced by the inflammatory cells released, cause nasal mucosal swelling [5,17].

The main four characteristics symptoms of this disease are rhinorrhea, sneezing, itching and nasal blockage [5,17,19].

Through systemic circulation, the inflammatory cells infiltrates in other tissues, where the adhesion molecules already exist. In this way, the allergic rhinitis also triggers a systemic inflammation, which lead to an augmented inflammation both the upper and lower airways. Thus, allergic rhinitis can also be associated with various comorbid conditions, according to Figure 1, such as: bronchial hyper-reactivity, allergic conjunctivitis, chronic hyperplastic rhinosinusitis, nasal polyposis, serous otitis media, sleep disorders, even asthma [12,20,21].

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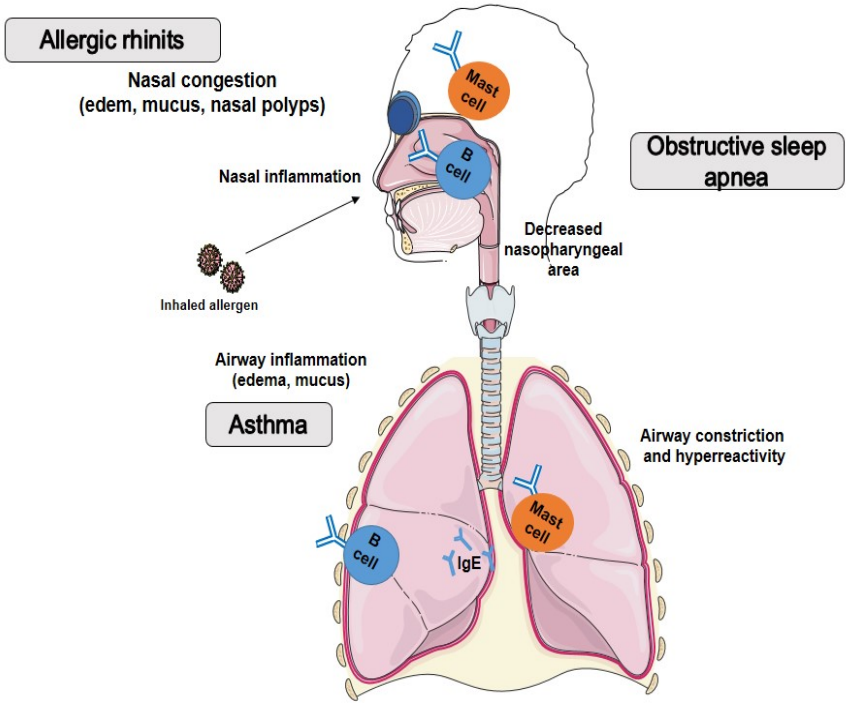

Figure 1. Chronic allergic respiratory syndrome.

In sensitized individuals, after the inhalation of nasal antigens, they pass through the mucosal epithelial cells, attaching to the mast cells IgE antibodies, which are distributed over the nasal mucosa. Thus, an IgE-mast-cell mediated early phase answer is obtained given by the antigen-antibody complex [5].

Histamine and peptide leukotrienes are chemical mediators released from mast cells, causing irritation to the mucosal blood vessel and to sensory nerve endings, thus occurring the early phase reaction symptoms (i.e. sneezing, nasal mucosal swelling and watery rhinorrhea) [17].

After 30 minutes of exposing to an allergen, the early phase symptoms appear and after 24 hours of exposing, the late phase response appear, characterized by tissue damage and remodeling.

As mentioned above, according to etiology, rhinitis classified into allergic (IgE-mediated), autonomic, infectious and unknown (idiopathic) diseases, detailed in Table 1 [22].

Table 1. Etiological classification of rhinitis.

	Description
Allergic (IgE-mediated)	Eosinophilic and Th2-cell infiltration of the nasal lining; Nasal mucosa inflammation caused by IgE; Depending on the severity and length of the symptoms, allergic rhinitis can also be characterized as intermittent or chronic.
Autonomic	Drug-induced (rhinitis medicamentosa) Non-allergic rhinitis with eosinophilia syndrome Vasomotor Hypothyroidism Hormonal
Infectious	Because of a bacterial, fungal, or viral infection
Unknown (idiopathic)	The etiology is unknown.

According to symptom duration and severity, and its impact on asthma, the allergic rhinitis have been classified in intermittent, persistent, mild and moderate-severe allergic rhinitis (Table 2) [22,23].

Table 2 Classification of allergic rhinitis based on the length and intensity of symptoms.

	Symptoms
Intermittent	Less than four days per week or four weeks in a row without symptoms
Persistent	More than four days each week or for more than four straight weeks, depending on the symptom,
Mild	Normal sleep No interference with regular activities, sports, or recreation Regular work/school No uncomfortable symptoms Abnormal sleep
Moderate-Severe	Impairment of daily tasks, sports, and recreational activities Issues at work or school Difficult symptoms

In the recent years, professional rhinitis and local allergic rhinitis have been diagnosticated more and more often by physicians. Although the prevalence of professional rhinitis is unknown, it is believed that the high-risk professions include farmers and workers in various manufacturing industries, veterinarians, laboratory workers or food-processing workers [13,24,25] and usually occurs within in the first two years of employment.

In professional rhinitis, the condition may be due to the exposure to respiratory irritants or due to the IgE-mediated due to allergen sensitization. In both cases, symptoms may occur immediately or after several hours since exposure; often being associated with ocular and/or pulmonary symptoms. According to literature, little evidence suggest that professional rhinitis will progress to professional asthma [13,25].

On the other hand, local allergic rhinitis is characterized by a localized allergic response in the nasal mucosa, leading to an increases of IgE production in the nasal mucosa as evidence [26-28].

Due to the fact that symptoms of local allergic rhinitis are very similar with one of allergic rhinitis and the detection of specific IgE in the nasal mucosa, one can assumed that local allergic rhinitis is also an IgE-mediated disease. The clinical evidences sustain the fact that local allergic rhinitis is not a precursor of allergic rhinitis due to the fact that the evolution of this disease does not go towards the typical allergic rhinitis in patients followed in the study [29].

The treatment plan is not fully set up, but some evidence suggests that allergen immunotherapy may lead to satisfactory outcomes as regards this type of rhinitis [26,28].

Asthma

Asthma is the most common chronic inflammatory diseases, in which the inflammatory process is characterized by hyper-reactivity in the bronchial system, with reversible airflow obstruction. Together with bronchial hyperreactivity and mucus release, bronchial system inflammation can also cause smooth muscle contraction, airway restriction due to mucosal oedema, and epithelial cell sloughing [30].

The most common type of asthma is represent by allergic asthma, manifesting by an induced immune system response, due to the inhaled allergens [30].

After an accurate classification of asthma severity, one can proceed to the implementation of therapy.

Infants' repeated wheezing and asthma have been related to viral infections, which are also likely the most frequent cause of a disease's exacerbation in older children and adults. The virus-induced immune response represent the main cause of the well-known clinical effect of viral infection.

In order to illustrate the link between viral infections and acute wheezing in children, adults, or both who have been diagnosed with asthma, viruses were first identified using either serology or culture during wheezing episodes [30] [31].

Inflammatory pathways that may contribute to airway blockage and lower airway symptoms have been identified through clinical research [32-35].

Additional epidemiological research suggests that atopy indicators and viral infections both independently and synergistically influence the likelihood of childhood wheeze [36,37].

There is no denying that some respiratory viruses, such as influenza, respiratory syncytial virus, and parainfluenza virus, can infect the tissues of the lower airway and cause inflammation and blockage. Some evidence even suggest that the rhinovirus infections can infect the lower airway, leading to the tissues inflammations and finally in the appearance of asthma [38-41].

These findings do, however, imply that, at least in certain circumstances, rhinovirus

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infections extend to the lower airways and cause bronchial inflammation that may be a factor in virus-induced asthmatic exacerbations.

The airway hyper-reactivity is one of the features of asthma, defined as an increased sensitivity of the airways to bronchoconstriction due to allergens or irritants. Several studies have been conducted to evidence the specific interactions between allergen and virus-induced inflammations [42-44].

Rhinovirus infections enhanced the risk of having late-phase asthmatic symptoms after inhaling whole lung antigen and increased airway hyperreactivity to histamine, methacholine, and allergen. Also, it was examined whether allergen exposure can make viral illnesses worse [45,46].

Although the exact mechanism by which respiratory viruses cause symptoms are still unknown, there are some data suggesting that the immune response to the virus is a key factor in pathogenesis of symptoms. For example, the severity of symptoms induced by the respiratory viruses, are closely linked with the influx of inflammatory cells, thus leading to an increases in cytokines and chemical mediators in nasal secretions [40, 47-49].

Another illustration of the etiology of symptoms is the fact that the morbidity of viral infections can be decreased through the passive transfer of specific T-cell subsets, as shown by investigations on rats [50-52].

There are a limited number of cells and chemical mediators that are likely to play the key roles in this process, namely the airway epithelial cell, which is thought to be the primary host cell for the majority of respiratory viruses, despite the fact that immune responses to viruses are complex and involve numerous airway cells, cytokines, and chemical mediators. The in vivo and in vitro studies showed that influenza and respiratory syncytial viruses can destroy high numbers of epithelial cells, but, just a small subset of epithelial cells can be infected with rhinovirus [53,54].

The initiation of airway immune responses and inflammatory processes can be conducted by viral replication with epithelial cells, as shown in Figure 2. Through viral replication, intracellular signaling pathways are triggered, thus leading to the secretion of multiple cytokines, chemokines, and adhesion molecules increases [55-57].

In this way, the virus and allergen-induced inflammation overlap, meaning that, during viral infections [40,49,58-60], the cytokines and chemokines which are increased in airway secretion can recruit and activate inflammatory cells (activated T cells, eosinophils and neutrophils) [61,62], which have been linked to asthma.

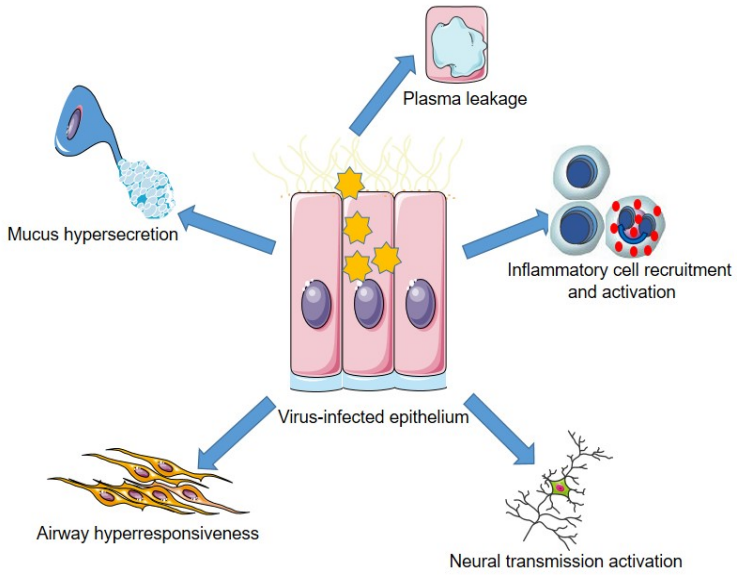

Figure 2. Effects of respiratory virus infection on airway tissues.

By upregulating adhesion molecules by cytokines (which is responsible for the recruitment of inflammatory cells) or by transudating plasma proteins from the vascular tissue of the nasal mucosa (which results in an increase in nasal secretions and congestive symptoms), some evidence suggested that endothelial cells are activated early during the course of upper respiratory tract infections [63,64].

Comorbidity between allergic rhinitis and asthma

The allergic symptoms of the upper and lower airways can be conceived of as manifestations of a shared atopic condition, and allergic rhinitis and asthma can be treated as a unified concept [65].

In addition, the epidemiological studies suggests a powerful relationship between them. Allergic rhinitis can occur in more than 75% of patients with asthma (either allergic or nonallergic), whereas asthma can affect up to 40% of patients with allergic rhinitis [15].

There are some studies which affirm that asthma occur often in patients which present moderate-to-severe persistent rhinitis as compare with those which present other types of allergic rhinitis. However, the strong interaction which exist between both is due to occupational environments [66].

Table 3 shows the differences or the similarities between the main forms of allergic rhinitis and asthma.

Table 3. Differences/similarities between allergic rhinitis (seasonal and perennial) and asthma.

Type of disease	Onset	Causes	Allergens	Symptoms
Seasonal allergic rhinitis	Progressive onset and occurs gradually over days to weeks. Often associated with conjunctivitis	Specific allergens	Tree pollen in spring Hay fever or grass pollen in summer Wood pollen in late summer or autumn	Sneezing, Hyper-secretion, Airflow limitation, Pruritus
Perennial allergic rhinitis	It is mild and chronic and can either increase or decrease in severity. Often associated with asthma	Year-round environmental exposure and exposure to allergens constantly	Dust mites Animal dander Molds	Nasal obstruction, Sneezing, Itching, Rhinorrhoea
Asthma	History of asthma or allergies, Significant stress, Obesity and/or smoking, Infections with respiratory viruses (respiratory syncytial virus and parainfluenza virus)	Unknown Allergens, irritants, or infections that promote inflammation of the small airways	Pollen, dust mites, animal fur, mold or feathers, Smoke, fumes and pollution, Medicines (ibuprofen, aspirin), Bronchiolitis	Wheezing, Breathlessness, Chest tightness, Coughing, Breathing faster, Fast heartbeat, Drowsiness, confusion, exhaustion or dizziness

For instance, allergic rhinitis appears at a younger age, being more frequently in firstborn children, and boys. Likewise, in children, among the risk factors for allergic rhinitis one can mention maternal cigarettes smoking, higher blood IgE levels (>100IU/ml before age 6), obesity, respiratory syncytial virus infection, air pollution, genetic predisposition etc. In adults, tobacco smoke, air pollution, eczema, exposure to a moisture environment, obesity, high consumption of aspirin, family history etc. are the main risk factors for these atopic disease [67,68].

Children are more susceptible to seasonal rhinitis whereas adults are more affected by perennial rhinitis, from which, those who are susceptible to dust mite are more prone to develop asthma than others who are allergic to pollen grains, for example.

As a result, allergens including mold, animal dander, and dust mites can cause both allergic rhinitis and asthma, which are both IgE mediated, to flare up; however, allergic rhinitis frequently manifests before the beginning of asthma [12].

Many clinical investigations also highlight the pathophysiological connection between allergic rhinitis and asthma, in addition to the epidemiological reports. For instance, bronchial hyper-reactivity is frequent in individuals with allergic rhinitis, without asthma symptoms, but, with all these, the asymptomatic airway hyper-reactivity is associated with an increased risk for developing asthma [69,70].

For example, it was shown that 40% of patients who suffer of allergic rhinitis develop hyper-reactivity to methacholine administration, in conclusion, the patients with hyper-reactivity were more likely to develop asthma over the following years [71].

Later, this finding were confirmed, and, in addition, it was demonstrated that the bronchial reactivity was correlated with the pollen season [72,73].

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Segmental bronchial stimulation in individuals with allergic rhinitis without asthma results in allergic inflammatory alterations in the nose, which serves as additional evidence of the pathophysiological relationship between the upper and lower airways [74].

The relationship between allergic rhinitis and asthma can be accounted by four mechanism. First of all, the nose has the role to prepare the inhaled air (warm, filter, humidifies and sterilizes through the submucosal glands, releasing the antibacterial enzymes); second, during an exacerbation of allergic rhinitis, all the compounds which produce inflammation in the upper airways, can be aspirated into the lower airways; third, during nasal inflammation, the cytokines are released in the bloodstream, leading to bronchoconstriction in the lower airways; and fourth, may occur a nasal-bronchial reflex, where histamine and bradykinin stimulate the afferent nasal sensory nerve, thus resulting the bronchial smooth muscle hyper-reactivity, due to the neural signal which ends up in central nervous system, activating the efferent vagus nerve [75].

The relationship between allergic rhinitis and asthma is probably complex, and there may be disagreement regarding the evidence for a nasal-bronchial reflex. Although nasal obstruction and aspiration of nasal secretions have long been recognized as significant factors, mounting evidence points to the systemic response as a key player in the link between allergic rhinitis and asthma. A proof for this affirmation could be the case of patients with allergic rhinitis without asthma, in which nasal allergen testing instigates bronchial airway reactivity and increase the eosinophil counts in the sputum samples [76].

Similarly happens with the bronchial and nasal biopsy specimens, it was found an increase in eosinophil's in both the nasal and the bronchial epithelium, at the 24-hour time point [77].

In addition, at patients with allergic rhinitis without asthma, the segmental bronchial provocation lead to the nose inflammation and to the increase of eosinophilia in peripheral blood [74].

From a different point of view, at patients with asthma without allergic rhinitis, the nasal biopsy was with eosinophil infiltration [78].

Eosinophilia ultimately results from an increase in inflammatory cytokines in both the upper and lower airways [79,80].

In summary, large studies have found that patients with severe form of asthma, often uncontrollable, frequently present severe nasal disease [81,82].

Allergic rhinitis in patients without asthma represent a risk factor for develop asthma both in the case of children as well as in adults [83,84].

In the case of children with allergic rhinitis, the development of asthma is frequently linked with allergy, whereas in adults with allergic rhinitis, the asthma development is independent of allergy [83,85].

Diagnosis and therapeutic treatments

Sneezing, nasal congestion, nasal itching, and rhinorrhea, as well as redness, tearing, and itching of the eyes (classic symptoms of allergic conjunctivitis, frequently associated with allergic rhinitis) are required for the diagnosis of allergic rhinitis.

Physical examination, particularly nasal examination (rhinoscopy and endoscopy), as well as various functional tests, are also necessary (peak nasal, inspiratory flow, rhinomanometry or acoustic rhinometry) [22] and after that an examination of the ears, sinuses, posterior oropharynx, chest and skin [22].

The history examination can include also the environmental history (allergen exposure or exposure to potential noxious substances at home or at work), as well as the use of recent medications (Aspirin, NSAIDs, beta-blockers, birth control, hormone replacement treatment, or angiotensin-converting enzyme inhibitors) or recreational drugs (cocaine) [22].

The patient history can include also the family history questions (e.g. comorbidities like asthma, snoring, sleep apnea, otitis media, nasal polyps, sinus involvement or mouth breathing) [22].

After the history and physical examination, the physicians can perform the diagnostic test, namely: in vitro and in vivo test to diagnose allergynasal challenge tests with allergens, the allergen-specific IgE test, hypersensitivity skin tests (to show an IgE-mediated allergic reaction), and a computed tomography scan (in order to exclude chronic rhinosinusitis or tumors) [86,87].

In conclusion, the screening for allergic rhinitis is very recommended, especially for asthmatic patients, since allergic rhinitis is present in majority of patients with asthma (up to 95%) [15,88].

A properly executed skin test is currently the best tool for determining the presence of allergen-specific IgE. The skin prick test is the most used way to check for IgE antibodies (the puncture skin or epicutaneous skin test). For the purpose of identifying specific IgE antibodies, Table 4 compares the benefits and drawbacks of in vivo skin testing versus in vitro serum testing [89].

Table 4. In vivo skin tests versus in vitro serum IgE antibody immunoassay in allergic diagnosis.

Skin test	Serum immunoassay
Cheap	No risk for patient
Greater sensitivity	Convenience for both patients and doctors
Wide allergen selection	Not suppressed by antihistamines
Results available immediately	Quantitative outcomes preferable to skin testing in children who are recalcitrant, have widespread dermatitis, or have dermatographism

When one obtain a negative result at the skin prick tests, but the allergy is still highly suspected, then, on the recommendation of the specialist, an intradermal testing, more sensitive but less specific, may be used. One can perform an in vitro test instead of a skin test, but only in the following cases: I) the patient has widespread dermatitis or dermatographism; ii) the patient cannot or has not stopped using antihistamines or other interfering medications; iii) the patient is very allergic owing to past experiences, therefore it is impossible to avoid the danger of anaphylaxis; and iv) the patient does not comply with skin test. Since antihistamines are known to suppress the skin test results, in order to avoid a false-negative skin test, the medication must be interrupted before skin tests are performed, as follows: Long-acting antihistamines should not be taken for 4 to 6 weeks, while short-acting antihistamines should not be taken for 36 to 48 hours.

In terms of the diagnosis of asthma, it could be challenging due to the reversibility of the airway restriction. But despite all of this, determining lung function and ensuring that airflow blockage is reversible are the most crucial measures in this regard. For the diagnosis of asthma, the information's regarding the patient's history is crucial. Among the symptoms reported by patient it counts: wheezing, episodic breathlessness, chest tightness, and cough that worsen at night and in the early hours of the morning. The recurrent exacerbations of the symptoms could be provoked by allergens, irritants, infectious agents, even hard exercise. If the treatment with bronchodilators and anti-inflammatory products works, i.e. the patient feels a relief of the symptoms, this one can be considered as a useful clinical marker of asthma [90].

An important parameter for managing the asthma is measuring the lung function (assessing the airflow limitation). But, as regards this method, one should note that, similar results can be obtain in the case of others disorders, such as rhinitis, cystic fibrosis, bronchiectasis, and chronic obstructive pulmonary disease [91].

Both pharmacological and non-pharmacological approaches can be used to treat allergic illnesses, while pharmacological preparations are frequently favored when non-pharmacological approaches fail or are insufficient to relieve allergy symptoms [92].

Several pharmaceutical preparations (local and systemic medications, intranasal decongestants, etc.) are utilized depending on the symptoms and kind of allergic disease [92,93].

Due to the strong connection between allergic rhinitis and asthma, it should not be surprising that the treatment for allergic rhinitis lead to the improvement of asthma symptoms. One can diagnose asthma by identifying a distinctive pattern of respiratory symptoms and expiratory airflow restriction, which varies for each patient [94].

The main treatment for allergic rhinitis is, as much as possible, allergen avoidance, to reduce or eliminate exposure, then pharmacotherapy and allergen immunotherapy.

Therapeutic options available, may include nasal saline irrigation, intranasal corticosteroids, oral antihistamines, a combination of intranasal corticosteroids and antihistamine sprays, leukotriene receptor antagonist and, finally, allergen immunotherapy. This therapeutic treatments can be used individually or in any combination. Besides the above therapies, decongestants and oral corticosteroids may be useful.

Allergen avoidance

Allergen avoidance alongside of irritants avoidance (e.g. dust mites, molds, pets, pollens, tobacco, smoke etc.) represents the first-line treatment of allergic rhinitis. The compliance with this avoidance recommendations, results in a significant reduction in symptoms within 4-6 months, leading to an affectively improvement of this disease [22].

Local and systemic decongestants

Local decongestants are sympathomimetic drugs which produces vasoconstriction by stimulate α1-adrenergic receptors. This lead to a local vasodilatation of the mucosal oedema that causes the nasal congestion [92].

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Local decongestants are indicated to alleviate acute symptoms, but it is not recommended to use it for more than 5 days, due to the appearance of undesirable effects, such as rebound rhinitis and conjunctivitis medicamentosa [92].

The most frequently used local decongestants are xylometazoline, phenylephrine and oxymetazoline [95].

The antihistamine-containing systemic decongestants stimulate 1-receptors, causing vasoconstriction that reduces oedema, redness, and itching. A systemic decongestant and an older type H1-antihistamine should not be taken together because doing so can make you drowsy and impair your motor coordination. Systemic decongestants often include phenylephrine, phenylpropanolamine, and pseudoephedrine. Phenylpropanolamine is contraindicated in individuals with uncontrolled hypertension and severe coronary artery disease since it has been reported to have caused hemorrhagic stroke in women who took it as an appetite suppressant [92].

Oral decongestants also have additional side effects such agitation, sleeplessness, headaches, and palpitations, thus their long-term usage may be restricted.

Antihistamines

H1-antihistamines are divided into second-generation (newer, nonsedating) and first-generation (older, sedating, multi-potent blockers) antihistamines based on pharmacological classifications (targeted receptors as well as side-effect profile) [96].

First-generation H1-antihistamines have the ability to pass the blood-brain barrier, but second-generation non-sedating H1-antihistamines have very limited or no ability to do so [4,97]

This is one of the main distinctions between the two classes. Promethazine, chlorpheniramine, dexchlorpheniramine, and cyclizine are first-generation antihistamines, while cetirizine (levocetirizine), loratadine, ebastine, fexofenadine, and mizolastine are second-generation antihistamines [2].

According to research showing that second-generation antihistamines can lessen sneezing, itching, and rhinorrhea when taken frequently during the peak symptom period or before to exposure to an allergen, they are the first-line pharmacological therapies advised for all patients with allergic rhinitis. Although they are efficient in reducing symptoms, first-generation sedating antihistamines have a deleterious effect on cognition and functioning and are therefore not always advised for the treatment of allergic rhinitis [22,98].

Antihistamines have, however, showed promise in the treatment of asthma when taken in conjunction with other drugs [99].

Intranasal corticosteroids

For patients with mild persistent or moderate/severe symptoms, the intranasal corticosteroids are also the first-line therapeutic options, being used alone or in combination with oral antihistamines, in agreement with the above. When taken carefully and consistently, intranasal corticosteroids can significantly reduce nasal mucosal inflammation and improve mucosal pathology. According to published research and meta-analyses, intranasal corticosteroids are more effective at controlling allergic rhinitis symptoms like nasal congestion and rhinorrhea than antihistamines and even leukotriene receptor antagonists [100-103].

Also, in patients with allergic rhinitis and concomitant asthma, intranasal corticosteroids relieve ocular symptoms and lessen lower airway symptoms [104-106].

The only typical side effects of intranasal corticosteroids are nasal irritation and stinging, although these may usually be avoided by aiming the spray slightly away from the nasal septum [22].

A combination of intranasal corticosteroid and antihistamine spray has also been demonstrated to be more efficacious than either agent alone, with a safety profile comparable to that of intranasal corticosteroids [107-110].

Oral corticosteroids, which have been shown to be efficient, can be used by patients with severe allergic rhinitis who have failed to respond to therapy with oral antihistamines and intranasal corticosteroids [22,111].

Leukotriene receptor antagonists

Because leukotriene receptor antagonists do not seem to be as effective as the previously mentioned therapeutic approaches, they can be used when oral antihistamines, intranasal corticosteroids, and/or the combination of both are not well tolerated or are ineffective in controlling allergic rhinitis symptoms [112-114].

However, allergen immunotherapy should be taken into consideration if the previously mentioned combination of pharmaceutical therapy is ineffective or intolerable [22,98].

Allergen immunotherapy

Allergen immunotherapy presume the gradually increasing quantities of subcutaneous administration of relevant allergens to a patient,

until the effective dose is reached, for inducing immunologic tolerance to the allergen. Seasonal allergic rhinitis brought on by pollens can be effectively treated by allergen immunotherapy (tree, grass and ragweed pollens) [115-118], as well as for treatment of allergic rhinitis caused by house dust mites. In order to control symptoms, this form of therapy should be offered carefully, only to patients who have not taken the necessary preventative measures and medication is not well tolerated [22].

It has been demonstrated that this treatment lowers a child's risk of developing asthma in the future if they have allergic rhinitis [116].

Sublingual immunotherapy is effective for the treatment of home dust mite- and grass-induced allergic rhinitis. This method is based on the administration of a tablet which contain an allergen extract under the tongue until it is dissolved-this is a way of desensitizing patients. The side-effects of sublingual immunotherapy are oral pruritus, throat irritation, and ear pruritus, but this symptoms are solved within a week after starting therapy [117].

This treatment should be avoided in people who have severe, unstable, or uncontrolled asthma, people who have severe pulmonary and cardiovascular disease concurrently, people who are pregnant, people who have autoimmune diseases or cancer, people who are taking beta-blocker therapy, and people who have active oral inflammation or scores [119].

Similar to adults, children can benefit from specialized immunotherapy, although children under the age of five should not receive it.

Conclusions

Allergic rhinitis and asthma frequently coexist as a single one disease concept, due to the fact that as the mucosal membranes of the nose and lungs are similar, most people with asthma also have rhinitis, this suggesting a worldwide health problem.

However, not all allergic rhinitis patients have asthma, because there are differences between them, the analysis of which could help to better understand one and the other of these diseases.

In addition, by understanding the pathophysiology of this disorders, one can improved the medical management.

Pharmacologic therapies ought to be chosen to enhance patients' quality of life.

Glucocorticoids and anti-leukotrienes are two medications that have been shown to be useful in treating both allergic rhinitis and asthma, whereas-and-adrenergic agonists are only beneficial in treating allergic rhinitis or asthma, respectively.

H1-antihistamines have been shown to work better for rhinitis than for asthma.

The medicine of choice for treating allergic rhinitis and asthma is intranasal corticosteroids.

It is noteworthy that effective rhinitis therapy can enhance concomitant asthma.

Asthma costs and hospitalizations rise when allergic rhinitis is left untreated; as a result, asthma can be avoided by treating allergic rhinitis aggressively and early.

For the symptoms of these conditions to be resolved earlier, more effectively, more affordably, and permanently, new treatments are required.

Conflict of interests

None to declare.

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