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Research Article

Allergic Rhinitis and Atopy: The Causative Role of Aeroallergens: A Review

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Abstract

The prevalence of Allergic Rhinitis (AR) has increased globally in recent times from 10 to 20% which can further deteriorate to atopy affecting adults and children equally. The main causative agents include aeroallergens which produce symptoms, not only like sneezing, itching, and nasal congestion, but also affecting the quality of life (QoL) and disturbed sleep. This review evaluates the risk parameters of allergic rhinitis which generally occur due to indoor and environmental aeroallergens, these interact with the host's immune system to increases the production of specific immunoglobins like IgE. These specific IgE antibodies bind to high-affinity IgE receptors on mast cells and basophils and trigger a sequence of events leading to allergic rhinitis, chronic rhinitis, and atopy. The propensity to produce IgE to allergens is referred as Atopy. This article examines the mechanism of the causative agents leading to the disease, with regards to the potential differences in health care and allergic rhinitis. The diagnoses, pathophysiology and subsequent treatment of the disease impacts an economic burden on the patients, further, co-morbidities associated with AR impose additional financial burden and can have a negative impact on the QoL of the patients. Hence this article observes the economic burden due to AR which is estimated at 10-40% of the country's economic burden. This review further highlights on improving the well-being of the patients through better diagnosis and utilizing currently available treatment options for Allergic rhinitis.

Keywords: Allergic Rhinitis; Allergens; Atopy; Treatment Options; Pharmacotherapy; Immunotherapy; Mechanisms; Economic Burden

Introduction

What is allergic rhinitis (AR)?

Allergic rhinitis affects 10 to 20% of the population and is one of the most common types of chronic rhinitis. [1]. In the past it was considered as a disorder that is localized only to the nose and nasal passages but the current research indicates that the prevalence of this disorder is increasing as it represents a component of systemic airway disease that involves the entire respiratory tract. The lower (trachea, bronchial tubes, bronchioles and lungs) and upper respiratory tracts (nose, nasal cavity, paranasal sinuses, pharynx and larynx) have a number of functional, physiological and immunological relationships between them and play an important role in the spread of the disorder. AR is generally triggered by aeroallergens. Aero-allergens could be two types: Seasonal (intermittent) and Perennial (Chronic and persistent), and can be found indoors or outdoors.

Atopy

The diseases which are recognised under the umbrella of atopic diseases include asthma, eczema, and conjunctivitis, with overlapping diagnostic symptoms. but the causative aeroallergens for these diseases may not be similar. The basis for this can be related to genetic predisposition or environmental factors. However, high levels of IgE as determined by skin prick test or Elisa

can induce chronic conditions which may or may not lead to life threatening conditions [3].

Further, Atopy is an immunological disorder involving the highly sensitive immune system which can react to even the smallest allergens or irritants which causes inflammation and frequent flare-ups. Generally, the diseases due to aeroallergens in atopic conditions such as rhinitis, atopy and relapse of asthma are diagnosed using skin prick test, and/or immunological test by checking the levels of a particular immunoglobulin IgE.

Mechanism involved: why some patients have atopy and some rhinitis?

MERK MANUAL describes: "The terms atopy and allergy are often used interchangeably but are different: Atopy is an exaggerated IgE-mediated immune response; all atopic disorders are type I hypersensitivity disorders. whereas, Allergy is any exaggerated immune response to a foreign antigen regardless of mechanism. The manual further describes that all atopic disorders are considered allergic and not viceversa. Both atopic and allergic disorders are due to exaggerated immune responses and can lead to autoimmune diseases.

The most common atopic disorder is Atopic-dermatitis or eczema which is a chronic relapsing inflammatory disease causing a severe itching on the skin, which results in skin infection many a times. This is more common in Children - about 10-20% of children in the United States and Western Europe suffer from this disease [4].

Another atopic disease is rhinitis, caused by the release of leukotrienes and histamines in the nose and bronchia, causing sneezing and nasal obstruction just like in asthma, nasal polyps can also be seen in rhinitis, IgE mediated allergic conjunctivitis is also one of the forms of allergic rhinitis.

Aero allergens

In this article we have tried to review and correlate the role of indoor and outdoor aeroallergens to a particular disease like atopy or rhinitis. As early as 1906, Clemens Von Piquet was the first author to introduce the word "allergy" and described the significant role of aeroallergens in the pathophysiology of allergic diseases.

He recognized that antigens induced reactivity changes in both protective immunity and hypersensitivity reactions [5] and are primarily responsible for the cause of asthma and rhinitis. Many allergens function in their natural state as enzymes by inducing proteolysis and are soluble proteins. The properties of allergen depend upon the size of the allergen (enhances aerodynamic properties) and its enzymatic activity such as increased mucosal permeability [5]. Some of the triggering factors that act as possible allergens are substances from natural resources, and the environment, these include; pollen, fungi, animal dander, house dust mites, domestic pets, and insects. Pollen grains are well studied as important aeroallergens and a cause of pollinosis, asthma and allergic rhinitis [6] these substances occur due to climate change and season change.

Risk factors and health effects

Risk factors

Heredity is a common risk factor for AR. In any family, a child can have a 30-50% inherited risk of developing allergies, if any one of the parents had been suffering from allergic reactions of any kind. Further rhinitis can also occur due to climate or seasonal changes and environmental exposures, in absence of genetic factors. Occupational exposure to seed dust, wood dust, animal dander, textile dust, chemicals, rubber latex, certain foods and spices storage mites, odours and fumes such as smoking or air pollution are considered as risk factors for AR. Pollens from various weeds like parthenium, or pollen from flowering plants and trees and grasses, present in the outdoor environment are also the major causes and risk factors for seasonal allergic rhinitis. Popular among the indoor pollutants are mites, pets, house dust, insects and molds which are the main causes of AR [7].

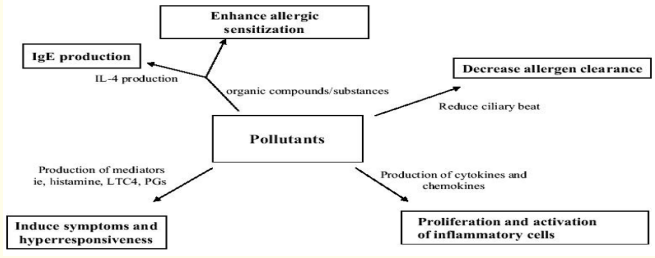

Figure 1: Possible effects of air pollution in allergic diseases.

Source: Wang DY., et al. [7]. Risk factors of allergic rhinitis: genetic or environmental?.

Health effects

Aeroallergens not only cause AR, but also allergic bronchial asthma, and in severe cases leading to atopy trailed by dermatitis and food allergies. Further other serious diseases like urticaria, angioedema, anaphylactic shock and allergic conjunctivitis are also due to environmental aeroallergens or IgE mediated drug allergies. Atopy occurs when the immune system is more sensitive to common allergic triggers that are aero-allergens or food allergens. A stronger-than-normal reaction occurs when exposed to allergens, such as dust, pollen, peanuts, or shellfish etc. also it is possible that allergies or asthma, causes atopy. Atopy occurs due a small set (30-50%) of common allergens in a population, as diagnosed by the skin prick test [8]. It was observed that the prevalence of the disease decreases with increase in the age of the individual. In a random young population about 50% of atopic (skin test positive) subjects had symptoms of atopy, which included asthma in about 50% [8].

Diagnosis and choice of treatment

The choice of selecting appropriate drugs, be it nasal decongestants, intranasal corticosteroids, or any antihistamines, or anticholinergics or immunotherapies, requires precise diagnosis to know whether it is allergic or non-allergic rhinitis. Besides, it is vital to look for patient gratification to comply for overall positive response of the interventions. This is possible only through understanding the pathophysiological and clinical outcome of these interventions. Hence, it is important to identify differential diagnosis of atopic rhinitis which may be - Chronic nonallergic (vasomotor) rhinitis; Rhinitis medicamentosa; Infectious rhinitis; or vernal keratoconjunctivitis. The most common preferred tests for these conditions is the Skin prick test and the measurement of total serum IgE [8]. But, due to the costs involved in carrying out skin prick test, several under-developed countries have not made it their routine.

The different diagnostic methods their advantages and disadvantages

Diagnostic methods are described in several hospital-based manuals, and have also been outlined above. The most common and standard allergy test is by the Skin Prick Test. In this test the allergen is placed on your arm in a small measured quantity and the surface of the that portion of the skin is pricked with a sterile needle to introduce the allergen inside the skin and this will initiate and immune response, and if you are allergic to this allergen then a small itchy spot will appear in less than an hour or less than an hour. Besides, the physical examination of the allergen by Skin-Prick-Test, a through history of the disease is recorded by asking the patient several relevant questions to establish the diagnosis of allergic rhinitis.

Guidelines for the diagnosis and treatment for allergic rhinitis were also published and widely accepted as Canadian Guidelines in 2007 [9].

Further, a second option or alternative to skin-prick test, is the Allergen- specific IgE test. This test is performed by collecting 3-5ml of the blood sample of the patient and performing Immunosobent assay or ELISA. this *in-vitro* assay provides the patient's specific IgE levels against the particular Allergen. IgE test uses an enzyme-labeled anti IgE antibody to detect the binding of serum IgE to the particular allergen. The advantage of this in-vitro test allows the doctor to see the results immediately for deciding the treatment options.

A third option is to check the CBP of the patients to detect for eosonophils and also serum IgE levels. Other options include Ophthalmic testing which may or may not have any advantage over the skin test or IgE test hence not included as routine test. To be more exhaustive we can think about primary research tolos for Nasal and bronchial challenge, only when the antigen extracts are not available.

Genetic aspects of AR

There is some data to suggest a genetic component to allergic rhinitis, but high-quality studies are generally lacking. Allergic rhinitis develops as a result of complex combination of environmental exposure and genetic susceptibility to certain allergens. Evidence to prove the hereditary component of AR came from the study of twins that has been validated [10]. Further, in the past decade it has been reported that allergic rhinitis occurs in genetically predisposed individuals. In this context, a study found that the chromosomes which harbour such genes were located on chromosome numbers 2,3,4, and 9. Other studies have demonstrated that some SNPs (single nucleotide polymorphism) on such genes relate to the pathogenesis of AR.

The chemistry of binding and interaction of the these molecules (SNPs) were recognized and related to the receptors on molecules like interleukins, leukotrienes chemokines, and eosinophils to name a few [10]. But, in the absence of proper controls, it has not been possible to demonstrate the direct association between occupationally respiratory allergens and occupational exposures in asthma patients. However, occupational respiratory allergens (OA) such as western red cedar, and some chemicals like trimellitic anhydride, and isocyanates, have been studied and have been correlated to HLA class II genes.

Immune response and the mechanisms of action and susceptibility according to the genetics of the individual

The immune response to the aero-allergens by humans reflects the pathophysiology of our defence mechanism, evidence suggests that our genes play a role in the immune response and therefore affect the patients' ability to combat the disease. The immune response can be stronger in some people depending on the age and gender of the individuals, since the genes for immune response occur on the X-chromosome and difference between individuals can be noticed in the fact that some show better protection from inflammation and tissue damage. The immune response to allergens triggers IgE antibodies which bind to the allergens and prevent tissue damage. The antibodies present on the mast cells and mucosal lining are released when the allergens appear. These mediate the release of large amounts of inflammatory mediators such as histamines in the early stages of rhinitis and release of cytokines, chemokynes and leutrokines in later stages of the disease, which activate eosonophils and basophils. Due to genetic defects the immune system produces less antibodies to effectively fight the infection or the disease. The way to treat allergies is eighter by inhibiting IgE production or by activating the effector pathway of cross-linking the cell surface IgE, but in case of abnormal regulation of the effector pathway it may lead to chronic or acute tissue damage in the patients. In the case of allergic rhinitis the precise mechanisms of the disease susceptibility or disease resistance in individuals with respect to the mechanism of action of the allergen- antibody reactions is not cearly understood [11,12].

Global economic burden of rhinitis allergies

The economic burden caused by allergic rhinitis varies across different regions of the world. From the literature survey it was certain that this disorder causes indirect, direct and intangible costs on the society. The two popular studies conducted by Hellgren., *et al*. [13] and Cardell., *et al*. [14] in Sweden had gained much importance in studying the economic burden of allergic rhinitis. Hellgren., *et al*. obtained results from 1213 adults and the productivity loss per person per year was observed to be €653 with a total productivity loss of € 2.7 billion a year. Cardell., *et al*. reported that the mean annual indirect cost was €750.8 and the direct cost was found to be €210.3. The cost for one patient per year was reported to be €961.1 with a total burden of €1.3 billion in the year 2016. Furthermore, A study performed by Colas., *et al*. (2017) on 498 patients in Spain reported that the direct cost per patient per year was found to be €553.80 and indirect costs were €1772.90, and US$266 million in South Korea (Pawankar R., *et al.* 2011). America reports 40 million people with AR costs them $5.3 billion yearly. The implications of such a burden were felt on the patient's productivity, and QoL (quality of life) besides their suffering due to exacerbations and comorbidity. All these reports on the economic burden of AR need to be updated, as information on current losses is not available nevertheless it gives the idea of its impact on global health. Several countries have not yet documented their economic burden.

Economic burden of rhinitis in India

According to the data that is reported by international study of asthma and allergies in childhood (ISSAC) studies [17] the prevalence and prominence of allergic rhinitis continues to increase in India. A study conducted in 1998 among children showed that in phase-I studies the prevalence rate of AR was 12 to 19% which increased to 12 to 24% in phase -3 trials [18].

However, statistics reflect that nearly 20-30% of the population suffers from allergic rhinitis, and there is a lack of information on analysing rhinitis economic burden in India. Thus, accurate and sufficient countrywide estimate and data are not available. In India the economic burden of allergic rhinitis depends on the cost of second-generation drugs. Various drug manufactures have revealed that some drugs like Fexofenadine costs INR 123.56, which could increase the financial burden of the patents [19] but levocetirizine was the cheapest at INR 2.3. Unfortunately, the enigma of the economic burden of AR remains a mystery to the patients and to the community at large.

Figure 2: Routes of aeroallergens exposure and their implications on human health.

Mechanisms of allergic rhinitis and its treatment

The mechanism of action of the allergens in AR patients is due to the development of specific immunoglobulin E (IgE) antibody in responses to indoor and outdoor environmental allergens with exposure over a period of time. Since IgE receptors also occur on the mast cells and basophils, a strong binding of the IgE antibodies occurs on these cells and on organs where these receptors occur [20]. In perennial rhinitis, there is an increase in CD4+ T memory cells, CD4+ T cells and B cells in the nasal mucosa. This is associated with an increase in the number of IL-4, IL-5 and IL-13 positive cells suggesting a Th2 pattern. Consequently, due to high-affinity binding of allergens to IgE in allergic rhinitis an inflammatory response occurs in the nasal mucosa which infiltrates to eosinophils, basophils, T-cells and mast cells. ~~This~~ The binding effect also triggers the release of cytokines and chemokines which are a group of major vasoactive mediators for the regulation of local and systemic IgE synthesis, which establish a communication with the bone marrow immune system for further release of the immunomodulators.

Figure 3: Immune response of an allergic person before and after immunotherapy.

Possible treatment options for allergic rhinitis

Possible treatment measures include therapeutic interventions such as control of rhinitis symptom, rescue medication requirements, and quality-of-life measures. Further, only a complete personalised treatment strategy can improve the patients' well-being.

Allergen avoidance

The initial step in managing AR is to prevent or minimise the exposure to all the causal allergens [21]. To avoid known and unknown allergens it is important to follow the traditional norms in the home interiors like frequent changing of bed covers dusting the house, removing pets from interiors and wearing masks when going out to avoid environmental allergens like pollen etc. as preventive measures for AR [22].

Pharmacotherapy

For the therapy of AR, a variety of pharmaceutical treatments are available. The first line of treatment for AR consists of H1-antihistamines, Intranasal corticosteroids (INCS), or a combination of both the drugs depending on the severity of symptoms of oral or intranasal conditions of AR.

Treatment	Rhinorrhoea	Sneezing	Nasal itch	Onset of action
Oral H1 antihistamines	++	++	+	1-3 hrs
Intranasal H1 antihistamines	++	++	+	< 30 minutes
Intranasal corticosteroids	+++	+++	+++	6-48 hrs
Intranasal corticosteroids + Intranasal H1 antihistamines	++++	++++	++++	10-60 minutes
Intranasal Chromones	+	+	+	15 minutes
Leukotriene receptor antagonist	+	+	+	1 hr

Table 1: Pharmacotherapeutic options.

+ to ++++ indicates the increasing levels of evidence of efficacy.

H1-antihistamines

H1-antihistamines are first-line treatments for patients with mild symptoms, available in oral, intranasal, and ocular forms. The HI- antihistamines are used to block histamine activity, as they aid in interrupting the receptor agonists. The pharmacodynamics and pharmacokinetics (PD-PK) properties of various antihistamines (H1) vary in their drug- gene and drug- drug interactions due to their varied structural chemistries. They are divided into three groups based on the H1 receptor occupancy: a) non-sedating, b) less-sedating, and c) sedating [13]. Some of the non-sedating antihistamines are Bilastine and Fexofenadine [23]. The second most popular less sedating oral H1-antihistamines include: desloratadine, loratadine, cetirizine, levocetirizine, and rupatadine [24]. First-generation oral H1-antihistamines like Diphenhydramine, Ketotifen is not generally prescribed owing to adverse effects, such as sedation [25]. Patient preference has always been for oral antihistamines for mild AR [26]. Some authors have reported that patients with ocular symptoms and mild allergies were treated with alcaftadine, azelastine, bepotastine, cetirizine, epinastine, ketotifen, and olopatadine (as eye drops) and azelastine and olopatadine (as nose sprays) [27].

Intranasal corticosteroids

The first line of treatment as suggested by Rodrigo and Neffen., *et al.* [28] for patients suffering from AR included, intranasal corticosteroids (INCS) such as, fluticasone propionate, fluticasone furoate, mometasone furoate, budesonide, triamcinolone acetonide, ciclesonide, and beclomethasone. The less effective drugs were leukotriene receptor antagonists. To avoid nasal irritation direct spray on the nasal mucosa is to be avoided [28].

INCS and intranasal H1-antihistamine fixed combination

In some countries like Australia fixed- dose combinations of INCS of the following drugs Fluticasone propionate-azelastine and mometasone-olopatadine and intranasal H1-antihistamine are prescribed for allergic rhinitis [29]. These drugs are more effective than the individual chemicals when administered separately and start working within a minute to an hour.

Other drugs

Montelukast and zafirlukast, both leukotriene receptor antagonists, are also used to treat AR. They have a similar effect to oral H1-antihistamines. In some instances a few other drugs for AR treatments, include chromones and ipratropium bromide, which are used for a limited number of symptoms. Chromones are generally regarded as safe, however their usefulness is reported as limited. The nasal spray containing ipratropium bromide is well tolerated, although it is solely useful for nasal discharge. From the available literature, it was observed that decongestions, such as phenylephrine or oxymetazoline sprays, and H1-antihistamines combined with sympathomimetic capsules or tablets, such as cetirizine hydrochloride, acrivastine, or desloratadine plus pseudoephedrine and few more were found to be useful for decongestions by some authors. The above mentions drugs were not recommended for long-time usage to prevent AR [30].

Herbal treatments, homoeopathy, and acupuncture are still widely used to treat AR, but there is very little evidence of using them as a possible treatment for allergic rhinitis [31].

AR pharmacotherapy in children

In many reports the treatment strategy for school- aged children included the following drugs Rupatadine, cetirizine, azelastine

hydrochloride, and the fluticasone propionate-azelastine in fixed combinations proved to be effective. In some countries, cetirizine can be given to children as young as six months old. INCS can also be prescribed to pre-schoolers, H1-antihistamines can be given to children over the age of one year, and cromoglycate or antihistamine eye drops can be given to children over the age of three [32].

AR pharmacotherapy in elderly patients

The diagnosis and recording of symptoms of rhinitis is the same for all age groups, also these patients were given similar treatment. The standard treatment of elderly individuals includes oral H1-antihistamines, intranasal H1-antihistamines, and the fixed combination of azelastine hydrochloride-fluticasone propionate [24].

Immunotherapy

So far there is no known perfect medical cure for Allergies**.** Various treatments which are available are to manage the symptoms of the disease. Immunotherapy is in the form of shots and is still in the developmental stages. Allergen immunotherapy involves the delivery of extracts of specific allergens to induce immune tolerance if the same allergen is exposed in the future. The method of administering these agents could be subcutaneous (SCIT) or sublingual (SLIT) routes these therapies are limited to IgE - mediated diseases in patients. One report has demonstrated the subcutaneous immunotherapy of specific allergens was able to reduce the symptoms of AR and subsequently increases the regulation by T-cells, which trigger the production of cytokines like TGF beta and some interleukins.

Figure 4: Allergic Rhinitis - an overview of the mechanisms of Intermediate and chronic rhinitis.

Source: (Bernstein DI., *et al*. 2016) [20].

When exposed to aeroallergens, a person can become hypersensitive. In the mucosa of the airways, B cells become activated and accumulate. These B cells produce lgE antibodies against aeroallergens and release them into the bloodstream [30]. When the same aeroallergen is exposed repeatedly, it causes an instant reaction that involves the cross-linking of cell bound IgE with the antigen and resulting in the fast release of allergic mediators. T cells result in delayed and persistent inflammatory response with symptoms like itching, swelling, and profuse secretions 6-10 hours later [34].

As a result of immunotherapy T lymphocytes instruct some of the B cells to produce IgG antibodies instead of IgE antibodies. IgG antibodies do not cause mast cell degranulation; instead, they bind to allergen molecules, preventing cross-linking and the release of allergic mediators [35]. Because only a few allergen molecules are available for IgE binding, allergic reactions are reduced or even stopped in some of the cases. Also, as a result of immunotherapy some of the T cells develop into regulatory T cells which reduce antibody production in B cells and effectively reduce allergic immune response [35].

The mechanisms of action of antihistamines and the pharmacogenomic and pharmacogenetic interaction

It is seen that the action of antihistamines and their PK and PD reactions in AR has not been completely documented however, Scientists have known for a long time (Wrighton and Stevens 1992) that the cytochrome P450 enzyme system consisting of at least 14 families of genes with somewhat similar sequences are the most important enzymes synthesized in the liver to deal with the metabolism of all drug molecules and to detoxify all drugs including antihistamines. Not many studies have dwelt on the details of the pharmacogenetics of Histamines in allergic rhinitis. The two most relevant enzymes such as CYP2D6 and CYP3A4 are known to interact with H1 antihistamines, by virtually blocking the H1 receptors and preventing the histamines from reaching the target, however the mutations in these genes may cause different reactions - which is yet to be demonstrated [34]. But this interaction bestows a great relief to the patients, since antihistamines have anti-inflamatory properties and patients feel relief from seasonal and perenial allergic rinitis and from nasal and non-nasal symptoms. Further, it has been shown that supression of cell- adhesión molecules (CAMs) expresion occurs with these antihistamine drugs [36].

To understand the pharmacodynamics and pharmacogenetics of these diseases and their treatments it is important to follow the effector pathways of the allergens and their immune response. The relationship between the various immune effector signaling pathways and how they modulate the therapeutic responses. Research in this área in rhinitis is very limited, hence further research may help us to understand the immuno- modulatory therapeutics and will be useful in overcoming tissue damage and inflamatory conditions [37]. This study may also lead us to discover new drugs or vaccines. So far seccond generation oral antihistamines and intranasal corticosteroides are the Golden standards for treatment for Allergic rhinitis. Some Health professionals have also demonstrated the usefulness of Allergen immunotherapies as well as decongestants and oral corticosteroides in select cases [37].

Discussion and Conclusion

The frequent causes of allergic rhinitis are mostly due a person's exposure to indoor or outdoor allergens which cause symptoms of discomfort like constant sneezing migraine and running nose. Growing evidence, in the last 3 decades, indicates that nasal reactivity to allergens can occur in individuals that have a lifelong tendency for the development of allergic reactions and can account for direct and indirect costs.. Epidemiologists have confirmed that allergic rhinitis and asthma occur due to the individuals' exposure to ubiquitous environmental aeroallergens. Available literature also suggests that patients suffering from allergic rhinitis could have had a previous history of the disease, however there is not much evidence from any multicentre studies or cross-sectional studies to document the same. Further, due to the lack of detail studies in immunopathology, the mechanism of inter-action of aero-allergen and antibody is still considered a grey area in the field of AR. The increased detectable levels of IgE in blood or nasal secretions, plus responses to BAT, SCIT and SLIT is the existing immunotherapeutic diagnosis for AR.

However, medical management of AR depends upon serum IgE (sIgE) and nasal reactivity to the aero- allergens.

Until in-vitro tests become available for clinical practice, the nasal allergen provocative test (NAPT), which determines the response of irritants/aero-allergens and the pathophysiology of the affected nasal parts will be valuable. It is most important to start the treatment for allergic rhinitis at an early stage, as it can proceed aggressively to worsen the condition and can lead to asthma or conjunctivitis or also become susceptible to co-morbidities. Among the symptoms of AR, migraine headaches are very common and immunotherapy is reported to decrease the frequencies of these symptoms.

As a preventive measure it is also crucial to educate the patients, especially the parents of children with rhinitis about how the disease can progress and lead to worse and uncomfortable conditions. It is also important to educate them and counsel them on how to prevent their exposure to allergens which can help them to reduce their economic burden. Patient counselling is one good option to a better management of allergic rhinitis. Understanding the complex mechanisms of sensitizations to allergens is eventually a challenge of the future, this can happen when much needed research in the fields of immunology, molecular genetics and pathology are given importance. This in turn will lead to better understanding of the disease and find better treatment options and better preventive measures, which is the need of the hour.

Conflict of Interest

The authors have no conflicts of interest that are directly relevant to the content of this manuscript.

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