

Diagnostic methods and management of allergic rhinitis

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Abstract:

We review herein the diagnosis and treatment of AR, including recent update of AR. A literature search for management of allergic rhinitis was performed in December, of 2017 through the MEDLINE/PubMed, Embase Databases. We searched with this method to be able to identified relevant articles pertaining to AR management. An intranasal glucocorticoid to be used on a continuous basis must be suggested. Integrating a nasal antihistamine with an intranasal glucocorticoid might provide additive impacts. In cases where pharmacotherapy is inefficient or otherwise appropriate to the patient, allergen-specific immunotherapy should be used. Two types of allergen immunotherapy are currently available: subcutaneous injections and rapidly dissolving sublingual tablets, the latter limited to the therapy of grass and ragweed allergy. Both kinds of therapy typically give sustained efficacy after the cessation of treatment.

Introduction:

Allergic rhinitis (AR) is a symptomatic problem of the nose generated after exposure to allergens via IgE-mediated hypersensitivity reactions, which are characterized by 4 principal symptoms of watery rhinorrhea, nasal blockage, nasal irritation and sneezing [1]. The frequency of AR is enhancing throughout the globe. In the United States, AR is estimated to impact roughly 60 million individuals, and the frequency has to do with 10-30% in adults and nearly 40% in youngsters [2],

[3].In Korea, the frequency of seasonal AR was 3.39% in accordance with the survey of 71,120 patients who visited the otolaryngology facilities of 23 tertiary recommendation centers between November 1999 and April 2000 [4].According to the surveillance of 42,886 Koreans utilizing the International Study of Asthma and Allergies in Childhood (ISSAC) questionnaire, 12-month occurrences of AR in primary and middle school kids (6-12 and 12-15 years) were 28.8% and 29.1%, respectively [5].AR is connected with a massive financial concern causing troubles in lifestyle such as work/school efficiency and sleep.

As A Result, Allergic Rhinitis and Its Impact on Asthma (ARIA) released the guidelines for AR and modified them in 2008 [6].The factors of the ARIA standards are as follows: AR is subdivided by symptom duration and the intensity of AR, a stepwise restorative approach is required relying on the ARIA category, and patients with consistent AR must be reviewed for asthma. There were some changes in the 2008 ARIA guidelines as compared to the 2001 guidelines: (1) intranasal corticosteroid ended up being a first-line medication which was second-line medicine in the 2001 guidelines, (2) second-generation antihistamines were chosen to first-generation one's, (3) leukotriene villains were gotten in into suggested drugs and (4) the duty of immunotherapy was re-evaluated.

We review herein the diagnosis and treatment of AR, including recent update of AR.

Methodology:

A literature search for management of allergic rhinitis was performed in December, of 2017 through the MEDLINE/PubMed, Embase Databases. We searched with this method to be able to identified relevant articles pertaining to AR management, the bibliographies of each these studies were searched for more relevant articles. All articles in the peer-reviewed English literature that

reported human subjects were included. of these articles were also used as a supplemental data source.

Discussion:

· **DIAGNOSIS OF AR**

The medical diagnosis of AR is based on a regular background of allergic signs and diagnostic tests [6]. When 2 or even more symptoms from watery rhinorrhea, sneezing, nasal obstruction and nasal pruritus continue for ≥ 1 hr on a lot of days, AR is highly suspected. In this situation, condition intensity need to be identified according to the ARIA guidelines and a confirmative medical diagnosis should be established by the skin prick examination or the serum-specific IgE level. Independent nasal stuffiness, mucopurulent rhinorrhea, mucoid postnasal drip, discomfort, frequent epistaxis or anosmia is generally not connected with AR.

Skin testing

Skin testing is the most important to discover offending allergens. There are various screening approaches including the scratch, prick/puncture, intradermal and patch tests. Amongst them, the skin prick examination is typically advised in medical practice. False-positive or false-negative responses are often stimulated in skin examinations, which implies that favorable responses to certain allergens in skin examinations does not always have a direct connection with actual allergic reactions in the nasal tooth cavity. There is controversy relating to the analysis of the test results, and requirements for positivity are various amongst allergic reaction clinics. Moreover, skin examinations have some issues. This test can be affected by some drugs, particularly

antihistamines, patients' age and test websites. If a patient has dermatologic disease, skin examinations are difficult to execute. Regardless of these weak points, skin testing is pertained to as the most vital analysis method. A previous research study on skin prick test results of 1,564 Korean AR patients reported that residence dust termites was the most typical allergen with a positive reactivity of 70% -80% (Table 1) [7].

Table 1.Positive rates of common offending aeroallergens (n=1,564)

Allergens	Positive rates(%)
Mite:	
Dermatophagoides farina	77.6
Dermatophagoides pteronyssinus	73.3
Epithelia:	
Cat hair	39.9
Dog hair	32.6
Pollens:	
Mugwort	23.4
Tree	18.8
Ragweed	18.2
Grass	14.1
Others:	
Cockroach	21.8
Fungus	6.0

Serum specific IgE level

Although the radioallergosorbent test (RAST) was the first approach to find serum-specific IgE, this examination has not been extensively made use of due to the fact that it calls for a radioactive isotope and pricey tools as well as since this examination could not find numerous antibodies all at once. The following technique is the multiple allergen simultaneous test (MAST). Considering that the MAST has some benefits over the RAST, it has been widely used. The MAST uses an image reagent instead of a radioactive isotope, does not need pricey devices and can discover multiple allergens simultaneously. This examination is not influenced by drugs such as antihistamines, is less intrusive and could be taken on in patients with dermographism. One issue with the MAST is

a reduced level of sensitivity as compared with the skin prick examination. Nonetheless, Finnerty et al [8] reported that the MAST shows 66.5% and 78.5% concurrence rates when the criteria for positivity are ≥ 3 mm and ≥ 5 mm, respectively, and they recommended the MAST rather compared to skin tests. The capsulated hydrophilic carrier polymer (CAP) system is a more exact in vitro test. Its treatment resembles that of the MAST, but it makes use of a strong phase that has a high fondness to antigens. The CAP system can spot allergens more quantitatively than the MAST using antigens bound to a great thread since antigens bind to the internal surface area of sponge-like cellulose polymer bubbles.

Clinical parameters associated with asthma

Guerra et al. [9] have reported that the extent of AR has a favorable relate to asthma and the risk of asthma occurrence is 5 times greater in AR patients with raised serum IgE. Silvestri et al. [10] have aimed out that the eosinophil count of the nasal cavity is associated with bronchial hyperresponsiveness which the changes in the number and distribution of eosinophils after nasal mucosal challenge are also connected with bronchial hyperresponsiveness. They recommend that the local inflammation of AR could forecast bronchial hyperresponsiveness. A domestic research of 83 pediatric AR patients and 32 regular kids reported that occurrence of bronchial hyperresponsiveness was greater in AR patients than in control subjects (32.5% vs. 9.4%) and that relentless AR and adult asthma are closely pertaining to bronchial hyperresponsiveness [11]. On top of that, it is recognized that bronchial hyperresponsiveness in AR patients is a predictor of asthma [12]. It has usually acknowledged that the growth and severity of asthma boost when a patient is animated to indoor allergens such as house dirt mites or cat dander. The occurrence of asthma more boosts in moderate to extreme AR patients animated to both interior and outside allergens.

TREATMENT

Avoidance

Avoidance of indoor irritants consisting of residence allergen is in some cases difficult. Therefore, couple of researches on avoidance of annoying irritants have been conducted. Consequently, the 2001 ARIA standards identified the avoidance as evidence D [1]. The 2008 ARIA guidelines have reported that there is the absence of evidence for performance of avoidance of house allergen or family pet animal dander [6]. Nevertheless, a previous research study has shown that cleaning with 60 °C hot water eliminates residence allergen and other irritants efficiently as compared with 30 °C water (26.8% vs. 0.6%) [13]. Evasion is necessary for work AR. The European Academy of Allergy and Clinical Immunology (EAACI) stated that the safest and most reliable treatment of work AR is the stringent avoidance of offending irritants [14]

Pharmacological treatment

The concept of pharmacological therapy is a stepwise strategy according to the intensity and duration (Fig. 1). The 2008 ARIA guidelines are different from the 2001 ARIA guidelines as adheres to: (1) leukotriene receptor antagonists could be made use of in all AR, (2) second-generation antihistamines are chosen to first-generation antihistamines and (2) topical steroids are related to as the most effective medicine for grown-up and pediatric AR patients.

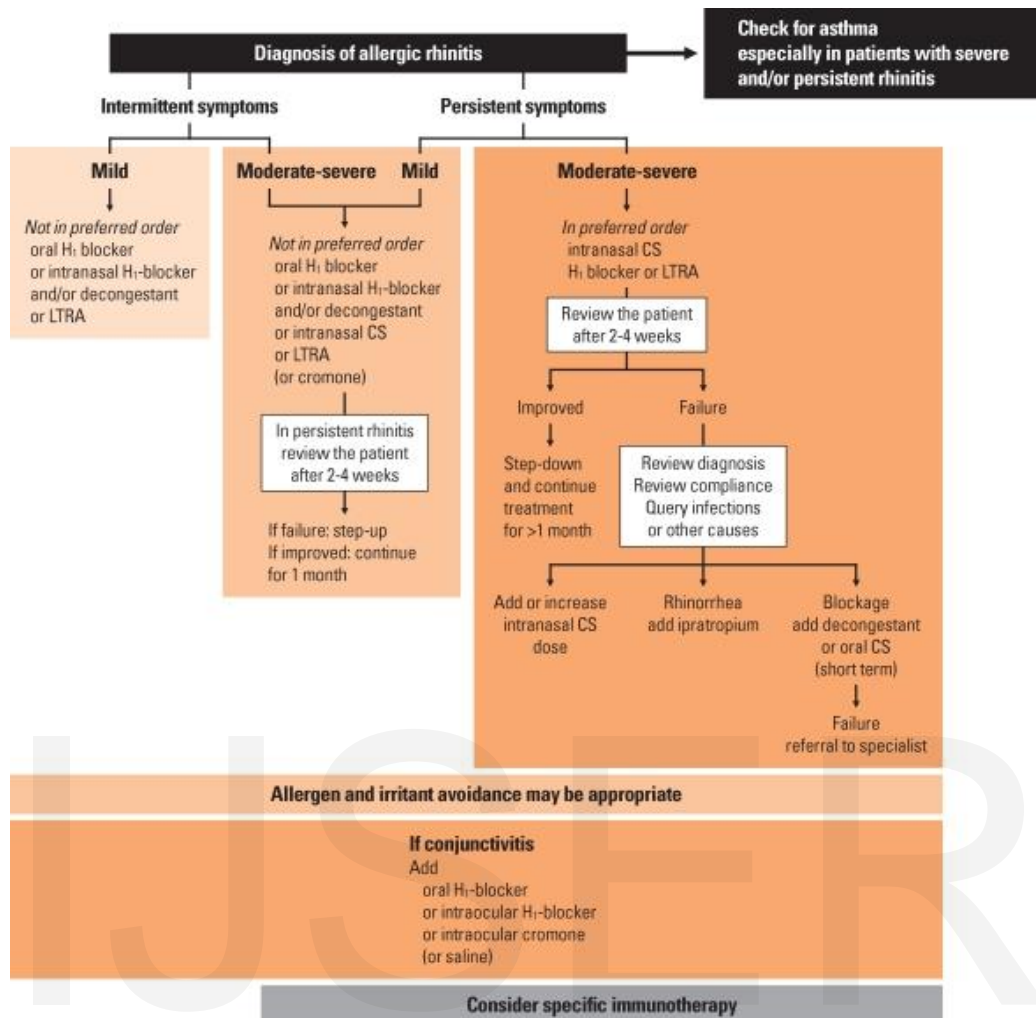


Figure1.Rhinitis management [6]

Oral antihistamines

First-generation antihistamines, which have been utilized since the early 1940s, have some side impacts such as sedation, memory disability and psychomotor disorder, which trigger lots of issues in professional practice. In contrast, second-generation antihistamines penetrate the blood-brain barrier a lot less than first-generation antihistamines, and therefore they have couple of adverse effects on the main nerves [15]. Therefore, the 2008 ARIA standards recommended second-generation antihistamines rather than first-generation antihistamines. Oral antihistamines are reliable in the treatment of rhinorrhea, sneezing, nasal itching and eye signs and symptoms yet less effective in nasal blockage [16]. Oral antihistamines have been reported to be secure and effective

in youngsters [17]. Terfenadine and astemizole were originally used second-generation antihistamines. These drugs have severe cardiac poisoning causing QT prolongation and torsade de pointes. When these antihistamines are provided together with macrolide anti-biotics or azole antifungal agents, the risk of cardiac negative effects rises due to the fact that these medications impact cytochrome p450 isoenzyme CYP3A4 activity. For that reason, terfenadine and astemizole have not been suggested in numerous nations. Considering that ebastine is metabolized by CYP3A4, it can additionally generate such medicine communications in theory. When high-dose ebastine (50 mg/kg/day) is offered to guinea pigs, QT prolongation is observed in electrocardiography. When ebastine 20 mg/kg/day is administered with ketoconazole 400 mg/kg/day or erythromycin 2,400 mg/kg/day, QT periods are lengthened up to 10 m sec with no medical relevance. Care should be taken in suggesting ebastine together with other drugs inhibiting CYP3A4 in patients with previous QT prolongation, liver failure or kidney disorder.

Intranasal antihistamines.

Topical antihistamines have been reported to reduce itching, sneezing and rhinorrhea [18]. Nevertheless, they are much less reliable than intranasal corticosteroids and inadequate in eye signs and symptoms [19]. Intranasal azelastine two times a day could decrease the signs and symptoms of seasonal AR patients who do not react to oral antihistamines. They have some negative effects such as mild sedation and metal taste [20].

Intranasal corticosteroids

Considering that intranasal corticosteroids are not absorbed systemically, they generate couple of systemic side impacts. Steroid fragments permeate the cellular membrane and bind to cytoplasmic steroid receptors. The steroid-receptor complicated is moved to the nucleus and binds to the

particular DNA site. The anti-inflammatory effect is generated by change in protein synthesis after binding of the steroid-receptor complex to DNA or by influencing various other transcription variables. Intranasal corticosteroids prevent both early and late reactions and lower IgE production and eosinophilia by inhibiting the secretion of cytokines consisting of IL-4, IL-5 and IL-13. When intranasal corticosteroids are carried out, eosinophils and basophils lower in 1 week [21]. Intranasal corticosteroids are efficient in all AR signs and symptoms, specifically nasal blockage and eye signs and symptoms [22]. The restorative effect of intranasal corticosteroids is encountered 7 hours after management [23] and gets to the maximal degree after 2 weeks.

Lately, budesonide, triamcinolone acetonide, fluticasone propionate, mometasone furoate and fluticasone furoate have been commonly used. For a far better choice of topical steroids, their pharmacological features must be considered. Although these medications have comparable clinical impacts, their systemic absorption rates are various. The systemic absorption rates of flunisolide, triamcinolone acetonide and beclomethasone dipropionate are 20-50%, whereas those of mometasone furoate and fluticasone propionate are very low ($\leq 0.1\%$ and $\leq 2\%$, specifically). Additionally, a lot of the intranasal corticosteroids are removed by first-pass hepatic metabolism.

Leukotriene receptor antagonists (LTRAs).

The role of leukotrienes in allergic responses is well understood. The effectiveness of LTRA has been shown in asthma. Just recently, some research studies on the efficiency of LTRAs in AR patients have been reported. As previously discussed, the 2008 ARIA standards re-evaluated the role of LTRAs. Passion in LTRAs has been enhancing with the principle of "one airway, one disease", and therefore several studies on LTRAs are being conducted. Care must be absorbed the medical usage of Pranlukast which is metabolized by hepatic CYP3A4 enzymes since its serum

concentration can be raised when administered with terfenadine, astemizole, ketoconazole or erythromycin.

Montelukast is effective in reducing nasal and eye signs in patients with seasonal AR and improves nasal blockage equivalent to loratadine [6]. The additive or synergic result of montelukast and loratadine is questionable. Some previous research studies have advocated that a mix of montelukast and loratadine has faster and a much better efficiency than montelukast or loratadine alone [24] whereas others have not [25]. Kurowski et al. [26] reported that montelukast plus cetirizine which was carried out 6 weeks prior to the plant pollen period properly stopped the exacerbation of seasonal AR symptoms. The additive effect of LTRAs and antihistamines requires even more investigations. Already, the pharmacological impacts of LTRAs are approximated to be much like those of antihistamines but less than those of intranasal corticosteroids in patients with seasonal AR [6].

Anti-IgE antibody.

Omalizumab, an anti-IgE recombinant humanized monoclonal antibody, conflicts with the interactions between mast cells/eosinophils and IgE by binding to free IgE and for this reason decreases serum free IgE [27]. It additionally reduces inflammatory reactions in blood or nasal mucosa [28] and expression of FcεRI located externally of pole cells or eosinophils [29]. Casale et al. [30] have shown that omalizumab pretreatment (300 mg) prior to and throughout the pollen season for 12 weeks with 3-4 weeks intervals reduces AR symptoms dramatically in patients with extreme seasonal AR. Although there were some negative responses, they mentioned that the incidence of adverse impacts of omalizumab such as headache, upper respiratory infection and sinusitis in the patient group is not considerably different from that of the placebo group. Urticaria could take place at the injection site, yet it subsides automatically or with the management of

antihistamines. While anti-IgE antibody treatment shows up to be handy in extreme asthma, it is controversial whether anti-IgE treatment is ideal as a treatment alternative for AR due to anaphylactic threat [31] and high prices.

Immunotherapy.

Immunotherapy is the only therapeutic choice that customizes the fundamental allergic mechanism by causing desensitization and creating an anergy state for upsetting irritants. Immunotherapy was originally presented for seasonal AR due to pollens. Today, its indications have been expanded to various other allergic illness because of hymenoptera, home dust mite, animal dander or fungi [32]. Extracts of upsetting allergens are infused subcutaneously with raising doses up until a maintenance dose is gotten to. The upkeep dose is administered for ≥ 3 years. Although subcutaneous immunotherapy is a well-established therapy choice, the danger of anaphylaxis has led to the growth of other administration courses such as the oral, sublingual or nasal course. Sublingual immunotherapy (SLIT) has been used for 20 years in European countries because of its non-invasiveness, reduced occurrence of negative effects and convenience of self-administration. Lately, it has changed subcutaneous immunotherapy. In Korea, sublingual immunotherapy for home dirt mites was initiated in 2007 [33].

Conclusion:

AR is worth treating properly, even when it is part of a myriad of allergic problems; as the nose is the entrance to the respiratory system, great rhinitis control could promote control of signs and symptoms elsewhere. AR, if poorly managed, causes troublesome symptoms and influence on everyday activities, quality of life and on various other areas of the respiratory tract, such as ears, sinuses, throat and lungs. Feasible reasons for difficult-to-treat cases consist of medical professional factors such as misdiagnosis and undertreatment or patient elements such as lack of concordance with treatment.

An intranasal glucocorticoid to be used on a continuous basis must be suggested. Integrating a nasal antihistamine with an intranasal glucocorticoid might provide additive impacts. In cases where pharmacotherapy is inefficient or otherwise appropriate to the patient, allergen-specific immunotherapy should be used. Two types of allergen immunotherapy are currently available: subcutaneous injections and rapidly dissolving sublingual tablets, the latter limited to the therapy of grass and ragweed allergy. Both kinds of therapy typically give sustained efficacy after the cessation of treatment.

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