Allergic rhinitis and its impact on asthma update (ARIA 2008): the Turkish perspective

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Allergic rhinitis is a symptomatic disorder of the nose induced after allergen exposure due to an IgE-mediated inflammation of the membranes lining the nose. According to its definition in 1929, "The three cardinal symptoms in nasal reactions occurring in allergy are sneezing, nasal obstruction and mucous discharge."

Allergic rhinitis is a global health problem. Patients from all countries, ethnic groups, and ages suffer from allergic rhinitis. Allergic rhinitis causes major illness and disability worldwide. It affects social life, sleep, school and work[1-4]. The economic impact of allergic rhinitis is substantial; however, rhinitis is still underdiagnosed and undertreated[5].

Epidemiology

Over 600 million patients suffer from this disease[6-9], but there are still differences between rural and urban areas and in developed and developing countries[8,10-12], possibly because of differences in immune reactions[13].

In Turkey, nationwide studies in both asthma and rhinitis are lacking. Most of the studies have concentrated on the prevalence of asthma in children and adults from different regions of the country. In general, three different methodologies have been used for the epidemiological studies of childhood asthma in Turkey[14-29]: International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire; American Thoracic Society (ATS) questionnaire adapted by the Turkish National Society of Allergy and Clinical Immunology; and Aberg's questionnaire. For the adult studies, on the other hand, a vast majority of studies have used the "European Community Respiratory Health Survey (ECRHS)"method.

These studies show that, depending upon the geographical region, the asthma prevalence in childhood varies between 2-15% and in adults between 2-5%[14-29]. The higher prevalence figures obtained in some childhood studies suggest that the prevalence of asthma decreases with age. Alternatively, these higher figures may be due to the fact that some of the wheezing illnesses in childhood may be mistakenly diagnosed as asthma.

Similar to the observation in various regions around the globe, asthma prevalence shows major variations among different cities and regions within Turkey. In general, the prevalence is higher in coastal regions, large cities and lower socioeconomic classes. Childhood infections, passive smoking, family history of asthma and allergies, premature birth, and living at lower altitudes and higher atmospheric pressure may increase the risk of asthma. The data suggest that asthma is more frequent in males in childhood and in females after adolescence in Turkey. Successive studies using the same methodology suggest that the prevalence is increasing in İstanbul, İzmir and Adana, while a more stable course has been seen in Ankara over the years[27,28,30].

Most of the epidemiological data on rhinitis are derived from studies that are basically conducted as an asthma study. These studies have shown that the prevalence of rhinitis ranges between 4.5-36.3% in children and 8.9-27.7% in adults[14-31]. The few studies that have investigated rhinitis specifically have shown that air pollution influences the frequency of rhinitis[32,33]. One study showed that seasonal symptoms are more frequent than perennial symptoms among university students[30]. Successive studies suggest that its prevalence is rather stable over the years. In

strong support of the ARIA (Allergic Rhinitis and its Impact on Asthma) concept, these studies have also shown that the prevalence of rhinitis in asthmatic patients approaches 100%, whereas the prevalence of asthma in patients with rhinitis is around 50%.

Using another approach, some studies have investigated the prevalence of atopy and asthma in more than three million Turkish immigrants living in Europe. These studies suggest that the prevalence rates are lower in children of this population compared to native Europeans, whereas atopy spectrum in adults is similar between the two populations[34-37].

ARIA Update

In 1999, during the ARIA World Health Organization (WHO) workshop, an evidence-based document was produced using an extensive review of the literature available up to December 1999[38]. The statements of evidence for the development of ARIA have followed WHO rules and were based on those of Shekelle et al.[39].

The ARIA document was intended to be state-of-the-art for the specialist as well as for the general practitioner and other health care professionals:

- To update their knowledge of allergic rhinitis.
- To highlight the impact of allergic rhinitis on asthma.
- To provide an evidence-based documented revision on the diagnosis methods.
- To provide an evidence-based revision on the treatments available.
- To propose a stepwise approach to the management of the disease.

However, an update of the ARIA guidelines was needed because:

- A large number of papers have been published within the past seven years extending our knowledge[40-45].
- The ARIA classification was proposed by an expert group and needed to be validated in terms of classification and management[38]. New studies showed consistently that "intermittent" and "persistent" are not synonymous with "seasonal" and "perennial"[46,47]. There are now several reports which have validated this classification[48,49], although some authors proposed to extend the severity of allergic rhinitis to three levels[50,51]. However, since this would not lead to a difference in treatment, the ARIA experts proposed to continue to classify the severity of rhinitis into "mild" and "moderate/severe".
- New methods of diagnosis have been proposed for allergic and non-allergic rhinitis[52-55]. The diagnosis of allergic rhinitis is often easy, but in some cases it may cause problems and many patients are still under-diagnosed, often because they do not perceive the symptoms of rhinitis as a disease.
- Moreover, there were gaps in our knowledge in the first ARIA document, which were more recently approached. These include:
  - o Some aspects of treatment like complementary and alternative medicine[41].
  - o Sports and rhinitis in athletes[42,56,57].
  - o Rhinitis and its links with asthma in children[58-62].

The ARIA update was started in 2004. Several chapters of ARIA were extensively reviewed using the Shekelle evidence-based model, and papers were published in peer-reviewed journals: tertiary prevention of allergy, complementary and alternative medicine, pharmacotherapy and anti-IgE treatment, allergen-specific immunotherapy, links between rhinitis and asthma, and mechanisms of rhinitis[40-45]. There was then a need for a global document that would highlight the interactions between the upper and the lower airways including diagnosis, epidemiology, common risk factors, management and prevention. Moreover, the allergy perspective should also be targeted to developing countries[63,64]. The ARIA 2008 update has been recently published[65].

The grading of evidence and recommendation for management evidence-based system of the ARIA 2008 update does not use the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach[66,67]. It is expected that some of the recommendations offered by the 2008 ARIA update may differ when the GRADE approach is achieved.

A large list of treatments was considered in the ARIA 2008 update[65]. Concerning pharmacologic treatments, intra-nasal corticosteroids are the

first-line therapy in patients with moderate to severe disease and are also effective on ocular symptoms[68], H_1-antihistamines are important treatments for all patients, and leukotriene receptor antagonists are particularly important for patients with rhinitis and asthma[69,70]. On the other hand, tertiary prevention of allergy is still a matter of debate since clinical trials do not usually show any efficacy of single allergen avoidance measures[40]. Sublingual immunotherapy has proven to be a safe and effective treatment[71-74] but clinical trials need to be standardized[75,76]. An algorithm of the management of allergic rhinitis is provided (Fig. 1). However, there is a continuous progress in our understanding of the mechanisms of allergic rhinitis and novel treatment approaches are constantly published[77].

Non-allergic rhinitis is still a matter of discussion[78] and may pose some problems in treatment[79].

Another important aspect of the ARIA was to consider comorbidities of allergic rhinitis, and in particular asthma. Epidemiologic studies have consistently shown that asthma and rhinitis often coexist in the same patients in every region of the world[80,31]. The vast majority of patients with asthma have rhinitis, but the prevalence of asthma in rhinitis patients still needs to be assessed[83,84]. The treatment of the nose does not considerably impact the lower airways, but there have been some compelling data suggesting that new studies with innovative methods need to be started[85,86]. Specific immunotherapy in patients with allergic rhinitis has a prolonged effect on the development of asthma when stopped[87].

The perception of patients and physicians about the links between asthma and rhinitis varies between countries, but appears to be higher than expected[88,89]. However, the knowledge is not directly translated into practice since fewer

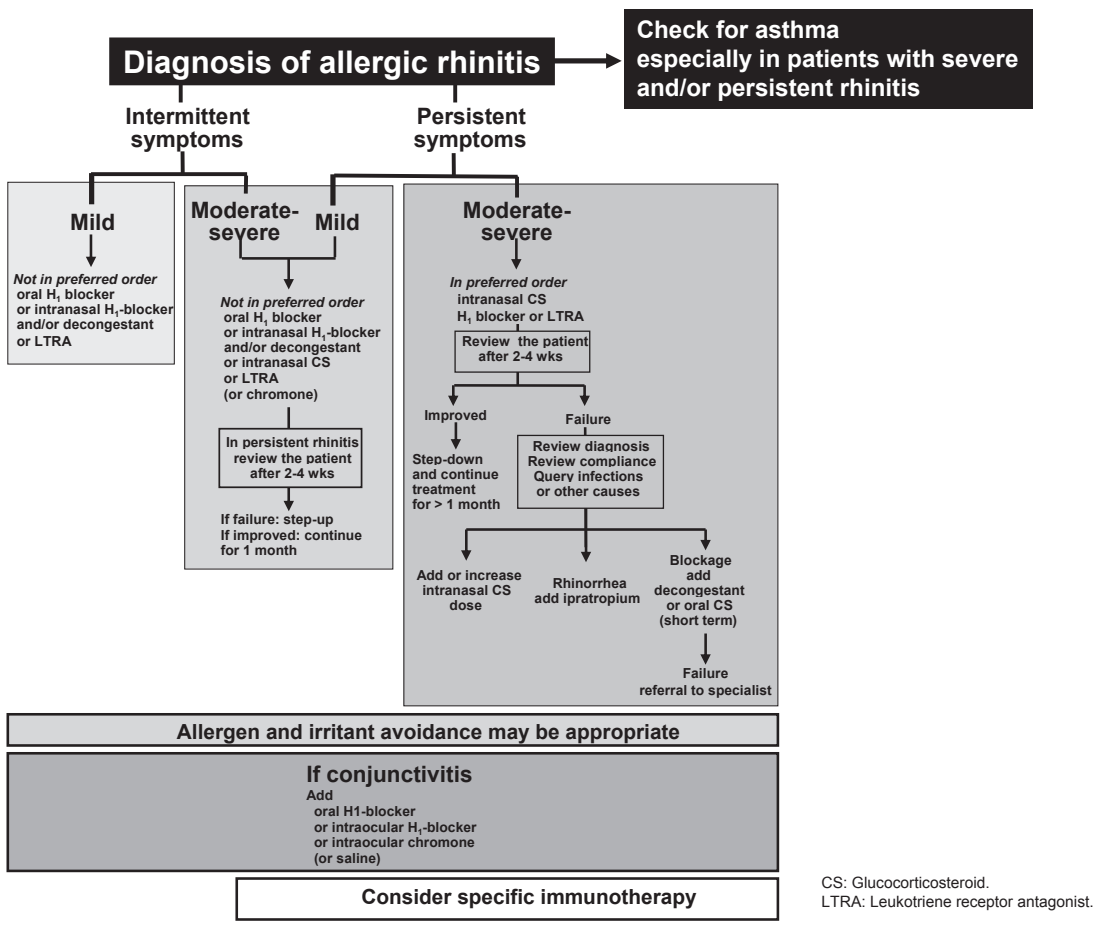

Fig. 1. Stepwise approach to the management of allergic rhinitis.

physicians co-prescribe treatments for rhinitis and asthma in the same patient.

The recommendations of the ARIA workshop in 1999 are still valid[38], and in particular, it is recommended that patients with allergic rhinitis, in particular if it is persistent, should be evaluated for asthma. Patients with asthma should be evaluated for rhinitis, and a combined strategy should be ideally used to treat the upper and lower airway diseases in terms of efficacy and safety.

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