Editorial
Allergy Asthma Immunol Res. 2018 January;10(1):1-3.
https://doi.org/10.4168/aair.2018.10.1.1
pISSN 2092-7355 • eISSN 2092-7363

AAIR
Allergy, Asthma & Immunology Research

Efficacy and Safety of Subcutaneous Allergen Immunotherapy for Allergic Rhinitis

Myung Hyun Sohn*

Department of Pediatrics, Severance Hospital, Institute of Allergy, Brain Korea 21 PLUS Project for Medical Science, Yonsei University College of Medicine, Seoul, Korea

Allergic rhinitis (AR), one of the most common allergic diseases, has an incidence rate that has been increasing constantly and a worldwide prevalence rate that is quite high, which make the social burden of AR substantial.[1,2] Because the diagnosis of AR is usually based on patients' subjective perceptions rather than on physicians' objective tests, unlike in the diagnosis of asthma and atopic dermatitis (AD), there are fewer studies about AR aside from those investigating allergic diseases in general.[3] Conversely, AR can be considered part of one airway disease along with asthma and a comorbidity of other allergic diseases; indeed, many studies about other allergic diseases have collected data about AR as well.[4]

Management of AR includes avoidance of environmental allergens, pharmacotherapy, and allergen specific immunotherapy (AIT).[5] If possible, allergen avoidance can be recommended. However, effective allergen avoidance is often not feasible.[6] A significant number of patients rely on pharmacotherapy, such as oral/topical antihistamines, nasal corticosteroids, or leukotriene receptor antagonists.[7] However, these therapies do not alter the natural course of AR and can cause side effects. Despite drug therapy, many patients continue to experience symptoms that reduce their quality of life.

By contrast with symptom suppression by pharmacotherapy, AIT aims to alter the immune system and could represent a cure for AR. The procedure of desensitization using pollen extracts for the treatment of AR has been used around for almost 100 years and was first initiated by Noon and Freeman in 1911.[8,9] The use of allergen-specific desensitization, now referred to as AIT, involves the administration of gradually increasing amounts of allergen to improve symptoms associated with subsequent exposure to the causative allergen.[10] The main difference between AIT and the other treatments is at present the only etiological treatment able to alter disease progression.[11]

AIT is indicated in patients with positive allergy skin testing and AR with poorly controlled symptoms using maximal pharmacotherapy as well as in those with coexisting allergy and asthma.[12] Relative indications include inability to tolerate pharmacotherapy or desire to avoid the need for medication. There are currently 2 forms of AIT available in Korea: subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT).

Several reviews and meta-analyses have focused on perennial and seasonal AR, assessing the efficacy of AIT in relieving symptoms, improving quality of life, and reducing use of medication.[13] Through a systemic review, Erekosima *et al.*[14] suggested that moderate to strong evidence supports the effectiveness of SCIT for the treatment of AR and asthma, particularly with SCIT regimens. A meta-analysis both directly and indirectly comparing SCIT with SLIT using data from 17 SCIT randomized controlled trials (RCTs) and 11 SLIT RCTs showed no statistically significant difference in quality of life between the 2 modalities.[15] A recent systemic review and meta-analysis reported that AIT is effective in improving symptom, medication, and combined symptom and medication scores in patients with allergic rhinoconjunctivitis while on treatment, and there is some evidence suggesting that these benefits are maintained in relation to symptom scores after discontinuation of therapy.[16] They identified 61 SCIT RCTs including 6,379 patients, 71 SLIT RCTs including 13,636 patients, and 2 intralymphatic immunotherapy RCTs including 56 patients.

In this issue of the *Allergy, Asthma and Immunology Research*, Lee *et al.*[17] reported a valuable study on the efficacy and safety of SCIT in routine clinical practice in Korean adults with AR

Correspondence to: Myung Hyun Sohn, MD, PhD, Department of Pediatrics, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea.
Tel: +82-2-2228-2050; Fax: +82-2-393-9118; E-mail: mhsohn@yuhs.ac
Received: November 3, 2017; Accepted: November 9, 2017
• There are no financial or other issues that might lead to conflict of interest.

sensitized to house dust mites (HDM). This large retrospective cohort study reviewed 304 patients with AR treated using SCIT targeting HDM alone or with pollens for at least 1 year, and showed that SCIT facilitated remission in 76.6% of patients with AR within 4.9 years on average. They also demonstrated that severe AR, specific IgE levels to HDM ≥17.5 kU/L, and duration of immunotherapy ≥3 years were identified as significant predictors of clinical remission during SCIT for patients with AR sensitized to HDM. There is no present consensus on optimal AIT duration.[13] Some reports show the carry-over effect persisting for at least 3 years after cessation of both SCIT and SLIT.[18,19] Another long-term follow-up study demonstrates the ongoing clinical benefit 12 years after discontinuation of SIT and the reduction in the onset of new sensitization, which is found 6 years after discontinuation of SIT, is sustained 6 years later.[20] Based on these long-term carry-over findings, manufacturers usually recommend a 3-year treatment duration.[13] A recent EAACI guidelines on AIT for AR also recommended that a minimum of 3 years of therapy be used to achieve long-term efficacy.[5]

Adverse reactions to SCIT range from local site reactions, such as skin pruritus, to systemic reactions, such as anaphylaxis and have previously been classified by the WAO.[21] Local reactions are frequent, in 26%-86% of SCIT injections, but are often well-tolerated.[11] A systematic review of SCIT in 2007 included 13 trials and reported severe anaphylactic reactions requiring adrenaline in 3.4% of cases.[22] Moreno *et al.*[23] demonstrated 3.7% of 423 SCIT patients experienced systemic reactions in a multicenter study. In the current issue of the *AAIR*, Lee *et al.*[17] found that 24% of patients experienced adverse reactions to SCIT and only 1 case of anaphylaxis developed.

In summary, SCIT is an effective and well-tolerated treatment option in the management of AR which has been practiced for almost a century and the only treatment that can affect the natural course of disease. However, SCIT still has disadvantages, such as visits to a doctor's office, repeated injections, and the risk of systemic allergic reactions. Further studies are needed to predict which individuals can respond favorably to AIT based on a molecular or component resolved diagnosis and to develop more convenient and effective routes other than injections.

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