Editorial

Step Up Approach in The Management of Pediatric Allergic Rhinitis

Nina Irawati,* Muhammad Irfan Ata Ul Awal**

**Allergy Immunology Division, Department of Otorhinolaryngology, Head and Neck Surgery Cipto Mangunkusumo Hospital – Faculty of Medicine Universitas Indonesia*
***Faculty of Medicine Universitas Indonesia*

Introduction

Allergic rhinitis (AR) is clinically characterized by two or more symptoms including itching, sneezing, nasal obstruction and rhinorrhoea. It is known to be caused by IgE-mediated hypersensitivity reaction in response to inhaled allergens.[1] It has been shown to have high burden of disease, as patients with AR show significant reductions in the number of healthy days, interruption of daily activities due to symptoms, and overall reduction in quality of life.[2] The International Study of Asthma and Allergies in Childhood (ISAAC) estimates the prevalence of AR across children and adults to be about 10-30% in the United States (US) and other developed countries.[3] Allergic rhinitis negatively impacts quality of life directly through, or from the consequences of, its symptoms such as sleep disturbances, fatigue, impaired learning and cognitive functions, leading to reduction in productivity, worsened school performances and may also lead to embarrassment.[4-7]

The Allergic March describes the natural history of allergic diseases over the course of infancy through adolescence, starting with atopic dermatitis, IgE-mediated food allergy, then asthma and AR in older children.[8] Patients with AR commonly present with associated multimorbidities which may further complicate their condition, including asthma, rhinosinusitis, atopic dermatitis, otitis media with effusion, sleep disordered breathing (SDB) and adenoid hypertrophy. Presence of AR with one or more morbidity will further increase the duration of disease, reduce quality of life and poses further challenges in determining the appropriate management strategy.[9]

Several major risk factors for AR have been identified, including family history of allergic diseases, gender (with males being more susceptible), first-born children, antibiotic exposure at early age, shorter breastfeeding period, cigarette smoke exposure during infancy, exposure to indoor allergens, poor hygiene, and high levels of circulating IgE at <6 years old.[10] The prevalence of AR is predicted to continually rise, owing to increased exposure to indoor allergen, air pollution, climate change, change of lifestyle, improved hygiene, use of pesticides and changed diet pattern.[11]

Management of Pediatric Allergic Rhinitis

Diagnosis of pediatric AR is done mainly through clinical examinations. Typical presentation includes sneezing, rhinorrhea, nasal

Korespondensi: **Nina Irawati**
E-mail: *ninairawati.sgt@gmail.com*

congestion resulting in mouth breathing, snoring, sleep apnea; and also nasal itching. Other common symptoms the examiner may find include cough or throat clearing, post nasal drip, irritability, fatigue and ocular symptoms (e.g., itching, burning and tearing). The symptoms may vary with age, with atypical presentations potentially occurring in preschool- and school-aged children.[12] Typical physical examination findings are facial grimacing, allergic shiners, nasal creasing, allergic facies, geographic tongue and Dennie-Morgan lines. Meanwhile, atypical presentations include eustachian tube dysfunction with ear pain on pressure changes, reduced hearing and Otitis Media with Effusion (OME), cough (which is often misidentified as asthma), poorly controlled asthma, and sleep disordered breathing (SDB) which may result in tiredness, poor school performance and irritability. Rhinosinusitis, which is characterised by rhinorrhoea, facial pain, headache, cough, halitosis and hyposmia may also be present in children with AR. Anterior rhinoscopy may reveal pale or bluish-grey, and sometimes inflamed, nasal mucosa. Other supporting tests such as specific IgE and Skin Prick Test can be done to establish the diagnosis and may also assist in identifying the specific causative allergen.[13,14]

The aim of management in pediatric AR is to control symptoms, decrease AR recurrency, prevent complications, improve patient's quality of life and prevent growth and developmental problems. The treatment is based on principles established by the Allergic Rhinitis and its Impact on Asthma (ARIA) study group, emphasizing on allergen avoidance, pharmacotherapy, education on self-management and immunotherapy if necessary; all in consideration of their cost-effectiveness.[14,15] The most recent guideline for pediatric AR treatment is based on the European Forum for Research and Education in Allergy and Airway Diseases (EUFOREA) paediatric AR management algorithm.[16] The algorithm highlights the importance of patient education on the disease itself and therapy adherence; as well as self-management strategies including avoidance of allergens/irritants and nasal saline sprays/douching. First line care is provided by pharmacists and general practitioners, with gradual escalation to specialistic care if there is no response to treatment. The guideline describes four levels of treatment which goes as following:

1. Step one: directed towards all patients showing two or more nasal symptoms consistent with AR, who have not received any therapy for AR previously. These patients should receive oral or nasal, non-sedative, antihistamines (anti-H1).
2. Step two: directed towards all patients with symptoms of nasal congestion or have experienced failure from treatment described in step one. These patients should receive nasal corticosteroids.
3. Step three: directed towards all patients with severe AR or patients who have experienced failure from treatment described in step two. These patients should be referred to a specialist, which will determine the appropriate course of treatment, which may include oral antihistamines if <6 years old, combination therapy of nasal corticosteroid and nasal antihistamines if >6 years old, and may also include add-on therapies, depending on additional symptoms (e.g., ocular itch, skin rash, sudden onset nasal blockage)
4. Step four: directed towards all patients aiming for long-term control of symptoms or patients who have experienced failure from treatment described in step four. Allergen immunotherapy (AIT) is given for these patients.[16]

Allergen Immunotherapy (AIT) is the only method available for disease-modifying treatment in AR. AIT re-modulates the reaction of human immune system to various allergens by shifting the inflammation response from Th2 cells to Th1, increasing production of IgG4, regulatory T cells and decrease specific IgE.[17-19] AIT can be administered through subcutaneous and sublingual route, with sublingual route being in favor for better safety and patient comfort.[20,21] A recent, large, systematic review has shown that AIT is beneficial in reducing both symptom score and medication score. SCIT is effective in the short term for both seasonal and perennial AR and SCIT given continuously for three years was shown to be effective in the long term for grass pollen-derived AR. SLIT is effective in the short term for seasonal AR and continuous administration of SLIT can be effective for perennial AR and for long term protection against grass pollen.[22] AIT is contraindicated for patients with uncontrolled asthma, eosinophilic esophagitis and history of severe systemic reactions to immunotherapy.[23]

Use of biologics, such as montelukast (anti-IgE), in pediatric AR is indicated for severely affected children with insufficient response to specific immunotherapy. The ef-

ficacy can be improved by combining the use of biologics and AIT. However, biologics are significantly more expensive than AIT and exhibits no disease-modifying effect for long term treatment.[24] Use of other methods like probiotics is promising in AR treatment, with significant remission rate of nasal symptoms ($p < 0.01$), reduction in total nasal symptom score ($p < 0.00001$) and improvements in total score of Paediatric Rhinoconjunctivitis Quality of Life Questionnaire ($p < 0.00001$). In addition, use of probiotics reduce the duration of cetirizine use ($p < 0.0005$) with no significant adverse reaction.[25]

Conclusions

Pediatric AR can reduce performance and QoL of affected children. The new pediatric AR guideline provides a better insight on the management of pediatric AR and helps to enable treatment of pediatric AR by primary healthcare providers. Prevention of irritant and allergen contact remains to be a very important step to reduce AR severity.

References

1. Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy. 2008 Apr;63 Suppl 86:8–160.
2. Leger D, Bonnefoy B, Pigearias B, de La Giclais B, Chartier A. Poor sleep is highly associated with house dust mite allergic rhinitis in adults and children. Allergy Asthma Clin Immunol. 2017 Aug 16;13:36.
3. Roberts G, Xatzipsalti M, Borrego LM, Custovic A, Halken S, Hellings PW, et al. Paediatric rhinitis: position paper of the European Academy of Allergy and Clinical Immunology. Allergy. 2013 Sep;68(9):1102–16.
4. Canonica GW, Bousquet J, Mullol J, Scadding GK, Virchow JC. A survey of the burden of allergic rhinitis in Europe. Allergy. 2007;62 Suppl 85:17–25.
5. Blanc PD, Trupin L, Eisner M, Earnest G, Katz PP, Israel L, et al. The work impact of asthma and rhinitis: findings from a population-based survey. J Clin Epidemiol. 2001 Jun;54(6):610–8.
6. Bousquet J, Neukirch F, Bousquet PJ, Gehano P, Klossek JM, Le Gal M, et al. Severity and impairment of allergic rhinitis in patients consulting in primary care. J Allergy Clin Immunol. 2006 Jan;117(1):158–62.
7. Hill DA, Spergel JM. The atopic march: Critical evidence and clinical relevance. Ann Allergy Asthma Immunol. 2018 Feb;120(2):131–7.
8. Mariño-Sánchez F, Valls-Mateus M, de Los Santos G, Plaza AM, Cobeta I, Mullol J. Multimorbidities of Pediatric Allergic Rhinitis. Curr Allergy Asthma Rep. 2019 Feb 22;19(2):13.
9. Zhang Y, Zhang L. Increasing Prevalence of Allergic Rhinitis in China. Allergy Asthma Immunol Res. 2019 Mar;11(2):156–69.
10. Cingi C, Bayar MN, Scadding GK. Will every child have allergic rhinitis soon? Int J Pediatr Otorhinolaryngol. 2019 Mar;118:53–8.
11. Zitelli B, McIntire S, Nowalk A. Zitelli and Davis' atlas of Pediatric physical diagnosis. 2017 May 11;
12. Schuler CF Iv, Montejo JM. Allergic Rhinitis in Children and Adolescents. Pediatr Clin North Am. 2019 Oct;66(5):981–93.
13. Brożek JL, Bousquet J, Agache I, Agarwal A, Bachert C, Bosnic-Anticevich S, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines—2016 revision. J Allergy Clin Immunol. 2017 Oct 1;140(4):950–8.
14. Scadding GK, Smith PK, Blaiss M, Roberts G, Hellings PW, Gevaert P, et al. Allergic Rhinitis in Childhood and the New EUFOREA Algorithm. Front Allergy. 2021 Jul 14;2:706589.
15. Gazi U, Bahceciler NN. Immune mechanisms induced by sublingual immunotherapy in allergic respiratory diseases. Clin Exp Immunol. 2022 Sep 29;209(3):262–9.
16. Zhang Y, Lan F, Zhang L. Update on pathomechanisms and treatments in allergic rhinitis. Allergy. 2022 Nov;77(11):3309–19.
17. Djuric-Filipovic I, Caminati M, Filipovic D, Salvottini C, Zivkovic Z. Effects of specific allergen immunotherapy on biological markers and clinical parameters in asthmatic children: a controlled-real life study. Clin Mol Allergy. 2017 Apr 3;15:7.
18. Liu W, Zeng Q, He C, Chen R, Tang Y, Yan S, et al. Compliance, efficacy, and safety of subcutaneous and sublingual immunotherapy in children with allergic rhinitis. Pediatr Allergy Immunol. 2021 Jan;32(1):86–91.
19. Epstein TG, Liss GM, Murphy-Berendts K, Bernstein DI. AAAAI/ACAAI surveillance study of subcutaneous immunotherapy, years 2008-2012: an update on fatal and nonfatal systemic allergic reactions. J

Allergy Clin Immunol Pract. 2014 Mar-Apr;2(2):161–7.
20. Dhami S, Nurmatov U, Arasi S, Khan T, Asaria M, Zaman H, et al. Allergen immunotherapy for allergic rhinoconjunctivitis: A systematic review and meta-analysis. Allergy. 2017 Nov;72(11):1597–631.
21. Roberts G, Pfaar O, Akdis CA, Ansotegui IJ, Durham SR, Gerth van Wijk R, et al. EAACI Guidelines on Allergen Immunotherapy: Allergic rhinoconjunctivitis. Allergy. 2018 Apr;73(4):765–98.
22. Rolinck-Werninghaus C, Hamelmann E, Keil T, Kulig M, Koetz K, Gerstner B, et al. The co-seasonal application of anti-IgE after preseasonal specific immunotherapy decreases ocular and nasal symptom scores and rescue medication use in grass pollen allergic children. Allergy. 2004 Sep;59(9):973–9.
23. Wang X, Tan X, Zhou J. Effectiveness and safety of probiotic therapy for pediatric allergic rhinitis management: A systematic review and meta-analysis. Int J Pediatr Otorhinolaryngol. 2022 Nov;162:111300.
24. Meirlaen L, Levy EI, Vandenplas Y. Prevention and Management with Pro-, Pre and Synbiotics in Children with Asthma and Allergic Rhinitis: A Narrative Review. Nutrients [Internet]. 2021 Mar 14;13(3). Available from: http://dx.doi.org/10.3390/nu13030934
25. Güvenç IA, Muluk NB, Mutlu FŞ, Eşki E, Altıntoprak N, Oktemer T, et al. Do Probiotics have a role in the Treatment of Allergic Rhinitis? A Comprehensive Systematic Review and Metaanalysis. Am J Rhinol. 2016 Sep 1;30(5):e157–75.