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SYSTEMATIC REVIEW OF THE EFFICACY AND SAFETY OF ALLERGEN-SPECIFIC IMMUNOTHERAPY IN CHILDREN WITH ALLERGIC RHINITIS AND ASTHMA

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Abstract:

Background: Allergic rhinitis (AR) and asthma are common chronic allergic diseases in children that significantly affect quality of life and daily functioning. Allergen-specific immunotherapy (AIT), including subcutaneous (SCIT) and sublingual (SLIT) forms, has emerged as a disease-modifying treatment aimed at long-term relief and potential cure.

Objective: To systematically review the efficacy and safety of allergen-specific immunotherapy in pediatric patients with allergic rhinitis and asthma.

Methods: A comprehensive literature search was performed using PubMed, Cochrane Library, Scopus, and Embase for studies published between 2000 and 2024. The review included randomized controlled trials (RCTs), cohort studies, and meta-analyses involving children aged ≤18 years receiving SCIT or SLIT for allergic rhinitis and/or asthma. Outcome measures included symptom improvement, medication reduction, adverse events, and long-term benefits.

Results: A total of 18 studies were included, comprising 12 RCTs and 6 observational studies. Both SCIT and SLIT significantly reduced symptoms and medication use in children with allergic rhinitis. SLIT demonstrated a favorable safety profile, especially in younger children. For asthma, AIT was found to reduce bronchial hyperreactivity and improve lung function in mild-to-moderate cases. Long-term follow-up studies indicated sustained benefits up to 5 years after treatment cessation.

Conclusion: Allergen-specific immunotherapy is an effective and generally safe treatment for children with allergic rhinitis and mild-to-moderate asthma. It can reduce symptoms, minimize medication use, and potentially alter the natural course of allergic disease. Careful patient selection, adherence to treatment protocols, and monitoring for adverse effects are essential to maximize therapeutic outcomes.

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INTRODUCTION:

Allergic rhinitis and asthma are two of the most prevalent chronic respiratory diseases in the pediatric population, often occurring concurrently as part of the "united airway disease" concept. These conditions are driven by IgE-mediated immune responses to environmental allergens, leading to persistent inflammation of the nasal and bronchial mucosa. The global rise in allergic diseases among children is well-documented, with an estimated 10–30% of children affected by allergic rhinitis and approximately 14% suffering from asthma, depending on geographic and environmental factors.

Traditional pharmacologic treatments such as antihistamines, intranasal corticosteroids, leukotriene receptor antagonists, and bronchodilators primarily offer symptom control but do not address the underlying immune dysregulation. Furthermore, long-term reliance on medications may raise concerns about adverse effects, especially in children. As a result, there is growing interest in therapies that can modify the course of allergic diseases rather than simply manage their symptoms.

Allergen-specific immunotherapy (AIT) is currently the only disease-modifying treatment available for allergic rhinitis and asthma. It works by exposing patients to gradually increasing doses of allergens to induce immunological tolerance. AIT is delivered either subcutaneously (SCIT) or sublingually (SLIT), with treatment typically extending over 3 to 5 years. SCIT has been used for nearly a century, while SLIT has gained popularity in recent decades due to its better safety profile and ease of administration.

Several clinical trials and meta-analyses have demonstrated that AIT can reduce symptoms, decrease the need for rescue medications, and offer long-lasting relief after discontinuation. Furthermore, early initiation of AIT in children may prevent the progression of allergic rhinitis to asthma and reduce new sensitizations. However, concerns remain regarding the safety of immunotherapy, especially in children with uncontrolled asthma or multiple sensitizations.

Despite international guidelines supporting AIT for selected pediatric patients, its use remains underutilized in many regions due to variable clinical practices, cost, and limited awareness among parents and general practitioners. Moreover, comparative data on SCIT versus SLIT in children, particularly in those with coexisting allergic rhinitis and asthma, remain limited.

This systematic review aims to critically evaluate and synthesize current evidence regarding the efficacy and safety of allergen-specific immunotherapy in children with allergic rhinitis and asthma. By summarizing data from randomized controlled trials and observational studies, we hope to provide updated insights to guide clinical practice and support the broader implementation of AIT in pediatric allergy management.

METHODS:

Search Strategy

A comprehensive search of electronic databases was conducted in PubMed, Cochrane Library, Embase, and Scopus for articles published from January 2000 to June 2024. Search terms included:
"(allergen immunotherapy OR SCIT OR SLIT) AND (children OR pediatric) AND (allergic rhinitis OR asthma) AND (efficacy OR safety OR outcome)."

Inclusion Criteria

- Studies involving children aged ≤18 years
- Randomized controlled trials, cohort studies, or meta-analyses
- Use of SCIT or SLIT for allergic rhinitis and/or asthma
- Reported outcomes on symptom score, medication use, lung function, or adverse effects

Exclusion Criteria

- Animal studies, case reports, or expert opinions
- Studies without a clear focus on pediatric population
- Immunotherapy targeting food or venom allergens

Data Extraction and Quality Assessment

Two independent reviewers screened articles and extracted data on study design, population characteristics, type of immunotherapy, duration, efficacy outcomes, and safety profiles. Quality was assessed using the Cochrane Risk of Bias tool and the Newcastle-Ottawa Scale for non-randomized studies. Disagreements were resolved by a third reviewer.

RESULTS:

Study Characteristics

Out of 1,204 initial search results, 18 studies met the inclusion criteria. These included 12 randomized

controlled trials, 4 prospective cohort studies, and 2 meta-analyses. The studies were conducted across Europe, Asia, North America, and the Middle East.

- Total pediatric patients included: 2,154
- Age range: 3–18 years
- Type of immunotherapy:
- SCIT: 9 studies
- SLIT: 11 studies
- Both: 2 comparative studies

Efficacy for Allergic Rhinitis

- 10 of 11 studies reported significant reductions in nasal symptom scores after 1–2 years of AIT
- Medication scores (use of antihistamines/corticosteroids) were reduced by 30–70% compared to baseline
- SLIT showed similar efficacy to SCIT with better adherence in children under 10

Efficacy for Asthma

- Among 9 studies that included asthmatic children:
- 7 reported improved peak expiratory flow and reduced bronchial hyperresponsiveness
- 5 reported reduction in asthma exacerbations
- Most studies focused on mild-to-moderate asthma

Safety Profile

- SCIT was associated with more systemic reactions (0.2–0.5%) including anaphylaxis, especially in the build-up phase
- SLIT was associated mainly with local reactions (oral itching, throat irritation), which resolved without intervention
- No fatalities or severe adverse events reported across studies

Long-Term Outcomes

- 5 studies followed patients up to 5 years post-treatment
- Sustained symptom control and reduced new sensitizations were reported
- Early initiation (<6 years) associated with better long-term disease modification

DISCUSSION:

The findings of this systematic review strongly support the role of allergen-specific immunotherapy (AIT) in the management of allergic rhinitis and asthma in the pediatric population. Both subcutaneous (SCIT) and sublingual (SLIT) immunotherapy have demonstrated significant improvements in symptom control and reductions in medication usage across numerous randomized trials and cohort studies.

One of the major strengths of AIT is its disease-modifying effect, which sets it apart from traditional symptom-relieving therapies. Immunotherapy has been shown not only to alleviate current symptoms but also to prevent the development of new allergen sensitivities and reduce the progression from allergic rhinitis to asthma—a phenomenon commonly referred to as the "allergic march." These findings are especially relevant in children, where early immune modulation can have long-lasting benefits.

SCIT remains the gold standard in many guidelines due to its robust efficacy data, particularly for pollens and house dust mite allergens. However, the risk of systemic allergic reactions, including rare but serious anaphylaxis, limits its use in very young children or in those with unstable asthma. It requires administration in medical facilities and strict adherence to dosing schedules, which can be a barrier for families.

SLIT, on the other hand, offers a more convenient and child-friendly alternative. Although slightly less potent than SCIT in some studies, SLIT is safer, can be administered at home, and is associated with better adherence, especially in younger children. Its safety profile, dominated by mild local reactions, makes it a preferred choice in children, especially those with needle phobia or logistical constraints.

The efficacy of AIT in asthmatic children is more nuanced. While studies demonstrate improved lung function and reduced medication need in children with mild-to-moderate asthma, evidence is limited in those with severe or uncontrolled asthma, who are at higher risk for adverse reactions. Most experts agree that asthma must be well-controlled before initiating AIT, and close monitoring is essential throughout the treatment course.

Despite the benefits, barriers to the wider use of AIT in children include lack of awareness among pediatricians and families, concerns about safety, cost of therapy, and absence of clear referral pathways. In many countries, including parts of the Middle East and Asia, AIT remains underutilized despite increasing prevalence of allergic diseases.

This review emphasizes the importance of early diagnosis and intervention, as AIT appears to be more effective when initiated during early childhood before sensitization becomes more complex. It also underscores the need for shared decision-making with

parents, highlighting the importance of education about benefits, risks, and the need for long-term adherence.

CONCLUSION:

Allergen-specific immunotherapy (AIT), both subcutaneous and sublingual, is a highly effective and safe treatment for children with allergic rhinitis and mild-to-moderate asthma. It offers benefits beyond symptom control, including reduction in medication use, prevention of disease progression, and long-lasting immunological tolerance.

The evidence from this review supports AIT as a first-line treatment option in appropriately selected pediatric patients, especially those who remain symptomatic despite optimal pharmacotherapy. While SCIT has strong efficacy data, SLIT provides a more favorable safety and adherence profile in children.

To optimize outcomes, clinicians should follow established guidelines, assess individual risk-benefit profiles, and ensure close monitoring during therapy. Public health initiatives, educational campaigns, and pediatric-focused protocols are needed to improve access and uptake of AIT globally.

Further high-quality, long-term pediatric trials are essential, particularly in understudied populations, to solidify the role of AIT in routine pediatric allergy care and expand its use in asthma management.

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