

**Efficacy of sublingual immunotherapy for allergic rhinitis in children: a systematic literature review**  
Eficacia de la inmunoterapia sublingual para la rinitis alérgica en niños: una revisión sistemática de la literatura

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### ABSTRACT

Allergic rhinitis (AR) is a prevalent chronic inflammatory condition affecting the nasal mucosa, predominantly mediated by immunoglobulin E (IgE) and affecting up to 40% of the global population. This study investigates the safety and efficacy of sublingual immunotherapy (SLIT) in treating pediatric AR, a preferred alternative to subcutaneous immunotherapy (SCIT) due to its non-invasive administration and reduced risk of severe adverse reactions. A systematic review of the literature up to June 2023 was conducted, including studies focusing on pediatric populations and examining long-term outcomes, safety profiles, and clinical effectiveness of SLIT. The findings reveal that SLIT is effective in reducing AR symptoms, medication usage, and improving quality of life in children, with a better safety profile compared to SCIT. Long-term SLIT treatment induces significant immunological changes, promoting a shift from IgE to IgG4, and increases in regulatory T cells and anti-inflammatory cytokines such as IL-10 and TGF-beta. Although some discrepancies exist in the efficacy results, particularly with low-dose allergen administration, the overall evidence supports SLIT as a safe and effective treatment for pediatric AR. Further research is needed to optimize treatment protocols and to better understand the long-term benefits and mechanisms of SLIT in this population.

**Keywords:** allergic rhinitis. sublingual immunotherapy. children. literature review.

### RESUMEN

La rinitis alérgica (RA) es una enfermedad inflamatoria crónica prevalente que afecta a la mucosa nasal, mediada predominantemente por inmunoglobulina E (IgE) y que afecta hasta al 40% de la población mundial. Este estudio investiga la seguridad y eficacia de la inmunoterapia sublingual (ITSL) en el tratamiento de la RA pediátrica, una alternativa preferida a la inmunoterapia subcutánea (SCIT) debido a su administración no invasiva y riesgo reducido de reacciones adversas graves. Se realizó una revisión sistemática de la literatura hasta junio de 2023, que incluyó estudios centrados en poblaciones pediátricas y que examinaron los resultados a largo plazo, los perfiles de seguridad y la eficacia clínica de la ITSL. Los hallazgos revelan que la ITSL es eficaz para reducir los síntomas de RA, el uso de medicamentos y mejorar la calidad de vida en los niños, con un mejor perfil de seguridad en comparación con la SCIT. El tratamiento a largo plazo con ITSL induce cambios inmunológicos significativos, promoviendo un cambio de IgE a IgG4 y aumentos de células T reguladoras y citocinas antiinflamatorias como IL-10 y TGF-beta. Aunque existen algunas discrepancias en los resultados de eficacia, particularmente con la administración de alérgenos en dosis bajas, la evidencia general respalda la ITSL como un tratamiento seguro y eficaz para la RA pediátrica. Se necesita más investigación para optimizar los protocolos de tratamiento y comprender mejor los beneficios y mecanismos a largo plazo de la ITSL en esta población.

**Palabras clave:** rinitis alérgica. inmunoterapia sublingual. niños. revisión de la literatura.

### INTRODUCTION

In otorhinolaryngology, allergic rhinitis (AR) is a frequent condition that affects atopic people after exposure to allergens. It is a chronic inflammatory non-infectious illness of the nasal mucosa, mostly caused by immunoglobulin E (IgE).

With a frequency of 10%–40%, AR affects over 500 million individuals worldwide. Its incidence is rising annually and its prevalence ranges from 4% to 38% in China (Zhang & Zhang, 2014)(Brożek et al., 2017). Depending on the kinds of allergens, allergic reactions may be classified as seasonal or perpetual. In contrast to perennial AR, which is mostly brought on by dust mites, cockroaches, and animal dander, seasonal AR is primarily brought on by inhaled allergens such as fungus and pollen. Paroxysmal sneezing, nasal congestion, nasal itching, and runny nose are the primary clinical signs of AR. Patients with bronchial asthma may have pulmonary symptoms like wheezing, coughing, shortness of breath, and chest tightness; some patients with AR also have psychological disorders like anxiety and depression; and patients with pollen allergy may have ocular symptoms like eye itching, lacrimation, eye redness, and burning sensation (Ji & Jiang, 2023).

Currently, immunotherapy, pharmacology, environmental management, and surgical treatment are the primary approaches often used to treat AR in clinical practice. Targeting the etiology of IgE-mediated type I allergic illnesses, specific immunotherapy (SIT) is the only treatment thought to be able to alter the course of allergic diseases naturally. In particular, SIT uses allergen extracts to build immunological tolerance, which subsequently helps AR patients' symptoms upon reexposure to allergens (Ridolo et al., 2014). Based on the various methods of administration, SIT may be divided into sublingual immunotherapy (SLIT) and subcutaneous immunotherapy (SCIT). The gold standard, SCIT, plays a significant role in the AR therapy. Subcutaneous immunotherapy, or SCIT, has a number of drawbacks, however. In order to get injections, patients must schedule frequent appointments with physicians, endure the discomfort of the injection, and doctors should be aware of potential adverse effects including anaphylaxis. Therefore, it is advised that SCIT only be carried out in establishments that have enough staff and equipment to address anaphylactic occurrences (Cox et al., 2007). Other means of administering allergens, such as intranasal, oral, and sublingual routes, have been developed in response to these problems. Sublingual immunotherapy (SLIT) has become the most popular option in Europe, taking the place of SCIT because to its many benefits, including noninvasiveness, home administration, and a lower incidence of serious adverse reactions than SCIT. With the development and widespread use of SLIT in clinical therapy, it has steadily evolved into a safe and effective immunological substitute; yet, disagreements persist about the best course of action between the two treatment modalities (Durham & Penagos, 2016). Furthermore, the majority of ongoing clinical trials for the treatment of AR concentrate on comparing the effectiveness of active and placebo medications; few research compare the efficacy of immunotherapies. diverse immunotherapies continue to encounter diverse selection hurdles in clinical application because of variations in SIT techniques as well as safety and effectiveness across various routes of delivery. Thus, the purpose of this research was to examine the safety and therapeutic effectiveness of SLIT in the management of AR.

## **METHODOLOGY**

Using a systematic method, we examined the safety and effectiveness of sublingual immunotherapy (SLIT) for the treatment of allergic rhinitis (AR) in children in this review. A thorough exploration of dependable databases, such as PubMed, MEDLINE, and the Cochrane Library, was carried out to find relevant research articles published till June 2023. The main search phrases were "children," "allergic rhinitis," "sublingual immunotherapy," and "efficacy." In order to guarantee thorough coverage of the subject, boolean operators were used to narrow the search queries.

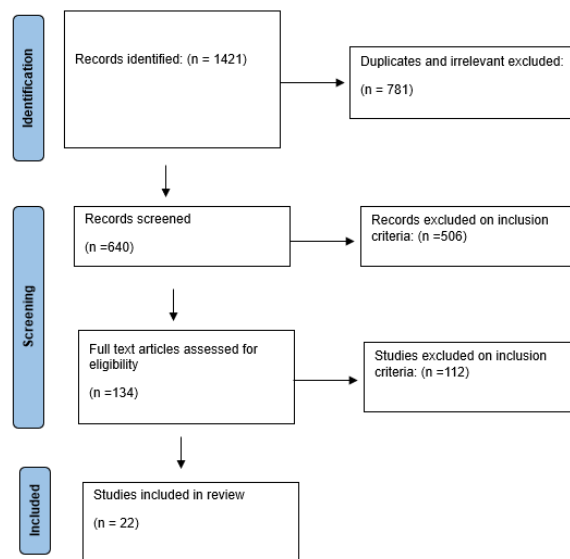
### **Inclusion and Exclusion Criteria:**

The following criteria were used to determine which studies were included in the inclusion and exclusion lists: they had to be published in English, concentrate on pediatric populations, and include information on the long-term effects, safety profiles, immunological changes, and clinical outcomes of SLIT. Studies that focused on adult populations, were not accessible in English, or lacked comprehensive outcome data were excluded. To guarantee that each chosen research was pertinent and applicable to the review's goals, each underwent a thorough evaluation process.

### **Data Categorization and Analysis:**

The clinical results, immunological markers, safety profiles, and long-term consequences of SLIT were the main foci of the chosen research. The focus of data capture was on adverse events, immunological changes, medication usage, and symptom ratings. Each study's insights were combined to provide a thorough summary of the safety and therapeutic effectiveness of SLIT in children with AR. An extensive examination of SLIT's effects on enhancing clinical results and guaranteeing patient safety during the treatment of pediatric allergic rhinitis was made possible by this methodical approach.

Figure 1: Prisma Flow diagram



Source: the authors.

## RESULTS

### Proposed mechanisms of SLIT

Numerous investigations have revealed that the immunologic alterations in SLIT are comparable to those in SCIT. Allergen-specific immunotherapy, or SLIT and SCIT, produces three main immunologic alterations: (1) controlling the immune response to the allergen, (2) decreasing the recruitment and activation of proinflammatory cells, and (3) modifying the immune response to the allergen by T cells. We also talk about the three previously stated mechanisms and oral (mucosal) tolerance.

### Regulation of allergen specific antibody response

Allergic diseases are characterized by serum allergen-specific IgE binding to mast cell surface FcεRI receptor. Serum IgE rises early in SCIT but decreases months later. This decrease reduces grass pollen allergy sufferers' seasonal IgE increase. Early symptomatic improvement following immunotherapy is unrelated to IgE level change, which happens later. Increasing allergen-specific IgG (mostly IgG1 and IgG4) improves clinical outcomes. IgA occasionally rises.

Similar to SCIT, allergen-specific IgG4 levels increased and IgE/IgG4 ratio decreased in SLIT. SLIT increased allergen-specific IgG and IgG4 levels (Radulovic et al., 2011), and another meta-analysis found that IgE/IgG4 ratio and skin reaction to allergen reduced in later phases of SLIT and clinical improvement (Wilson et al., 2005). IgG4, a blocking antibody, may stop the allergic inflammatory cascade caused by IgE antigen recognition. Thus, immunotherapy effectiveness depends on the shift from IgE to IgG4 and IgE/IgG4 ratio (Scadding & Durham, 2011). Changing allergen-specific IgE levels was contentious (Kim et al., 2010). HDM-specific IgE did not change between SLIT and placebo groups in asthmatic children after 2 years of HDM SLIT. In our AR patients, 12-month SLIT raised specific IgE for *Dermatophagoides farinae* but not *pteronyssinus* (Kim et al., 2010). However, grass pollen SLIT increased *Phleum pratense*-specific serum IgE time- and dose-dependently, demonstrating an allergen-specific immune system action [13]. Changing IgA has been noted. SLIT with grass pollen allergen increased dose-dependently antigen-specific serum IgA and HDM allergen increased it. Thus, allergen-specific IgG (and IgA) without IgE alterations may contribute to SLIT clinical reactions.

### Reduction of proinflammatory cell recruitment and activation

SCIT inhibits allergen-induced mucosal proinflammatory cell recruitment and activation. When SCIT works, mast cell, eosinophil, and basophil recruitment and activation in the epidermis, nasal cavity, conjunctiva, and bronchial mucosa diminish following allergen exposure. SCIT affects mast cell and basophil activation threshold and peripheral T cell immunological tolerance. SCIT also boosts IL-10 synthesis, which suppresses mast cell proinflammatory cytokines, eosinophil functions, and

Th0 and Th2 cell IL-5 production. Like these reactions, SLIT reduced basophil in the conjunctiva or nasal cavity following allergen exposure. SLIT for grass pollen and HDMs lowered local or systemic eosinophil cationic protein (ECP) (Kim et al., 2010).

### Changes in allergen specific T cell response

Allergic inflammation requires Th1-Th2 equilibrium. SCIT increases Th1 and decreases Th2 cytokines. In grass pollen SCIT, nasal mucosa or skin regularly shifted from Th2 to Th1 profile, although systemic alteration was inconsistent. This indicated that immunologic alteration affects peripheral blood and target organs.

Maintaining immunologic tolerance of peripheral T cells by antigen-specific regulatory T cells is the key to SIT. SCIT triggers regulatory T cells to release IL-10 and TGF- $\beta$  (Passalacqua & Durham, 2007). IL-10 regulates Th1 and Th2 responses. IL-10 increases IgG4 rather than IgE class switching, lowers MHC class II expression, mast cell and eosinophil activation, and migration. TGF- $\beta$  inhibits Th1 and Th2 responses, generates regulatory T cells, and causes B-cell IgA class switching.

T cell response in SLIT is unclear. Some found that SLIT with grass pollen did not affect T cell activity, cytokine generation, cell proliferation, or dendritic and T cell numbers in epithelium and lamina propria (Rolinck-Werninghaus et al., 2005). Other studies utilizing HDM SLIT revealed it lowers Th2 cytokine IL-13, peripheral monocyte proliferation, ECP, and prolactin and increases IL-10. Because active T cells generate prolactin, T cell activity may have decreased.

### Induction of oral mucosal immune tolerance

SLIT captures allergens via Fc $\epsilon$ RI and/or other structures on oral mucosal Langerhans-like DCs. DCs upregulate coinhibitory molecules (B7H1 and B7H3) or release IL-10 to trigger protolerogenic pathways in oral mucosa (Novak et al., 2011). Allergen absorption reduces DC maturation and CCR7 expression, which recruits DCs to peripheral lymphoid organs. DCs with lower CCR7 expression and slower maturation after allergen uptake during migration to lymphoid tissue may present antigens to T cells outside local draining lymphoid tissues, such as in the oral mucosa. Oral DCs stimulate CD4+ CD25+ Foxp3+ Treg cells, which increase in the oral epithelium during SLIT. SLIT also increased peripheral blood Foxp3+ Treg cells, IgG4, IL-10, IL-18, and signaling lymphocytic activation molecule in mononuclear cells. In pollen SLIT patients, monocytes and B cells expressed more programmed cell death ligand 1 and produced less IL-4 (Piconi et al., 2010).

### Efficacy of SLIT

According to meta-analyses, SLIT is therapeutically effective for treating asthma and both adult and pediatric AR (Radulovic et al., 2011)(Wilson et al., 2005). In 2008, the ARIA group recognized the effectiveness of SLIT for treating rhinitis patients with birch, cypress, grass, olive, Parietaria, and HDM (Passalacqua et al., 2011).

Comparing SLIT to a placebo group, some early research found that it had no desensitizing impact against HDM and grass pollen allergen (Bufe et al., 2004). Furthermore, only severe AR was clinically improved by SLIT, and at least three years of therapy were needed. SLIT effectiveness has been confirmed by a number of research carried out throughout time. The effectiveness of sublingual immunotherapy (SLIT) in treating children with allergy rhinitis (AR) during the COVID-19 pandemic was investigated by Liu et al. (Liu et al., 2021). The research included the recruitment of 335 AR children receiving SLIT who were sensitized to house dust mite (HDM). Utilizing ratings for symptoms and medications, the clinical efficacy and safety were assessed at various intervals. While still considerably lower than baseline levels ( $p < 0.05$ ), the total nasal symptoms score (TNSS) and the total medication score (TMS) rose during the COVID-19 pandemic compared to the same time last year ( $p < 0.05$ ). There were no significant variations in the incidence of negative responses at various times. Additionally, they discovered that the decent response group's household cleaned their bedding more often. Amidst SLIT therapy, there were no notable alterations in the levels of tIgE or sIgE. Sublingual immunotherapy (SLIT) for mite-sensitized allergy rhinitis (AR) was investigated by Wen-Bo Chen for its long-term effectiveness (Chen et al., 2020). The 3- and 6-year follow-up scores for both groups' symptoms and medication were much lower than their baseline levels; however, the SLIT group's ratings were significantly lower than the PT group's. Between the 3- and 6-year follow-ups in the SLIT group, no discernible changes were seen.

There have been disagreements on SLIT's effectiveness in pediatrics. Children with HDM allergy who were given low dosage allergens for two years did not exhibit any changes in immunologic markers, according to a research (Pajno et al., 2000). Through a thorough meta-analysis, Zao Ji assessed the safety and therapeutic effectiveness of sublingual immunotherapy for allergic rhinitis (AR) (Ji & Jiang, 2023). Twenty-two studies including 4,941 AR patients and five interventions—pharmacotherapy, sublingual immunotherapy with pollen extract, subcutaneous immunotherapy with dust mite, and sublingual immunotherapy with grass mix—were conducted. Sublingual immunotherapy dust mite, subcutaneous immunotherapy\_dust mite, sublingual immunotherapy\_grass mix plus pollen extract, placebo, and pharmacotherapy were the

most effective treatments for AR, according to the results of a network meta-analysis conducted based on symptom scores following various interventions for AR. Significantly, there were fewer side effects and increased safety with sublingual immunotherapy. In order to evaluate the effectiveness and safety of *Dermatophagoides farinae* (Der.f) extracts for sublingual immunotherapy (SLIT) in treating allergy rhinitis (AR) in children and adults, Lina et al. (2023) carried out a retrospective investigation (Lin et al., 2017). Children under four years old were the primary focus of this study. Pharmacotherapy and sublingual immunotherapy with Der.f extracts were administered for three years to a total of 573 patients with AR, ages three to 69. Evaluations were conducted at each visit using the visual analogue score (VAS), total medication score (TMS), total nasal symptoms score (TNSS), and adverse events (AEs). In compared to the baseline values, TNSS, TMS, and VAS considerably improved during the course of the three-year therapy ( $P < 0.01$ ). Furthermore, among young children aged 3–6 years, there was a substantial improvement in nasal symptoms and a decrease in medication usage ( $P < 0.01$ ). Adverse events (AEs) of a severe system were not recorded.

According to a recent Position Paper by the World Allergy Organization, SLIT for pollen and HDM was effective in treating children with AR who were at least five years old, and it may be safe to use in children who were at least three years old (Passalacqua et al., 2011). The long-term impacts of stopping SLIT have been recognized, but the implications of stopping SCIT have not yet been well demonstrated (Bousquet et al., 1998). There was a higher improvement after three years of SLIT compared to two years, according to a research including 137 patients with HDM AR (Tahamiler et al., 2007). The effectiveness of sublingual immunotherapy (SLIT) and its immunological effects in treating juvenile patients with allergy rhinitis (AR) were investigated by Zeng et al. (Zeng et al., 2023). In comparison to the 1 year and 2 year groups, the 3 year group's total nasal symptom score (TNSS), rescue medication score (RMS), and SMS were substantially different. The following outcomes were noted in the 3-year group at the conclusion of the 2-year period after SLIT cessation: The following improvements were noted: 1) the serum levels of IL-10, TGF-beta, and IL-35 had risen greatly; 2) the TNSS, RMS, and SMS had significantly improved; and 3) the percentages of regulatory T cells, regulatory B cells, and follicular regulatory T cells had strongly increased.

SLIT has been shown to have a preventive impact on asthma. The effectiveness of sublingual immunotherapy (SLIT) in treating patients with asthma and allergic rhinitis (AR) was assessed by Ma et al, by a systematic review and meta-analysis (Ma et al., 2023). The inclusion criteria were satisfied by 10 studies with 1722 patients in total. Both the total asthma symptom score (TASS) and the total rhinitis score (TRSS) were considerably lower in the SLIT group compared to the placebo group (weighted mean difference [WMD] =  $-1.23$ , 95% CI:  $-1.39$ – $-1.06$ ,  $P < .001$ ). In terms of therapy-related adverse events (RR =  $2.82$ , 95% CI:  $1.77$ – $4.48$ ,  $P < .001$ ) and overall treatment costs (SMD =  $0.71$ , 95% CI:  $0.45$ – $0.97$ ,  $P < .001$ ), the SLIT group exhibited greater results. Between the SLIT and placebo groups, there was no discernible change in the percentage of exhaled nitric oxide (FeNO) ( $P = .158$ ), forced expiratory volume in 1 second (FEV1) ( $P = .237$ ), inhaled corticosteroids (ICS) dosage ( $P = .195$ ), or direct treatment costs ( $P = .630$ ).

### Safety and adverse events

The better safety profile of SLIT over SCIT is one of its benefits. In comparison to SCIT, the primary benefit of SLIT is its safety. Anaphylaxis is one of the serious side effects that SCIT may sometimes cause. 3.3% of patients exposed to grass allergen and 0.7% of patients exposed to birch allergen had systemic adverse effects, according to a DBPC research. 3.7% of patients undergoing SCIT and 0.9% of injectable patients had systemic adverse effects, according to a postmarketing monitoring study (Moreno et al., 2004).

In order to examine the effectiveness and safety of sublingual immunotherapy (SLIT) and subcutaneous immunotherapy (SCIT) for children with allergic rhinitis (AR), Yang and Lei carried out a systematic review and meta-analysis (Yang & Lei, 2023). Treatment-related adverse events (TRAEs), new sensitizations, asthma development, overall improvement, and symptom scores (SSs), medication scores (MSs), and combination symptom and medication scores (SMSs) were among the outcomes that the researchers assessed. The findings suggested that, when taking safety and effectiveness into account, SLIT would be a better AIT than SCIT for treating juvenile AR. This information might help doctors make decisions.

There were no instances of death. There have been six reports of anaphylactic instances, including two cases after the use of a combination of several allergens (Eifan et al., 2007). One happened during the latex rush protocol therapy, while the other one appeared six times (60 drops instead of 10 drops) above the recommended dosage for HDM SLIT. Two patients, a 13-year-old boy with swelling of the tongue, angioedema of the eyes, and generalized urticaria, and a 27-year-old female with asthma symptoms, generalized itching, fainting, and abdominal cramps, were among the remaining two who had previously stopped SCIT due to severe systemic side effects (De Groot & Bijl, 2009).

Younger children's safety with SLIT has been investigated. A research conducted on 65 children between the ages of 3 and 7 revealed that adverse effects, such as urticaria, oral pruritus, and gastrointestinal issues, were not more severe in

younger children than in older children (Fiocchi et al., 2005). SLIT is safe for children under the age of five, according to a second trial that included 126 pediatric patients between the ages of three and five. All nine adverse effects—six gastrointestinal, two oral itching, and one minor stomach pain—occurred during the up-dosing phase and were documented in 7 children (5.6% of patients and 0.2/1,000 doses). Lowering the dose resolved every issue. In children, multiple allergen SLIT did not increase the probability of an unpleasant response compared to mono-allergen SLIT, according to another research (Agostinis et al., 2008).

## **DISCUSSION**

AR, a common and long-lasting inflammatory disease of the nasal mucosa mostly brought on by immunoglobulin E (IgE), impacts a large number of people worldwide, including children. Because it is less intrusive, can be administered at home, and has a reduced risk of serious adverse responses than SCIT, SLIT has become the treatment of choice.

Significant improvements in total nasal symptom scores (TNSS), medication scores (TMS), and visual analogue scores (VAS) are indicative of the effectiveness of SLIT in controlling AR symptoms, as supported by the evaluated studies collectively (Liu et al., 2021; Chen et al., 2020; Ji & Jiang, 2023). According to Lin et al. (2017), these results were consistently shown in a variety of patient demographics, including very young children between the ages of three and six. This is consistent with the results of meta-analyses and systematic reviews that have shown the efficacy of SLIT against a range of allergens, such as grass pollen and house dust mites (HDM) (Radulovic et al., 2011; Wilson et al., 2005). Research by Liu et al. (2021) and Chen et al. (2020) showed that SLIT has long-lasting benefits that persist even in difficult situations like the COVID-19 pandemic, dramatically reducing total nasal symptoms scores (TNSS) and total medication scores (TMS).

Long-term research also shows that SLIT has long-term advantages in addition to providing instant relief. For example, Zeng et al. (2023) discovered that three years of SLIT resulted in significant changes in blood levels of immunoregulatory cytokines including TGF-beta and IL-10, as well as in the TNSS and rescue medication score (RMS). These results highlight the possibility that SLIT may cause long-lasting immunological alterations that support long-term symptom alleviation. Longer treatment durations (e.g., three years vs two years) generate better outcomes, according to Passalacqua et al. (2011) and Tahamiler et al. (2007), highlighting the significance of continued therapy for best results.

On the other hand, there are some differences in the research about the effectiveness of SLIT in pediatric populations. Children with HDM allergy receiving low-dose allergens showed no discernible alterations in immunologic markers, according to Pajno et al. (2000). Variations in patient groups, allergen dose, and research designs may be to blame for this disparity. Notwithstanding these discrepancies, the majority of the research indicates that SLIT is a useful tool for treating AR in kids.

Comparable to subcutaneous immunotherapy (SCIT), SLIT is equally effective in reducing symptoms. According to Passalacqua et al. (2011), the World Allergy Organization's Position Paper on SLIT for pollen and HDM allergens, it has improved safety characteristics and comparable therapeutic results to SCIT, hence it is recommended for use in children five years of age and older. Based on its decreased frequency of treatment-related side events and its ability to be given at home, which improves adherence to the treatment regimen, SLIT is a better alternative for treating juvenile AR, according to Yang and Lei's meta-analysis from 2023.

One of the review's main highlights is the safety profile of SLIT, which has a lot less treatment-related adverse events (TRAEs) than SCIT (Yang & Lei, 2023). This makes SLIT a safer choice, particularly for young children (Fiocchi et al., 2005; Agostinis et al., 2008), who are more vulnerable to the intrusive character of SCIT and its possible systemic effects. SLIT's safety credentials are further reinforced by the lack of severe systemic adverse events, such as anaphylaxis, and the low occurrence of minor adverse effects, such as oral pruritus and gastrointestinal symptoms (Moreno et al., 2004; Eifan et al., 2007; De Groot & Bijl, 2009). Multiple studies have established that SLIT is safe for children under five. Adverse events in younger children were not more severe than in older children, according to studies by Fiocchi et al. (2005) and Agostinis et al. (2008), and multiple allergen SLIT did not increase the likelihood of adverse responses compared to mono-allergen SLIT (Fiocchi et al., 2005; Agostinis et al., 2008).

Even if SLIT is well supported by research, there are some limitations that should be taken into account. The generalizability of the results may be impacted by differences in the patient demographics, length of therapy, and research designs across the evaluated studies. Furthermore, even though SLIT has shown encouraging results, further study is required to examine the effectiveness of the therapy for additional allergens as well as in larger populations. Dosing regimes and treatment durations should also be optimized (Tahamiler et al., 2007). Long-term research evaluating the long-term effects of SLIT after treatment ends might be beneficial as well (Bousquet et al., 1998).

## CONCLUSION

In conclusion, sublingual immunotherapy (SLIT) has been shown to be a safe and effective treatment option for children suffering with allergic rhinitis (AR). It has shown to be just as effective as standard subcutaneous immunotherapy (SCIT), but with a far better safety record. By causing allergen-specific immunological changes, such as elevated IgG4 and IgA levels, lowered IgE/IgG4 ratios, and increased regulatory T cell activity, SLIT successfully lowers symptom ratings, medication usage, and improves overall clinical outcomes. Even while some early studies questioned the effectiveness of SLIT, later investigations have continuously shown its therapeutic effects, particularly for seasonal allergens like grass pollen and perennial allergens like home dust mites. Particularly in pediatric populations, SLIT is a better option than SCIT because to its noninvasiveness, adaptability for home administration, and decreased frequency of serious adverse events. With its potential to prevent the development of asthma and to manage AR, these results provide support to the wider use of SLIT in clinical practice, providing a viable and safer therapeutic alternative for kids.

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