Efficacy of Sublingual Immunotherapy in the Treatment of House-Dust Mite Induced Allergic Rhinitis

Sirena Saleet, PA-S
Faculty Advisor: Kevin Basile, PT, MD
Department of Medical Science

Abstract

House-dust mite (HDM) induced allergic rhinitis (AR) is a chronic condition associated with rhinorrhea, nasal obstruction, nasal pruritus and sneezing. The current mainstay of treatment is intranasal corticosteroids, which have shown variable degrees of symptom control among patients. Immunotherapy works to increase peripheral immune tolerance by administration of the allergen itself. This study examined multiple randomized controlled trials to determine if sublingual immunotherapy (SLIT) is a viable treatment option for allergic rhinitis.

Introduction

- Allergic rhinitis affects approximately 10-30% of adults and 40% of children, with an estimated 60 million people suffering from the condition in the United States.
- The presence of allergic rhinitis significantly affects a person's quality of life, contributing to issues like missed time at work or school, poor performance in daily activities, and lack of sleep. Total economic toll has been roughly $6 billion annually in the United States through direct and indirect costs of therapy and occupational burden.
- Not all patients experience equivalent resolutions of symptoms on intranasal corticosteroids and chronic use is required to achieve continued relief.
- Immunotherapy not only has the potential to decrease acute symptoms of allergic rhinitis, but is also the only treatment with disease-modifying potential with long-term use.

Figure 1. Pathophysiology of Allergic Rhinitis

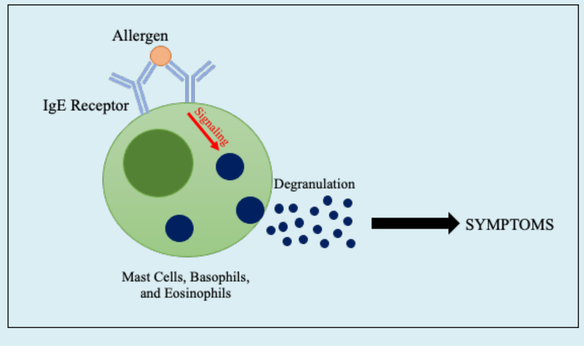

Figure 1. Pathophysiology of Allergic Rhinitis. Allergic rhinitis is an IgE antibody-mediated hypersensitivity reaction typically occurring after exposure to a specific allergen. Allergen exposure triggers degranulation in mast cells, basophils and eosinophils. Degranulation results in the release of cytokines, histamines, and chemotactic factors. The release of these factors results in symptoms like rhinorrhea, nasal obstruction, nasal pruritus, and sneezing. The immune system has an intricate memory allowing a similar response to occur with subsequent exposure to identical or similar allergens.

Methods

Literature search was performed in April 2020

Sources	• Pubmed • Clinical Key
Search Terms	"Immunotherapy" AND "allergic rhinitis" AND "dust-mite" AND "sublingual"
Inclusion Criteria	• Published in the last 5 years (2015-2020) • Human clinical trials • Published in peer reviewed journal
Exclusion Criteria	• Systematic reviews or meta-analyses • Clinical trials involving animals

Results

The evidence compiled through five randomized controlled trials showed statistically significant symptom improvement in patients treated with SLIT in comparison to a placebo. Total combined rhinitis scores measured in three studies showed a reduction of greater than 15% in active groups. Total symptom scores showed a significant decrease in all studies analyzed. There were mixed significant and non-significant results in the measurement of medication scores after SLIT. Quality of life surveys showed improvement in active groups and the safety profile was favorable in all studies.

Table 1. Comparison of Results

Study	TCRS	Total symptom scores	Medication score	QOL	Safety Profile
Demoly et al (2016)	S	S	S	S	S
Guo et al (2017)	N/A	S	S	S	S
Nolte (2016)	S	S	S	S	S
Okamoto (2018)	N/A	S	NS	N/A	S
Okubo (2017)	S	S	NS	S	S
KEY					
Categories **S = significant** **NS = not significant** **N/A = not reported**	TCRS = Total combined rhinitis score S = ≥15% ↓ in active groups compared to placebo NS = <15% ↓ in active groups compared to placebo	Total symptom scores S = ↓ in active groups compared to placebo NS = ↑ or no change in active groups compared to placebo	Medication score S = ↓ in active groups compared to placebo NS = ↑ or no change in active groups compared to placebo	QOL = quality of life measured by questionnaire S = ↑ in active groups compared to placebo NS = ↓ or no change in active groups compared to placebo	Safety profile S = was determined safe NS = was determined unsafe due to excessive toxicity

Discussion

Overall, the study designs were similar in that they all used randomized double-blind placebo-controlled trials, which contributed to the validity of the studies. However, variable dosing and outcome measurements make comparison difficult and reveal the need for standardization in this field. Extension of the one-year duration of intervention should be considered to determine the long-term effects of SLIT.

Table 2. Comparison of Study Designs

Study	Design	Total N	Age range (years)	Duration of Intervention	Dosing	Outcome measurements
Demoly et al (2016)	Randomized, placebo-controlled	992	18-65	1 year	6 SQ, 12 SQ, or placebo	TCRS, rhinitis symptoms, MS, QOL
Guo et al (2017)	Randomized, placebo-controlled	48	5-55	1 year	"5 drops"	NSS, TNSS, ACS, MS
Nolte (2016)	Randomized, placebo-controlled	1482	≥ 12	1 year	12 SQ or placebo	TCRS, DSS, DMS, QOL
Okamoto (2018)	Randomized, placebo-controlled	438	5-16	1 year	300 IR or placebo	AASS, RTSS, ARTSS; ARMS, ISS,
Okubo (2017)	Randomized, placebo-controlled	946	12-64	1 year	10,000 JAU, 20,000 JAU or placebo	TCRS, rhinitis symptoms, MS, QOL, symptom free days, symptom severe days
KEY						
SQ = Standardized quantity; JAU = Japanese Allergy Units; TCRS = total combined rhinitis score; MS = medication score; QOL = quality of life; NSS = nasal symptom score; TNSS = total nasal symptom score, ACS = allergic conjunctivitis score; DSS = daily symptom score; DMS = daily medication score; AASS = average adjusted symptom score; RTSS = Rhinitis total symptom score; ARTSS; average rhinitis total symptom score; ARMS = average rescue medication score; individual symptom score						

Table 3. Validity Assessment of the Evidence

Study	Statistical Power	Adequate treatment timeline	Blinding	Intention-to-treat
Demoly et al (2016)	A	A	A	A
Guo et al (2017)	I	A	A	A
Nolte (2016)	A	A	A	A
Okamoto (2018)	A	A	A	A
Okubo (2017)	A	A	A	A
KEY				
Categories **A = Adequate** **M = Marginal** **I = Inadequate**	Statistical power A = sample size > 400 M = sample size > 100 I = sample size <100	Timeline A = well defined timeline (i.e. dosing up regulation, follow up and data collection outlined) I = no defined timeline	Blinding A = double blind M = single blind I = no blinding	Intention-to-treat A = All patients enrolled in the study were included in the analysis I = Not all patients enrolled in the study were included in the analysis

Conclusion

SLIT should be considered as an alternative or adjunct in the treatment of HDM-induced AR. SLIT has shown statistically significant symptomatic relief and a favorable safety profile. However, further research is required before SLIT can be recommended in place of the current standard of care. Cost-benefit analysis and more long-term studies are necessary for better assessment of where SLIT belongs on the treatment continuum.