

Sublingual Immunotherapy Versus Subcutaneous Injection Immunotherapy in Children With House Dust Mite Allergy: A Randomized Controlled Trial

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Abstract

Background

Subcutaneous Immunotherapy is an effective treatment for allergic diseases. It decreases the new sensitizations in individuals who were monosensitized. It may be associated with mild local symptoms with difficult to apply in children. The aim of the current study is to compared Sublingual Immunotherapy versus Subcutaneous Injection Immunotherapy in Children with House Dust Mite allergy.

Methods

In an open-label randomized clinical trial included 20 children aged (6–13) years with House Dust Mite allergic asthma and/ or rhinitis who were admitted to Al Assad University Hospital over 1 year between January 2014 to January 2015. The patients were divided into 2 groups according to a randomized schedule, one of them was treated with Subcutaneous Injection Immunotherapy (SCIT), and the other received Sublingual Immunotherapy (SLIT). We monitored the patients every 3 months over 1 year to evaluate the clinical improvement, side effects of the treatment, drug dependence.

Results

The current study showed remarkable and fast improvement of the clinical symptoms with a decrease in the need for the medication in the Sublingual Immunotherapy group compared to the Subcutaneous Injection Immunotherapy group with a significant difference. There was no difference observed in safety between the two groups, and side effects were mild in both groups.

Conclusion

The current study confirmed that the use of the Sublingual Immunotherapy group is more rapid and effective in children with allergic diseases.

Background :

Allergic diseases in children have increased significantly in recent years and now affect up to 35% of children (1). It is a result of the interaction between genetic and environmental factors to produce high levels of immunoglobulin E (IgE), which can activate the immune system (2). One of the most common allergens worldwide is house dust mite with its major strains are *Dermatophagoides pteronyssinus* and *Dermatophagoides farina* (3). Subcutaneous Injection Immunotherapy (SCIT) using standardized house dust mite extracts is effective in treating allergic asthma and rhinitis, but it has limitations such as the discomfort of repeated injections and side effects (4). Therefore the current study aimed to compared Sublingual Immunotherapy (SLIT) versus SCIT in children with House Dust Mite allergic asthma and /or rhinitis.

Material And Methods:

The current study was reviewed and approved by the ethical committee of Al-Assad University Hospital. Informed consent was obtained from the patient's parents.

Eligibility criteria:

An open label randomized clinical trial included 20 children aged (6-13) years with House Dust Mite allergic asthma and/ or rhinitis diagnosed by skin prick test (SPT) who were referred to the pediatric clinic at Al-Assad University Hospital over 1 year between January 2014 to January 2015.

Initial management and Randomization:

On admission, a detailed history was taken and a clinical examination was performed. Any medications received by the patient were noted. After enrolment patients were randomly allocated to one of the two study groups. We used random number tables for the randomization. The medications were constituted in both groups as follows:

Group A: received SCIT @ Alustal 1st set of injections (0.01 IR/ml each week for 4 weeks, then 0.1 IR/ml each week for 4 weeks, then 1 IR/ml each week for 4 weeks, then 10 IR/ ml each week for 5 weeks). The maintenance dose repeats with regular intervals between injections from 2,3,4 weeks to 6 weeks maximum. Treatment maintenance for at least 3 years.

Group B: received SLIT @ Stalloral (Blue cap 15IR/ml, red cap 100/ml, violet cap 300IR/ml). The dose is (1, 2, 3, 4, 5) drops under tongue from the blue cap at the first 5 days accordingly, then (1, 2, 3) drops under tongue from the red cap at the next 3 days accordingly, then (1, 2, 3, 4) drops under tongue from the violet cap at the next 4 days. Treatment maintenance (4 drops under tongue from violet cap daily) for at least 3 years.

Assessment of response:

All clinical variables by fill out a questionnaire of clinical improvement, drug dependence, and any side effects noted by the patient or physicians were recorded every 3 months over one year.

Statistical methods:

All data were analyzed using Statistical Package for social sciences (SPSS version 20). Descriptive statistical parameters (mean and standard deviation, frequencies, and percentage) were calculated for each quantitative variable. Between-group comparisons of qualitative data were done using the Chi-Square test or Fisher’s exact test. We used Friedman Test to compare the mean of several related populations and the Mann Whitney test to study the difference between the means of two independent groups. The results were considered significant at the 5% level ($p < 0.05$).

Results:

From January 2014 to January 2015, 20 patients presented with House Dust Mite allergic asthma and/ or rhinitis diagnosed by skin prick test (SPT). The mean age of the study patients were (8 ± 2.5) years. Both studied groups were matched regarding sex and age with no statistical difference (**Table 1**). There was a statistically significant difference in the clinical symptoms, drug dependence after treatment begun on the second day of treatment in group B (**Table 2**). There was no difference between the studied groups according the drug's effects ($p = 0.326$) (**Table 3**).

Table (1): Baseline characteristics of the patients in the study groups

		Group A	Group B	p-value
Sex	Male, n(%)	6(60)	5(50)	0.7
	Female, n(%)	4(40)	5(50)	
Age		9.2 ± 2.7	8.1 ± 2.8	0.1

Table (2): Comparison of clinical improvement between studied groups

		Group A				Group B				p-value
		1st visit, n(%)	2nd visit, n(%)	3rd visit, n(%)	4rd visit, n(%)	1st visit, n(%)	2nd visit, n(%)	3rd visit, n(%)	4rd visit, n(%)	
symptoms	Improve	2(20)	4(40)	6(60)	7(70)	10(100)	10(100)	8(80)	8(80)	0.0001
	No difference	7(70)	3(30)	2(20)	2(20)	0(0)	0(0)	2(20)	0(0)	
	Worse	1(10)	3(30)	2(20)	1(10)	0(0)	0(0)	0(0)	2(20)	
Drug dependence	No difference	10(100)	10(100)	3(30)	3(30)	10(100)	3(30)	0(0)	0(0)	0.0000
	More use	0(0)	0(0)	3(30)	0(0)	0(0)	0(0)	0(0)	2(20)	
	less use	0(0)	0(0)	4(40)	7(70)	0(0)	7(70)	10(100)	8(80)	

Table (3): side effects of the treatment in studied groups

		Side effects				p-value
		No reaction	Local reaction (edema, redness)	Itchy skin	Systemic reaction (Anaphylactic shock)	
Group A	1st visit, n(%)	10(100)	0(0)	0(0)	0(0)	0.326
	2nd visit, n(%)	10(100)	0(0)	0(0)	0(0)	
	3rd visit, n(%)	6(60)	4(40)	0(0)	0(0)	
	4rd visit, n(%)	6(60)	3(30)	0(0)	1(10)	
Group B	1st visit, n(%)	9(90)	0(0)	1(10)	0(0)	
	2nd visit, n(%)	8(80)	1(10)	1(10)	0(0)	
	3rd visit, n(%)	9(90)	1(10)	0(0)	0(0)	
	4rd visit, n(%)	9(90)	0(0)	1(10)	0(0)	

Discussion:

We conducted the present study to investigate the role of SLIT versus SCIT in patients presented with House Dust Mite allergic asthma and/ or rhinitis diagnosed by skin prick test (SPT). The study showed remarkable and fast improvement of the clinical symptoms with a decrease in the need for the medication in the Sublingual Immunotherapy group compared to the Subcutaneous Injection Immunotherapy group with a significant difference. The current study is the first at the local researches that compared the effectiveness of the SLIT compared to the SCIT. In Allergen immunotherapy (AI), the patient takes escalating doses of allergen that gradually decrease the IgE-dominated response and encouraging the body to produce more CD4 + T regulatory cells that secrete IL-10 and TGF- β (5). Besides, SLIT is characterized by an increase in IgG4 antibodies and a decrease in IgE antibodies, as well as diminished mast cells and basophils (6). Sporta.D conducted

that SLIT improves symptom scores for asthma and allergic rhinitis by decreasing medication usage that in agreement with the European literature and the current study (7). Chelladurai et al. showed little difference in treatment effectiveness were from 4 studies; two favored SCIT in reducing medication use and two favored SLIT, while a birch study found SLIT to be more effective (8). Although both SCIT and SLIT appear to be effective in allergic asthma, Nelson's meta-analysis and literature supportive of a SCIT predominance in clinical efficacy (9, 10).

There are some limitations of this study. Firstly, the study was open-label randomization with its limitation which may increase the selection bias. Secondly, cases of this study were small and selected from a single center, and thus, it may be not generalized to other pediatric populations.

Conclusion

The present study showed that the use of the Sublingual Immunotherapy group is more rapid and effective in children with allergic diseases. Present results require further double-blind controlled trials to confirm the potential clinical benefit of SLIT in children with House Dust Mite allergic asthma and/ or rhinitis.

List Of Abbreviations

SCIT: Subcutaneous Injection Immunotherapy.

SLIT: Sublingual Immunotherapy.

AI: Allergen immunotherapy.

IgE: immunoglobulin E.

SPT: skin prick test.

Declarations

Data Availability:

We can't share patient data due to our hospital's privacy policy, which is concerned with maintaining patient confidentiality and refuses to publish or share data. Also, the informed consent signed by the parents to participate in the study prevents the sharing of information with the non - Study researchers.

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Statement of Ethics:

All parents whose children were studied gave informed consent for sharing of this research. Ethical clearance for this study was obtained from the Ethical Committee of the University of Tishreen Hospital

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None.

CONFLICT OF INTEREST STATEMENT:

None declared.

Author Contributions:

Both authors developed and carried out sample collection. Literature review, the data analysis and read through the final data were done by both authors .

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