Research Article

Efficacy of sublingual immunotherapy in adult allergic asthma from Minia University hospitals

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Abstract
Background: specific immunotherapy is the sole treatment for changing the natural course of allergic diseases and minimizing the risk of an exacerbation. Sublingual immunotherapy is may be preferred worldwide considering the favorable safety profile and absence of anxiety provoking injections. Many updated recommendations of its use with reports emphasize the need for a methodological control of research projects in order to increase their objectivity. **Patients and methods**: this study is designed to be open labeled, randomized and double armed parallel groups; 80 adult asthmatic patients were screened for mild to moderate persistent asthma by history, clinical examination ,chest X ray ,FEV1 , then screened for atopic sensitized patients with total IgE and skin prick test . Then patients were randomized into 2 equal groups, group 1 received ICS plus SLIT for 9 months and group 2 received ICS for the same period. Serum total IgE was evaluated before and after treatment, every 3 months FEV1 was evaluated and monthly clinical evaluation by Asthma symptom control sheet, medication score were done throughout the entire period. **Results**: 80 patients were randomized into 2 equal groups, group 1 received ICS plus SLIT for 9 months and group 2 received ICS for the same period. In group 1 serum level of total IgE after treatment show a significant decrease while FEV1 after treatment show significant increase. In group 2 serum level of total IgE after treatment show no significant difference while FEV1 show no significant difference.
Conclusion: Serum level total IgE is a good biomarker significantly decreased with SLIT therapy.
Keyword: SLIT, allergen immunotherapy, allergic diseases, atopic, asthma, asthma control, asthma exacerbations, lung function.

Introduction
Allergic diseases result from an unbalanced response of the specific immune system generating allergen-specific immunoglobulin E antibodies, which mediate various clinical symptoms, such as asthma and allergic rhinitis, upon re-exposure to allergen Aim of work[(1)], The most prevalent form of asthma is allergic asthma where individuals have a genetic predisposition for the development of an antigen specific IgE mediated response to common aeroallergens[(2)]. Dendritic cells in the airway epithelium and sub mucosa detect inhaled allergens, including house dust mite (HDM), pollen, fungal spores and cockroach antigen. The IgE antibody bound to high affinity receptors on dendritic cells facilitates the uptake and internalization of these allergens[(3)], specific immunotherapy (SIT) by the sublingual route (sublingual immune-therapy, SLIT) has been increasing in accep-tance in clinical practice, mainly in Central Europe, it is currently the most used form of specific immunotherapy in children. This is due to its ease of administration and documented safety.[(4)], currently numerous treatments aimed at managing the symptoms associated with asthma exist. Although these treatments may offer symptom relief, they have potential side effects that may be experienced by the patient. Furthermore, the majority of current treatments do not resolve the underlying immunological mechanism causing asthma. This has led to researchers shifting their attention to the possible use of immunotherapy; Allergen immunetherapy rehabilitates the immune system. This involves administering increasing doses of allergens to accustom the body to substances that are generally harmless (pollen, house dust mites) and thereby induce specific long-term tolerance.[(5)].

Patients and methods
This study will be conducted on 80 adult patients with mild to moderate bronchial asthma disease, screened for mild to moderate

persistent asthma by history, clinical examination, chest X ray, FEV1, then screened for atopic sensitized patients with total IgE and skin prick test.

This will divide into two groups:
Group one: 40 adult asthmatic patients on sublingual immunotherapy in addition to pharmacotherapy
Group two: 40 adult asthmatic patients on pharmacotherapy alone.

Inclusion criteria: adult patients with clinical and functional diagnosis of Asthma (stable disease)
Exclusion criteria: Patients on specific allergen immunotherapy, Pregnant females, Patients currently on oral antihistamines, or any other drugs that inhibit the SPT reaction, Patients with positive dermographism, Asthmatic patient presented by pneumonia, Asthma with other systemic disease.[6]

Results

Table (1): Distribution of the studied patients according to socio-demographic characteristics

Socio-demographic characteristics	Cases (n= 40)	Control (n=40)	P-value
Age #	27.9 ±8.4	29.7±9.05	0.3
Sex			
Male	16 (40)	17 (42.5)	0.8
Female	24 (60)	23 (57.5)	
Residence			
Urban	33 (82.5)	28 (70)	0.2
Rural	7 (17.5)	12 (30)	
Marital status			
Single	27 (67.5)	15 (37.5)	0.007
Married	13 (32.5)	25 (62.5)	
Education			
Illiterate	0 (0.0)	5 (12.5)	0.002
Primary	2 (5.0)	11 (27.5)	
Secondary	24 (60)	16 (40)	
University	14 (35)	8 (20)	
Occupation			
Not working	28 (70)	28 (70)	0.3
Manual/free workers	4 (10)	8 (20)	
Clerical	2 (5.0)	2 (5.0)	
Professional	6 (15)	2 (5.0)	
Smoking status			
Non-smoker	37 (92.5)	38 (95)	0.9
Smoker/ Ex-smoker	3 (7.5)	2 (5.0)	

#Quantitative data represented by Means ± SD

Table (2): Distribution of the studied patients according to medication:

Type of medication	Group1 (n= 40)	Group2 (n=40)	P-value
ICS	27 (67.5)	33 (82.5)	0.03
SABA	9 (22.5)	5 (12.5)	
LABA	0 (0.0)	2 (5.0)	
Combination	4 (10)	0 (0.0)	

Table (3): Distribution of the studied patients according to family history:

Family history	Group1 (n= 40)	Group2 (n=40)	P-value
Positive	26 (65)	37 (92.5)	0.003
Negative	14 (35)	3 (7.5)	

Table (4): Distribution of the studied patients according to associated atopy:

Associated Atopy	Group1 (n= 40)	Group2 (n=40)	P-value
No	4 (10)	5 (12.5)	0.3
Urticaria	3 (7.5)	0 (0.0)	
Rhinitis	33 (82.5)	35 (87.5)	

Discussion

The introduction of sublingual immunotherapy has shown to be in some ways, an effective alternative to subcutaneous immunotherapy. The indications are quite similar for both and there is a significant patient preference for the sublingual approach. This particularly applies to children. Allergen delivery through the sublingual-swallow route appears more effective than sublingual or oral route alone, suggesting that absorption through the GI tract potentiates induction of tolerance [7]

In the present study, there was significant correlation between asthma and family history (P-value0.003) as in[8] which found a positive family history predicts an increased risk of asthma.

In our study, there was significant correlation between asthma and high eosinophilia count (P-value 0.001) as in [9] which found count–response relation exists between blood eosinophil counts and asthma-related outcomes. Blood eosinophil counts could add predictive value to Global Initiative for Asthma control-based risk assessment.

Our study was in agreement with[10] which found coexistence of asthma and allergic rhinitis is frequent, that allergic rhinitis usually precedes asthma, and that allergic rhinitis is a risk factor for asthma. Finally, studies that have examined the age of onset of atopic as a confounding factor for the development of asthma and allergic rhinitis have suggested that early age atopic may be an important predictive factor for respiratory symptoms that continue into late childhood.

Conclusion

SLIT appears to be efficacious and safe in asthmatic adult with sensitivity to multiple allergens. We also demonstrated that SLIT, with high allergen dosing and rush dosage schedule, is safe and provides clinical benefits in asthmatic adult. Further studies on lager groups of patients and longer treatment durations are needed to confirm these results. Additional studies are necessary to evaluate immunologic mechanism behind SLIT and the cost effectiveness of SLIT.

Recommendation

It is known that our study had limited numbers of patients so, we recommend making studies on larger scale. Serum total IgE level is recommended to be followed after course of sublingual immunotherapy.

References

1. Busse WW and Lemanske RF Jr. Asthma. N Engl J Med. 2003;344(5):350–62 (PubMed)

2. Holgate ST. Innate and adaptive immune responses in asthma. Nat Med May 4 2012; 18(5):673–83.
3. GINA (2014) Global Initiative for Asthma. Global strategy for asthma management and prevention. http//www.ginasthma.org
4. Bateman ED, Hurd SS, Barnes PJ, Bousquet J, Drazen JM, FitzGerald M, Gibson P, Ohta K, O'Byrne P, Pedersen SE, Pizzichini E, Sullivan SD, Wenzel SE, Zar HJ. Global strategy for asthma management and prevention: GINA executive summary. Eur Respir J 2008; 31: 143-178 [PMID: 18166595 DOI: 10.1183/ 09031936.00138707]
5. Blackwell DL, Lucas JW, Clarke TC. Summary health statistics for U.S. adults: national health interview survey, 2012. Vital Health Stat 10 2014; (260): 1-161 [PMID: 24819891]
6. Feary, J. (2018). 1737b Occupation and asthma, BMJ Publishing Group Ltd.
7. Leynaert, B., F. Neukirch, P. Demoly and J. Bousquet (2011). "Epidemiologic evidence for asthma and rhinitis comorbidity." Journal of Allergy and Clinical Immunology 106(5): S201-S205.
8. Lue, K. H. (2009). "Clinical and immune-logic effects of sublingual immunotherapy in asthmatic adult a double-blind, rando-mized, placebo-controlled study." Pediatric allergy and immunology 17(6): 408-415.
9. Milligan, K. L., E. Matsui and H. Sharma (2016). "Asthma in urban children: epidemiology, environmental risk factors, and the public health domain." Current allergy and asthma reports 16(4): 33.
10. Brozek, J., et al., Global A, Asthma European N, Grading of Recommendations Assessment D,Evaluation Working G: Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines: 2010 revision. J Allergy Clin Immunol, 2010. 126: p. 466-476.