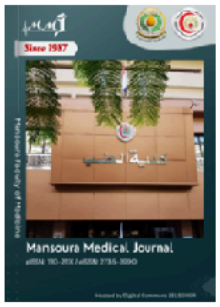
MANSOURA MEDICAL JOURNAL

ISSN - Print: 1110-211X - Online: 2735-3990

journal homepage: mmj.mans.edu.eg



Volume 52 | Issue 3 Article 5

Effectiveness of allergen immunotherapy in cigarette smokers with allergic airway disorders

Heba Wagih Abdelwahab

Chest medicine department, Faculty of Medicine, Mansoura university. Egypt

Mostafa Bakeer

Chest medicine department, Faculty of Medicine, Mansoura university. Egypt, mbekeer10@hotmail.com

Ahmed Mohamed Fouda

Chest medicine department, Faculty of Medicine, Mansoura university. Egypt

ORIGINAL STUDY

Effectiveness of allergen immunotherapy in cigarette smokers with allergic airway disorders

Heba W. Abdelwahab, Mostafa Bakeer*, Ahmed M. Fouda

Chest Medicine Department, Faculty of Medicine, Mansoura University, Mansoura, Egypt

Abstract

Background: **Exposure to environmental tobacco smoke (ETS) is associated with several medical diseases especially allergy, but little is known about the effects of cigarette smoking on allergen immunotherapy (AIT) response.**

Aim: **This study aims to explore any association between cigarette smoking and response to AIT in patients with allergic airway disorders.**

Patients and methods: **The study was conducted on patients with allergic airway disorders who received subcutaneous immunotherapy. All patients were assessed as regards smoking history including pack-year index and dependence, symptoms, and medication scores. Patients' demographic and clinical data were collected. A statistical analysis was then performed.**

Results: **A total of 54 patients were enrolled 48 (88.9 %) males and 6 (11.1 %) females, with mean age of 30.6 ± 12 years. Coincidence of Allergic rhinitis and bronchial asthma was the most frequent in 23 (42.6 %) patients. Nonsmoker patients were the most frequent representing 63 %, followed by current smokers in 29.6 %. Symptom and medication scores in current smokers were highly and significantly better after AIT ($P = 0.001$, 0.005, respectively), ex-smoker showed significant improvement as regards symptoms score ($P = 0.05$), but with no significant improvement as regards medication score ($P = 0.06$). Among nonsmokers, there was a highly significant improvement in both symptom and medication scores after AIT (P=<0.000). As regards medication response about smoking status, ex-smokers and nonsmokers had better statistically significant responses to treatment in comparison with smokers (P1:0.001, P2:0.003).**

Conclusion: **Smoking status has no significant effect on symptom improvement in patients with allergic airway diseases receiving allergy immunotherapy.**

Keywords: Allergen immunotherapy, Allergic rhinitis, Asthma, Smoking

1. Introduction

Allergy can be defined as an adverse immune-mediated hypersensitivity response to common substances in the environment. Allergic diseases are common, and their prevalence is increasing in all countries, resulting in morbidity and mortality in all age groups (Douglass and O'Hehir, 2006).

Atopic dermatitis is a prevalent chronic inflammatory skin condition, affecting 15–30 % of children and 2–10 % of adults. In the past three decades, there has been a notable increase in prevalence, particularly in industrialized countries, leading to a significant economic burden (Asher et al., 2006; Schram et al., 2010). Several patients with atopic dermatitis have been observed to develop allergic rhinitis and asthma in subsequent years due to the so-called 'atopic march' (Spergel, 2010; Weidinger et al., 2008; Marenholz et al., 2006).

Allergic rhinitis is a widespread condition that impacts individuals of all ages, with a peak in incidence during the teenage years. Its significance is often disregarded, leading to underdiagnosis, misdiagnosis, and inadequate treatment, which can have deleterious effects on health and societal costs. Although allergic rhinitis is not life-threatening, it is clinically significant due to its association with various complications, being a substantial risk factor for poor asthma control, and negatively affecting

Received 10 June 2023; revised 2 September 2023; accepted 9 November 2023.
Available online 18 December 2023

* Corresponding author at: Chest Medicine Department, Faculty of Medicine, Mansoura University, ElGomhouria Street, Mansoura, 35516, Egypt.
E-mail address: mbekeer10@hotmail.com (M. Bakeer).

https://doi.org/10.58775/2735-3990.1398

quality of life and workplace or school productivity (Greiner et al., 2011).

It is a well-established fact that nasal allergy and asthma often coexist, with around 20–50 % of allergic rhinitis sufferers experiencing concurrent asthma and more than 80 % of asthma patients experiencing chronic nasal symptoms. This high level of agreement is not unexpected given the pronounced pathophysiological and histological similarities between the two disorders (Corren, 2007).

Cigarette smoking is a current epidemic that proves to be costly and puts a significant health burden on society. It is estimated that there are well over one billion smokers globally, with tobacco use being the leading preventable factor in worldwide illness and premature death (Polosa et al., 2008).

Adults and older children with asthma who smoke have more severe symptoms and poorer quality of life associated with their asthma compared with non-smokers with asthma (Siroux et al., 2000). Moreover, reduced response to inhaled and oral corticosteroids has been observed in asthmatic patients who smoke (Tomlinson et al., 2005). The prevalence rate of smoking amongst adults with rhinitis is also comparable to the general population (Olsson et al., 2003).

2. Patients and methods

This study is an ex post facto study, which was conducted in the outpatient Allergen Immunotherapy Clinic at the Chest Medicine Department. Mansoura University Hospitals, Egypt, through the period from May 2020 to May 2022. This study was conducted within the required ethics guidelines of the Mansoura institutional research board ethics committee (R.20.04.796). Informed consent was obtained from every case after an explanation of the study. All the candidates participating in this study were enrolled voluntarily having the right to freely refuse to participate in the study without any affection for the provided medical service.

Patients diagnosed to have allergic airway diseases (bronchial asthma and allergic rhinitis), attended an allergen immunotherapy (AIT) clinic for a scheduled visit, and on AIT regularly without interruption for at least one year were considered eligible for participation. Meanwhile, we excluded patients with established diagnoses of chronic obstructive pulmonary disease (COPD), interstitial lung diseases, chronic cardiac problems, and patients refusing to participate in the study. Due to the limitations associated with coronavirus disease 2019 (COVID-19) pandemic, sample size was relatively small. Immunotherapy used was formed in the AIT preparation unit at Mansoura University.

The demographic and clinical-related data which include the patient's age, sex, diagnosis of allergic disorder, and allergen sensitization pattern, were recorded.

Based on smoking history, categories of smokers, ex-smokers, and never-smokers were employed in the analyses in accordance with Centers for Disease Control and Prevention (CDC) definitions (Jamal et al., 2012) along with pack years to determine the level of cumulative exposure. To measure the amount a person has smoked over a long period of time, the pack year index was used. This is calculated by multiplying the number of packs of cigarettes smoked/day by the number of years the person has smoked. Additionally, the Fagerström test for nicotine dependence was assessed (Fagerström and Furberg, 2008).

The effectiveness of immunotherapy was evaluated by means of a four-point scoring system for both symptoms and medication (Eifan et al., 2010). Patients were directed to maintain a diary throughout their treatment, assessing their symptoms on a daily basis using the four-point scale: 0 (no symptoms) to 3 (severe symptoms) for each rhinitis symptom (sneezing, nasal discharge, itching and nasal obstruction) and asthma symptom (wheezing, breathlessness, dyspnoea and cough).

The patients were required to document every time they used medication on a diary card. A score of 1 was assigned to the use of β-2 agonists and antihistamines, while a score of 2 was given for inhaled or intranasal steroids. A score of 3 was attributed to the use of corticosteroids, specifically oral prednisolone greater than or equal to 5 mg or dexamethasone greater than or equal to 8 mg. These scores were then used to calculate the total medication score (TMS). The individual symptom and medication scores were recorded daily throughout the entire study period, and the mean of the 3 monthly scores was recorded during the 3-monthly study visit.

The improvement level was assessed as complete response, partial response and no response in both symptom and medication scores (Eifan et al., 2010). Complete response: patients with lack of symptoms and withdrawal of medicines (both symptoms as well as medication scores = 0), Partial response: decline in symptom and/or medication scores but not reaching 0, and No response: in both symptom and medication scores.

2.1. Statistical analysis

The data collected were prepared, tabulated and statistically analysed using the social science statistical software package (SPSS) version 16. Numerical values for categorical data were presented in

percentages, whilst continuous data were presented either as Mean (SD) or median (interquartile range), based on the Shapiro–Wilk test's results, which determined whether the data adhered to normal distribution assumptions or not. Comparison of paired ordinal data (pre/post-treatment symptom score, pre/post-treatment medication score) was performed using Wilcoxon Signed Ranks Test. The comparison between two groups was conducted using Mann–Whitney *U* and independent *t*-test based on data distribution. For the three groups, analysis of variance (ANOVA) was utilized for normally distributed data, and Kruskal–Wallis test for non-normally distributed data. The significance test was conducted using χ^2 test or Fisher's exact test for categorical variables.

3. Results

A total of 54 patients were enrolled 48 (88.9 %) males and 6 (11.1 %) females, with mean age of 30.6 ± 12 years. Coincidence of Allergic rhinitis and bronchial asthma was the most frequent in 23 (42.6 %) patients followed by Allergic rhinitis alone in 22 (40.8 %) patients. Asthma alone was found in only 9 (16.6 %) patients. Current smokers represented 29.6 % of the studied patients. Regarding the Sensitization pattern, 35 patients have molds as an allergen representing 64.8 %, followed by pollen in 32 (59.3 %) patients, meanwhile wheat was the least frequent allergen presented in two patients only. Before starting AIT, 27 (50 %) patients had moderate symptom score and the other half had severe symptom score (Table 1).

As regard symptom and medication scores after AIT treatment in current smokers, there was a highly significant improvement after AIT ($P = 0.001$) as regard symptoms score and significant improvement in medication score ($P = 0.005$), ex-smoker showed also significant improvement as regard symptoms score ($P = 0.05$), but with no significant improvement as regard medication score ($P = 0.06$). Among nonsmokers, there was a highly significant improvement in both symptom and medication scores after AIT (P=<0.000) (Table 2).

As regard improvement in symptom score in relation to smoking status, there is no statistically significant difference in response when comparing smokers, ex-smokers, and nonsmokers (P 1:0.4, P 2:0.3). When assessing the effect of smoking duration, index and dependence by Fagerstrom score on improvement in symptom score, no statistically significant difference was found. As regard medication score improvement in relation to smoking status, ex-smokers and nonsmokers had better statistically significant responses to treatment in comparison with smokers (P 1:0.001, P 2:0.003), Meanwhile smoking duration, index, and dependence by Fagerstrom score showed no statistically significant effect on medication response (Tables 3 and 4).

Table 1. Demographic data of studied patients.

	N (54) (%)
Age: years (mean ± SD)	30.6 ± 12
Sex	
Males	48 (88.9)
Females	6 (11.1)
Diagnosis	
Allergic rhinitis	22 (40.8)
Bronchial asthma	9 (16.6)
Allergic rhinitis and bronchial asthma	23 (42.6)
Sensitization pattern[a]	
Molds	35 (64.8)
Pollens	32 (59.3)
Cotton dust	6 (11.1)
Feather	24 (44.6)
Mite	32 (59.2)
Pigeon	12 (22.2)
Wheat	2 (3.7)
Hay dust	24 (44.4)
Wool	10 (18.5)
Smoking status	
Current smokers	16 (29.6)
Ex-smokers	4 (7.4)
Nonsmokers	34 (63)
Baseline symptom score	
0	0
1	0
2	27 (50)
3	27 (50)
Baseline medication score	
0	0
1	12 (22.2)
2	35 (64.8)
3	7 (13)

[a] Not mutually exclusive.

4. Discussion

Tobacco smoking and exposure to ETS have both been implicated in several medical diseases especially allergy, but little is known about the effects of cigarette smoking on AIT response.

In this study we tried to explore any association between cigarette smoking and response to AIT in patients with allergic airway disorders.

Our study proved the efficacy of AIT regard symptoms and medications scores in current smokers and nonsmokers. However ex-smoker showed significant improvement as regard symptoms score with no significant improvement as regard medications score.

Regard smoking status there was no difference in improvement in symptom score when comparing smokers, ex-smokers, and nonsmokers.

Table 2. Symptom and medication scores after allergen immunotherapy treatment among studied patients.

	N (%)	*P* value
Current smokers		
Symptoms score before AIT 0/1/2/3	0/0/10/6 (0/0/62.5/37.5)	Z = −3.4[a]
Symptoms score after AIT 0/1/2/3	9/7/0/0 (56.2/43.8/0/0)	*P* = 0.001
Medication score before AIT 0/1/2/3	0/4/10/2 (0/25/62.5/12.5)	Z = −2.8[a]
Medication score after AIT 0/1/2/3	1/9/5/1 (6.2/56.2/31.2/6.2)	*P* = 0.005
Ex-smokers		
Symptoms score before AIT 0/1/2/3	0/0/3/1 (0/0/75/25)	Z = −1.8[a]
Symptoms score after AIT 0/1/2/3	4/0/0/0 (100/0/0/0)	*P* = 0.05
Medication score before AIT 0/1/2/3	0/2/2/0 (0/50/50/0)	Z = −1.8[a]
Medication score after AIT 0/1/2/3	4/0/0/0 (100/0/0/0)	*P* = 0.06
Nonsmokers		
Symptoms score before AIT 0/1/2/3	0/0/14/20 (0/0/41.2/58.8)	Z = −4.9[a]
Symptoms score after AIT 0/1/2/3	4/15/11/4 (11.8/44.1/32.4/11.8)	*P* < 0.000
Medication score before AIT 0/1/2/3	0/6/23/25 (0/17.6/67.6/14.7)	Z = −4.7[a]
Medication score after AIT 0/1/2/3	17/8/8/1 (50/23.5/23.5/2.9)	*P* < 0.000

[a] Wilcoxon Signed Ranks Test; allergen immunotherapy (AIT).

Table 3. Symptom response in relation to smoking parameters.

	No response *N* (%)	Partial response *N* (%)	Complete response *N* (%)	*P* value
Smoking status				X^2:0.8, *P* 1:0.4
Current smokers (r)	3 (18.8)	13 (81.2)	0	X^2:2.1, *P* 2:0.3
Ex-smokers	0	4 (100)	0	
Nonsmokers	5 (14.7)	25 (73.5)	4 (11.8)	
Smoking duration (mean ± SD)	7 ± 1	13.8 ± 6		*t*: −1.01, *P* = 0.3
Pack year index				Z: −0.9 *P*: 0.3
Median (min–max)	7.2 (0.5–14)	12 (1–45)		
Fagerstrom score (mean ± SD)	5.7 ± 2.8	5.1 ± 2		t:0.4, *P* = 0.6

(r): reference.

These findings corroborate certain previous studies. In a retrospective analysis of asthmatic children, factors that predicted positive clinical outcomes from allergen-specific immunotherapy were assessed. The cases were subsequently categorized into a group that demonstrated clinical effectiveness and another that exhibited clinical inefficacy based on the decrease in pulmonary symptoms and pharmaceuticals used as required. They found that the response to passive smoking did not differ significantly between the ineffective clinical response group and the effective clinical response group (Peng and Liu, 2013).

Also, Di Lorenzo et al. (Di Lorenzo et al., 2009) failed to demonstrate that tobacco smoke exposure correlated with the therapeutic effect of allergen specific immunotherapy. They assessed the efficacy on the basis of clinical response (reduction in nasal

Table 4. Medication response in relation to smoking parameters.

	No response *N* (%)	Partial response *N* (%)	Complete response *N* (%)	*P* value
Smoking status				X^2:15,
Current smokers (r)	8 (50)	7 (43)	1 (7)	*P* 1:0.001
Ex-smokers	0	0	4 (100)	X^2:10.2,
Nonsmokers	6 (18)	11 (32)	17 (50)	*P* 2:0.003
Smoking duration				*P* = 0.6[a]
Median (min–max)	12 (7–24)	15 (15–15)	10 (5–15)	
Pack year index				*P* = 0.4[a]
Median (min–max)	12 (5–30)	4.5 (1–20)	15 (2–45)	
Fagerstrom score (mean ± SD)	6 ± 1.8	4.4 ± 1.7	4.8 ± 2.9	*P* = 0.3[b]

(r): reference.
[a] Kruskal–Wallis test.
[b] ANOVA test.

and pulmonary symptoms) and reduction of the pharmacotherapy taken on an as-needed basis (e.g., oral second-generation H1-antihis-tamine for rhinitis and inhaled short-actingb2-agonist for asthma symptoms).

Additionally, a prospective study on 163 patients was conducted to explore any association between smoking habits (duration and quantity) and quality of life results after sublingual immunotherapy in allergic rhinitis (Katotomichelakis et al., 2015).

The study concluded that smoking habits did not influence the success of sublingual immunotherapy with regards to quality of life outcomes.

On the other hand, some studies had showed conflicting results.

Li et al. (2014) investigated various predictive factors of clinical response to allergy immunotherapy in children with asthma and rhinitis, encompassing allergen skin-prick test responses, serum specific and total IgE levels and blood eosinophil counts. The study divulged that early exposure to tobacco smoke was linked with an unproductive clinical response to AIT. Nevertheless, the researchers utilized distinct criteria than ours to evaluate AIT response. They considered AIT to have been effective if a patient reached 3 years immunotherapy, no longer need for medications or reduced dose to 25 % and symptoms became well-controlled and quality of life was satisfactory during follow-up for 2 years, and an overall assessment by the parents and children at the end of immunotherapy was a 'noticeable' or 'mild' improvement. If the conditions above were not met, the AIT was considered to have been ineffective.

Additionally, another retrospective study assessed the factors that might affect the efficacy of AIT (Romantowski et al., 2019). In addition to smoking history, the study analyzed other factors like age, sex, type of allergy (rhinitis, asthma, or both), type of allergen, type of vaccine and type of AIT (Subcutaneous or sublingual). They found that there were no differences in the efficacy of AIT regard the assessed risk factors, except for smoking history. The study concluded that smoking is negatively associated with AIT. The difference to our study was that they included patients treated with specific AIT for grass pollen and house dust mites. Additionally, the efficacy of AIT was assessed with the use of Allergy Control Score (ACS), patients received two Allergy Control Score: concerning symptoms and medication before AIT and at least 1 year after the initiation of AIT.

Furthermore, a randomized study was performed to determine whether passive smoking influences the outcome of therapies in children with allergic respiratory diseases (Marogna et al., 2011).

This study found a decreased clinical response to both drug therapy and immunotherapy.

In contrast to our study, they included pediatric patients till 17 years old. Also, they assessed efficacy of sublingual immunotherapy rather than subcutaneous immunotherapy used in our study. Furthermore, the enrolled patients were sonosensitizer to house dust mites.

Finally, it seems that the impact of smoking on allergy development needs to be further investigated. A unified method of subjective and objective assessment of AIT should be developed.

The limitation in our study was small study population in addition to subjective assessment of the efficacy of AIT. Thus, our results need further confirmation from multicenter rather than one center study.

4.1. Conclusion

Smoking status has no significant effect on clinical response to AIT in patients with allergic airway disorders.

Source(s) of support

No.

Conflicts of interest

No.

Acknowledgements

No.

References

Asher, M.I., Montefort, S., Björksteán, B., et al., 2006. ISAAC Phase Three Study Group. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. Lancet 368, 733–743.

Corren, J., 2007. The connection between allergic rhinitis and bronchial asthma. Curr. Opin. Pulm. Med. 13, 13–18.

Di Lorenzo, G., Mansueto, P., Pacor, M.L., et al., 2009. Evaluation of serum s-IgE/total IgE ratio in predicting clinical response to allergen-specific immunotherapy. J. Allergy Clin. Immunol. 123, 1103–1110.

Douglass, J.A., O'Hehir, R.E., 2006. 1. Diagnosis, treatment and prevention of allergic disease: the basics. Med. J. Aust. 185, 228–233.

Eifan, A.O., Akkoc, T., Yildiz, A., et al., 2010. Clinical efficacy and immunological mechanisms of sublingual and subcutaneous immunotherapy in asthmatic/rhinitis children sensitized to house dust mite: an open randomized controlled trial. Clin. Exp. Allergy 40, 922–932.

Fagerström, K., Furberg, H., 2008. A comparison of the Fagerström Test for Nicotine Dependence and smoking prevalence across countries. Addiction 103, 841−845.
Greiner, A.N., Hellings, P.W., Rotiroti, G., et al., 2011. Allergic rhinitis. Lancet 378, 2112−2122.
Jamal, A., Dube, S.R., Malarcher, A.M., et al., 2012. Centers for disease control and prevention (CDC). Tobacco use screening and counseling during physician office visits among adults–national ambulatory medical care survey and national health interview survey, United States, 2005-2009. MMWR Suppl. 61, 38−45.
Katotomichelakis, M., Tripsianis, G., Daniilidi, A., et al., 2015. Smoking effects on quality of life of allergic rhinitis patients after sublingual immunotherapy. Rhinology 53, 325−331.
Li, Q., Li, M., Yue, W., et al., 2014. Predictive factors for clinical response to allergy immunotherapy in children with asthma and rhinitis. Int. Arch. Allergy Immunol. 164, 210−217.
Marenholz, I., Nickel, R., Ruschendorf, F., et al., 2006. Filaggrin loss-of-function mutations predispose to phenotypes involved in the atopic march. J. Allergy Clin. Immunol. 118, 866−871.
Marogna, M., Massolo, A., Colombo, F., et al., 2011. Children passive smoking jeopardises the efficacy of standard anti-allergic pharmacological therapy, while sublingual immunotherapy withstands. Allergol. Immunopathol. 39, 60−67.
Olsson, P., Berglind, N., Bellander, T., et al., 2003. Prevalence of self-reported allergic and non-allergic rhinitis symptoms in Stockholm: relation to age, gender, olfactory sense and smoking. Acta Otolaryngol. 23, 75−80.
Peng, W., Liu, E., 2013. Factors influencing the response to specific immunotherapy for asthma in children aged 5-16 years. Pediatr. Int. 55, 680−684.
Polosa, R., James, D., Russo, C., et al., 2008. Cigarette smoking is associated with a greater risk of incident asthma in allergic rhinitis. J. Allergy Clin. Immunol. 121, 6.
Romantowski, J., Specjalski, K., Jakub, Ł., et al., 2019. Smoking history is negatively associated with allergen specific immunotherapy efficacy: a retrospective analysis. Postepy Dermatol. Alergol. 36, 673−676.
Schram, M.E., Tedja, A.M., Spijker, R., et al., 2010. Is there a rural/urban gradient in the prevalence of eczema? A systematic review. Br. J. Dermatol. 162, 964−973.
Siroux, V., Pin, I., Oryszcyn, M.P., et al., 2000. Relationships of active smoking to asthma and asthma severity in the EGEA study. Eur. Respir. J. 15, 470−477.
Spergel, J.M., 2010. From atopic dermatitis to asthma: the atopic march. Ann. Allergy Asthma Immunol. 105, 99−106.
Tomlinson, J.E.M., McMahon, A.D., Chaudhuri, R., et al., 2005. Efficacy of low and high dose inhaled corticosteroid in smokers versus nonsmokers with mild asthma. Thorax 60, 282−287.
Weidinger, S., O'Sullivan, M., Illig, T., et al., 2008. Filaggrin mutations, atopic eczema, hay fever, and asthma in children. J. Allergy Clin. Immunol. 121, 1203−1209.