

Clinical research

Does treatment with sub-lingual allergen-specific immunotherapy reduce adenoid size and improve quality of life among Egyptian children?

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Abstract

Introduction: Adenoidal hypertrophy is a paediatric problem. Adenoidectomy contributes to post-operative complications. Allergic rhinitis is a major health problem. Its prevalence in Egypt and the Middle East is up to 9%. The aim of the present study was to evaluate the effect of sub-lingual immunotherapy on adenoid size and/or quality of life among children suffering from adenoid hypertrophy with allergic rhinitis in Suez Canal University Hospital.

Material and methods: Forty-six children suffering from adenoid hypertrophy and allergic rhinitis were recruited for this purpose. Skin prick test was administered to identify the causative allergen. All patients received sub-lingual immunotherapy. Lateral X-ray, serum total immunoglobulin E, symptoms, and sign score were recorded for all patients before and after the treatment.

Results: The nasal symptoms and adenoidal size of the examined patients were significantly decreased after immunotherapy was applied, and thus there was an improvement in the quality of life among those patients.

Conclusions: It was concluded that sub-lingual immunotherapy was an alternative treatment of adenoidectomy in children with moderate adenoid hypertrophy with allergic rhinitis. Surgical treatment for children who suffer from severe adenoid hypertrophy with allergic rhinitis could not be considered as obligatory because medical treatment has no effect on the size of adenoids nor on quality of life.

Key words: adenoid hypertrophy, allergic rhinitis, sub-lingual immunotherapy, Egypt.

Introduction

Adenoidal hypertrophy (AH) is a paediatric problem resulting from antigenic stimulation due to severe or chronic inflammation, leading to obstruction of the nasal passages, Eustachian tubes, and blocking the clearance of nasal mucus [1]. Anatomically, the adenoid size reaches its maximum size by the age of 6 years, then gradually decreases at the age of 9 years [2].

Adenoidectomy is considered the typical modality treatment in those patients. Although it plays an important role in relieving obstructive

symptoms, it may lead to some serious complications, such as bleeding (4–5%) and postoperative respiratory compromise (27%) [3].

Allergic rhinitis (AR) is a major health problem that affects 10 to 40% of the global population [4, 5]. In terms of allergic rhinitis and its impact on asthma (ARIA), AR is seen as increasing the production of immunoglobulin (Ig) E of the mucosa after exposure to the allergen, leading to sneezing, nasal obstruction, and mucus discharge [4–6]. The prevalence of AR in Egypt and the Middle East is up to 9% [7].

The wide spread of indoor and outdoor allergens and the small chances of avoiding them raise the appearance and efficacy of allergen-specific immunotherapy (ASIT), despite its effects on the immune system [8].

Sub-lingual immunotherapy (SLIT) stimulates T-helper (TH) 1 and the regulatory T-cells to migrate into the bloodstream and mucosa after the production of interferon γ (IFN- γ) and interleukin (IL)-10 a few days after its administration [9].

The safety, ease of administration, patient compliance, and reduced side effects of SLIT (manifested in oral pruritus and throat irritation) increase its usage worldwide [8].

The aim of the current study was to evaluate the effect of SLIT on adenoid size and/or quality of life (QoL) among children suffering from adenoid hypertrophy with AR in Suez Canal University Hospital.

Table I. Type of allergens among the studied patients ($n = 46$)

Allergen	Studied population ($N = 46$)	
	<i>N</i>	%
HDM	34	74.0
HD	42	52.2
Tobacco	14	30.4
Aspirin	8	17.4
Latex	8	17.4
Cockroach	8	17.4
Dog epithelium	6	13.0
Cat epithelium	6	13.0
Timothy grass	6	13.0
Aspergillus fumigatus	4	8.7
Banana	4	8.7
Bermuda grass	4	8.7
Mixed pollen	4	8.7
Soya bean	4	8.7

Material and methods

This study was conducted at the Otolaryngology Department in the Suez Canal University Hospital affiliated to the Faculty of Medicine in Ismailia in Egypt from June 2013 to March 2016. The studied population was 46 children of both sexes, with age range from four to nine years, suffering from AH and AR, with no previous history of ASIT administration, and with exclusion of those having: anaphylaxis (i.e. after the first dose of immunotherapy), chronic infections, immunodeficiency diseases, asthma uncontrolled by pharmacotherapy, and/or irreversible airway obstruction and malignancy. Severity of nasal and adenoid symptoms were assessed [10, 11], as well as full head and neck-examinations, anterior and posterior rhinoscopy, cold mirror test, nasopharyngoscopy, and radiological assessment for of AH and AR were conducted.

The adenoidal nasopharyngeal ratio was measured by detecting many landmarks on the nasopharyngeal X-ray as follows:

- Q: the point of maximal convexity of the adenoid shadow,
- O: a line running tangential to the basiocciput,
- T: the posterior border of the hard palate,
- X: the antero-inferior aspect of the sphenobasi-occipital synchondrosis,
- N: the distance between T and X,
- A: a line drawn from Q to X,
- N: a line drawn from T to X.

The degree of nasopharyngeal airway obstruction by the adenoid was classified and scored as follows [12]:

- normal (AN ratio < 0.50) = 0 points,
- mild (AN ratio 0.50 – 0.62) = 1 point,
- moderate (AN ratio 0.63 – 0.75) = 2 points,
- severe (AN ratio 0.76 – 0.88) = 3 points.

Skin prick test for the allergens of house dust (HD), house dust mites (HDM), cockroach, mixed pollen, mixed feathers, *Aspergillus fumigatus*, Timothy grass, sheep wool, hay dust, latex, tobacco, mixed mould, dog epithelium, cat epithelium, Bermuda grass, *Alternaria tenuis*, milk, banana, egg, strawberry, *Salonecea*, mixed fish, mango, maize, soy-bean, wheat, cocoa, and mixed nuts was performed.

All patients received SLIT drops for five months according to skin reactivity. Allergen extracts were serially diluted to five concentrations according to weight/volume (w/v) ratio into (1 : 50000 w/v, 1 : 5000 w/v, 1 : 500 w/v, 1 : 50 w/v, and 1 : 5 w/v).

Lateral X-ray, serum total IgE, and symptoms and signs severity score were done for all patients before and after five months of treatment.

QoL assessment was conducted for all patients, using a seven-point scale for severity of allergic rhinitis on sleep patterns at night, work performance, and social and/or recreational activities.

Ethical considerations

The study work had the approval from the Ethics Committee of the Faculty of Medicine, Suez Canal University (FOMSCU) in Ismailia, Egypt.

Statistical analysis

The gathered data were processed using SPSS version 20 (SPSS Inc., Chicago, IL, USA). Quantitative data were expressed as means \pm SD, while qualitative data were expressed as numbers and percentages (%). Student's *t*-test was used to test significance of difference for quantitative variables. A probability value of $p < 0.05$ was considered statistically significant.

Results

The demographic characteristics of the children in this study showed an age range from 4 to

9 years with a mean 5.6 ± 1.7 years and with a predominance of female patients over male patients (65.2% vs. 34.8%, respectively) (Table I).

The nasal and non-nasal symptoms among the studied population showed statistical improvement before and after immunotherapy and are represented in Tables II–IV.

For the effect of medication on nasal and non-nasal symptoms before immunotherapy, we found that no medications had been used in nine and 17 cases, respectively, and for the moderate relief, it was four and two cases, respectively. Also, the effect of immunotherapy could substantially decrease the serum levels of total IgE after its administration for months.

Table V shows that changes occurred in the size of adenoids among the studied population after immunotherapy in comparison with its size before immunotherapy. These were expressed in numbers and percentages including the mean and

Table II. Nasal symptoms among the studied patients before and after treatment ($n = 46$)

Variables	Before		After		P-value
	N	%	N	%	
Sneezing:					< 0.0001**
None	8	17.4	18	39.1	
Mild	18	39.1	20	43.5	
Moderate	16	34.8	6	13.0	
Severe	4	8.7	2	4.3	
Runny nose:					0.0002**
None	18	39.1	30	65.2	
Mild	22	47.8	12	26.1	
Moderate	6	13.0	4	8.7	
Congestion:					0.015*
None	16	34.8	24	52.2	
Mild	20	43.5	16	34.8	
Moderate	10	21.7	6	13.0	
Itching:					0.009**
None	14	30.4	22	47.8	
Mild	20	43.5	20	43.5	
Moderate	12	26.1	4	8.7	
Post nasal:					0.37
None	16	34.8	22	47.8	
Mild	20	43.5	14	30.4	
Moderate	6	13.0	8	17.4	
Severe	4	8.7	2	4.3	

*Significant p -value < 0.05 , **highly significant p -value < 0.01 .

Table III. Non-nasal symptoms among the studied patients (n = 46)

Variables	Before		After		P-value
	N	%	N	%	
Eye symptoms:					0.030*
None	32	69.6	38	82.6	
Mild	12	26.1	8	17.4	
Moderate	2	4.3	0	0.0	
Throat symptoms:					0.05*
None	26	56.5	32	69.6	
Mild	14	30.4	10	21.7	
Moderate	6	13.0	4	8.7	
Chronic cough:					0.002**
None	18	39.1	28	60.9	
Mild	20	43.5	14	30.4	
Moderate	8	17.4	4	8.7	
Ear symptoms:					0.18
None	28	60.9	32	69.6	
Mild	12	26.1	12	26.1	
Moderate	6	13.0	2	4.3	
Headache:					0.030*
None	32	69.6	38	82.6	
Mild	14	30.4	8	17.4	

*Significant p-value < 0.05, **highly significant p-value < 0.01.

Table IV. Total nasal and non-nasal symptoms among the studied patients before and after immunotherapy (n = 46)

Total symptoms	Before		After		P-value
	N	%	N	%	
None	18	0.0	0	39.1	0.0007**
Mild	38	82.6	20	43.6	
Moderate	4	8.7	6	13.0	
Severe	4	8.7	2	4.3	

**Highly significant p-value < 0.01.

Table V. Adenoid size among the studied population before and after immunotherapy (n = 46)

Adenoid size	Before		After		P-value
	N	%	N	%	
AN 0.62 > 0.75	30	65.2	28	60.9	
AN ≥ 0.75	16	34.8	18	39.1	
Mean size (SD)	0.70 (0.06)		0.69 (0.06)		0.009**

**Highly significant p-value < 0.01, SD – standard deviation.

standard deviation as well as the statistical significance test and the *p*-value. The size of adenoid was measured by the adenoidal nasopharyngeal ratio (AN), as explained in the materials and methods section.

Also, we found that the effect of immunotherapy caused moderate improvement of symptoms in 30 cases and severe improvement in 16, out of a total of 46, with a significant relationship ($p < 0.0001$) (Table VI). Table VII shows that there was a statistically significant decrease of serum level of total IgE after immunotherapy. The relation between quality of life (QOL) and severity of adenoidal hypertrophy among the studied patients before and after immunotherapy presented in Table VIII.

Discussion

Because the adenoids are located on the roof of nasopharyngeal cavity, this permits close contact with allergens that settle onto the mucous membrane [13]. The early exposure to allergens in childhood permits the development of natural acquired immunity [14].

This study was conducted on 46 children with an age range of 4–9 years because AH increases during this span and declines by the age of 12 years. This copes with Somayajj *et al.* [15] and Evcimik *et al.* [16] who conducted their study on the same age range.

In the present study, the most common allergens found in these children were, in descending order, HDM (74.0%), HD (52.2%), tobacco

Table VI. The clinical rating scale for adenoidal symptoms among the studied patients before and after immunotherapy ($n = 46$)

Variables	Before		After		P-value
	N	%	N	%	
Snoring:					0.0002**
Absent	0	0.0	6	13.1	
Present on a few occasions during sleep	0	0.0	16	34.8	
Present whenever asleep	28	60.9	10	21.7	
Present whenever asleep or awake	18	39.1	14	30.4	
Mouth breathing:					< 0.0001**
Absent	0	0.0	8	17.4	
Present on a few occasions during sleep	8	17.4	16	34.8	
Present whenever asleep	30	65.2	14	30.4	
Present whenever asleep or awake	8	17.4	8	17.4	
Obstructive breathing during asleep:					0.17
Absent	30	65.2	34	73.9	
Present on a few occasions during sleep	12	26.1	8	17.4	
Present, fewer than 5 episodes daily	4	8.7	4	8.7	
Present, more than 5 episodes daily	0	0	0	0	

**Highly significant *p*-value < 0.01.

Table VII. Percentages of total IgE levels among the studied patients before and after immunotherapy ($n = 46$)

Total IgE	Before		After		P-value
	N	%	N	%	
ULN	5	21.8	6	26.1	0.51
1–2-fold ULN	7	30.4	11	47.8	0.009**
3–4-fold ULN	4	17.4	2	8.7	0.1
> 4-fold ULN	7	30.4	4	17.4	0.03*

*Significant *p*-value < 0.05, **highly significant *p*-value < 0.01, ULN – upper limit of normal.

Table VIII. The relation between quality of life (QoL) and severity of adenoidal hypertrophy among the studied patients before and after immunotherapy ($n = 46$)

Variables	Moderate ($n = 30$)				Severe ($n = 16$)				P-value
	Before		After		Before		After		
	N	%	N	%	N	%	N	%	
QOL terribly affected	0	0.0	0	0.0	4	25.0	4	25.0	< 0.0001**
QOL affected almost all time	0	0.0	0	0.0	6	37.5	4	25.0	
Quality of life often affected	2	6.7	2	6.7	2	12.5	2	12.5	
QOL occasionally affected but tolerable	14	46.6	10	33.3	4	25.0	4	25.0	
QOL hardly affected	12	40.0	2	6.7	0	0.0	2	12.5	
Quality of life mildly affected	2	6.7	10	33.3	0	0.0	0	0.0	
Excellent QOL	0	0.0	6	20.0	0	0.0	0	0.0	

**Highly significant p-value < 0.01.

(30.4%), aspirin (17.4%), latex (17.4%), cockroach (17.4%), dog epithelium (13.0%), cat epithelium (13.0%), and Timothy grass (13.0%). The abundance of HDM in Egypt is attributed to the geographic situation and the climatic condition of our country, as revealed by Kenawy *et al.* [17] in their research – HDM is the focus allergen in their work.

SLIT stimulate the TH 1 and regulatory T-cells to migrate into the bloodstream and mucosa after the production of IFN- γ and IL-10 a few days after its administration [9]. It remains the only aetiological treatment for allergic diseases [18]. In this study, we found that SLIT induced reduction of the serum level of total Ig E, the severity of sneezing, running nose, congestion, itching, eye symptoms, throat symptoms, chronic cough, and headache after 5 months of its administration as well as improvement in QoL among the treated children due to the alteration of immune response. Several studies were in consistent with ours, such as Niederberger [19], Chang *et al.* [20], and Rolinck-Werninghaus *et al.* [21].

The ordinary medical treatment usually improves the symptoms of AH as well as adenoid size. Many meta-analyses conducted in this area, such as the one by Cengel and Akyol [22], concur that mometasone decreases the adenoid dimensions and improves related symptoms in the long term.

For intranasal budesonide, Gozal and Gozal [23] stated that its usage with a dose of 32 μ g/nostril once daily in children with mild obstructive sleep apnoea syndrome effectively reduced the apnoea-hypopnoea index and adenoid dimensions measured (by lateral X-rays) and polysomnographies (PSG). Also, this effect persisted for at least 8 weeks after cessation of therapy.

Jung *et al.* [24] concluded that children with sleep disorders in breathing due to AH could be

effectively treated with a 4-week course of mometasone furoate. In a systemic review, six out of seven studies showed that the treatment with nasal corticosteroids improved nasal obstructive symptoms and reduced adenoid size, and its effect was sustained for a long time [25].

Meanwhile, the views regarding beclomethasone nasal spray are completely different from the other nasal sprays; Lepcha *et al.* [26] and others indicated that there was no significant change in nasal symptoms nor in the adenoidal size in the general paediatric population.

In this study, regarding adenoid size, we reported that there was a minimal significant decrease from 0.70 mm before to 0.69 mm after SLIT, while the clinical rating scale for adenoidal symptoms including snoring, mouth breathing, and obstructive breathing during sleep showed significant improvement. The improvement of these symptoms can be explained in terms of the amelioration of AR, while the minimal change of adenoid size can be attributed to the short period of treatment. Additionally, the QoL was remarkable in children with moderate AH compared to those who suffered from severe hypertrophy.

AR influences the occurrence of AH; it is considered an important risk factor in children allergic to HDM when compared with normal one [27].

It is very clear that there is similarity of clinical symptoms of AR and adenoid hypertrophy. Thus, it is important that the allergists and otolaryngologists take account of the allergic background of AR and adenoid hypertrophy [28].

In conclusion, surgical treatment for children who suffer from severe AH with AR is obligatory, because medical treatment has no effect on adenoid size or QoL, while sub-lingual immunotherapy is recommended as an alternative treatment of adenoidectomy in children with moderate ad-

enoid hypertrophy with AR because QoL shows significant improvement in such cases.

Conflict of interest

The authors declare no conflict of interest.

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