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Long-term efficacy of allergen specific immunotherapy in atopic dermatitis patients in relation to quality of life

KEY WORDS

Atopic dermatitis; DLQI; allergen specific immunotherapy

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Summary

Introduction. Atopic dermatitis (AD) is an inflammatory, chronically relapsing and highly pruritic skin disorder that considerably effects patients' life. Dermatology Life Quality Index (DLQI) is often applied in clinical research in order to evaluate the impact of AD on daily performance of patients. **Aims.** The aim of the study was to evaluate the long-term effect of allergen specific immunotherapy (ASIT) on the quality of life in AD patients. **Materials and methods.** 15 patients suffering from AD, allergic to house dust mites or grass pollen allergens, who were previously treated with ASIT participated in the study. Our treatment with allergy vaccinations was performed during the time period between 1995 and 2001. DLQI questionnaires have been filled by the patients before the treatment, after termination of ASIT and after 2 - 12 years of the observational period. **Results.** The statistical tests revealed a significant difference between the DLQI before ASIT was introduced and after termination of ASIT. Every answer except two (describing the influence of skin condition on preventing from working or studying and on sexual life) of these periods also disclosed statistically significant difference. As for the relation between the DLQI after ASIT and the actual one the tests revealed non significant difference, also regarding to every single answer of the questionnaire. **Conclusions.** In relation to improvement of quality of life in AD patients, this study confirms the effectiveness of ASIT and it discloses the persistence of its results in long-term aspect.

Introduction

Atopic dermatitis (AD) is an inflammatory, chronically relapsing, and highly pruritic skin disorder. AD affects more than 10% of children and 2% of adults. In industrialized countries the prevalence has increased significantly in last years, it has doubled or even tripled. AD is often associated with other atopic diseases such as asthma or allergic rhinitis. The etiology of atopic dermatitis is complicated and it is based on defects concerning the immunologic system that leads to IgE-mediated sensitization and epithelial barrier dysfunction. Both dysfunctions result in inflammatory skin lesions that vary with age in localization and clinical manifestation. In each stage, itching that continues throughout the day and worsens at night causes sleep

loss and considerably affects patient's and family unit's life (1). The successful treatment of atopic dermatitis is based on complex management: optimal moisturization, topical anti-inflammatory treatment (corticosteroids and calcineurin inhibitors), first-generation antihistamines to decrease the itch and sleeping disturbances and the adequate skin infections treatment. The patient education is still one of the most important tools to improve patients' health status. Other therapeutic options may be considered in severe cases, such as oral corticosteroids, ultraviolet phototherapy, cyclosporine A, azathioprine (2). Although optimistic researches reporting the benefit influence of allergen-specific immunotherapy (SIT) on atopic dermatitis patients have appeared (3,4,5), this method still remains contro-

versial. SIT as an only known casual allergy treatment involves complicated mechanisms that need further investigations. The evidences of SIT efficacy in atopic dermatitis were summarized by Comapalati et al and Bea et al (6,7).

Aims

The aim of the study was to evaluate the long-term effect of allergen specific immunotherapy (SIT) on the quality of life in AD patients.

Material and methods

Fifteen patients suffering from AD, allergic to house dust mites (n - 7), grass pollen allergens (n - 7) or house dust mites and grass pollen allergens (n - 1), who were previously treated with SIT, participated in the study. SIT was performed subcutaneously for five years for each allergen. In case of one patient treated with two types of allergen vaccines, SIT lasted for eight years in total. At the baseline patients presented moderate and/or severe AD, and clinical characteristics were one of the inclusion criteria for the treatment with allergen vaccinations. At the baseline patients were evaluated on the basis of W-AZS index (Severity and Extensiveness of skin Inflammation in Atopic Dermatitis Index) with the mean value of 102,6 points.

Depending on the type of airborne sensitization, patients were treated with allergen vaccinations of an appropriate composition (mites or grass pollen allergens extracts). In case of a patient with airborne sensitization to mite as well as grass pollen allergens, first the mite allergy vaccine has been introduced and thereafter SIT with the second vaccination (after one year of the treatment), composed of grass pollen allergens extract was started. For our study allergy vaccines, Novo-Helisen® Depot, Nexter - Allergopharma (Katowice, Poland and Reinbek, Germany) have been selected. SIT was performed according to the international European guidelines, and it was a perennial type of treatment. The starting dose was 0,05 ml of 50 TE/ml concentration, followed by injections administered every 7-14 days with increasing amount dosages, finally reaching the maintenance dose of 1 ml of 5000 TE/ml allergen concentration. Maintenance doses while reached in the course of treatment, were administered monthly.

The age of patients ranged from 5 to 46 years (mean age: 20,4) and the group was composed of 20% males and 80% females. Our treatment with allergy vaccinations was performed during the time period between 1995 and 2001. Dermatology Life Quality Index (DLQI) questionnaires have been filled by the patients before the treatment, after termination of SIT, and af-

ter 2 - 12 years of the observational period. DLQI is one of the most practical and easy measure that was developed in 1994 by the team at the Department of Dermatology, Cardiff University (**table 1**). This simple questionnaire for routine clinical is often used to describe the impact of the disease and its treatment on patient's lives. It was used in over 1000 publications and it is available in over 21 languages. The DLQI is the most frequently used instrument in studies of randomized controlled trials in dermatology. It is a questionnaire that consists of ten simple questions concerning symptoms and feelings, daily activities, leisure, work, and school, personal relationships and treatment (8). The score for each question is from 0 to 3 points, summed giving a range from 0 (no impact on life) to 30 points (maximum impairment of life quality).

Results

Friedman Test (Nonparametric Repeated Measures ANOVA) and Dunn's Multiple Comparisons Test were used to statistical analysis (**table 2,3**). Also the average DLQI results comparison is presented (**table 3**). It reveals the constant improvement of quality of life in the time course. We did not observe any statistical significant difference in DLQI results depending on presented type of allergy.

Before SIT and after SIT

The tests revealed significant difference between the DLQI before SIT was introduced and after termination of the treatment, what can be considered as an important factor of success of SIT in our AD patients. In case of all answers except two (describing the influence of skin condition on preventing from working or studying and on sexual life) the difference was statistically significant.

Before SIT and the present time point (now) (after 2 - 12 years of the observational period)

The quality of life before SIT was performed has been improved till today, although the statistical analysis only in some questions revealed significant improvement.

After SIT and the present time point (now) (after 2 - 12 years of the observational period)

As for the relation between the DLQI after SIT and the actual one the tests revealed non-significant difference also regarding to every single answer of the questionnaire.

Table 1 - Dermatology Life Quality Index (DLQI).

DERMATOLOGY LIFE QUALITY INDEX				
Hospital No:	Date:	DLQI		
Name:	Diagnosis:	Score:		
Address:				
The aim of this questionnaire is to measure how much your skin problem has affected your life OVER THE LAST WEEK. Please tick ⇒ one box for each question.				
1. Over the last week, how itchy, sore painful or stinging has your skin been?	Very much A lot A little Not at all	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
2. Over the last week, how embarrassed or self conscious have you been because of your skin?	Very much A lot A little Not at all	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
3. Over the last week, how much has your skin interfered with you going shopping or looking after your home or garden ?	Very much A lot A little Not at all	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	Not relevant	<input type="checkbox"/>
4. Over the last week, how much has your skin influenced the clothes you wear?	Very much A lot A little Not at all	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	Not relevant	<input type="checkbox"/>
5. Over the last week, how much has your skin affected any social or leisure activities?	Very much A lot A little Not at all	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	Not relevant	<input type="checkbox"/>
6. Over the last week, how much has your skin made it difficult for you to do any sport ?	Very much A lot A little Not at all	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	Not relevant	<input type="checkbox"/>
7. Over the last week, has your skin prevented you from working or studying ?	Yes No	<input type="checkbox"/> <input type="checkbox"/>	Not relevant	<input type="checkbox"/>
If "No", over the last week how much has your skin been a problem at work or studying ?	A lot A little Not at all	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
8. Over the last week, how much has your skin created problems with your partner or any of your close friends or relatives ?	Very much A lot A little Not at all	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	Not relevant	<input type="checkbox"/>
9. Over the last week, how much has your skin caused any sexual difficulties ?	Very much A lot A little Not at all	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	Not relevant	<input type="checkbox"/>
10. Over the last week, how much of a problem has the treatment for your skin been, for example by making your home messy, or by taking up time?	Very much A lot A little Not at all	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	Not relevant	<input type="checkbox"/>

Please check you have answered EVERY question. Thank you.

Table 2 - The statistical analysis of DLQI questions before SIT, after SIT and now.

Question	Before SIT and AFTER SIT	Before SIT and now	After SIT and now
1. Over the last week, how itchy, sore, painful or stinging has your skin been?	SIGNIFICANT	SIGNIFICANT	NON SIGNIFICANT
2. Over the last week, how embarrassed or self conscious have you been because of your skin?	SIGNIFICANT	SIGNIFICANT	NON SIGNIFICANT
3. Over the last week, how much has your skin interfered with you going shopping or looking after your home or garden ?	SIGNIFICANT	SIGNIFICANT	NON SIGNIFICANT
4. Over the last week, how much has your skin influenced the clothes you wear?	SIGNIFICANT	SIGNIFICANT	NON SIGNIFICANT
5. Over the last week, how much has your skin affected any social or leisure activities?	SIGNIFICANT	SIGNIFICANT	NON SIGNIFICANT
6. Over the last week, how much has your skin made it difficult for you to do any sport ?	SIGNIFICANT	NON SIGNIFICANT	NON SIGNIFICANT
7. Over the last week, has your skin prevented you from working or studying ? / Over the last week how much has your skin been a problem at work or studying ?	NON SIGNIFICANT	NON SIGNIFICANT	NON SIGNIFICANT
8. Over the last week, how much has your skin created problems with your partner or any of your close friends or relatives ?	SIGNIFICANT	NON SIGNIFICANT	NON SIGNIFICANT
9. Over the last week, how much has your skin caused any sexual difficulties ?	NON SIGNIFICANT	NON SIGNIFICANT	NON SIGNIFICANT
10. Over the last week, how much of a problem has the treatment for your skin been, for example by making your home messy, or by taking up time?	SIGNIFICANT	SIGNIFICANT	NON SIGNIFICANT
DLQI – total score	SIGNIFICANT	SIGNIFICANT	NON SIGNIFICANT

Table 3 - Average DLQI results (max. - 30 points).

	Before SIT	After SIT	Now
Average DLQI result (points)	20,0	9,0	4,0

Discussion

Skin diseases such as AD can have a great impact on patients' lives in terms of psychological well-being, everyday activities and functioning in the society. Therefore, the quality of life improvement has become a major object to achieve in various clinical trials.

In this study we show that SIT has a long-term efficacy in AD patients. The initial average DLQI result has been reduced after SIT was completed (what reflects in statistical analysis as a significant difference) and after then the score still has a decreasing

tendency, although it is of no statistical significance. Every single question of the DLQI questionnaire has been analysed separately in addition. We are able to show a significant improvement in case of six questions (except two, concerning preventing from working or studying and sexual life) before and after SIT was performed. Then, the value of quality of life obtained due to the treatment with allergy vaccination has become stabilized till today, although statistical analysis revealed no significant difference. On the basis of the comparison between DLQI score before SIT and now, we observe that in two of ten questions (concerning sport, relation with relatives and friends) the actual

score has been decreased; it was not that satisfying as after SIT, but anyhow not that distressing as before SIT. In case of other two questions, regarding preventing from working or studying and sexual life, we did not observe any influence of SIT on this part of the quality of life of our patients.

The long-term comparison of quality of life in AD patients who were treated with SIT has not been described so far. Besides, even the effectiveness of SIT in AD patients using the quality of life measures has been poorly described in the medical literature. Bae JM et al performed a systemic review of efficacy of allergen-specific immunotherapy for atopic dermatitis (7). Almost all of the trials mentioned in the review did not analyse the patient's quality of life as an important factor describing success of treatment.

Novak N et al showed a clinically important reduction of the total DLQI due to SIT in the trial, although it was not always statistically significant. The AD group obtained the following median DLQI score before -5.7, and after active treatment (SIT) -6.0 (5).

The long-term efficacy defined by quality of life measures was highlighted in articles dedicated to rhinoconjunctivitis. Stephen R. Durham performed a double-blind, placebo-controlled trial, that involved a group of two hundred thirty-eight participants with a clinical history of grass pollen-induced allergy, presenting symptoms interfering with usual daily activities or sleep. The significant decrease in days with severe symptoms, and the improved quality of life in the active group, supported the clinical relevance of the primary efficacy end points, and emphasized the relevance of sublingual grass SIT treatment from the patient perspective (9).

Also Didier et al describes improvement in quality of life over the fourth pollen period in patients with rhinoconjunctivitis. Besides, it is highlighted that this improvement may be underestimated, due to the higher rescue medication use in placebo-treated group compared to the active group (10).

Conclusions

The current study was designed to assess whether SIT in AD patients displays a long-term efficacy in relation to quality of life. SIT has been shown to improve patients' well-being, not only just after SIT was performed, however it also has a beneficial sustained influence years after its termination.

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