Phototherapy for allergic rhinitis: a prospective, randomized, single-blind, placebo-controlled study

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***Abstract*:** Phototherapy has a profound immunosuppressive effect, and phototherapeutic methods using both ultraviolet (UV) and visible light are therefore widely used for the therapy of various inflammatory skin diseases. It is also proposed that phototherapy, using a combination of UV-A (25%), UV-B (5%) and visible light (70%), may represent a therapeutic alternative in patients with allergic rhinitis. Seventy nine patients were randomly assigned to receive either a combination of UV-A (25%), UV-B (5%) and visible light (70%), in the phototherapy group, or low-intensity visible light, in the control group. The efficacy of treatment was assessed by means of total nasal symptom score before treatment and 1 month after the end of treatment. Total nasal scores decreased in both groups but the decrease was highly significant in the active treatment group when compared with the placebo ($p < 0.001$). This study demonstrates that phototherapy may be an effective modality in the treatment of allergic rhinitis especially in cases of which commonly used drugs either are contraindicated and/or have insufficient efficacy.

***Keywords*:** allergic rhinitis, phototherapy, rhinophototherapy, UV, ultraviolet

Introduction

Allergic rhinitis is considered to be one of the most frequent health problems. A costly and highly prevalent disease with a major effect on the quality of life, it is also considered to be a risk factor for asthma [Salib and Howarth, 2003; Togias, 2003; Kay, 2001]. Despite the fact that new antihistamines and local steroids have been used with good results, complete resolution of the symptoms is practically difficult. In a special subsets of patients, such as pregnant and breastfeeding women, application of these drugs is disputed [Law *et al*. 2003]. As a result, the above characteristics of allergic rhinitis firmly show the need for effective treatment modalities.

Phototherapy has a profound immunosuppressive effect, and phototherapeutic methods using both ultraviolet (UV) and visible light are therefore widely used for the therapy of various inflammatory skin diseases [Koreck *et al*. 2005a]. It is also proposed that phototherapy, using a combination of UV-A (25%), UV-B (5%) and visible light (70%) (UVAB), may represent a therapeutic alternative in patients with allergic rhinitis. Various papers on the successful results of phototherapy treatment on allergic symptoms have been published [Kemény and Koreck, 2007; Csoma *et al*. 2006; Koreck *et al*. 2005a, 2005b, 2007]. Koreck and colleagues assessed the efficacy of phototherapy in allergic rhinitis and stated that phototherapy locally reduced the number of inflammatory cells [Koreck *et al*. 2005b]. They also revealed that UVAB (UV-A, UV-B, visible light) significantly suppressed the clinical symptoms of allergic rhinitis.

Herein, we aimed to investigate the efficacy of phototherapy treatment on patients with allergic rhinitis by means of total nasal symptom score (TNSS).

Materials and methods

Study design

We conducted a prospective, randomized, single-blind, placebo-controlled study in patients with a history of at least 2 years of moderate-to-severe persistent allergic rhinitis that was not controlled

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by anti-allergic drugs. Positive skin test results and an elevated level of specific IgE antibody confirmed the diagnosis. The study was performed out of the pollen season. The study protocol was approved by the Ethics Committee of the University and a written consent form was obtained for each volunteer (Approval No. 31120743). The patients were provided with the necessary information on the nature and scope of the clinical study. All participants were required to submit a signed informed consent form at least 24 hours before the start of treatment.

Seventy nine patients were prospectively and randomly assigned into two groups using computer-generated randomization: 41 in the UVAB (UV-A, UV-B, visible light) group and 38 in the VIS (low-intensity visible light) group. Volunteers with significant nasal structural abnormalities, those with asthma, those with an upper or lower respiratory tract infection within 4 weeks or nasopharyngeal pathology diagnosed via fiber-optic endoscopy, and those who had used any of the following drugs were excluded from the study: systemic corticosteroids within 4 weeks, topical corticosteroids within 2 weeks, membrane stabilizers within 2 weeks, antihistamines within 1 week, nasal decongestants within 3 days, or immunotherapy within 5 years prior to the study. Illuminations were performed with the same device (Rhinolight III; Rhinolight Ltd, Szeged, Hungary) by the same examiner. Each intranasal cavity was irradiated three times a week for 2 weeks with increasing doses as shown in Table 1. During the course of the investigation, no rescue medication was allowed. The signs and symptoms of allergic rhinitis were scored by the volunteer before and after the treatment.

Table 1. The treatment protocol used for the illumination of the patients' nasal cavities either with UVAB or VIS lights. The starting dose of 2 minutes is equal to 1.6 J/cm^2. Upon every consecutive treatment, the dose was raised by 0.2 J/cm^2, reaching the highest dose of 2.4 J/cm^2 achieved at the fifth visit.

Visit	Length of treatments per nostril (min:s)
	First week
1	2:00
2	2:15
3	2:30
	Second week
4	2:45
5	3:00
6	3:00

Assessing the efficacy of treatment

TNSS is considered as the most common and best established parameter for the clinical assessment of allergic rhinitis. The signs and symptoms of allergic rhinitis were scored by the patient using TNSS before treatment and 1 month after the end of treatment. TNSS is the sum of the scores for the four nasal symptoms graded by the patient before and after the treatment. Nasal symptoms included in the study are nasal obstruction, nasal itching, nasal discharge and sneezing. All symptoms were graded on a four-point scale using the following system: 0, none; 1, mild (symptoms that are present but not particularly bothersome); 2, moderate (symptoms that are bothersome but do not interfere with daily activities); and 3, severe (symptoms that are bothersome and interfere with daily activities or disturb sleep).

Statistical analyses

Data were analyzed using the SPSS (Statistical Package for Social Sciences) 13.0 for Windows. The distribution of variables was checked initially by Shapiro–Wilk test. A chi-squared test was used in order to compare the sex distribution and house types of UVAB and VIS groups. A comparison of the age distribution of groups was done by using an independent samples *t*-test. The initial symptoms of cases such as nasal discharge, sneezing, nasal congestion and itching were compared with Mann–Whitney *U*-test. The variation of these symptoms along the treatment period was compared by Wilcoxon signed rank tests. Independent samples *t*-tests were used in order to evaluate the efficacy and satisfaction evaluation scores of UVAB and VIS groups. Results were expressed as mean $\pm$ standard deviation (SD) and p-value < 0.05 was considered as statistically significant.

Results

The UVAB group consisted of 41 patients (24 female, 17 male), and the VIS group consisted of 38 patients (26 female, 12 male). There was no difference in average age between the two groups ($p = 0.392$). The most common allergens that the patients were sensitive to were mites and pollens. For the UVAB group, a statistically significant difference was found between scores of nasal obstruction, nasal itching, nasal discharge, and sneezing before and after phototherapy

($p < 0.001$) (Table 2). When the scores of nasal obstruction, nasal itching, nasal discharge and sneezing variables for the VIS group were compared, it was observed that there was a decrease in the severity of symptoms but this decrease was milder when compared with that of the active treatment group ($p < 0.001$) (Table 3).

Total nasal symptom scores decreased in both groups but the decrease was highly significant in the active treatment group when compared with placebo ($p < 0.001$). According to these results it is possible to state that the phototherapy treatment with UVAB proved to be more efficient than VIS. The therapy was well tolerated in both groups. The subjects were not given any medicine during the treatment period, not even rescue medications. Dryness in the nose was the only side effect reported in the UVAB group.

Discussion

Allergic rhinitis is considered as a very important disorder due to its high incidence and severe impairment of quality of life. Intranasal steroids and antihistamines are the gold standard of medical therapy but there are many patients who do not desire to take any medication for the relief of allergic rhinitis, or cases where these medications may be contraindicated due to various reasons.

A treatment application like phototherapy may be very suitable especially in such cases where commonly used drugs are either contraindicated and/or have insufficient efficacy. In a pilot study, Kemény and Koreck compared the efficacy of UVAB with an oral antihistamine, fexofenadine and stated that TNSS in the UVAB group was significantly lower [Kemény and Koreck, 2007]. Although phototherapy probably will not be a competing treatment method with antihistamines or nasal steroids, it would be very suitable before the allergy season as a concomitant treatment of ongoing medication. The ease of application, especially in cases where commonly used drugs are either contraindicated and/or have insufficient efficacy, is another important advantage of the present method.

In a recent study, it was also reported that UVAB does not have any harmful effects on the DNA of nasal mucosa cells [Mitchell *et al.* 2008; Koreck *et al.* 2007]. Although the current data suggest that the nasal mucosa has effective mechanisms to repair UV-induced DNA damage, more studies are needed to clearly state that 'UVAB does not have any harmful effects on the DNA of nasal mucosa cells'.

The present study focused only on clinical efficacy, but previous studies worked on the mechanism of the efficacy of phototherapy. In these studies, irradiation of the nasal mucosa resulted in a significant decrease in local interleukin-5 (IL-5). T lymphocytes are major sources of IL-5.

Table 2. Total nasal symptom scores for the UVAB group. A highly significant difference was observed before and after treatment for all variables ($p < 0.001$).

	Baseline (mean ± SD)	After treatment (mean ± SD)	*p*-value
Nasal obstruction	2.64 ± 0.12	0.85 ± 0.16	$p < 0.001$
Nasal itching	2.68 ± 0.14	0.75 ± 0.14	$p < 0.001$
Nasal discharge	2.48 ± 0.10	0.45 ± 0.11	$p < 0.001$
Sneezing	2.56 ± 0.16	0.5 ± 0.11	$p < 0.001$

SD, standard deviation.

Table 3. Total nasal symptom scores for the VIS group. A significant difference was observed before and after treatment for all variables ($p < 0.01$).

	Baseline (mean ± SD)	After treatment (mean ± SD)	*p*-value
Nasal obstruction	2.35 ± 0.12	1.13 ± 0.18	$p < 0.01$
Nasal itching	2.55 ± 0.12	1.01 ± 0.16	$p < 0.01$
Nasal discharge	2.65 ± 0.13	1.06 ± 0.12	$p < 0.01$
Sneezing	2.38 ± 0.12	1.02 ± 0.14	$p < 0.01$

Thus, apoptosis of these cells after phototherapy might be the basis of the underlying mechanism of decreased IL-5 production. Memory T cells have an important role in the perpetuation and maintenance of allergic process. Apoptosis of these cells after phototherapy might have a long-term beneficial effect. Phototherapy also resulted in a decreased number of eosinophils and a decreased level of ECP in the nasal lavage fluid. This might be attributed to the direct proapoptotic effect of UVAB on eosinophils and to the decreased local IL-5 level [Koreck *et al*. 2005b]. It has also been shown that UV-A light significantly inhibited histamine release from human basophiles and a human mast cell line and that UV-B light had an inhibitory effect only on mast cells [Koreck *et al*. 2005b]. So phototherapy might be a promising new treatment modality in different inflammatory and immune-mediated mucosal diseases as reported [Kemény and Koreck, 2007]. It may also be successful in treating persistent allergic rhinitis. The present study revealed that UVAB treatment was significantly more efficient than placebo. A statistically significant difference was found between all variables, in the phototherapy group before and after the treatment. However, the efficacy of placebo light on self-assessed symptoms, namely congestion, sneezing and itching, was very striking. This result can be explained by the psychological aspect of the disease.

The most important restriction of phototherapy is the area of the nasal mucosa that we cannot reach with this application. We believe that the clinical results will improve when UVAB transmission and distribution to whole or a larger area of nasal mucosa can be achieved. In our study group, the only side effect reported was dryness in the nose. After the study, this problem was solved by using a seawater gel (Tonimer Gel®, Istituto Gansssini S.p.A., Milano, Italy) which is a natural decongestive agent that has a high humidifying effect. Now we routinely advise patients to use it during phototherapy period. Although we did not observe any major side effects with the protocol that we applied, it is important to work out the frequency of repeated phototherapy applications and possibility of unexpected side effects in continuous or frequent usage.

In clinical studies, performing a double-blind study is always preferred. However, in this study it was almost impossible to do that. The UV filter that we had attached to the nozzle was detectable by the physicians. So we performed a single-blind study. We believe that it did not affect the patients because the decrease in subjective symptoms was also noticeable in placebo group.

Conclusion

This study demonstrates that phototherapy is an effective modality in the treatment of allergic rhinitis especially in cases of which commonly used drugs either are contraindicated and/or have insufficient efficacy. Further studies are needed in order to plan an ongoing treatment of phototherapy at certain intervals for permanent relief of symptoms.

Conflict of interest statement

The authors do not have a financial relationship with any organization or company, nor has the research been sponsored by any commercial organization. This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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