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Short Time Efficiency of Rhinophototherapy in Management of Patients with Allergic Rhinitis Resistant to Medical Therapy

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ABSTRACT

Allergic rhinitis is one of the most common health problems with a major effect on the quality of life. We intended to treat Allergic Rhinitis (AR) in patients who are either unresponsive to antihistamines or their job requires optimal alertness that may be disturbed by antihistamine's side effects and those who do not comply with the regular use. We tried short term phototherapy and evaluated its effect on AR.

As phototherapy is effective in the treatment of atopic dermatitis (AD) and the same allergens can produce both AD and AR, phototherapy is proposed as a new tool in the AR treatment. In AD, phototherapy causes induction of apoptosis in infiltrating T cells and other immunomodulatory effects. We performed a randomized single-blind study to investigate the effect of low-dose phototherapy in AR patients. Among AR patients who did not respond to local and systemic therapy, we chose 62 allergic patients all above 25 years of age with moderate to severe AR whose disease was verified by allergy skin test or specific IgE to allergens; then, they were randomly divided into 31 patients as treatment group and 31 patients as control group.

In treatment groups, we used a mixture of UVA, UVB and visible light. In the control group, we used visible light alone as placebo. Then we evaluated the level of response to treatment in two groups and compared them according to Total Nasal Symptom scores (TNSS) and Global Severity Scores (GSS) and Rhinoconjunctivitis Quality of Life Questionnaires (RQLQ) symptom scores.

We found out that phototherapy in the treatment group in comparison with placebo was effective in treatment of AR *(p-value* <0.001*)*. However, we recommend that for substantiation of the claim, further investigations are still required.

Keywords: Allergic rhinitis; Phototherapy; Quality of life; Treatment

INTRODUCTION

Allergic rhinitis (AR) is one of the most common allergic disease with a major effect on the quality of life. Allergic Rhinitis symptoms have been found to impair personal productivity. Several studies showed that patients with moderate to severe allergic rhinitis had a significant decrease in physical, and social activity.[2] Sleep loss due to AR may lead to daytime fatigue and poor concentration in school, resulting in learning impairment. It is a high-cost and high-

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prevalence disease. AR is also considered to be a risk factor for asthma and worsening asthma in patients who have both asthma and rhinitis. Rhinosinusitis is common in patients with allergic rhinitis and significant portion of patients have concomitant otitis media with effusion.[2] Typical signs and symptoms of AR include a combination of congestion, sneezing, rhinorrhea, and pruritus of the nose, eyes and oral mucosa.[2] We aimed to treat AR in patients who were either unresponsive to antihistamines or their job required optimal alertness that may be disturbed by antihistamine's side effects like drivers or those who did not comply with the regular use.[1] As phototherapy is effective in the treatment of allergic disease like atopic dermatitis (AD) and the same allergens can produce both AD and AR, it seems that phototherapy can be helpful in AR treatment. We aimed to try short term phototherapy and evaluate its effect on AR. Koreck et al assessed the efficacy of phototherapy in AR and stated that phototherapy locally reduced the number of inflammatory cells.[1] Allergic Rhinitis and Its Impact on Asthma (ARIA) is the guideline used in this study for classification and assessment of its severity of AR.[3] Phototherapy including ultraviolet (UV) and visible light has a profound immunosuppressive effect. Therefore, phototherapy is widely used for therapy of various inflammatory skin diseases, such as AD.[14] The major mechanisms of immunosuppression induced by the various forms of phototherapy in the skin involve the induction of apoptosis in infiltrating T cells, reduction in the number and function of Langerhans cells, and induction of immunomodulatory cytokines such as IL-10.[2] Koreck et al found that irradiation with low doses of UV-B, UV-A and visible light was capable of significantly inhibiting the wheal formation even at suberythematous doses in skin prick tests.[2] In allergic cases, the Th2 lymphocytes play an important role and TH2 require interleukin (IL)-4 for development. These cells secrete the cytokines IL-4, IL-5, and IL-13, which all have a central role in induction of IgE production and recruitment and survival of eosinophil at sites of allergic reaction like nasal mucosa.[2] Thus, apoptosis of these cells after phototherapy might be the basis of the underlying mechanism of decreased IL-5 production. The potential therapeutic strategy for the resolution of allergic rhinitis by phototherapy is suppression of prolonged eosinophil survival induced by IL-5.[1] In patients who are either unresponsive to treatments or their job requires optimal alertness that may be disturbed by antihistamine's side effects, phototherapy might serve as a new tool in the therapeutic procedure for AR.

MATERIALS AND METHODS

We conducted a prospective randomized, single-blind study, which was approved by the Ethics Committee of Shiraz University of Medical Science in Iran. Signed informed consent obtained from the patient prior to conducting any study-related procedures. This study was performed from April to July 2014. The study included 62 patients with a history of at least 2 years of moderate to severe persistent AR that was not controlled by local or systemic drugs such as antihistamines or corticosteroids. The diagnosis of AR was confirmed by positive skin test or specific IgE to aeroallergens. The study was done in pollen season. Inclusion criteria included: 1. Men and women, 25–60 years of age. 2. Out-patients, with a history/diagnosis of allergic rhinitis for at least two years prior to the first visit. 3. Allergy verified by a positive skin-prick test or specific IgE determination within two years prior to first visit, or at first visit 4. Patients with diagnosis of AR who did notrespond satisfactorily to previous local or systemic antihistamines/corticosteroids, or did not want or could not be treated with these drugs due to side effects or any other reasons. 5. Patients with moderate to severe disease, where the global severity score (GSS) was>6 out of the 10-point scale in the last 3 days before enrollment. Exclusion Criteria included: 1. Known light-induced skin disease (photodermatosis). 2. Ongoing fungal, viral or bacterial respiratory infection. 3. Abnormalities in the nose (e.g. severe septum deviation or polyps) that disturb phototherapeutical treatment, as judged by the investigator. 4. Drug contraindication (photosensitive drugs): digitoxin, doxepin, amiodarone, trimethoprim, chlorpropamide, piroxicam, doxycycline, promethazine. Therapeutic Class Wash-Out Period for Systemic corticosteroids was 4 weeks; for intranasal cromolyn sodium and intranasal corticosteroids, 2 weeks; for intranasal decongestants, 3 days; for intranasal or systemic antihistamines, 1 week; and for immunotherapy it was 5 years before the beginning of the study. 5. Patients<25 years of age. 6. Pregnant women. 7. Patients unable to give informed consent because of senility, mental illness, dementia or communication

difficulties. 8. Patients with nasopharyngeal tumors. All participants fulfilling the inclusion criteria were enrolled after the beginning of the pollen season. Sixty nine patients were randomly assigned to the two groups: 34 patients in the treatment group and 35 in the control group. Three patients from the treatment group, and four from the control group were excluded, because diagnose changed in progress of research or development of phototherapy complications. These two groups of patients were fairly homogeneous regarding their clinical findings. The study population consisted of 23 males and 39 females. The mean age of the treatment group was 36.84 years (range, 25 to 59 years) and in the control group it was 36.42 years (range, 25 to 60 years). In the pretreatment evaluation, there was no statistically significant differences between age, sex, mean age, total nasal symptom scores (TNSS), palate itching, conjunctivitis and Rhinoconjunctivitis Quality of Life Questionnaires (RQLQ) scores ($p>0.05$). The total RQLQ scores of the two groups were significantly homogenous at baseline (Figure.5) ($p<0.05$). There was also no difference in compliance for the medication of each group. Demographic data is shown in Table 1.

Phototherapy was done using Rhinolight (Rhinolight Ltd., Szeged, Hungary) according to the protocol described by Koreck et al.[1] The light emitted consisted of more than 70% of visible light, 25% of UV-A, and less than 5% of UV-B lights. The light was emitted with a special light cable onto the surface to be treated. Treatments lasted 2-3 minutes. Both the patient and the physician wore glasses filtrating UV light. Each intranasal cavity was irradiated 3 times a week for 2 weeks with increasing doses (starting dose, 1.6 J/cm2) as shown in Table 2. At every consecutive treatment, the dose was raised by 0.2 J/cm2; therefore, the top dose was 2.4 J/cm2 and this was achieved at the fifth treatment session.

The probe was turned round in the nasal cavity during phototherapy but irradiation to nasal septum was avoided. Irradiations were performed with the Rhinolight 180 m W lamp. This equipment is applied for treatment with either the active or placebo.

The treatment group for active intervention received phototherapy with Rhinolight and the control group received placebo phototherapy (420 nm wavelength filter used to cut UV light, Schott FG13) with only visible light. After starting the phototherapy, 3 patients were excluded from the treatment group, because they did not meet the inclusion criteria. One of them was photosensitive, another one because of unilateral severe nasal mucosal edema after the second dose of phototherapy and the third one due to discontinuation of his treatment. In the control group, also two females and two males were excluded from the study because of discontinuation of their treatment by themselves. We did not use other drugs during the study period in the treatment (phototherapy) group.

During the course of the investigation, the only rescue medication allowed was cetirizine (10 mg/day). The mean dose of cetirizineused in the treatment group was 261.39±98.92 mg and in the control (placebo) group it was 335.48±60.83 mg during the study (three months). Each patient kept a diary of daily symptoms on a scale of 0 to 3 (0 indicating no symptoms and 1, 2, and 3 indicating mild, moderate, and severe symptoms, respectively) for nasal obstruction, nasal itching, rhinorrhea, sneezing, itching of the palate, and eye symptoms. An independent investigator and a volunteer jointly examined and calculated the weekly symptom scores. TNSS, a sum of scores for sneezing, rhinorrhea,

Table 1. Demographic data of both groups

	Treatment group N (31)	Placebo group N (31)	*p*-value
Age (year)	36.84±10.364	36.42±9.889	0.871
Men %	35.5%	45.2%	0.437
Women %	64.5%	54.8%	0.437
Sneezing	2.61±.667	2.23±.805	0.117
Nasal obstruction	2.10±.831	2.19±.703	0.558
Nasal itching	1.87±.991	1.74±.930	0.217
Rhinorrhea	2.74±.682	2.58±.672	0.232
TNSS	9.29±1.901	8.74±1.770	0.673
Palate itching	1.48±.962	1.10±.944	0.296
Conjunctivitis	1.81±1.078	1.58±.765	0.120

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nasal itching, and nasal obstruction and GSS, a sum of TNSS, itching of the palate, and eye symptom scores which are considered the most common and best established parameters for the clinical assessment of AR, was also calculated. The efficacy of treatment was assessed by clinical findings, TNSS, GSS, and RQLQ scores. We evaluated the TNSS and GSS of the patients in this study before the treatment, at the second week, sixth week, and 12th week after treatment. All symptoms were graded according to the severity (0, none; 1, mild; 2, moderate; 3, severe). Quality of life was investigated using the Iranian validated form of RQLQ (4, 5). Also, we evaluated the patients before the treatment, at the first and third months after the treatment with RQLQ, scores. The RQLQ had 28 questions in seven domains (activity limitation, sleep problems, nose symptoms, eye symptoms, non-nose non-eye symptoms, practical problems and emotional function) and each question was scaled from 0 (not impaired at all) to 6 (severely impaired). Our data about RQLQ scores were assessed at the baseline before treatment, one month and three months after treatment. RQLQ was grouped according to the following seven domains, namely sleep (three items), non-nasal eye symptoms (seven items), practical problems (three items), nasal symptoms (four items), eye symptoms (four items), activities that have been limited by nose or eye symptoms (three items), and emotional function (four items); they were then compared statistically. The only significant side effect of phototherapy was nasal mucosal dryness. We recommended that local ophthalmic vitamin A should be used for prophylaxis then. When the patient developed nasal mucosal swelling, treatment was postponed for 1-2 days. If nasal mucosal swelling was aggravated and caused ulceration or bleeding, therapy was stopped until symptoms revolved.

Statistical Analyses

Data were analyzed using SPSS version 18.0 microsoft, US. For comparing demographic data such as age distribution, we used Student's t-test and for evaluation of a sex distribution Chi-square test was applied. Sample size was estimated considering the power of the study to be 95% with 5% level of significance. Variation of mean values of nasal symptom scores such as TNSS, GSS and RQLQ scores during the treatment periods within the groups and the variation during the treatment period for all parameters between the groups were compared using repeated measurements. For evaluation of the effects within subjects, Sphericity and Greenhouse Geisser were applied. Results were expressed as mean and a $p<0.05$ was considered statistically significant.

RESULTS

In the placebo group, 31 patients completed the treatment and four patients from this group did not complete the study. These four patients withdraw from the treatment because of occupational or familial problems. In the treatment group, 31 patients completed the treatment. Three patients were excluded from the study, one because of photosensitivity which was determined at the beginning of the treatment protocol and two due to severe nasal mucosal edema and bleeding. The mean dose of cetirizine which was used in the treatment group was less than that of the control group and the difference between them was statistically significant *(*$p<0.001$). Treatment groups had statistically significant improvements from their baseline TNSS and GSS after 2 weeks, 6 weeks and 12weeks of treatments *(*$p<0.05$*)*, (Figure 2, Table 4). A statistically significant difference was found in the treatment group in comparison with the placebo group in the scores of nasal discharge, nasal obstruction, sneezing, nasal itching, itching of the palate and conjunctivitis before and after phototherapy *(*$p<0.05$), (Figures 1,2, Table 4). A statistically significant difference was found between the baseline and second, 6th and 12th week in the scores of nasal discharge, nasal obstruction, sneezing, nasal itching, itching of the palate and conjunctivitis before and after phototherapy in the treatment group in comparison with the placebo one *(*$p<0.05$), (Figures 1,2, Table 4). However, no statistically significant difference was found between these scores for the placebo group between the baseline and second, 6th and 12th week after treatment *(*$p<0.05$*)*, (Figure 1, Table 4). The total RQLQ scores of the two groups were significantly homogenous at baseline ($p<0.05$) (Figure 5). The RQLQ measures revealed that phototherapy was effective in improving the quality of life overall and in seven separate domains of treatment group *(*$p<0.05$*)* (Table 5, Figure 3). Treatment groups showed statistically significant improvements from their baseline RQLQ scores after one month and three

months of treatments (p<0.05), (Figure 3, Table 5). A statistically significant difference was found in the treatment group in comparison with the placebo group in the RQLQ scores before and after phototherapy (p<0.05), (Table 5). A statistically significant difference was found between the baseline before treatment, in comparison with the first and third months after treatment in the RQLQ scores in two groups, including sleep, non-nasal eye symptoms, practical problems, nasal symptoms, eye symptoms, activities that have been limited by nose or eye symptoms and emotional function. (p<0.05), (Figures 3, 4, Table 5). But, overall there were no improvement seen in the quality of life and in seven separate domains of the placebo group (p<0.05) (Table 5, Figure 4). Intranasal phototherapy was well tolerated. The side effects included dryness and edema of the nasal mucosa, nasal burning sensation and headache which occurred significantly in the treatment group. This side effect was not seen in the placebo group (Table 3). The nasal mucosal dryness, edema and burning sensation were controlled by emollients. The headache of patients ameliorated during the first two weeks after phototherapy without any treatment.

Table 2. Phototherapy protocol

Phototherapy	Time: Minutes & Seconds
First week	
First	2
Second	2.15
Third	2.30
Second week	
Forth	2.45
Fifth	3
Sixth	3

Table 3. The Side effects of phototherapy in both groups

Phototherapy side effects	Treatment	Placebo
Dryness	4	0
Severe mucosal edema	1	0
Severe mucosal dryness	2	0
Headache	2	0
Nasal burning sensation	2	0

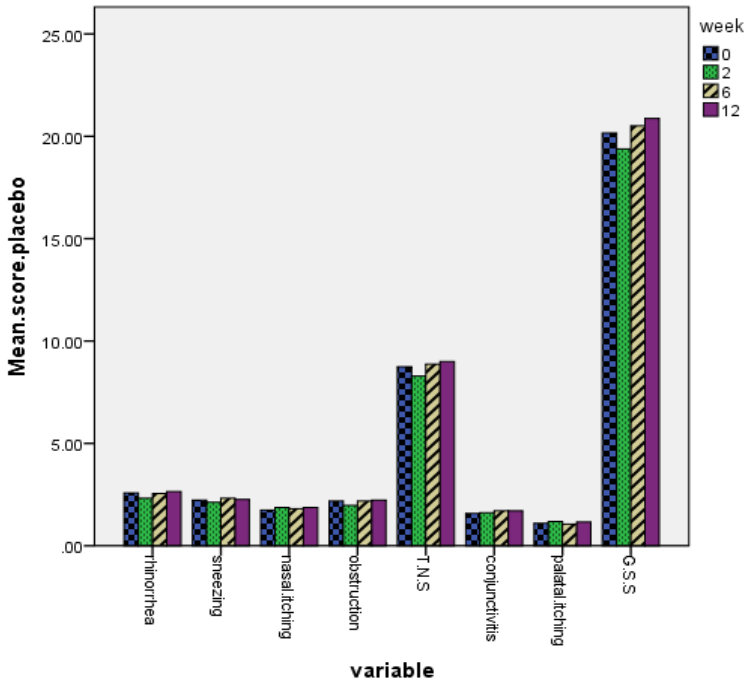

Figure 1. Mean scores of nasal symptoms Total Nasal Symptom scores (TNSS) and Global Severity Scores (GSS) in the placebo group at the baseline and after 2, 6, 12 weeks after treatment

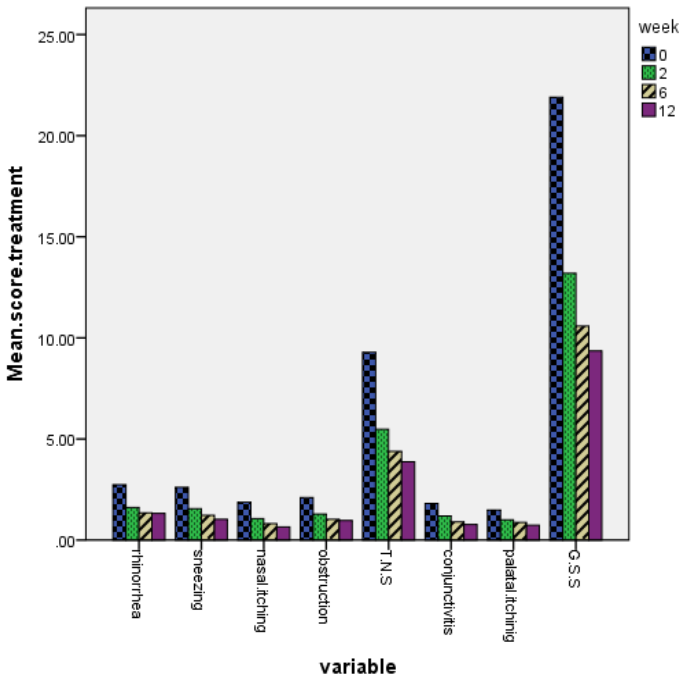

Figure 2. Mean scores of nasal symptom Total Nasal Symptom scores (TNSS) and Global Severity Scores (GSS) in the treatment group at the baseline and 2, 6, 12 weeks after treatment.

Table 4. Symptomatic scores of the nose, eyes and palate, at baseline and after 2 weeks, 6 weeks and 12 weeks of treatment in both groups (1: Treatment, 2: placebo).

Parameter	Treatment group	Baseline Mean±SD	Second week Mean±SD	6th week Mean±SD	12th week Mean±SD	*p*-value*	*p*-value**	*p*-value***
Rhinorrhea	1	2.74±0.682	1.61±0.888	1.35±0.915	1.32±1.013	<0.001	<0.001	<0.001
	2	2.58±0.672	2.32±0.653	2.55±0.723	2.65±0.661			
Sneezing	1	2.61±0.667	1.55±0.850	1.23±0.762	1.03±0.795	<0.001	<0.001	<0.001
	2	2.23±0.805	2.13±0.806	2.32±0.832	2.26±0.815			
Nasal obstruction	1	2.10±0.831	1.29±0.783	1.03±.948	0.97±1.048	<0.001	<0.001	<0.001
	2	2.19±0.703	1.97±0.752	2.19±0.749	2.23±0.762			
Nasal itching	1	1.87±0.991	1.06±0.892	0.81±0.833	0.65±0.839	<0.001	<0.001	<0.001
	2	1.74±0.930	1.87±0.922	1.81±0.910	1.87±0.922			
TNSS	1	9.29±1.901	5.48±2.308	4.39±2.216	3.87±2.680	<0.001	<0.001	<0.001
	2	8.74±1.770	8.29±1.936	8.87±2.029	9.00±2.000			
Conjunctivitis	1	1.81±1.078	1.19±0.980	0.90±0.944	0.77±0.920	<0.001	<0.001	<0.001
	2	1.58±0.765	1.61±0.882	1.71±0.902	1.71±0.864			
Palate itching	1	1.48±0.962	1.00±0.856	0.87±0.763	0.74±0.682	<0.001	<0.001	<0.001
	2	1.10±0.944	1.19±1.014	1.06±0.929	1.16±1.003			
GSS	1	12.65±3.14	7.71±3.43	6.32±3.026	5.39±3.730	<0.001	<0.001	<0.001
	2	11.10±2.37	10.97±2.70	11.32±2.74	11.55±2.87			

TNSS, Total Nasal Symptom Scores; GSS, Global severity scores; Group 1, interventional phototherapy; Group 2, placebo phototherapy. The *p*-values* of comparisons between baseline and second week, 6th week and 12th week scores using Student's t-test. The *p*-values** of between-group comparison (Group 1 versus 2) using Student's t-test with Bonferroni correction. The *p*-value*** evaluate the effect within time-groups in variables.

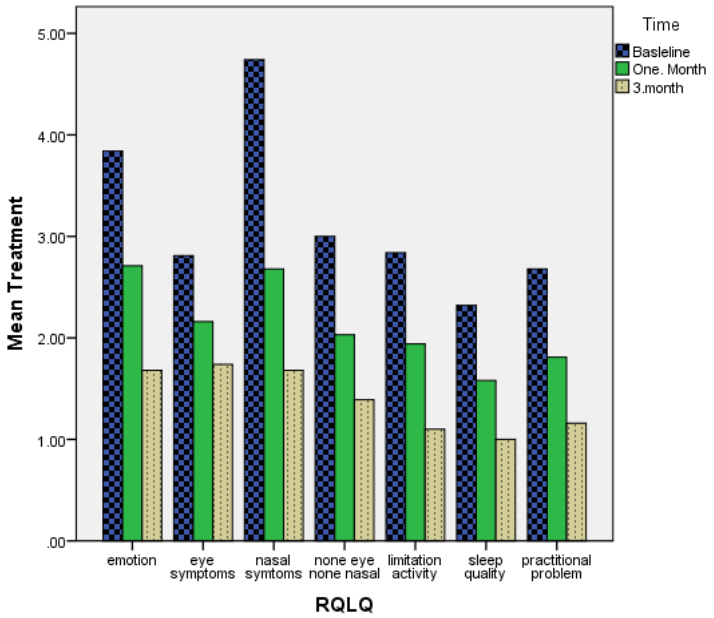

Figure 3. Mean Rhinoconjunctivitis Quality of Life Questionnaires (RQLQ) symptom scores of the treatment group

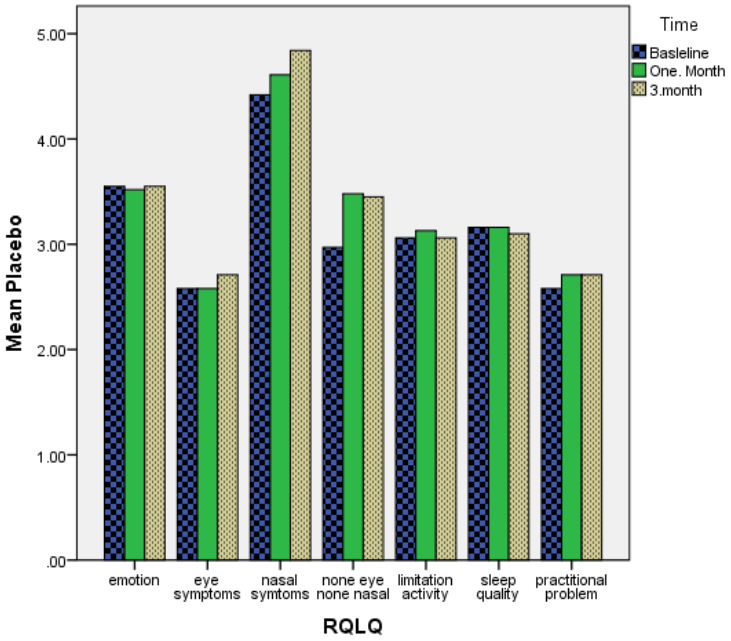

Figure 4. Mean Rhinoconjunctivitis Quality of Life Questionnaires (RQLQ) symptom scores of the placebo group

Table 5. Comparison of the baseline and post-treatment Rhinoconjunctivitis Quality of Life Questionnaires (RQLQ) symptom scores, at the first and third months between the two groups.

RQLQ domains	group	Baseline (Mean+_SD)	First month (Mean+_SD)	Third month (Mean+_SD)	*p*-value*	*p*-value**	*p*-value***
Emotional function	1	3.84±1.393	2.71±1.160	1.69±1.194	<0.001	<0.001	<0.001
	2	3.55±1.410	3.52±1.208	3.55±1.179			
Eye symptoms	1	2.81±1.078	2.16±1.003	1.74±0.965	<0.001	<0.001	<0.001
	2	2.58±0.765	2.58±0.848	2.71±0.864			
Nasal symptoms	1	4.74±0.930	2.68±0.909	1.68±1.222	<0.001	<0.001	<0.001
	2	4.42±0.807	4.61±0.882	4.84±0.779			
None eye none nasal	1	3.0±0.775	2.03±0.706	1.39±0.715	<0.001	<0.001	<0.001
symptoms	2	2.97±0893	3.48±1.092	3.45±1.150			
Limited activity	1	2.84±0.680	1.94±0.680	1.10±0.790	<0.001	<0.001	<0.001
	2	3.06±1.181	3.13±1.384	3.06±1.389			
Practical problems	1	2.68±0.871	1.81+_0.833	1.16±0.860	<0.001	<0.001	<0.001
	2	2.58±1.119	2.71±1.039	2.71±1.039			
Sleep quality	1	2.32±0.748	1.58±0.672	1.00±0.730	<0.001	<0.001	<0.001
	2	3.16±1.241	3.16±1.241	3.10±1.165			
Total RQLQ Scores	1	22.22±2.96	14.90±2.67	9.74±3.99	<0.001	<0.001	<0.001
	2	22.32±2.86	23.19±3.21	23.41±3.12			

RQLQ, Rhinitis Quality Of Life Questionnaire; Group 1, interventional phototherapy; Group 2.placebo phototherapy. The *p*-values* of comparisons between baseline with first month and third month scores using Student's t-test. The *p*-values** comparison between-groups (Group 1 versus 2) using Student's t-test with Bonferroni correction. The *p*-value*** evaluate the effect within time-groups in variables.

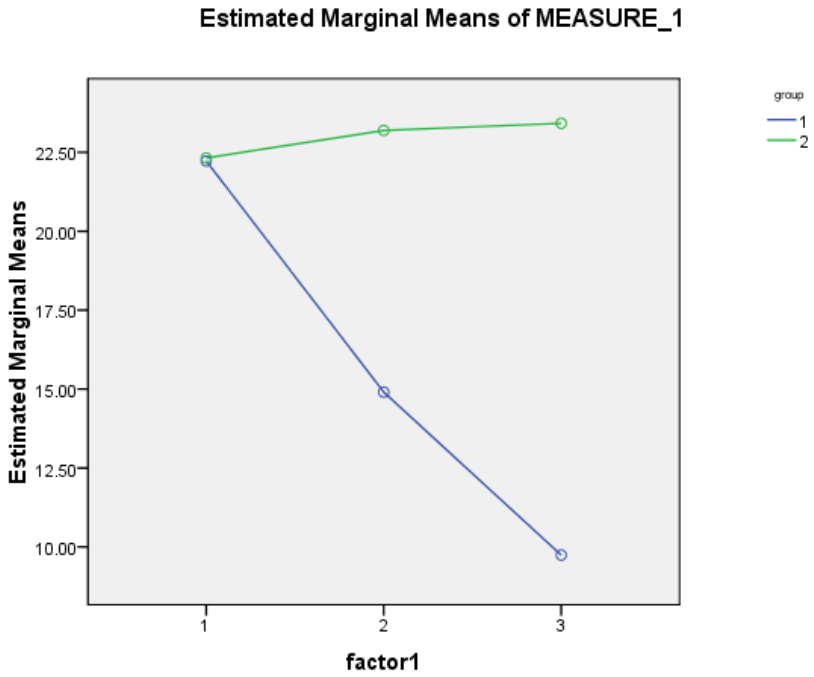

Figure 5. Total Rhinoconjunctivitis Quality of Life Questionnaires (RQLQ) scores of treatment (blue line) and placebo groups (green line) at baseline (1), and one month (2) and three months (3) after phototherapy. The total RQLQ scores of the two groups were significantly homogenous at baseline (1) (p<0.05).

DISCUSSION

AR is one of the most common health problems with a major effect on the quality of life. Seasonal AR is a very common allergic disorder with a complex problem. The treatment of AR includes elimination of the inhaled allergens from the patient's environment, specific pharmacotherapy, and immunotherapy. According to ARIA treatment guidelines, for moderate/severe rhinitis, intranasal corticosteroids are suggested as the first-line therapy in combination with oral or intranasal antihistamines.[6] Moderate to severe AR had been shown to adversely affect performance at work and school and, therefore, may have significant effects on physical and emotional functioning, which results in absences from school and work. In addition, chronic nasal inflammation may aggravate or lead to the development of asthma, sinusitis, and middle ear disease.[2] The patients experiencing one month of rhinitis symptoms per year noted the most significant quality of life impairment. Sleep loss may play an important role in determining quality of life. It may lead to daytime fatigue and poor performance in school or other occupations.[2] We conducted short term phototherapy and evaluated its effect on AR. Phototherapy has a profound immunosuppressive effect, and phototherapeutic methods using both UV and visible light are therefore widely used for the therapy of various inflammatory skin diseases, including atopic dermatitis.[1] As phototherapy is effective in the treatment of allergic disease like AD with the same allergens as AR, phototherapy is proposed to be helpful AR treatment. Koreck et al reported that phototherapy significantly reduced the clinical symptoms of AR.[1] The goal of our study was to assess the efficiency of short time phototherapy in treatment of AR *in* patients who are either unresponsive to treatment or there is contraindication for antihistamine use. Koreck et al showed that phototherapy with a mixture of UVA, UVB and visible light locally reduced the number of inflammatory cells and the level of mediators.[1] AR is an IgE mediated disease. In the case of allergy, the Th2 subset plays a central role and allergic inflammation is associated with a shift in the cytokine balance toward a TH2 predominance. These cells secrete the cytokines IL-4, IL-5, and IL-13, which all are central to the production of IgE and recruitment of eosinophil. IL-5 promotes the maturation, activation, and prolonged survival of eosinophils at the sites of allergic reaction. IL-5 is a cytokine that exerts its main effects on eosinophils, enhancing histamine release from the basophils.[2] In Koreck et al study, irradiation of the nasal mucosa resulted in a significant decrease in local IL-5 and apoptosis of T lymphocytes which are major sources of IL-5. Therefore, apoptosis of these cells, suppression of prolonged eosinophil survival and significant decrease in local IL-5 after phototherapy might be the potential treatment strategy of phototherapy for resolution of AR. Similar results concerning eosinophil, and IL-5 levels and T lymphocytes are observed after other therapies of AR, such as topical glucocorticoids or immunotherapy. In this study, Rhinophototherapy was tolerated well and significantly reduced the clinical scores of sneezing, rhinorrhea, and nasal itching as well as the TNS. Koreck and colleagues suggests that intranasal phototherapy might also be an alternative for patients with symptoms not controlled by antihistamines.[1] In our study, nasal phototherapy with UVA, UVB and visible light resulted in a significant decrease in nasal itching, nasal obstruction, rhinorrhea, sneezing (TNSS) itching of palate and eye symptoms (GSS. A statistically significant difference was found in the treatment group in comparison with the placebo group in the RQLQ scores before and after phototherapy*)*. Therefore, quality of life improved after phototherapy treatment in patients who received interventional phototherapy in contrast to the placebo group. Albu and colleagues assessed the effect of intranasal phototherapy in comparison with intra-nasal azelastine in the treatment of seasonal AR. They demonstrated that both azelastine and intranasal phototherapy are able to significantly improve nasal symptoms in patients afflicted by AR. Nevertheless, intranasal phototherapy reduced the nasal obstruction better than azelastine. After a 14-day treatment period, the RQLQ scores revealed that both treatments were effective in improving the quality of life overall and in seven separate domains.[6] Çadalli Tatar and colleagues evaluated the effects of Rhinophototherapy on the quality of life in persistent AR. They found that adding phototherapy to medical treatment, using combined UVA, UVB, and visible lights, is beneficial. They evaluated the patients in detail by all symptom scores, the RQLQ scores and visual analog scale (VAS) scores, showing that adding phototherapy to medical therapy is more effective than medical therapy for persistent AR patients.[7] The conclusions of these studies conformed to our results. Brehmer and co-workers assessed endonasal phototherapy with Rhinolight for the treatment of AR. They recommended that avoidance of the allergen is

usually not possible and symptom relief is often limited, despite the availability of a number of pharmacological options. Specific immunotherapy demands a high level of cooperation on the part of the patient at least for 3 years. They reported that intranasal phototherapy has been effective in treatment of AR.[8] Demirbaş and colleagues assessed the effect of endonasal phototherapy on the quality of life, nasal obstruction and the other symptoms in AR with VAS, sinonasal outcome test-20 (SNOT-20), and acoustic rhinometry. They concluded that endonasal phototherapy is an effective modality in the treatment of AR symptoms of patients who resistant to anti-allergic drugs and has positive effects on the quality of life. However, no effect on nasal obstruction was found with acoustic rhinometry, which is an objective method.[9] In our study, phototherapy was effective in treatment of nasal obstruction subjectively. But because of some limitations, we could not assess nasal obstruction objectively. Leong reviewed previous articles to assess intranasal phototherapy in the treatment of AR, with particular emphasis on clinical efficacy, scientific basis and safety. Most studies demonstrated symptomatic improvement in the quality of life scores. No improvement in objective measures of the nasal airflow was demonstrated.[10] Leong reported that phototherapy treatment results in DNA damage but does not appear to predispose the patient to carcinogenesis.[10] However, long-term prospective studies are required to verify this. The quality of published studies was variable and thus the current strength of recommendation for intranasal phototherapy is currently weak.[10] Edina Garaczi and colleagues showed that intranasal phototherapy represents an efficient therapeutic modality for the treatment of patients with seasonal AR. They ultimately found that intranasal phototherapy is more efficient than fexofenadine in reducing clinical symptoms for seasonal AR.[11] Lee et al compared symptom improvement before and after phototherapy in Korean patients with perennial AR. The total RQLQ scores significantly improved about 45% from the baseline after 4 weeks. These results indicated that phototherapy was an effective procedure for treating perennial AR.[12] Cingi et al valuated the effects of phototherapy on quality of life in AR cases. They found a statistically significant difference between all variables, including the TNSS, in the phototherapy group before and after the treatment in comparison with the control group (p<0.001).[13] Short term phototherapy may cause erythema, skin pain, pruritus, and pigmentation. Potential long term complications may include premature skin aging and cutaneous malignancies.[14] Koreck et al assessed UV-induced DNA damage in the nasal epithelium in AR patients undergoing intranasal phototherapy. They have shown for the first time that nasal mucosa exposed to UV light possess the capacity to repair DNA damage which suggests that the multistep process of carcinogenesis has not been triggered. However they recommended that more studies are needed in the future to characterize UV complications.[15] Agrawal et al showed UV radiation used in procedures like teeth whitening increases carcinogenic risks for oral tissues compared to the skin.[16] David et al assessed the molecular response of nasal mucosa to therapeutic exposure to broad-band ultraviolet radiation. They showed that human nasal mucosa was capable of efficient repair of UV-induced DNA damage and suggest that UV phototherapy can be used in the treatment of AR.[17] About the carcinogenic effect of phototherapy, we confronted contradictory conclusions in different studies. Therefore, our judgment about carcinogenic effect of phototherapy depends on prolonged observation and accurate assessment of patients who received this treatment. Our study was based on subjective measures. We could not assess objective measures like acoustic rhinometry, level of cytokines (IL-5, IL-4 or IL-13), or eosinophil and mast cell counts in the nasal lavage before and after phototherapy due to some limitations including assessment expenditures, probable investigator and volunteer bias. These measures could result in augmentation of our study potency. Due to suspected effect of phototherapy on nasal mucosal cytokines it can be used as add on therapy on other cytokine involved problems such as nasal polyposis with Aspirin exacerbated respiratory disease.[18] Both groups had permission from authors to receive cetirizine 10mg/day. This also had bias effect. Of course, the mean dose of cetirizine which was used in the treatment group was less than that of the control group and the difference between them was statistically significant. The difference between the two groups during three months of the study may be due to the effect of phototherapy in the treatment group. Because of time restriction and cost limitation, we did not compare the results of intranasal phototherapy with previous treatment (intranasal/ oral corticosteroids and intranasal Antihistamines). This is a limitation of the present study. Physicians other than the investigators assessed the scores, which could reduce the bias effect in this study. Pollination depends on climatic conditions,

humidity, environmental temperature and windflaw. All of them could be variable during the study, so symptom scores could vary during the study period.

CONCLUSION

Our findings demonstrated that phototherapy was an efficient therapeutic procedure for the treatment of patients with AR. Phototherapy has beneficial effects on the quality of life of patients, especially in whom commonly used drugs are contraindicated and/or have insufficient efficacy. Whether intranasal phototherapy with combination of UVA, UVB and visible light will be a standard treatment of AR or not should be evaluated in future studies and clinical trials.

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