Phototherapy in Allergic Rhinitis

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Efficacy of endonasal phototherapy for relieving the symptoms of allergic rhinitis: Meta-analysis.

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Background: Endonasal phototherapy can relieve the symptoms of allergic rhinitis (AR) for the patient. However, there is no consensus on whether or not endonasal phototherapy is effective in reducing the symptoms of AR.

Objective: The goal of this meta-analysis was to perform a systematic review of the available literature on the effects of endonasal phototherapy on symptoms of AR.
Methods:

- Two authors independently searched medical literature databases from their inception of article collection to July 2014.
- Studies that scored the nasal symptoms of AR and quality of life related to AR before and after endonasal phototherapy, and that compared the effects of phototherapy (treatment groups) with sham treatment (sham group) or antihistamine administration (antihistamine group) were included in the analysis.
Methods:

- The outcomes of interest were total nasal symptom scores, disease-specific quality of life questionnaire assessments, and endoscopic findings (discharge and turbinate hypertrophy).
- Overall, a total of 13 trials met the inclusion criteria of this study, with a total sample size of 679 patients.
Results:

- Phototherapy significantly reduced nasal symptoms compared with pretreatment values and improved quality of life.
- The endoscopic findings also significantly improved after phototherapy.
- In addition, the symptom score and disease-specific quality of life after treatment were significantly lower in the treatment group versus the sham group, and were similar to those in the antihistamine group.
Conclusions:

- Phototherapy could provide nasal symptom relief and improve quality of life related to AR.
- However, when considering the insufficient evaluation of the efficacy of phototherapy according to the treatment methods and the high heterogeneity apparent in some parameters, further clinical trials with robust research methodologies should be conducted to confirm the results of this study.
Introduction

- Allergic rhinitis (AR) is one of the most common allergic diseases, caused by the inhalation of allergens, which can affect both children and adults.
- The worldwide prevalence of physician diagnosed AR is 7–14%, which makes it a considerable global health problem.
Introduction

– Although AR has been regarded as a nuisance rather than a significant health problem, a number of studies have indicated that AR can be associated with significant morbidity, not only limited to its physical symptoms but including significant impact on learning, performance, and productivity at work and school as well as a patient’s quality of life (QOL).
Introduction

– One type of Complementary and alternative medicines (CAM) treatment is phototherapy, which is defined as the application of light to a pathologic area to promote tissue regeneration, reduce inflammation, and relieve pain.
– Significant suppression of clinical AR symptoms after phototherapy treatment with ultraviolet (UV) and visible light has been reported.
– In addition, marked improvement in the clinical symptoms of AR was found after narrow-band red-light phototherapy as well as a low-level energy laser and far infrared ray.
MATERIALS AND METHODS

– Criteria for considering studies for this review were the following: randomized or case-controlled trials of the effect of any method of endonasal phototherapy, such as UV and visible light, narrow-band red light, low-level energy laser, or far infrared ray, on AR-related symptoms or QOL were included.

– Children or adults with a history of moderate-to-severe AR that was not controlled by conventional antiallergic treatment were included.
MATERIALS AND METHODS

– Studies with **more than eight patients** per treatment group were included, which compared the effect of phototherapy before and after treatment or with a control (sham or antihistamine)
MATERIALS AND METHODS

– Studies were **not eligible for inclusion** if
– (1) patients **underwent additional procedures**, such as turbinoplasty or vidian neurectomy;
– (2) patients **with significant** nasal structural abnormalities, bronchial asthma, upper respiratory tract infection within the past 2 weeks, or a lower respiratory infection within 4 weeks before the start of the study;
MATERIALS AND METHODS

– Studies were not eligible for inclusion if

– (3) patients were treated with systemic corticosteroids within the previous 4 weeks, topical corticosteroids or cromolyn sodium within 2 weeks, antihistamines and decongestants within 1 week before the beginning of the study, or immunotherapy in the past 2 years; or

– (4) multiple reports were based on the same trial data.

– (5) if clinical outcomes of interest were not clearly reported with quantifiable data or if it was not possible to extract and calculate the appropriate data from the published results.
MATERIALS AND METHODS

Figure 1. Diagram of the study selection.
MATERIALS AND METHODS

The risk of bias for each study was evaluated by using the Cochrane Risk of bias tool to assess the quality of the enrolled studies.

Table 1  Summary of studies included in the meta-analysis

<table>
<thead>
<tr>
<th>Study, y</th>
<th>Sample Size</th>
<th>Comparison</th>
<th>Outcome Measurement Analyzed</th>
<th>Judgment of Risk of Bias</th>
<th>Type of AR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lee, ^3^ 2013</td>
<td>42</td>
<td>Before vs. after treatment</td>
<td>Total symptom score and life quality</td>
<td>High</td>
<td>Perennial</td>
</tr>
<tr>
<td>Moustafa et al., ^16^ 2013</td>
<td>60</td>
<td>Before vs. after treatment</td>
<td>Total symptom score and endoscopic finding</td>
<td>High</td>
<td>Perennial</td>
</tr>
<tr>
<td>Yıldırım et al., ^15^ 2013</td>
<td>31</td>
<td>Before vs. after treatment</td>
<td>Total symptom score</td>
<td>High</td>
<td>Perennial</td>
</tr>
<tr>
<td>Brehmer and Schon, ^13^ 2011</td>
<td>10</td>
<td>Before vs. after treatment</td>
<td>Total symptom score</td>
<td>High</td>
<td>Seasonal</td>
</tr>
<tr>
<td>Csoma et al., ^12^ 2004</td>
<td>8</td>
<td>Before vs. after treatment</td>
<td>Total symptom score</td>
<td>High</td>
<td>Seasonal</td>
</tr>
<tr>
<td>Garaczi et al., ^13^ 2011</td>
<td>18</td>
<td>Before vs. after treatment</td>
<td>Total symptom score</td>
<td>Low</td>
<td>Seasonal</td>
</tr>
<tr>
<td>Albu and Baschir, ^14^ 2013</td>
<td>39</td>
<td>Before vs. after treatment</td>
<td>Total symptom score and life quality</td>
<td>Low</td>
<td>Seasonal</td>
</tr>
<tr>
<td>Neuman, ^9^ 2007</td>
<td>78</td>
<td>Phototherapy vs. antihistamine</td>
<td>Total symptom score and endoscopic finding</td>
<td>Low</td>
<td>Perennial</td>
</tr>
<tr>
<td>Cingi et al., ^5^ 2010</td>
<td>41</td>
<td>Before vs. after treatment</td>
<td>Total symptom score</td>
<td>Low</td>
<td>Seasonal</td>
</tr>
<tr>
<td>Emberli, ^26^ 2009</td>
<td>101</td>
<td>Phototherapy vs. sham</td>
<td>Total symptom score</td>
<td>Unclear risk</td>
<td>Seasonal</td>
</tr>
<tr>
<td>Csoma et al., ^7^ 2006</td>
<td>13</td>
<td>Before vs. after treatment</td>
<td>Total symptom score</td>
<td>High</td>
<td>Seasonal</td>
</tr>
<tr>
<td>Koreck, ^8^ 2011</td>
<td>25</td>
<td>Before vs. after treatment</td>
<td>Total symptom score</td>
<td>Low</td>
<td>Seasonal</td>
</tr>
<tr>
<td>Cingi et al., ^17^ 2009</td>
<td>100</td>
<td>Before vs. after treatment</td>
<td>Total symptom score</td>
<td>High</td>
<td>Seasonal</td>
</tr>
</tbody>
</table>
MATERIALS AND METHODS

- Outcomes analyzed: Nasal symptoms AR score, disease specific QOL questionnaire, Endoscopic findings (discharge & Turbinate hypertrophy).

- Pre- and postprocedural values or between postprocedural and control (sham or antihistamine) during a follow-up period (within 1 month after starting the endonasal phototherapy).
Results

- 13 studies with 679 participants were reviewed and included in meta analysis
- Change in Nasal Symptoms Scores and QOL After Phototherapy
- Change in Endoscopic Findings After Phototherapy
- Phototherapy Versus Control (sham or antihistamine group) (change of nasal symptoms scores)
Results

Change in Nasal Symptoms Scores and QOL After Phototherapy

– 10 studies assessed the efficacy of phototherapy on the reduction of nasal symptom scores
– Phototherapy significantly reduced the total symptom score (p <0.0001)
– Reduction scores for nasal itching (p <0.0001)
– Reduced nasal obstruction (p <0.0001)
– Reduced Rhinorrhea (p <0.0001)
– Reduced sneezing (p <0.0001)
– All compared to pretreatment values
Results
Change in Nasal Symptoms Scores and QOL After Phototherapy

- 4 studies assessed the efficacy of phototherapy on **improvement of QOL**
- Phototherapy significantly improved sleep \( p = 0.0354 \)
- Practical issues \( p = 0.0478 \)
- Non–hay fever symptoms \( p = 0.0050 \)
- Nasal symptoms \( p = 0.0303 \)
- Limited activity \( p = 0.0409 \)
- **Eye symptoms** \( p = 0.0121 \)
- Emotional problems \( p = 0.0081 \)
- Compared to pretreatment values.
Results

Change in Nasal Symptoms Scores and QOL After Phototherapy

- To standardize the patients according to the type of AR, they performed subgroup analysis (perennial or seasonal AR).
- These analyses revealed that phototherapy had a significantly greater effect in improving the symptom and QOL in patients with seasonal AR than in patients with perennial AR.
- Phototherapy produced no statistically significant effect on nasal itching and sneezing in patients with perennial AR, despite the large effect size.
Results
Change in Endoscopic Findings After Phototherapy

- 2 studies assessed the efficacy of phototherapy on improvement of endoscopic findings.
- Significantly improved nasal discharge (p < 0.0001)
- Turbinate hypertrophy (p < 0.0083)
- As compared to pretreatment value
Results
Phototherapy Versus Control (sham or antihistamine group) (change of nasal symptoms scores)

– 6 studies involved a comparison of the reduction in nasal symptom scores between phototherapy treatment and a control.
– Control groups were divided in two groups such as sham or antihistamine group.
– In 2 of the 6 studies, phototherapy significantly reduced the nasal itching score, nasal obstruction and rhinorrhea compared with antihistamine group.
– However, no differences were detected in sneezing or total symptoms score.
– Phototherapy exhibited a weak significant reduction in symptoms compared with the antihistamine values.
Results

Phototherapy Versus Control (sham or antihistamine group) (change of nasal symptoms scores)

- **Conversely, in 4 of the 6 studies, phototherapy significantly reduced all symptom scores compared with the sham group**
Discussion

- Their results indicated that the nasal symptom score (total symptom score, nasal itching score, nasal obstruction, rhinorrhea, and sneezing) and QOL (sleep, practical issues, non-hay fever symptoms, nasal symptoms, limited activity, eye symptoms, and emotional problems) after phototherapy were significantly lower compared with the respective pretreatment values.
In the endoscopic findings, phototherapy significantly improved nasal discharge and turbinate hypertrophy compared with pretreatment values.

The nasal symptom score and QOL questionnaire were used as reliable measurements to assess the severity of rhinitis and the efficacy of therapeutic interventions.

In addition, the endoscopic findings reported by clinicians served as objective criteria for the assessment of the appearance of the mucosa and associated nasal inflammation.
Discussion

- **Phototherapy significantly reduced** the nasal *itching* score, nasal *obstruction*, and *rhinorrhea* compared with the *antihistamine group*.
- However, **no significant** differences were detected between phototherapy and antihistamine treatment for sneezing and total symptom score.
- Conversely, when compared with a *sham treatment*, phototherapy improved all nasal symptom measurements.
Discussion

– In particular, among the symptoms considered, the improvement in nasal obstruction was relatively higher with phototherapy as opposed to antihistamines.

– This finding can be explained by the fundamental mechanisms of action of the two different treatments.

– In contrast to antihistamines, which predominantly influence histamine-mediated features of the allergic process, phototherapy has a different, more-complex mechanism of action.
Discussion

- A previous study demonstrated that **apoptosis of T lymphocytes** in skin disease reduces the number and function of dendritic cells and increases immunomodulatory cytokines.
- Similar results concerning immunomodulatory cytokines and T lymphocytes have been observed after other well-established AR therapies, such as topical glucocorticoids or immunotherapy.
Limitations

First limitation pertains to the lack of multicenter, double-blinded, and randomized trials, and the short follow-up period.

The second limitation was that they could not evaluate the objective measurements such as nasal airflow or inflammatory markers.

The third limitation was that they could not evaluate the long-term adverse effects of endonasal treatment.
Conclusion

– This meta-analysis demonstrated that phototherapy for treatment of AR could decrease symptomatic complications and improve QOL regarding rhinoconjunctivitis, although the mechanism of action is not clear.

– In the future, if more basic science and clinical trials regarding this novel approach are conducted, then phototherapy might be regarded as a mainstream treatment for AR.
Phototherapy for allergic rhinitis: a prospective, randomized, single-blind, placebo-controlled study.

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Background

- 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.
Methods

- Seventy-nine (79) 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.
Results

- 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).
Conclusion

- 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
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%) (UVAB), may represent a therapeutic alternative in patients with allergic rhinitis.

Phototherapy in allergic rhinitis locally reduced the number of inflammatory cells.
Materials & Methods

Study Design

– 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 by anti-allergic drugs
– Positive skin test results and an elevated level of specific IgE antibody confirmed the diagnosis.
– Out of pollen season
Materials & Methods

Study Design

- Seventy-nine (79) patients were prospectively and randomly assigned into two groups using computergenerated randomization:
  - 41 in the UVAB (UV-A, UV-B, visible light) group
  - 38 in the VIS (low-intensity visible light) group
Materials & Methods

Exclusion

- significant nasal structural abnormalities,
- asthma, those with an
- upper or lower respiratory tract infection within 4 weeks
- nasopharyngeal pathology diagnosed via fiberoptic endoscopy,
Materials & Methods

Exclusion

- those who had used any of the following drugs
  - 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
Materials & Methods

– 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

**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/cm². Upon every consecutive treatment, the dose was raised by 0.2 J/cm², reaching the highest dose of 2.4 J/cm² achieved at the fifth visit.

<table>
<thead>
<tr>
<th>Visit</th>
<th>Length of treatments per nostril [min:s]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>First week 2:00</td>
</tr>
<tr>
<td>2</td>
<td>Second week 2:15</td>
</tr>
<tr>
<td>3</td>
<td>2:30</td>
</tr>
<tr>
<td>4</td>
<td>2:45</td>
</tr>
<tr>
<td>5</td>
<td>3:00</td>
</tr>
<tr>
<td>6</td>
<td>3:00</td>
</tr>
</tbody>
</table>
Materials & Methods
Assessing the efficacy of the 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.
Materials & Methods
Assessing the efficacy of the treatment

– Nasal symptoms included in the study were 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).
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.
Results

- 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)

- 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)
Results

- **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.
Results

- 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

– In a pilot study, Keme´ny and Koreck compared the efficacy of UVAB with an oral antihistamine, fexofenadine, and stated that TNSS in the UVAB group was significantly lower [Keme´ny 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.
Discussion

- 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.
Discussion

– 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. 2010; Korecket 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’.
Discussion

MOA

- Previous studies worked on the mechanism of the efficacy of phototherapy.
- Irradiation of the nasal mucosa resulted in a significant decrease in local interleukin-5 (IL-5).
- T lymphocytes are major sources of IL-5.
- Thus, apoptosis of these cells after phototherapy might be the basis of the underlying mechanism of decreased IL-5 production.
Discussion

MOA

- **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 **eosinophil cationic protein (ECP)** in the nasal lavage fluid.
Discussion

MOA

– It has also been shown that UV-A light significantly inhibited histamine release from human basophils and a human mast cell line and that UV-B light had an inhibitory effect only on mast cells
Discussion
placebo effect!

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.
Discussion

– The **most important restriction** of phototherapy is the area of the nasal mucosa that we cannot reach with this application

– They believe that the clinical results will improve when UVAB transmission and distribution to whole or a larger area of nasal mucosa can be achieved
Discussion

– In clinical studies, performing a **double-blind study** is always preferred.
– However, in this study it was **almost impossible** to do so; the UV filter that we had attached to the nozzle was detectable by the physicians and so we performed a single-blind study.
– They believe that 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.
Thank You ...