

Histopathological effects of intranasal phototherapy and nasal corticosteroids in allergic rhinitis in a rabbit model



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ABSTRACT

Allergic rhinitis is one of the most common health problems and has a major effect on quality of life. Although new-generation antihistamines and nasal steroids are the main treatment options, complete resolution cannot be obtained in some patients. Besides common side effects such as nasal irritation and epistaxis, the use of these drugs is controversial in some patients, such as pregnant or breastfeeding women. These findings highlight the need for new treatment options. Although phototherapy has been successfully used in the treatment of atopic dermatitis, which is an IgE-mediated disease and shares several common pathogenic features with allergic rhinitis, there are limited studies about its role in the treatment of allergic rhinitis. In this study, we aimed to evaluate and compare the histopathological effects of intranasal phototherapy (Rhinolight) and nasal corticosteroid treatment on the nasal mucosa in allergic rhinitis in a rabbit model and we found that both treatment options significantly reduced inflammation in the nasal mucosa without increasing apoptosis of mucosal cells.

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1. Introduction

Allergic rhinitis is one of the most common health problems and has a major effect on quality of life [1]. It is characterised by nasal symptoms including rhinorrhea, itching, sneezing, and nasal congestion [2]. Allergic rhinitis involves nasal inflammation that results from IgE-mediated immune responses to specific allergens [2,3]. Although new-generation antihistamines and nasal steroids are the main treatment options, complete resolution cannot be obtained in some patients. Besides common side effects such as nasal irritation and epistaxis, the use of these drugs is controversial in some patients, such as pregnant or breastfeeding women [4,5]. These findings highlight the need for new treatment options.

Although phototherapy has been successfully used in the treatment of atopic dermatitis, which is an IgE-mediated disease and shares several common pathogenic features with allergic rhinitis [6], there are limited studies about its role in the treatment of allergic rhinitis [7–9]. In this study we aimed to evaluate and compare the histopathological effects of intranasal phototherapy

(Rhinolight) and nasal corticosteroid treatment on the nasal mucosa in allergic rhinitis in a rabbit model.

2. Materials and methods

A total of 24 male New Zealand rabbits (20–24 weeks of age, 2000–3000 g) were used in the study. Animals were purchased from Uludağ University Faculty of Medicine Animal Application and Research Center, Bursa, Turkey. The study was approved by the Committee of Animal Research of Abant İzzet Baysal University Institute for Experimental Medicine Research, Bolu, Turkey. All the animals were kept in individual rubber-covered iron cages and were given free access to food (*ad libitum*) and water. All animals were exposed to a consistent light/dark schedule of 12 h of light followed by 12 h of dark, and they were kept at a room temperature of 22–24 °C with 40–60% moisture. The animals were randomly divided into four groups of six. Groups 1 and 2 were control groups. We did not perform intranasal phototherapy, intranasal corticosteroid treatment (ICS), or ovalbumin (OVA) sensitisation in group 1, and OVA sensitisation was performed in group 2 without any treatment. After ovalbumin sensitisation, intranasal phototherapy was performed to group 3. Group 4 was composed of animals that were treated with ICS (mometasone furoate) after OVA sensitisation.

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2.1. Ovalbumin sensitisation

Animals were sensitised with OVA. The 0.4% OVA solution was prepared using OVA emulsified in Tween 80 in combination with Al(OH)₃ and mixed with 100-ml saline. Animals in groups 2, 3, and 4 were sensitised by intraperitoneal administration of 5-ml OVA on days 0, 2, 4, and 6. Subsequently, intraperitoneal injection of 10 µl of the same solution was performed intranasally once per day for 7 days. To confirm the sensitisation, rabbit serum anti-ovalbumin IgE values were measured by a specific enzyme-linked immunosorbent assay technique. Original MyBioSource (MyBioSource Inc. San Diego CA; USA) brand reagent was used.

2.2. Intranasal phototherapy

Each intranasal cavity was irradiated three times per week for 2 weeks with increasing doses of radiation, as shown in Table 1. The phototherapy treatment was started with a dose of 1.6 J/cm² for 2 min, and the dose was increased by 0.2 J/cm² for each consecutive treatment. The highest dose was 2.6 J/cm². The irradiation was performed with a broad band light source (Rhino-light, Hungary, 180 mW, spectral composition 5% UVB, 25% UVA and 70% visible light).

2.3. Histopathological evaluation

After completion of the phototherapy, animals were sedated by intraperitoneal injection of ketamine (80 mg/kg) and xylazine (5 mg/kg). After sedation, the nasal septum was totally resected. Biopsy materials were fixed in 10% formaldehyde and embedded in paraffin. For histological evaluation, paraffin-embedded tissue specimens were cut into 5-µm slices using a microtome. Mucosal structures were stained with hematoxylin–eosin, and toluidine blue was used to demonstrate the mast cells. The TUNEL (Gen Script apoptosis kit) assay was used to confirm the occurrence of epithelial apoptosis. A Nikon photomicroscope was used to obtain images of specimens.

3. Results

Nasal mucosa and concha structure were normal in the control group (Group 1). In the untreated allergic rhinitis group (Group 2), there were widespread inflammatory cells, mainly neutrophils and mast cells, in the intraepithelial and submucosal layers. Significant intraepithelial goblet cell hypertrophy and hyperplasia were also seen. Loss of cilia and vascular congestion were detected in some parts of the nasal epithelium, as shown in Fig. 1.

In the positive control group treated with mometasone furoate, intraepithelial and submucosal inflammation and goblet cell hypertrophy were significantly decreased compared to group 2. There was no vascular congestion, and the distribution of cilia was normal (Fig. 1).

In the intranasal phototherapy group, intraepithelial and submucosal inflammation was also significantly lower compared to group 2. Although hypertrophic goblet cells were seen in some areas, they were decreased in intensity and number. Cilial structures were normal, and no change was seen in the structure of chondrocytes (Fig. 1).

Table 1
Treatment regimen for intranasal phototherapy.

Week	1	1	1	2	2	2
Treatment number	1	2	3	4	5	6
Treatment dose (J/cm ²)	1.6	1.8	2.0	2.2	2.4	2.6

We performed the TUNEL assay to show the apoptosis of epithelial cells and in connective tissue. There was no difference in apoptosis among the groups. The TUNEL-positive cell count did not increase in the treated groups. These results show that intranasal phototherapy did not induce apoptosis in epithelial cells and the nasal septum.

4. Discussion

In this study we showed that intranasal phototherapy significantly decreased inflammation and goblet cell hypertrophy and hyperplasia in an allergic rhinitis model without inducing apoptosis. This is the first study that compares the histopathological findings related to intranasal phototherapy and nasal steroid (mometasone furoate) treatment. We showed that intranasal phototherapy has similar histopathological effects as mometasone furoate on nasal mucosa in an allergic rhinitis rabbit model.

Allergic rhinitis is an IgE-mediated inflammatory disease of the nasal mucosa and is an increasingly common condition that has a major impact on human health [10]. The prevalence of allergic rhinitis varies between 4.6% and 31.8% [11]. Traditional treatments include elimination of the inhaled allergens, pharmacotherapy, and immunotherapy [12]. For pharmacotherapy, nasal corticosteroids in combination with antihistamines are suggested as the first-line treatment [12].

Although phototherapy has been successfully used in the treatment of atopic dermatitis, which shares several common pathogenic features with allergic rhinitis [6], there are limited studies about its role in the treatment of allergic rhinitis [7–9]. The immune response in allergic rhinitis involves the release of inflammatory mediators and activation and recruitment of lymphocytes, eosinophils, and mast cells to the nasal mucosa [2]. It has been shown that intranasal phototherapy significantly reduces individual nasal symptom scores in allergic rhinitis [8]. The mechanism of action of intranasal phototherapy in allergic rhinitis includes T cell and eosinophil apoptosis and decreasing the release of inflammatory mediators [13]. In this study, we showed that intranasal phototherapy significantly reduced allergic inflammation and also reduced nasal epithelial damage. It has been known that UV radiation leads to DNA damage, which may induce apoptosis of cells and result in tissue damage. In our study, we also evaluated the apoptotic effect of intranasal phototherapy and did not find increased apoptotic activity. These results suggest that rhinophototherapy is a safe treatment option in allergic rhinitis.

As mentioned above, nasal corticosteroids are the cornerstone drugs in treatment of moderate to severe allergic rhinitis [14,15]. Nasal corticosteroids cause a reduction in the number of inflammatory cells and cytokines within the nasal mucosa of patients with allergic rhinitis [16]. Besides common side effects such as nasal irritation and epistaxis, nasal corticosteroids may cause nasal septum perforation and *Candida* overgrowth [4]. When these adverse effects are taken into account, intranasal phototherapy may be an option in the treatment of allergic rhinitis. Only one study has evaluated the additive effect of rhinophototherapy in patients receiving nasal corticosteroids and antihistamines; the authors reported that improvements in a quality of life questionnaire, nasal symptom scores, and VAS were statistically significant in the rhinophototherapy group [17]. To our knowledge this is the first study that compares the histopathological effects of intranasal phototherapy and nasal steroids. In our study we showed that intranasal phototherapy is as effective as nasal corticosteroids in reducing the number of inflammatory cells in the nasal mucosa. We also showed that none of the treatment options increases apoptosis in the nasal septal mucosa. These results suggest that intranasal phototherapy may be an alternative in the treatment of allergic rhinitis.

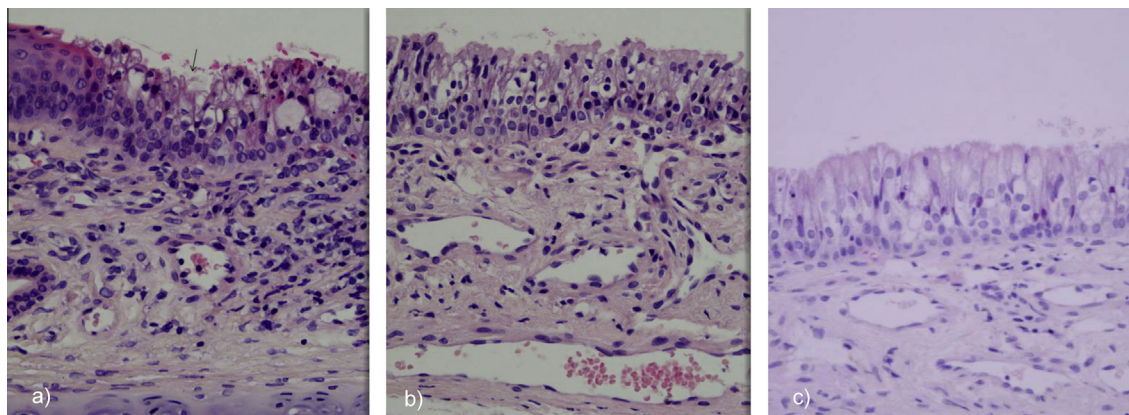


Fig. 1. (a) Histopathological findings of untreated allergic rhinitis group (Group 1). (b) Histopathological findings of animals that were treated with ICS (mometasone furoate) after OVA sensitisation. (c) Histopathological findings of animals that were treated with intranasal phototherapy after OVA sensitisation.

5. Conclusion

In this study the histopathological effect of nasal steroids and intranasal phototherapy was compared for the first time. Both treatment options significantly reduced inflammation in the nasal mucosa without increasing apoptosis of mucosal cells.

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The English in this document has been checked by at least two professional editors, both native speakers of English. For a certificate, please see: <http://www.textcheck.com/certificate/6Pie4r>.

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