Inhibition of immediate type hypersensitivity reaction by combined irradiation with ultraviolet and visible light

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Abstract

Recently we found that ultraviolet B (UVB) irradiation in erythematous doses significantly inhibited the immediate type hypersensitivity reaction in the skin. In the present study we investigated the effects of different wavelengths on the skin prick test reaction (SPT). The forearm of ragweed allergic patients was irradiated with increasing doses of ultraviolet A (UVA), visible light (VIS) or combined UVB, UVA and VIS light, referred to as mUV/VIS. SPTs were performed 24 h after irradiation both on irradiated and non-irradiated control skin areas using ragweed extract. UVA and VIS irradiation led to a slight, not significant inhibition of allergen-induced wheal formation. Mixed irradiation with mUV/VIS light resulted in a dose-dependent inhibition of the allergen-induced wheal formation. The inhibition was significant already at suberythematous doses. As there is a good correlation between SPT and the nasal symptoms in patients with hay fever these data suggest that phototherapy with mUV/VIS light might be an effective and safe treatment modality for immediate type hypersensitivity reactions in the skin and nasal mucosa.

Keywords: Immediate type hypersensitivity; Skin prick test; Phototherapy

1. Introduction

Phototherapy has a profound immunosuppressive effect and phototherapeutic methods utilizing both ultraviolet (UV) and visible (VIS) light are therefore widely used for the therapy of various inflammatory skin diseases such as psoriasis and atopic dermatitis [1–4]. It has been also shown that UV irradiation of skin inhibits the development of contact hypersensitivity and induces hapten-specific tolerance, which can be adoptively transferred in mice. The major mechanisms of immunosuppression induced by the various forms of phototherapy in the skin involve apoptosis induction in infiltrating T cells, reduction in the number and function of Langerhans cells, and the induction of immunomodulatory cytokines such as IL-10 [5–8].

Recently, we have found that UVB irradiation was capable to significantly inhibit the immediate type hypersensitivity reaction in the skin at erythematous doses and that 308 nm xenon chloride (XeCl) eximer laser is effective for the treatment of allergic rhinitis [9]. The goal of our present study was to evaluate the effect of different wavelengths on the immediate type hypersensitivity in the skin. As skin prick test (SPT) is the most widely used in vivo test for the diagnosis of immediate type allergic reaction we tested the capacity of different wavelengths to inhibit the wheal formation in SPT on irradiated and non-irradiated skin areas. We found that mixed irradiation with UVB, UVA and
visible light is capable to inhibit SPT reaction even after a single irradiation with suberythematous doses.

2. Materials and methods

2.1. Effect of different wavelengths on the immediate hypersensitivity reaction in the skin

2.1.1. Patients

The study protocol was approved by the Human Investigation Review Board of the Szeged University. Informed consent was obtained from 19 patients with a history of at least 2 years of ragweed-induced allergic rhinitis, 7 men and 12 women, aged 21–58 years (mean age 32.98 years) with skin types II/III. Patients discontinued tacking any treatment 2 weeks prior to the performance of SPTs. All patients had a positive SPT with a wheal formation of at least 10.0 mm in diameter.

2.1.2. Irradiation protocol

Five patients received UVA irradiation (Waldmann-PUVA 4000, Germany, range: 320–400 nm). On one forearm three areas were irradiated with increasing doses of UVA (0.5, 1 and 2 J/cm²). Seven patients were irradiated with increasing doses of visible (VIS) light (2, 4, 6 and 8 J/cm²) (Rhinolight-VIS, Hungary, range: 395–600 nm). In 7 patients irradiation was performed with increasing doses of mixed UVB (5%), UVA (25%) and VIS (70%), referred to as mUV/VIS light (2, 4, 6 and 8 J/cm²) (Rhinolight-mUV/VIS, Hungary, range: 310–600 nm). Measurements were performed with Scientech Vector H410 (Scientech Inc., Boulder, CO) and Jobin-Yvon H-20UV (Ocean Optics, RK Duiven, The Netherlands).

2.1.3. Skin prick test

The SPT is a method that is widely used to investigate the immediate hypersensitivity reaction to a specific allergen in the skin [10,11]. SPTs were performed with ragweed extract (Soluprick-Epipharm Allergie-Service GmbH) on the irradiated skin areas from one forearm and non-irradiated control skin areas from the other forearm, 24 h after irradiation. Twenty-microlitre aliquots of the test solution were placed on the patients' forearm, with a distance of more than 3 cm between individual application sites. Sterile 0.9% sodium chloride solution and histamine hydrochloride were used for negative and positive controls respectively. The test results were evaluated after 20 min and the induced wheal was measured by digital planimetry.

2.2. Statistical analyses

The differences in wheal formation after irradiation were analyzed statistically by means of Friedman repeated measures ANOVA, followed by Dunnett's multiple-comparison test. Spearman's rank correlation test was applied to analyze the correlation between the irradiation doses and the inhibition of wheal formation. Differences were considered significant at $p < 0.05$.

3. Results

UVA irradiation resulted in a slight inhibitory effect on allergen-induced wheal formation (Fig. 1(a)). The inhibition rate was 8.97% at 0.5 J/cm², 14.22% at 1 J/cm² and 10.13% at 2 J/cm², but the changes did not reach statistical significance ($p = 0.069$). No correlation was found between the inhibition of allergen-induced wheal formation and the UVA dose.

Similar results, mirrored by a slight, statistically not significant inhibition of wheal formation, were obtained 24 h after VIS irradiation (Fig. 1(b)). The inhibition was 6.5% at 2 J/cm², 7.19% at 4 J/cm², 6.11% at 6 J/cm² and 6.74% at 8 J/cm², at neither of these doses changes proof to be significant ($p = 0.406$). No correlation was found between the inhibition of allergen-induced wheal formation and the VIS dose.

Mixed irradiation with mUV/VIS light resulted in a dose-dependent inhibition of the allergen-induced wheal formation ($r = 0.463, p = 0.0132$) (Fig. 1(c)). The inhibition was 33.92% at 2 J/cm², 54.74% at 4 J/cm², 68.96% at 6 J/cm² and 82.87% at 8 J/cm². The inhibition was statistically significant at the doses of 4, 6 and 8 J/cm² ($p < 0.05$). The two lowest doses did not produce erythema on the skin, the proportion of UVB light in mUV/VIS was 0.1 J/cm² for 2 J/cm² and 0.2 J/cm² for 4 J/cm². The use of higher, erythematous doses of mUV/VIS light (0.4 J/cm² UVB for 8 J/cm² mUV/VIS) led to almost complete inhibition of wheal formation.

4. Discussion

The goal of our study was to assess the inhibitory effect of different wavelengths on the immediate-type hypersensitivity reaction. We evaluated the inhibitory effect on the antigen-induced wheal formation in SPT. Although, we found that UVA and VIS light alone had only a slight inhibitory effect on immediate type skin test reaction, the addition of these wavelengths to UVB light in the form of mUV/VIS, resulted in a synergistic effect. We have previously found that UVB irradiation with the 308 nm XeCl excimer laser significantly suppressed allergen-induced wheal development only at erythematous doses [9]. In the present study we found that a single irradiation with a suberythematous dose of UVB resulted in an inhibition of SPT when irradiation was performed using a combination of UVB, UVA and VIS light (mUV/VIS). Vocks et al. found compara-
ble inhibition rates of wheal formation (48%) only after three irradiation with suberythematous doses of UVB [12]. These results suggest that mUV/VIS irradiation has a more profound and rapid inhibitory effect on immediate type skin reaction than UVB alone. The underlying mechanism might be the synergistic effect of different wavelengths on histamine release. In the skin prick test, the antigen induces a rapid release of histamine from the sensitized cells and results in the development of a wheal in 10–20 min. It has been shown that UVA light significantly inhibited histamine release from human basophils and a human mast cell line and that UVB light had an inhibitory effect only on mast cells [13]. The effect of in vitro UVA irradiation of basophils is characterized by a biphasic dose dependent action on histamine release: low doses are followed by a significant inhibitory effect, in contrast high doses are followed by histamine liberation [14]. The strong inhibition of SPT reaction by mUV/VIS might therefore be explained by the combined actions of the different wavelengths on the skin mast cells.

We reported recently that UVB irradiation of the nasal mucosa with medium doses of XeCl laser resulted in the significant improvement of clinical symptoms of hay fever, while low doses had no effect [9]. An important step towards the application of phototherapy for the treatment of allergic rhinitis is to identify the clinically effective wavelengths, which combine the advantages of high efficacy and few side effects. It is well known that repeated irradiation with UV light in high doses has a carcinogenic potential and this depends on the cumulative dose [15]. Although, the UVB doses we used for the treatment of allergic rhinitis were much lower than those leading to an increased risk of cancer; reduction of UVB doses might further improve safety of intranasal phototherapy.

Our data showed that comparable inhibitory effect on allergen-induced wheal formation might be achieved by irradiation with suberythematous doses of mUV/VIS light as with higher erythematous doses of UVB alone. It has been shown that there is a good correlation between the SPT reaction and the nasal symptoms in patients with hay fever and that reduced immediate skin sensitivity is observed after long-term successful immunotherapy [10,11]. These data suggest that phototherapy with mUV/VIS light might be effective not only in inhibiting immediate type hypersensitivity in the skin but also in the nasal mucosa and that phototherapy using mUV/VIS light might be an effective and safe treatment modality for allergic rhinitis.

5. Abbreviations

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<tr>
<td>MED</td>
<td>minimum erythema dose</td>
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<td>mUV/VIS</td>
<td>mixed ultraviolet and visible light</td>
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<td>SPT</td>
<td>skin prick test</td>
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Fig. 1. The inhibitory effects of different wavelengths on wheal formation in SPT. Irradiation with increasing doses of UVA light resulted in a slight, not significant inhibition of wheal formation in SPT (a). Irradiation with increasing doses of VIS light resulted in a slight, not significant inhibition of wheal formation (b). Irradiation with increasing doses of mUV/VIS light resulted in a significant, dose dependent inhibition of wheal formation in SPT (c). Significant decreases (*p < 0.05) were observed 24 h after irradiation at 4 J/cm² (p = 0.01), at 6 J/cm² (p < 0.001) and at 8 J/cm² (p < 0.001).
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References