Ultraviolet-A1 phototherapy modulates Th1/Th2 and Tc1/Tc2 balance in patients with systemic lupus erythematosus

A. Szegedi, E. Simics, M. Aleksza¹, I. Horkay, K. Gaál, S. Sipka¹, J. Hunyadi and E. Kiss¹

Objective. Ultraviolet-A1 (UVA1) phototherapy is effective for a variety of dermatological diseases. We examined the effectiveness and reliability of low-dose UVA1 phototherapy (60 kJ/m²/treatment) in patients suffering from systemic lupus erythematosus (SLE). We studied the changes in immunological parameters.

Methods. The patients received a 9-week course of phototherapy according to the following regimen: five times a week during the first 3 weeks, three times a week during the second 3 weeks and twice during the last 3 weeks. Among other things, we analysed the proportions of T helper 1 (Th1), Th2, T cytotoxic (Tc1) and Tc2 cell populations in the peripheral blood of patients by flow cytometric detection of intracytoplasmic interferon γ (IFN-γ) and interleukin 4 (IL-4).

Results. Our study showed the improvement of clinical symptoms determined by the subjective clinical disease activity scoring and the SLE Disease Activity Index (SLEDAI). By the end of UVA1 phototherapy, the mean value of SLEDAI had decreased from 7.2 ± 5.6 to 0.9 ± 1.8, which was significant (P = 0.005). Immunological investigations detected a decrease in the frequency of IFN-γ-producing Th1 and Tc1 cells and a decrease in the Th1/Th2 and Tc1/Tc2 ratios after UVA1 therapy.

Conclusion. According to the literature, IFN-γ has a pathogenic role in the development of SLE. We observed a decreased proportion of IFN-γ-secreting cells, which we think is presumably one of the beneficial effects of UVA1 therapy. On the basis of our study, UVA1 phototherapy does seem to be an effective adjuvant in the treatment of SLE patients.

Key words: Phototherapy, Systemic lupus erythematosus, Th1, Th2, IFN-γ.

Sensitivity to ultraviolet light is a characteristic feature in systemic lupus erythematosus (SLE) [1]. The wavelengths responsible for inducing SLE flares are thought to be within the UVB (280–320 nm) and UVA2 (320–340 nm) wavebands and not in the UVA1 region (340–400 nm) [2, 3]. In these patients UVB phototherapy or photochemotherapy is contraindicated because of the risks of inducing skin and systemic flares. The first observation that broadband UVA (320–400 nm) had a therapeutic effect on SLE was made by McGrath et al. on mice with a model of SLE [4] and a further study in the same animal suggested that UVA1 wavelengths were primarily responsible [5]. Phototherapy resulted in prolongation of their survival, a reduction in the level of anti-DNA antibodies and the improvement of the cell-mediated immune response [4]. Since then open studies [6–8] and three randomized, controlled, crossover trials [9–11] have shown that UVA1 can decrease signs and symptoms in SLE patients.

Articles that have appeared on the beneficial effects of UVA1 therapy on patients suffering from SLE are promising, but there is little information about the immunological changes occurring during UVA1 treatment. The question of whether UVA1 phototherapy can be used in SLE patients has been studied only by two research teams so far. Therefore, in this uncontrolled study, our aim was to analyse the immunological changes resulting from UVA1 therapy and the mechanism of these changes. We also examined the safety and effectiveness of this treatment modality in this patient population.

Materials and methods

Patients

Nine Caucasian patients (eight females and one male) with SLE who fulfilled the updated American College of Rheumatology classification criteria for SLE were studied [12]. The patients' previous clinical symptoms, autoantibody profile and therapy are shown in Table 1. All our patients had mild or moderate lupus and had been in a stable condition without any flare for at least 3 months before the study. Their immunosuppressive therapy was not changed within a 3-month period before the UVA1 treatment or during the study period. Six patients received daily corticosteroids (in the form of 4–8 mg methylprednisolone), one of whom also needed monthly cyclophosphamide infusions to control alveolitis. The other three patients were on NSAIDs (Table 1). Exclusion criteria included severe or rapidly fluctuating disease, the use of photosensitizers, and photosensitivity to UVA determined by minimal erythema dose. No potential participants were excluded on the basis of UVA photosensitivity. All the patients had Fitzpatrick skin type 2. The mean age of patients at the time of the study was 46.6 yr (range, 19–74 yr) and the mean disease duration was 9.3 yr (range 3–26.5 yr). Autoantibody profile since the onset of lupus included ANA (in all patients), anti-double-stranded (ds) DNA (in four out of nine), anti-extractable nuclear antigens (anti-ENA) (2/9), anti-Sm (6/9), anti-SS-A (anti-Ro) (4/9), anti-SS-B (anti-La) (4/9) and antiproteinase (2/9), anticientromere (1/9), and anti-mitochondrial antibody (1/9). At entry,

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### Table 1. Individual data for patients

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Duration of disease (yr)</th>
<th>Previous clinical symptoms</th>
<th>Previous autoantibody positivity</th>
<th>Previous therapy</th>
<th>Therapy at the entry of the study</th>
<th>Autoantibody positivity at the entry of the study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>74</td>
<td>Photosensitivity, arthritis, butterfly rash, mononeuritis multiplex, KCS, XO, panniculitis</td>
<td>ANA, anti-ENA, anti-Sm</td>
<td>M</td>
<td>8 mg M</td>
<td>ANA (homogen)</td>
</tr>
<tr>
<td>Patient 2</td>
<td>23</td>
<td>Leucopenia, thrombocytopenia, CNS, necrotizing vasculitis, livedo reticularis, Raynaud’s</td>
<td>ANA, anti-ENA, anti-Sm</td>
<td>M, cyclosporin</td>
<td>8 mg M</td>
<td>Negative</td>
</tr>
<tr>
<td>Patient 3</td>
<td>46</td>
<td>Butterfly rash, photosensitivity, polyarthritis, KCS, Raynaud’s phenomenon, myositis, cutaneous vasculitis</td>
<td>ANA, anti-ds-DNA, anti-cardiolipin</td>
<td>M</td>
<td>8 mg M</td>
<td>Negative</td>
</tr>
<tr>
<td>Patient 4</td>
<td>53</td>
<td>Photosensitivity, polyarthritis, leucopenia, butterfly rash, Crohn’s disease, Raynaud’s</td>
<td>ANA, anti-ENA, anti-Sm</td>
<td>M, HY, azathiopine</td>
<td>8 mg M</td>
<td>Negative</td>
</tr>
<tr>
<td>Patient 5</td>
<td>67</td>
<td>Polyarthritis, photosensitivity, leucopenia, butterfly rash, KCS, thyroiditis</td>
<td>ANA, anti-SS-A, anti-SS-B, ACA, ANA, anti-Sm</td>
<td>M, IVC</td>
<td>8 mg M + IVC</td>
<td>Negative (granular)</td>
</tr>
<tr>
<td>Patient 6</td>
<td>57</td>
<td>Polyarthritis, glomerulonephritis (WHO IV)</td>
<td>ANA, anti-SS-A, anti-SS-B</td>
<td>M</td>
<td>M, methotrexate, HY, cyclosporin A</td>
<td>ANA, anti-SS-A</td>
</tr>
<tr>
<td>Patient 7</td>
<td>19</td>
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<td>ANA, anti-ds-DNA, anti-Sm, anti-SS-B, ACA, ANA, anti-Sm</td>
<td>M</td>
<td>8 mg M</td>
<td>ANA (granular)</td>
</tr>
<tr>
<td>Patient 8</td>
<td>52</td>
<td>Photosensitivity, polyarthritis, leucopenia, butterfly rash, pleurisy, alveolitis, KCS</td>
<td>ANA, anti-Sm, anti-SS-A</td>
<td>M, HY,</td>
<td>4 mg M</td>
<td>Negative (granular)</td>
</tr>
<tr>
<td>Patient 9</td>
<td>28</td>
<td>9.3 ± 7.5</td>
<td>ANA, anti-SS-A, anti-SS-B</td>
<td>M, HY,</td>
<td>NSAID</td>
<td>Negative</td>
</tr>
</tbody>
</table>

KCS, keratoconjunctivitis sicca; XO, xerostomia; CNS, central nervous system involvement; ACA, anti-centromere antibody; AMA, anti-mitochondrial antibody; M, methylprednisolone; IVC, i.v. cyclophosphamide; HY, hydroxychloroquine.
only four patients were positive for antinuclear autoantibody in higher than 1:200 dilution, as detected by indirect immunofluorescent staining in the HEp-2 cell line; other immune serological data were in the normal range (Table 1). Patients gave informed consent, which was in accordance with the Declaration of Helsinki. The local ethical committee approved the study.

Radiation source
Irradiation was administered in a specially constructed cabinet containing 25 TL/10 R/100 W tubes (Philips International, Eindhoven, The Netherlands). The TL/10 R tubes were coated with strontium borate phosphor that converted UVC irradiation to UVB and UVA. The irradiance had a spectrum of 340–450 nm and a peak wavelength of 365 nm. The amount of UVC in the light emitted by the lamp was 0% and the amount of UVB was less than 0.1%.

Treatment regimen
The treatment was carried out during the winter months to minimize concomitant exposure to natural sunlight. The patients were clothed in undergarments and were wearing protective goggles. The phototherapy was performed with a UVA1 dose of 60 kJ/m² per treatment. The patients received a 9-week course of phototherapy according to the following regimen: five times a week during the first 3 weeks, three times per week during the second 3 weeks and twice during the last 3 weeks. We began the UVA1 phototherapy during the first 3 weeks, three times per week during the second 3 weeks and twice during the last 3 weeks. We began the UVA1 phototherapy five times a week during the first 3 weeks, three times per week during the second 3 weeks and twice during the last 3 weeks. We began the UVA1 treatment during the winter months to minimize concomitant exposure to natural sunlight. The patients were clothed in undergarments and were wearing protective goggles. The phototherapy was performed with a UVA1 dose of 60 kJ/m² per treatment. The patients received a 9-week course of phototherapy according to the following regimen: five times a week during the first 3 weeks, three times per week during the second 3 weeks and twice during the last 3 weeks. We began the UVA1 therapy with half of the therapeutic dose and gradually increased (30–40–50 kJ/m²/day) the amount of radiation until we reached the dose of 60 kJ/m² per day by the second week.

Clinical assessment
The patients’ symptoms were examined before starting phototherapy and after the ninth week. Two systems were used by the physician for clinical assessment of SLE disease activity: the SLE Disease Activity Index (SLEDAI) [13] and a subjective clinical disease activity scoring system [6]. The SLEDAI consists of 19 items, which represent nine organ systems. With the SLEDAI, the disease activity was determined by the physician, according to the patients’ evaluation, using 10 clinical parameters previously found especially useful for assessing the effectiveness of this therapy. These were scored subjectively as none, mild, moderate or severe, corresponding to a scale ranging from 0 to 3. The symptoms examined included rash, joint pain, headache, stomatitis, malaise, disturbed sleep pattern, impaired level of activity and the need for pain medication. Further symptoms were the duration of morning stiffness (0 = none, 1 = 1 h, 2 = 2–3 h, 3 = ≥3 h) and the onset of fatigue after getting up (0 = ≥12 h, 1 = 8–12 h, 2 = 4–8 h, 3 = ≤4 h). The aim of the assessment of the clinical symptoms was to evaluate the efficacy and safety of the therapy.

Laboratory studies
All the laboratory examinations were done before and after the 9-week course of UVA1 phototherapy. The patients’ blood was drawn prior to the first phototherapy and within 24 h after the last phototherapy into preservative-free heparin tubes. The blood samples were used within 2 h after drawing. Total complement activity and immune complex levels were measured by passive hemagglutination. Complement 3 (C3), C4 and immunoglobulins (IgG, IgA, IgM) were determined by nephelometry.

Autoantibodies to ENA (Sm, Sm/RNP, SS-A, SS-B), dsDNA, cardiolipin (CL) and β2-glycoprotein I were measured by enzyme-linked immunosorbent assay (ELISA) (Hycore Biomedical, UK). ANA was determined with an indirect immunofluorescence (IIF) technique using HEp-2 cells. The test was considered positive at or above 1:200 dilution. ANCA was detected by IIF on separated granulocytes.

Lymphocyte subsets (CD3+, CD4+, CD8+, CD19+) were analysed with an Epics XL-4 flow cytometer (Coulter, Hialeah, FL, USA). Monoclonal antibodies against CD3, CD4 and CD8 cells were purchased from Sigma-Aldrich (Schnelldorf, Germany) and Becton Dickinson (Mountain View, CA, USA).

With the examinations mentioned above, we monitored disease activity and the safety and beneficial effect of the therapy.

Determination of intracytoplasmic cytokines
We measured these in SLE patients before and after UVA1 phototherapy and, to obtain reference values, also in 30 healthy volunteers, who did not receive phototherapy. We determined the proportions of CD4+ and CD8+ cells, which can produce IFN-γ or IL-4 cytokines [14]. To activate the whole blood, we used phorbol myristate acetate and ionomycin (Sigma-Aldrich; 25 ng/ml; 1 μg/ml) for 4 h at 37°C. Activation was done in the presence of brefeldin-A (Sigma-Aldrich; 10 μg/ml), which inhibits intracellular transport. After 4 h, the surface CD4 and CD8 molecules were labelled with anti-human CD4-Quantum Red or anti-human CD8-Quantum Red (Sigma-Aldrich; 25 μg/ml–50 μg/ml), followed by lysing and cell membrane permeabilization of red blood cells (Lysing Solution and PermeaBilizing Solution; Becton Dickinson). Finally, IFN-γ and IL-4 in the cytoplasm was reacted with anti-human IFN-γ-FITC (fluorescein isothiocyanate/anti-human IL-4–phycocerythrin (20 μl; Becton Dickinson). Fixation was carried out with paraformaldehyde solution. The samples were measured with a flow cytometer. We determined the proportions of IFN-γ- and IL-4-positive cells among 5000 CD4+ and CD8+ cells.

Minimal erythema dose (MED) determination
Before and after therapy, the minimal erythema dose was determined using UVB and UVA radiation (Saalmann multimeter SBB LT400, UVB spectrum 280–320 nm, peak wavelength 295 nm, UVA spectrum 320–400 nm, peak wavelength 365 nm) as described [15].

Statistical analysis
Statistical processing of the data was carried out with SPSS for Windows 9.0 (standard version, SPSS Inc. 1989–2001). Changes were analysed by Student’s paired t-test and the Mann–Whitney test. P values <0.05 were considered statistically significant. No adjustments were made for multiple comparisons.

Results
Clinical assessment
The effectiveness of UVA1 therapy was characterized by improvement in the patients’ clinical condition, which was determined by SLEDAI and the subjective clinical disease activity scores. At baseline, SLEDAI ranged from 2 to 17, and the mean value was 7.2 ± 5.6 (s.d.). SLEDAI decreased in all patients after phototherapy, the score ranging from 0 to 4 and the mean value was 0.9 ± 1.8. The decrease was statistically significant (P = 0.005).
According to the subjective clinical disease activity scores, all symptoms improved with the exception of morning stiffness. In spite of this, the decrease in activity scores was statistically significant only with regard to skin rashes (Fig. 2).

Minimal erythema dose

In all patients, MED with UVA was normal before and after UVA1 therapy (MED UVA >16.2 J/cm²). MED with UVB was decreased compared with normal value in six patients before therapy (<0.04 J/cm²), but by the end of therapy MED was normal with UVB (>0.06 J/cm²) in all patients.

Laboratory studies

Several immunological parameters were determined before and after the 9-week UVA1 therapy. At baseline, ANA was shown by indirect immune fluorescence on HEp-2 cells in only four patients, and ANA remained positive even after treatment (Table 2). The levels of other autoantibodies, determined by ELISA, were normal before and after therapy. Total complement activity, immune complex level, concentrations of complement proteins C3 and C4 and immunoglobulins were also measured at baseline and 9 weeks later. These values were all within normal ranges and did not show any significant changes due to the UVA1 therapy. The same results were obtained when we determined lymphocyte subpopulations before and after treatment (data not shown).

The proportions of T helper 1 and 2 (Th1 and Th2), T cytotoxic 1 and 2 (Tc1 and Tc2) cells were determined by intracytoplasmic cytokine staining. After the 9 weeks of UVA1 therapy, the frequency of IFN-γ-producing Th1 and Tc1 cells decreased compared with that before therapy. The percentages of both Th1 and Tc1 cells in the peripheral blood of lupus patients after UVA1 treatment became significantly lower than those in healthy controls (Fig. 3A, Table 2). On the other hand, the percentage of Th2 cells significantly increased, while the proportion of Tc2 cells did not change significantly after UVA1 therapy (Fig. 3B, Table 2). As a result of these changes, the Th1/Th2 ratio decreased significantly after week 9 compared with the value before therapy; the Tc1/Tc2 ratio also decreased, though this decrease was not significant (Fig. 4, Table 2).

Discussion

In our study, low-dose UVA1 irradiation mitigated clinical symptoms in nine SLE patients. SLEDAI decreased significantly as a consequence of the therapy. Furthermore, we found that subjective clinical disease activity scores decreased by the end of the therapy, with the exception of morning stiffness. However, this change was statistically significant only in the case of skin rashes.

Like us, McGrath et al. found a significant decrease in most symptoms in an uncontrolled study using similar average doses (60 kJ/m² per day) and the same subjective clinical disease activity scores. They detected non-pronounced improvement in the case of stomatitis and disturbed sleep pattern [8]. This difference in the degree or pattern of decrease in the subjective clinical activity scores between our study and the one mentioned above could be attributed to the different study populations. In the first of the three randomized, patient- and observer-blinded, controlled, crossover studies that have been published, McGrath et al. suggested that low-dose UVA1 irradiation effectively diminished signs and symptoms of disease activity in SLE [9]. Polderman et al. published two other studies, which reported a direct comparison of change with UVA1 vs visible light. In the first study, a UVA1 therapy of 3 weeks (five times weekly, 6 J/cm² per day) and a visible light treatment were compared; they concluded this treatment was strongly suggestive of lowering disease activity [10]. In the other, recent publication, using the same treatment regimen with higher daily UVA1 dose (12 J/cm²/day), the difference between the two groups was significant [11]. Both investigators stated that during UVA1 phototherapy no side-effects were observed, and we could confirm their findings, since neither our laboratory parameters nor the clinical signs indicated activation of SLE. We found improvement in the clinical picture of the patients, and in the case of six patients, the UVB photosensitivity that existed before therapy decreased. This may be have been due to thickening of the horny layer and pigmentation induced in the epidermis by UVA1.

SLE is an autoimmune disorder involving several organs and it is characterized by variable disease activity. In the background of this disease there is complex immunological dysregulation. According to a previous idea, Th1 cells and their cytokines (IL-2, IFN-γ) are involved in cell-mediated autoimmune diseases, and Th2 cells and their cytokines (IL-4, IL-5, IL-10, IL-13) are expected to play a key role in the development of antibody-mediated autoimmune diseases such as SLE [16–18]. However, on the basis of recent studies it seems that this paradigm of cytokines in autoimmune syndromes cannot be dogmatically predicted and their effects may be much more complex than the simplistic Th1/Th2 definition dictates [19]. Publications examining immunological alterations in animal models of SLE have reported dominance of Th1 cells and have shown that IFN-γ is a major effector molecule in this disease [19]. Concentrations of IFN-γ and IL-12 were also increased in the serum of lupus patients,
particularly those in the active stages of the disease, and an increase in the Th1/Th2 ratio has been detected in peripheral mononuclear cells [20–22]. These data suggest that, besides Th2 cells, Th1 cells also play a pathogenic role in certain phases of SLE. Furthermore, type 1 cytokines may also be produced by CD8\(^+\) Tc1 cells.

Interestingly, in our study we observed that after 9 weeks of UVA1 therapy, the frequency of IFN-γ-producing Th1 cells and, significantly, Tc1 cells decreased compared with the baseline values, and both became significantly lower than control values. On the other hand, the changes in the proportions of Th2 and Tc2 cell populations were not so congruent with each other. The percentage of IL-4-secreting Th2 cells increased significantly, while the proportion of Tc2 cells decreased during the UVA1 therapy, so both were comparable to those of controls. Accordingly, the level of autoantibodies did not rise during the UVA1 therapy. Due to these changes in lymphocyte subsets during the phototherapy, there was a prominent decrease in the Th1/Th2 and Tc1/Tc2 ratios.

It is known that Th1 differentiation is driven by IL-12 and interestingly UVA1 releases IL-10, a cytokine that decreases IL-12 levels [23]. The production of IL-10, induced by UVA1, could result in decreased IL-12 secretion and a decreased percentage of IFN-γ-producing T cells. Since IFN-γ plays an important role in the pathogenesis of SLE, this mechanism may be one of the beneficial effects of UVA1 in the treatment of lupus patients.

The UVA band (320–400 nm) was separated into two parts (UVA2, 320–340 nm, and UVA1, 340–400 nm) because the biological effect of UVB turned out to have properties similar to those of UVA2. Consequently, UVA2 can be considered an extension of UVB [24]. In some respects, UVB and UVA1 have opposing effects and while UVB is contraindicated for SLE

### Table 2. Individual data for patients before and after 9 weeks of UVA1 phototherapy

<table>
<thead>
<tr>
<th>Patient</th>
<th>ANA</th>
<th>SLEDAI</th>
<th>Th1 proportion (%)</th>
<th>Tc1 proportion (%)</th>
<th>Th1/Th2 ratio</th>
<th>Tc1/Tc2 ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12</td>
<td>190.4</td>
<td>39.6</td>
<td>1.8</td>
<td>19.4</td>
<td>12.5</td>
</tr>
<tr>
<td>2</td>
<td>14</td>
<td>129.6</td>
<td>57.3</td>
<td>4.6</td>
<td>12.6</td>
<td>48.8</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
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<td>34.7</td>
<td>6.2</td>
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<tr>
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<td>4</td>
<td>70.1</td>
<td>75.6</td>
<td>0.7</td>
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<td>13.5</td>
</tr>
<tr>
<td>5</td>
<td>4</td>
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<td>64.7</td>
<td>1.1</td>
<td>4.9</td>
<td>13.0</td>
</tr>
<tr>
<td>6</td>
<td>3</td>
<td>40.3</td>
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<td>0.9</td>
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<td>64.7</td>
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<td>2</td>
<td>103</td>
<td>12.6</td>
<td>0.9</td>
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<td>59.7</td>
</tr>
<tr>
<td>Mean±S.D.</td>
<td>270.2±166.6</td>
<td>154.8±196.09</td>
<td>154.8±196.09</td>
<td>154.8±196.09</td>
<td>154.8±196.09</td>
<td>154.8±196.09</td>
</tr>
</tbody>
</table>

Fig. 3 (A) Proportions of IFN-γ-producing CD4\(^+\) Th1 and CD8\(^+\) Tc1 lymphocytes before and after UVA1 therapy. After 9 weeks of UVA1 therapy, the frequency of Th1 and Tc1 cells decreased compared with values before therapy, and became significantly lower compared with healthy controls (controls: Th1, 22.1±6.25%; Tc1, 43.4±8.45%). (B) The proportion of IL-4-producing CD4\(^+\) Th2 and CD8\(^+\) Tc2 lymphocytes before and after UVA1 therapy. The percentage of Th2 cells significantly increased, while that of Tc2 cells decreased after UVA1 therapy, although both percentages approached those in controls (controls: Th2, 1.12±0.62%; Tc2, 0.59±0.58%).

![Graph](image1)

![Graph](image2)

Fig. 4. Th1/Th2 and Tc1/Tc2 ratios in patients before and after AV-A1 therapy. The Th1/Th2 ratio significantly decreased after week 9 compared with the value before therapy; the Tc1/Tc2 ratio also decreased, though this decrease was not significant.

Interestingly, in our study we observed that after 9 weeks of UVA1 therapy, the frequency of IFN-γ-expressing Th1 cells and, significantly, Tc1 cells decreased compared with the baseline values, and both became significantly lower than control values. On the other hand, the changes in the proportions of Th2 and Tc2 cell populations were not so congruent with each other. The percentage of IL-4-secreting Th2 cells increased significantly, while the proportion of Tc2 cells decreased during the UVA1 therapy, so both were comparable to those of controls. Accordingly, the level of autoantibodies did not rise during the UVA1 therapy. Due to these changes in lymphocyte subsets during the phototherapy, there was a prominent decrease in the Th1/Th2 and Tc1/Tc2 ratios.

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patients, UVA1 has several beneficial effects. UVA1 can penetrate more deeply than UVB, so it can reach the dermis and its circulating blood and lymph cells, and can promote photoreactivation [25]. UVA1 induces immediate apoptosis of T and B lymphocytes [26] and also inhibits the release of tumour necrosis factor α [27]. Regarding cell-mediated immunity (CMI), the effects of UVA1 are contradictory. Some publications showed that UVA photons inhibit cis-urocanic acid-induced immunosuppression [28] and increase the numbers of immunoonhancing CD1α+ DR+ dendritic cells in irradiated skin [23]. In other studies, UVA1 radiation increased the level of cis-urocanic acid [27] and reduced Langerhans cell density in human skin [29, 30]. In an animal model (New Zealand Black × New Zealand White F1 mice), UVA1 improved lymphocyte responses to phytohaemagglutinin and lipopolysaccharide [4]. In our study UVA1 therapy caused a decrease in the proportion of IFN-γ-producing Th1 and Tc1 cells in the peripheral blood of lupus patients, which could lead to impairment of CMI. In conclusion, our study, in agreement with the results of McGrath’s and Polderman’s groups, demonstrated an improvement in the clinical symptoms of SLE following UVA1 phototherapy. There were no adverse events during the therapy and the disease did not relapse. As a new finding in our results, we emphasize that one of the beneficial effects of UVA1 therapy is probably the decrease in the frequency of INF-γ-producing T cells (Th1, Tc1), and this also results in a decreased Th1/Th2 and Tc1/Tc2 ratio. UVA1 phototherapy can be an effective and safe adjuvant therapy to the traditional pharmacological therapies in SLE patients. In our opinion, further examinations of larger patient populations are necessary in the future to learn more about the effectiveness and mechanisms of UVA1 therapy.

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The authors have declared no conflicts of interest.

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