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HIGH-DOSE NARROWBAND ULTRAVIOLET A1 INDUCES THE REGRESSION OF DERMAL FIBROSIS IN ANIMAL MODEL OF SCLERODERMA

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Background: Ultraviolet A1 (UVA1) phototherapy implications for systemic sclerosis still remain area of research. The wide spectral waveband of UVA1 could react with many chromophores in the skin, leading to different effects of the immune system.¹ In accordance with the physical properties of UVA1 and the optical features of the skin, the narrowband UVA1 would influence collagen metabolism with a reduced chance of side effects. None of the previously conducted studies evaluated the effectiveness of narrowband UVA1 on dermal fibrosis.

Objectives: The main objective of the present study was to define the impact of high-dose of 365±5 nm UVA1 on the dermal thickness in pre-established, bleomycin-induced mouse model of scleroderma.

Methods: Forty two DBA/2 line mice were randomly divided into the following 6 groups (7 animals in each): group I – mice injected with sodium chloride (NaCl) for 3 weeks; group II – mice injected with bleomycin (Bleo) for 3 weeks; group III – mice injected with NaCl for 8 weeks; group IV – mice injected with Bleo for 3 weeks and then with NaCl for 5 weeks; group V – mice injected with Bleo for 8 weeks; group VI – mice injected with Bleo for 8 weeks and parallel treated with average cumulative dose of 1200 J/cm² of UVA1 for the last 5 weeks (the treatment group). Light source emitting a narrow band UVA1 of 365±5 nm and 21 mW/cm²; power density was used in the study. Histological analysis was performed for the evaluation of dermal thickness. The Mann – Whitney U test was used for statistical analysis.

Results: After bleomycin injections that spanned a period of 3 and 8 weeks, the dermal thicknesses were significantly (p=0.002) higher (group II – 433.69±54.37 µm and group V – 497.43±57.83 µm, respectively) as compared to that of the healthy controls (group I – 166.04±25.29 µm and group III – 178.18±42.35 µm, respectively). The 3 weeks of bleomycin injections and the following 5 weeks of NaCl did not cause any spontaneous regression of dermal fibrosis (group IV – 443.87±41.77 µm; group II – 433.69±54.38 µm; p=0.482). Dermal thickness in mice injected with bleomycin for 8 weeks and irradiated with UVA1 for the last 5 weeks was significantly lower than that in mice challenged only with bleomycin for 8 weeks (group VI – 253.96±31.83 µm and group V – 497.43±57.83 µm, respectively; p=0.002). Furthermore, treatment with 1200 J/cm² of UVA1 in parallel with profibrotic stimulus of bleomycin resulted in a lower dermal thickness as compared with pre-existing fibrotic changes in the group IV observed after 3 weeks of bleomycin injections (group VI – 253.96±31.83 µm and group IV – 443.87±41.77 µm; p=0.002) (figure 1).

Abstract AB0186 – Figure 1

Conclusions: The cumulative dosage of 1200 J/cm² of narrowband UVA1 not only prevented the progression of dermal fibrosis, but also induced the regression of pre-existing fibrotic changes in bleomycin-induced mouse model of scleroderma.

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AB0187

THE ASSOCIATION BETWEEN ACTIVITY OF PURINE AND PYRIMIDINE METABOLISM ENZYMES AND DISEASE ACTIVITY IN SYSTEMIC SCLERODERMA PATIENTS

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Background: Recent studies report various metabolic disturbances in systemic sclerosis (SSc) patients. Purine and pyrimidine metabolic pathways are closely interrelated, underlying the central processes of cellular life. Alterations of the enzymes that control these metabolic conversions can disturb proliferation and differentiation of lymphocytes, therefore contributing initiation and progression of the immunopathological phenomena.

Objectives: to characterise enzymatic patterns of the major purine and pyrimidine metabolic pathways enzymes in blood plasma and lysed lymphocytes depending on the SSc activity.

Methods: 51 SSc patients and 30 healthy controls were enrolled in the study. Mean age of patients (Mean ±SD) was 42.8±1.3 years, mean SSc duration was 7.9±0.7 years. The diagnosis was verified in accordance with the international standards (ACR/^{EULAR} 2013). Disease activity was assessed in accordance with the national classification.¹ Adenosine deaminase (ADA; EC 3.5.4.4); adenosine kinase (AK; EC 2.7.1.20); guanylate kinase (GK; EC 2.7.4.8), dihydroorotate dehydrogenase (DODH; EC 1.3.1.14); IMP dehydrogenase (IMPDH; EC 1.1.1.205); purine nucleoside phosphorylase (PNP; EC 2.4.2.1); thymidine kinase (TK; EC 2.7.1.21); thymidine phosphorylase (TP; EC 2.4.2.4); uracil/thymidine dehydrogenase (UDH; EC 1.1.7.99.4); cytidine deaminase (CDA; EC 3.5.4.5) activities were measured in blood plasma and lysed lymphocytes.

Results: We revealed substantial changes in enzymatic activities related to both purine and pyrimidine metabolism in SSc. The increased DODH (p<0.001), IMPDH (p<0.001), PNP (p<0.001), TK (p<0.001), TP (p<0.01), UDH (p<0.001) activities in plasma and AK (p<0.001), IMPDH (p<0.001), TK (p<0.001) activities in lysed lymphocytes; the decreased ADA (p<0.001), GK (p=0.02), PNP (p<0.001) activities in lysed lymphocytes were observed in SSc patients in comparison with healthy controls. Plasma AK, DODH, IMPDH, PNP, TK, UDH activities positively correlated with SSc activity, as well as lymphocytic AK, IMPDH, TK activities did. Negative correlations with SSc activity were revealed for plasma ADA, GK, TP, and also for lymphocytic ADA, GK, DODH, PNP, TP, UDH, CDA. Plasma and lymphocytic adenosine deaminase as well as adenosine kinase activities were the most informative for minimal SSc activity detection, being a promising candidate marker.

Conclusions: The changes in enzymatic activity of purine and pyrimidine metabolism participate in pathogenesis of SSc. The enzymatic patterns studied can be used as auxiliary markers of SSc activity. The correction of purine and pyrimidine metabolism changes can be considered as one of the promising ways of increasing the effectiveness of SSc treatment.

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