DE GRUYTER OPEN

Acta Medica Marisiensis 2018;64(1):17-21 DOI: 10.2478/amma-2018-0003

RESEARCH ARTICLE

Clinical and Therapeutic Trial for the Efficacy of Narrow Band - UVB Phototherapy versus Systemic Therapy in Moderate and Severe Atopic Dermatitis of the Adult

Gyula Laszlo Fekete*, László Fekete

University of Medicine and Pharmacy Tirgu Mures, Romania

Objectives: The aim of this clinical and therapy study was to evaluate the efficacy of NB-UVB phototherapy versus systemic therapy in moderate-to-severe atopic dermatitis of the adult. **Material and methods**: The subjects of the study were divided into two groups of 25 adult patients with moderate and severe atopic dermatitis according to the inclusion criteria. The first group of 25 patients were treated with systemic corticosteroids while the second group of 25 patients were treated with NB-UVB phototherapy. At the end of the study, after all the data were centralized, we performed a statistical analysis of the results, comparing the two groups as well as the efficacy of the different therapies. **Results**: In group I the clinical efficacy of the systemic corticosteroid treatment was achieved, on average, at 4 weeks in patients with moderate atopic dermatitis and at 6 weeks in patients with severe atopic dermatitis. In group II the clinical effecacy of NB-UVB phototherapy was achieved, on average, at 6 weeks for patients with moderate atopic dermatitis and at 8 weeks for those with the severe form. In both groups, the total IgE serum levels were elevated at the beginning, and they became normal throughout the clinical improvement. Remarkable therapy-related side effects were found in the first study group. **Conclusion:** We conclude that NB-UVB phototherapy had similar efficacy in treating moderate-to-severe atopic dermatitis with minimal side effects compared to systemic corticosteroid therapy.

Keywords: atopic dermatitis, narrow band UVB, systemic treatment

Received 13 August 2017 / Accepted 4 January 2018

Introduction

In 1801, Ritter discovered ultraviolet rays (UV); in 1820, Home describes how solar radiation causes erythema, regardless the power of the emitted heat, and points out the fact that the pigments of dark skinned persons protect against inflammation caused by sunlight [1]. In 1858, the inflammatory effect of UV radiation is proven as a result of a mere laboratory accident. Finsen in 1900 recognized the therapeutic effect of UV radiation, therefore he was awarded the third Nobel Prize in 1903 [2]. UV radiation has both positive and negative biological effects on the human skin. The beneficial effects include: germicidal effect, pigmentogen effect, stimulation of the vitamin D synthesis, and the therapeutic effects on certain skin diseases. The immunomodulatory-suppresive effect of the UV radiation can be both advantageous and harmful [3]. In the 90's Parrish demonstrated that the erythema-causing effect and the therapeutic effects of the UV-B radiation are caused by different wavelengths [4]. In 1984, Fischer demonstrated that the wavelength of 313 nm is the most effective in the treatment of psoriasis. Consequently, UV-B emission lamps appeared with a wavelength of 311nm +/- 2nm in narrowband, named narow-band UVB, NB-UVB.

Atopic dermatitis is an immuno-allergic, inflamatory, non-infectious, itchy skin condition, with chronic evolution, that appears mainly at genetically predisposed individuals. Atopic dermatitis is a widespread skin disease, and its prevalence increases steadily from year to year. Men and women are equally affected, moreover, it accounts for approximately 10% -20% of the dermatological consultations. This skin condition typically affects children in their early childhood but can occur at any age. At the adults, the onset of the disease is between the ages of 20-40 years and it persists with exacerbations and remissions throughout the patient's lifetime. Moderate and severe forms of atopic dermatitis at adults are estimated to vary between 5-10% of the cases. The treatments used in these clinical forms includes emollients and antipruritic agents, systemic corticosteroids, cyclosporine, biological treatment and either UVB or NB-UVB phototherapy. Phototherapy is rather inaccessible for the patients due to the fact that hospitals and private clinics are not equipped with the ultimate NB-UVB phototherapeutic devices. [5].

Objectives

The aim of this clinical and therapy study was to evaluate the efficacy of NB-UVB phototherapy versus systemic therapy in moderate and severe atopic dermatitis of the adult. We also wanted to monitor the total IgE serum levels, as a paraclinic evaluation for the efficacy of the therapy, the side effects that appeared during the study and the long-term adverse effects reported at the end of the study, for all the patients treated with phototherapy.

* Correspondence to: Gyula Laszlo Fekete
E-mail: dermafek@yahoo.com

Material and methods

The subjects of the study were selected from the patients who presented themselves at the Dermatology Clinic and Outpatient Mures County Clinic Hospital of Tirgu Mures between November 2015 and August 2016. We obtained the study agreement of the Ethics Commission of the Mures County Clinic Hospital and of the Ethics Committee for Research of the University of Medicine and Pharmacy Tirgu Mures, with the decision no.1537 / 2016 respectively, 24/2016.

Patients were selected according to the followng inclusion/exclusion criteria:

Inclusion criteria:

– Clinically confirmed onset or acute exacerbation of moderate or severe atopic dermatitis
– Age over 20 years

Exclusion criteria:

– Acute morbid conditions
– Decompensated chronic diseases
– Age under 20 years
– Patients who did not sign the informed consent.

A study datasheet was performed every patient's case containing: personal information, medical history, both clinical and dermatological examination, treatments and investigations that are going to be performed, as well as the evolution of the affected skin area during the study. The weekly clinical evaluation, the adverse effects, and the possible new flares were monitored. All patients obtained topical treatment with emollients. In both groups, we monitorized the total serum IgE levels at the beginning and at the end of the treatment, as a paraclinic evaluation of treatment efficacy, as it is a well-known the fact that IgE serum levels are maximum in acute exacerbations, decreasing under therapy. We used the immunoturbidimetric method to determine IgE serum levels, and the device used was an Abbot-type Immunoassay, model c 2000 Architect. The subjects were divided into two groups of minimum 25 adult patients with moderate or severe atopic dermatitis according to the above mentioned criteria. The 25 patients from *group I* were treated with *systemic therapy,* using systemic corticosteroids (0.5 to 1 mg/kgprednisone) until clinical response was achieved: 0.5 mg/kg in medium forms and 1 mg/kg for those with severe forms. The systemic treatment was stopped at clinical recovery and the topical treatment was continued as a maintenanc therapy. The 25 patients from *group II* were treated with *NB-UVB phototherapy*. A minimal erythema dose (MED) was carried out for the optimal dosing, knowing that different skin phototypes require different UV doses. The phototherapeutic treatment dosing protocol was as follows:

– The starting dose is 70% of the MED at 1000W power of the device
– Increasing the dose with 10-30%
– Weekly exposure: 3 times per week
– Total exposure: 15-30 (5-10 weeks) of exposures depending on clinical response. For performing the phototherapeutic treatment and to obtain minimal erythema dose, it was used Dr Honle 1000 W NB-UVB phototherapeutic device, which could irradiate an entire hemibody, the patients being irradiated in the front and in the back, with a 1000 W transmit power. At the end of the study, after all the data were centralized, we performed an analysis of the results, comparing the two groups as well as the efficiency of the different therapies.

Results

Group I

Out of the 25 patients included in our study, with relapses, 18 were women (72%) and 7 were men (28%), including 16 suffering from moderate (64%), and 9 from severe form (46%). Of whom, 19 patients (3 men and 16 women) had phototype I (76%), 6 patients (4 men and 2 women) had phototype II (46%). In 5 cases (20%) the treatment was stopped due to gastrointestinal symptoms such as vomiting, nausea, gastric hyperacidity, and in 3 cases a symptomatic treatment was prescribed, while continuing the corticosteriod therapy. The average age of the study population was 29.4 years, all of them were suffering from atopy from childhood, the average of the onset being 16.5 years. The clinical efficacy of the systemic corticosteroid treatment was obtained on average at 4 weeks in patients with moderate atopic dermatitis and at 6 weeks for the patients with severe atopic dermatitis. (Figure 1) The IgE serum levels were elevated at the beginning, and they became normal with clinical improvement. For those with severe forms the average value of total IgE was of 486 IU/ml while for those with moderate form the average value was 280 IU/ml. (Figure 2)

Group II

During the study period 25 patients with relapses were included, 15 women (60%) and 10 men (40%), of whom 15 suffered from moderate forms (60%), and 10 suffered of severe forms, (40%). Out of them, 17 patients (9 male, 8 female) had phototype I (68%), and 8 had phototype II (32%) (6 male and 2 female). The average age of the subjects was 27.2 years, all suffered from atopy from childhood, the average of the onset of the disease being 15.7 years. The clinical efficacy of NB-UVB phototherapy was achieved, on average, at 6 weeks for those with moderate atopic dermatitis and at 8 weeks in those with the severe forms. (Figure 3) Aside from one case (female, phototype I, moderate form), the total serum IgE levels were elevated at the beginning, and they became normal through the clinical improvement. For those with severe froms, the average value of the total IgE was of 526 IU/ ml, while for those with moderate forms the average was 320 IU/ml. (Figure 4) Immediate side effects were observed at two women, with phototype I and severe clinical forms; the phototherapy was interrupted, for two sessions, because of grade I burn, after which we continued according to the proto-

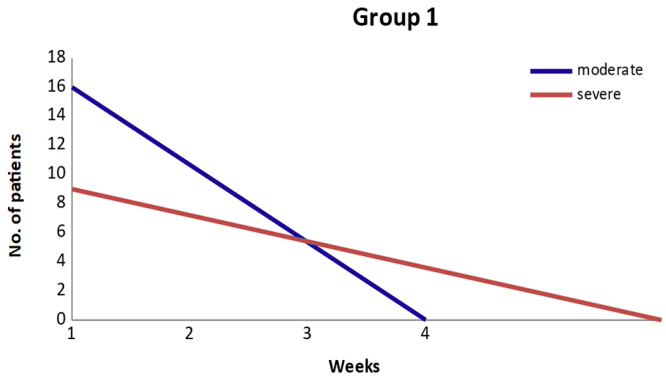

Fig. 1. Clinical efficacy of the treatment at group 1

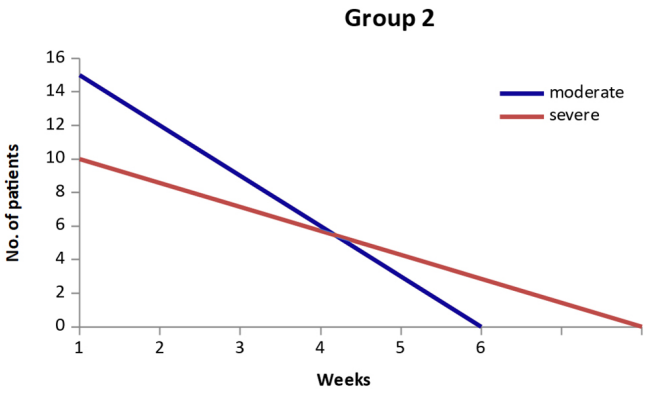

Fig.3. Clinical efficacy of the treatment at group 2

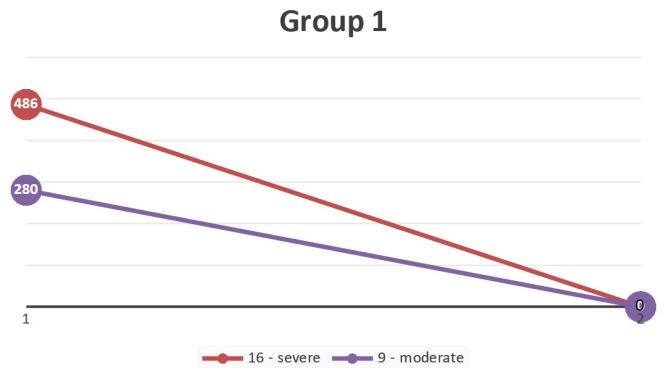

Fig.2. The dynamics of IgE levels at the clinical endpoint for group 1 (IU/ml)

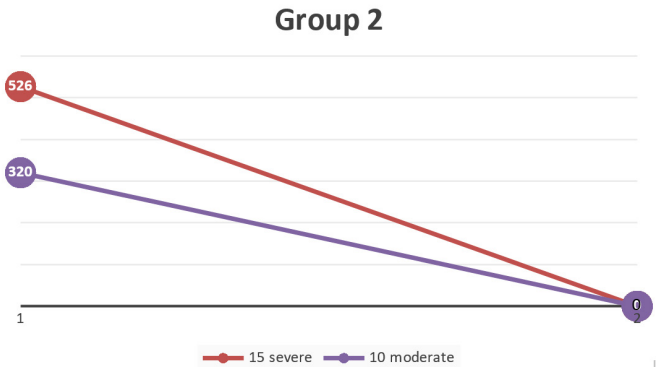

Fig. 4. The dynamics of IgE levels at the clinical endpoint for group 2 (IU/ml)

col. No adverse effects were detected in 6 months after the treatment.

Discussions

UV radiation are divided in function of the radiation wavelength into the UV A, B and C. Generally, the UV-C effect appears only as an inflammation. The UV-B radiation is responsible for the therapeutic effect. The effects of the UV-A radiation are mainly pigmentogene effects, erythematous manifestations occuring in approximatively 1000 x higher dose than the UV-B radiation. UV-B radiation therapies are used as monotherapy or in multiple combinations with local agents used for more than a half century with documented results, particularly in psoriasis, vitiligo and some chronic dermatoses [6]. The adverse effects can be divided into short-term effects such as sunburn, induced hyperkeratosis and pigmentogenesis, and long-term effects like the induction and development of skin cancers and photodermatoses [7]. The beneficial effects of UVB consist in blocking DNA synthesis in hyperproliferative conditions, like in psoriasis, induction of apoptosis in keratinocytes in eczema, and immunomodulatory effect by induction of IL-10, and by decreasing the NK-cell activity in atopic dermatitis [8]. The clinical effects of these new therapies are documented by several studies, and they have proved to be superior to broadband UV treatment, due to the shorter exposure, with longer remissions and with more moderate side effects [9]. In the phototherapeutic treatment of the atopic dermatitis a well-defined protocol for psoriasis is used, with the indication of moderate and severe atopic dermatitis of the adult. Phototherapy is not indicated under the age of 12 years [10]. NB-UVB therapy can also be used with protocols adjusted to several chronic skin conditions, such as: chronic urticaria, nodular prurigo, different etiologies of pruritus, alopecia areata, lichen sclero-atrophic, seborrheic dermatitis, mycosis fungoides, etc. [11]. In addition to the treatments used for these clinical forms, systemic treatment with corticosteroids, cyclosporine, and biological therapies are also used. [12-15]. In the systemic treatment of the study population, in group I we used systemic corticosteroids, since they are the most accessible systemic therapies. Atopic dermatitis is considered to be a multifactorial disorder, whose clinical expression depends on complex interactions like: hereditary predisposition, functionally altered skin barrier, immunological and neuro-endocrine abnormalities and a series of trigger or aggravating factors of skin lesions. Both sexes are equally affected. The study subjects were chosen to include men and women, approximately equal. The clinical and laboratory characteristics of these patients are: intense cutaneous pruritus, marked xerosis, the association of other allergic diseases, increased IgE serum levels, as well as the appearance of typical skin lesions of a chronic eczema covering large areas of the skin [16]. Concerning the effi-

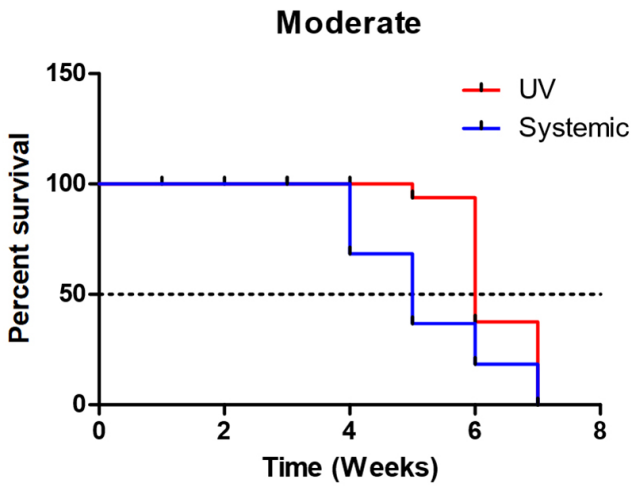

Fig. 5. Survival analysis test for patients with moderate clinical form

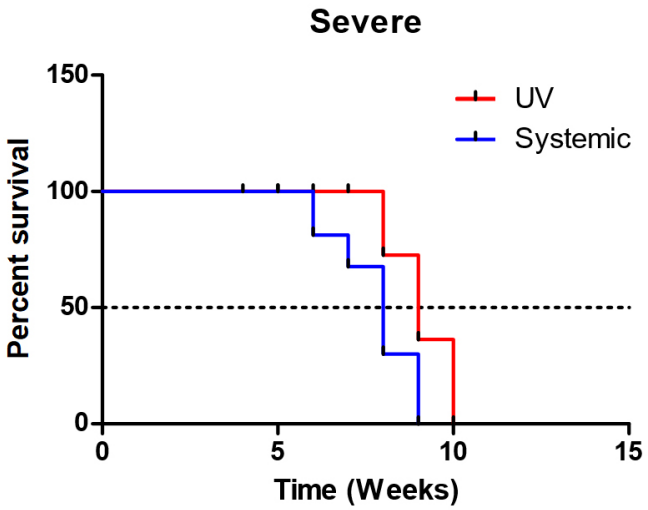

Fig. 6. Survival analysis test for patients with severe clinical form

cacy of the treatments both of them were efficient, and the difference of the time until recovery between the two groups has been clinically significant. We done the survival analysis Log-rank test to compare the efficacy of the treatment at patients with moderate and severe clinical forms from both groups. At patients with moderate clinical forms the survival curves were significant different with p value of 0.0036. (Figure 5)

At patients with severe clinical forms the survival curves were significant different with p value of 0.0013. (Figure 6) The systemic treatment is more practical, the phototherapeutic therapy requiring a more difficult management of the patients. During the study, the dynamics of IgE serum levels were directly correlated with the clinical evolution and efficacy of the treatment, it was elevated at the beginning, and it became normal throughout the clinical improvement. Similarly, IgE serum levels were also correlated with the clinical form of the disease, having been more elevated in the severe forms of the disease that corresponds with the literature datas [17]. Regarding adverse effects, in group I with patients on systemic corticosteroids, we have had a drop to 20% of the patients due to the gastrointestinal side effects. In group II there was no evidence of short-term side effects, while the long-term adverse effects will be followed and documented.

Conclusions

As a conclusion we can say that phototherapy had similar efficacy with minimal side effects compared to systemic drug therapy. The management of patients treated with phototherapy is much more difficult. The dynamics of serum IgE levels during the study are directly correlated with the clinical evolution and efficacy of the treatment. Side effects are more severe in patients receiving systemic treatment than in those who are treated with phototherapy, this type of treatment being an effective alternative. At the moment, phototherapy is rather inaccessible for patients, due to the fact that hospitals and private clinics are not equipped with the ultimate NB-UVB photohterapeutic devices.

Conflict of interest

None to declare.

Acknowledgments

This work was funded by grant no. 16479/2015 / of University of Medicine and Pharmacy Târgu Mures and Sc. Cattus Srl company.

References

1. Ritter J W. - Kurze Mitteilung uber die Endeckung der Uv-Strahlen. Ann. Phys 1801,7:527.
2. Hölze E. - Photodermatosen und Lichtreaktionen der Haut. Wissenschaftliche V mbH, Stuttgart, 2003,31-33.
3. Horkay Irén - Klinikai photodermatologia, Ed. Medicina, Budapest, 2008, 29-39.
4. Parrish JA, Jaenicke KF. - Action spectrum for phototherapy of psoriasis. J Invest. Dermatol.,1981: 76:359.
5. Brown SJ. - Atopic eczema. Clin Med (Lond), 2016,16(1):66-69.
6. Vangipuram R, Feldman SR. - Ultraviolet phototherapy for cutaneous diseases: a concise review. Oral Dis., 2016, 22(4):253-259.
7. Rodenbeck DL, Silverberg JI, Silverberg NB.- Phototherapy for atopic dermatitis. Clin Dermatol. 2016, 34(5):607-613.
8. Fernández-Guarino M, Aboin-Gonzalez S, Barchino L, et al. - Treatment of moderate and severe adult chronic atopic dermatitis with narrow-band UVB and the combination of narrow-band UVB/UVA phototherapy. Dermatol Ther. 2016, 29(1):19-23.
9. Horkaylrén - Ultraibolya fény okozta kórélettani változások a bőrben. Bőrgyógy. Vener. Szl., 2005, 81: 95-97.
10. Sokolova A, Lee A, D Smith S. - The Safety and Efficacy of Narrow Band Ultraviolet B Treatment in Dermatology: A Review. Am J Clin Dermatol, 2015, 16(6):501-531.
11. Patrizi A, Raone B, Ravaioli GM. - Management of atopic dermatitis: safety and efficacy of phototherapy. Clin Cosmet Investig Dermatol, 2015, 5;8:511-520.
12. Notaro ER, Sidbury R. - Systemic Agents for Severe Atopic Dermatitis in Children. Paediatr Drugs, 2015, 17(6):449-457.
13. Totri CR, Eichenfield LF, Logan K, et al. - Prescribing practices for systemic agents in the treatment of severe pediatric atopic dermatitis in the US and Canada: The PeDRA TREAT survey. J Am Acad Dermatol, 2017, 76(2):281-285.
14. Simon D, Bieber T. - Systemic therapy for atopic dermatitis. Allergy, 2014, 69:46-55.

15. Cornish KS, Gregory ME, Ramaesh K. - Systemic cyclosporin A in severe atopic kerato-conjunctivitis. Eur J Ophthalmol, 2010, 20(5):844-851.
16. Weinhold A, Obeid R, Vogt T, Reichrath J. - Prospective Investigation of 25(OH)D3 Serum Concentration Following UVB Narrow Band Phototherapy in Patients with Psoriasis and Atopic Dermatitis. Anticancer Res, 2016, 36(3):1439-1444.
17. Sidbury R, Davis DM, Cohen DE, et al. - American Academy of Dermatology. Guidelines of care for the management of atopic dermatitis: section 3. Management and treatment with phototherapy and systemic agents. J Am Acad Dermatol, 2014, 71(2):327-349.