

ORIGINAL ARTICLE

Dead Sea ultraviolet climatotherapy for children with atopic dermatitis

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SUMMARY

Background

Atopic dermatitis (AD) is a common, chronic, and relapsing inflammatory skin disorder. Moderate to severe cases represent an extremely disabling disease, for both children and their parents. Dead Sea climatotherapy (DSC), recognized as a natural treatment for patients with skin diseases, takes advantage of the selectively scattered ultraviolet irradiation (UV) present at the lowest terrestrial site on the earth.

Objectives

To investigate the impact on short-term results of DSC in moderate to severe AD children from the Czech Republic treated 4 weeks at the Deutsches Medizinisches Zentrum (DMZ), Israel, and to correlate their results to the cumulative UVA and UVB irradiation doses received during treatment.

Patients and Methods

Seventy-two patients aged <19 years were divided into three groups and treated in March 2014, October 2014, and March 2015 with gradually increasing sun exposure during 28 consecutive days. Daily and cumulative exposure doses of UVB and UVA were calculated through patients' recorded sun exposure logs. The SCORing Atopic Dermatitis (SCORAD) index was recorded immediately after DSC and 3 months later by the same dermatologist.

Results

Good clinical results were observed in all groups, with overall improvement in SCORAD reaching $87.5 \pm 13.4\%$ and $71.3 \pm 21.3\%$ immediately after DSC and 3 months later, respectively. No side effects were observed during the treatments. Higher cumulative exposure times correlated with better results and enhanced remission.

Conclusion

Dead Sea climatotherapy represents a valuable option for the treatment of AD in children. Medically controlled and prescribed sun exposure seems to directly and positively influence the results obtained.

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Atopic dermatitis (AD) is a common, chronic, and relapsing inflammatory skin disorder, which can be exacerbated by many trigger factors such as psychological stress, changes in season and climate, irritants, allergens, and infections. On the individual level, moderate to severe AD is a physically and socially extremely disabling disease, with significant reduction of both patient's and parent's quality of life. Topical therapy remains the mainstay of treatment among phototherapy and various systemic therapies (1).

The Dead Sea basin is recognized as a natural treatment center for patients with various cutaneous and rheumatic diseases. Psoriasis is the major skin disease treated at the Dead Sea with an 85% success rate after 4 weeks in both adults and children (2–4). The number of publications regarding the treatment of AD at the Dead Sea is significantly lower (5).

The unique climatic conditions at the Dead Sea are due to its latitude and altitude, ca. –420 m below mean sea level (m m.s.l.), the lowest terrestrial site on the earth. They include high barometric pressure and, consequently, an increased partial oxygen pressure, high and stable temperature, low humidity, paucity of rainfall, and a unique composition of the solar spectrum. The solar rays entering the earth's atmosphere must traverse a longer optical path length before being incident on the surface of the Dead Sea basin, viz. it being the lowest terrestrial site. The attenuation of solar rays due to scattering by air molecules, aerosols, and water vapor is inversely proportional to the wavelength raised to a power. As a result, there is a natural wavelength-selective filtration phenomenon of the solar spectrum (6–8).

It was observed that the relative irradiation intensities within the UVB spectrum between erythema and the therapeutic wavelengths are also a function of time of day. This also being a result of the natural wavelength-selective filtration, viz. the erythema wavelength range, is located around 300 nm, whereas the therapeutic range is centered about 311 nm. Therefore, patient sun exposure time intervals should be scheduled for early morning or late afternoon hours when the optical path lengths are longer, that is enhanced selective filtration, in order to reduce their exposure to the deleterious erythema rays. This also avoids the hot midday hours (9).

Natural sun and in particular the composition of the solar spectrum incident at the Dead Sea basin have been proven to be highly effective in suppressing clinical features of psoriasis. While the cardinal effect of this solar climatotherapy involves local immunosuppression of affected lesions, it has been shown that solar rays have, in addition, immunoregulatory effects on

immunologically active circulating blood cells (10). Recently, the induction of regulatory T cells (Tregs) has been suggested as one of the mechanisms mediating the clinical effect of UV treatment (11). Vitamin D produced by sun exposure has also been shown to contribute to the immunological changes present in allergic diseases (12).

Atopic dermatitis patients achieve significant improvement when treated by artificial phototherapy, and moderate to severe cases are commonly treated by this therapeutic option. Sun exposure is often reported as a positive factor of improvement in patients suffering from AD (13).

The Dead Sea water has a unique salt composition and concentration. The total salt content is about 340 g/l, which is about ten times higher than the salt content in the oceans' waters. The salt content is uniquely high in potassium, magnesium, calcium, chlorides, bromides, and various other trace elements. This combination of solar, climatic, and balneo-therapeutic factors is unequaled anywhere else in the world.

In the present paper, we investigate the impact on short-term results of Dead Sea climatotherapy (DSC) in moderate to severe AD children from Czech Republic who spent 4 weeks at the DMZ Medical Center. Climatotherapy treatment utilizes climatic factors present in a specific area, for a pre-determined period of time, under medical supervision. During their stay at the Dead Sea, the AD patients undergo mainly sun exposure following a personnel exposure protocol. It should be noted that atopic dermatitis lesions are often open and bloody, making any contact with salt water extremely painful. Consequently, only few of the young patients experienced Dead Sea baths and only during the third or fourth week of their stay. The length of such baths was recorded in the daily log and was included when determining their daily and cumulative sun exposure doses. The number of patients experiencing Dead Sea baths and their corresponding cumulative sun exposure time was not sufficient to warrant a separate study.

PATIENTS AND METHODS

Our population consisted of Czech patients followed at the University Hospital of Kralovske Vinohrady, Prague, Czech Republic.

Inclusion and exclusion criteria

Male and female ≤ 19 years with diagnosed atopic dermatitis were included in the study. Exclusion criteria included renal failure, known photosensitivity, lupus

erythematosus suspected or diagnosed, tendency to sudden loss of consciousness and/or dizziness, chemotherapy and active malignancy, serious concomitant, chronic disease, and drug abuse.

The patients were selected and assessed regarding their willingness and approval of their parents to participate in the study. Prior to participation, the two Czech principal investigators (AM and PA) obtained written approvals from the hospital ethics committee (Helsinki forms) and other local regulatory bodies as regards the treatment protocol.

Screening was performed at University Hospital of Kralovske Vinohrady, Prague, Czech Republic. A member of the study research team approached individual patients who were potential candidates for participation and explained the purpose, procedures, and intent of the study. Interested parents and patients were invited to join the study and parents were asked to sign a written informed consent prior to initiation of any study-related procedure.

Study procedures

After enrollment and initial screening, patients were randomized into three groups of 24 patients each that were scheduled to undergo climatotherapy at the Dead Sea during March 2014, October 2014, and March 2015. Evaluations were performed for all groups at several stages:

- Time 0 (before Dead Sea climatotherapy) and Time 1 (immediately after Dead Sea climatotherapy) at the DMZ Medical Center, in Israel.
- Time 3 (3 months after the initiation of the DSC treatment) at the University Hospital of Kralovske Vinohrady, Prague, Czech Republic.

The three groups ($n = 72$) received sun exposure at the Lot Spa Hotel, Israel, following a personal protocol. All patients in the group were exposed to Dead Sea sun (after examination and approval of the physician in charge) twice a day (morning and afternoon) over a period of 28 days wearing bathing suits only. The sun exposure protocol was divided into two sessions during the day, the morning, and the afternoon, thus avoiding hours in which UV irradiation is intense. The patients were initially exposed twice daily for 10, 15, or 20 min, according to their skin photo-type (skin types II, III, and IV). Increments of ~20% were done every 3 days up to a maximum of twice a day 60-min sun exposures. During the treatment, regular consultations and controls were scheduled, and the patients used only emollients

and creams without any active ingredient. Children were not allowed outdoors during midday hours. They were allowed to perform outdoor activities, after application of sun blockers creams, at other times of the day. It should be noted, nevertheless, erythema, viz. incipient redness, was observed in some patients, at different times of their treatment and the physicians adapted the sun exposure protocol accordingly. These events were treated by simple topical treatment and not considered as a side effect, as long as the treatment was not suspended.

The patients/parents were asked to keep a log of their daily sun exposure time intervals so that the daily and cumulative exposure dose of UVB/UVA per patient could be calculated in units of standard erythema dose (SED) and W/m^2 for UVB and UVA, respectively.

Data

The demographic data included gender and age (Tables 1 and 2), number of years since the diagnosis of AD (age of disease), and familial status regarding skin disease. The clinical data collected at the three selected times (T0, T1, and T3) included SCORAD (SCORing Atopic Dermatitis) (14) calculated after examination by the same physician, questionnaire on the quality of life for both children and parents, concomitant and sporadic treatment received.

The average duration of the disease was 7 years for all patients involved in the study and for each of the three groups. The incidence of family history of AD was found in 33% of the study population, without differences between groups (data not shown).

The UVB and UVA irradiation intensities have been monitored continuously at a meteorological station located on the western shore of the Dead Sea, at Neve Zohar, approximately 6 km from Ein Bokek, since January 1995. The site parameters are as follows: latitude $31^{\circ}12'N$; longitude $35^{\circ}22'E$; altitude (m m.s.l.) -375 .

The instrumentation utilized to measure the UV irradiation has been described in detail in previous publications (6–8). In the present study, the units for measuring UVB intensity have been revised. Viz., the UVB meter utilizes a detector with a spectral response, which mirrors the erythema action spectra (15), and the irradiation intensity is measured in minimum erythema dose per hour (MED/h). One MED/h is defined as a dose, which causes incipient redness of skin type 2 after 1 h of irradiation and has been defined for this instrument as 21 mJ/cm^2 . This is equivalent to 2.1 SED (standard erythema dose), which is defined as

Table 1. Composition according to groups

Session	Patients	Sex (female/male)	Average age (year)	Age range (year)
March 2014	17	8/9	11.6 ± 5.0 (%Cv = 42.9)	17.8–2.4
October 2014	24	15/9	9.6 ± 5.4 (%Cv = 55.8)	18.4–2.6
March 2015	22	15/7	9.8 ± 4.4 (%Cv = 45.4)	18.7–3.6
All groups	63	38/25	10.2 ± 5.0 (%Cv = 48.5)	18.7–2.4

Table 2. Composition according to skin type

Skin type	Patients	Sex (female/male)	Average age (year)	Age range (year)
Skin type II	26	14/12	9.5 ± 4.8 (%Cv = 50.8)	17.8–2.4
Skin type III	37	24/13	10.4 ± 5.1 (%Cv = 49.0)	18.7–2.6

100 J/m² = 10 mJ/cm² (16) and is independent of skin type. It should be emphasized that the UVB and UVA irradiation intensities measured are those incident on a horizontal surface and may be assumed to be the maximum possible dose received by an ambulatory or stationary body with a non-planar contour. It should also be noted that a relatively high fraction of the UV irradiance at the Dead Sea is diffuse; consequently, the position of the body relative to the sun is of lesser importance (9).

RESULTS

The efficacy of the DSC was determined by the changes in the individual patients' SCORAD upon arrival at the Dead Sea and that after 28 days of DSC, reported as percent of improvement. The daily exposure doses of UVA and UVB received by each patient were calculated by cross-referencing the daily exposure time intervals recorded in their individual logs with the concurrently measured UVA and UVB irradiation intensities at the Neve Zohar meteorological station.

Cumulative values per group or skin type for the UVA and UVB doses and exposure time as well as the average improvement achieved after 28 days of DSC treatment and that 3 months after the conclusion of the DSC treatment are shown in Tables 3 and 4. Average values are reported in the tables together with their respective standard deviations and percent coefficient of variation (%Cv). The coefficient of variation is defined as the ratio of the standard deviation to the average value and is used to indicate the degree of spread of the individual values in the database.

It should be noted that two patients with skin type IV have been excluded for this analysis. Also, seven patients

failed to appear for their 3-month control examination and therefore were also excluded from our study analysis. Consequently, the results reported are based upon 63 patients.

DISCUSSION

We observed excellent results for the three groups of patients after Dead Sea climatotherapy and sustained good results after 3 months. The overall average improvement in SCORAD immediately after DSC for 63 patients was 87.5 ± 13.4% with a relatively low Cv of 15.3%. Three months later, the average SCORAD index was still low, viz. with an overall average improvement of 71.3 ± 21.3% (Table 3).

Serious side effects were not observed during the 4-week stay for all groups. Simple polymorphic light eruptions and sometimes increased itch were present, a common side effect of DSC (17). The relatively slow increase in sun exposure times and the close follow-up of the children by parents, monitors, and medical team during the stay assured a good compliance to the scheduled treatments.

Of course, the long-term side effects are much more noteworthy. Even if 'a carcinogenic risk related to UV radiation has not been excluded', we can stipulate, while comparing the doses of UV radiation delivered by artificial phototherapy to children, and the lack of any short-term side effect, that we do not increase significantly the risk of skin cancer in our patients. Moreover, the strict daily control of the sun exposure during the stay prevents very efficiently any sunburn, which remains a central event increasing the skin cancer risk.

Cumulative irradiation doses are scarcely reported regarding phototherapy for AD and even though some

Table 3. Results according to groups

Session	Patients	Average UVA (W/m ²)	Average UVB (SED)	Cumulative exposure time (h)	Improvement* (%)	Improvement after 3 months† (%)
March 2014	17	847.96 ± 241.66 (%Cv = 28.5)	93.22 ± 25.39 (%Cv = 27.2)	31.2 ± 8.2 (%Cv = 26.2)	84.2 ± 17.2 (%Cv = 20.4)	66.4 ± 21.5 (%Cv = 32.4)
October 2014	24	847.34 ± 73.47 (%Cv = 8.7)	91.79 ± 8.57 (%Cv = 9.3)	39.4 ± 3.3 (%Cv = 8.4)	84.5 ± 12.8 (%Cv = 15.2)	64.0 ± 17.8 (%Cv = 27.8)
March 2015	22	1105.87 ± 68.77 (%Cv = 6.2)	138.66 ± 7.94 (%Cv = 5.7)	38.6 ± 2.5 (%Cv = 6.5)	93.2 ± 8.4 (%Cv = 9.0)	83.5 ± 20.3 (%Cv = 24.3)
All groups	63	937.79 ± 184.61 (%Cv = 19.7)	108.54 ± 26.64 (%Cv = 24.5)	36.7 ± 6.1 (%Cv = 16.7)	87.5 ± 13.4 (%Cv = 15.3)	71.3 ± 21.3 (%Cv = 29.9)

*Improvement = (SCORAD_{arrival} - SCORAD_{departure})/SCORAD_{arrival}•†Improvement = (SCORAD_{arrival} - SCORAD_{after 3 months})/SCORAD_{arrival}•**Table 4.** Results according to skin type

Skin type	Patients	Average UVA (W/m ²)	Average UVB (SED)	Cumulative exposure time (h)	Improvement* (%)	Improvement after 3 months† (%)
Skin type II	25	941.04 ± 245.06 (%Cv = 26.0)	111.09 ± 32.42 (%Cv = 29.2)	33.5 ± 7.8 (%Cv = 23.3)	86.3 ± 14.9 (%Cv = 17.2)	72.0 ± 23.9 (%Cv = 33.2)
Skin type III	37	925.74 ± 146.61 (%Cv = 15.8)	105.00 ± 22.81 (%Cv = 21.7)	38.7 ± 4.1 (%Cv = 10.7)	88.0 ± 12.5 (%Cv = 14.2)	69.4 ± 21.3 (%Cv = 30.7)

*Improvement = (SCORAD_{arrival} - SCORAD_{departure})/SCORAD_{arrival}•†Improvement = (SCORAD_{arrival} - SCORAD_{after 3 months})/SCORAD_{arrival}•

suggestions have been proposed, there is still a lack of consensus about them (18, 19). When compared to artificial UV exposure, the UVB doses reached by our young patients in this study are lower than the classical ones in adults (161 SED) but higher than the ones proposed by Wulf and Bech-Thomsen (20). Since narrow-band UVB (NB-UVB) treatment became the option of choice for many skin conditions including AD (21), it is difficult to compare cumulative doses between artificial and natural UVB doses. The same remark can be done regarding UVA doses, as UVA is never used solely but only with prior additional psoralen intake, orally or in bath or together with NB-UVB (22).

We found in this study some differences between the three groups regarding their results and their UV doses. If the average improvements for the March 2014 and October 2014 groups are essentially the same (exceeding 84%), for the March 2015 group the average is approximately 10% higher, at 93.2%. It is interesting to note, as a possible explanation, that the average cumulative doses of UVA and UVB for the March 2015 group are significantly higher than that for the other two groups, by about 30% for UVA and almost 50% for UVB.

The average daily UVA and UVB irradiation intensities during the month of March exceed usually that for the month October by approximately 10%. This may explain the observed difference in DSC treatment efficacy between March 2015 and October 2014 groups,

since the cumulative exposure times are similar. But the observed difference in treatment efficacy between March 2015 and March 2014 groups may be again explained by the significant difference in their cumulative sun exposure times, viz. exceeding 20%.

In this study, we found that treatment efficacy was essentially the same for both skin types II and III, exceeding 86% SCORAD improvement (Table 4).

We found it of interest to estimate the threshold or minimum cumulative doses of UVA and UVB required to achieving a SCORAD improvement exceeding 80% upon completion of the 28 day DSC treatment. In order to arrive at such values, the SCORAD improvement (in percent) of the individual patients was plotted as a function of their cumulative doses of UVA and UVB (Figs 1 and 2, respectively). It is observed from these figures that a cumulative UVA dose exceeding 800 W/m² and a cumulative UVB dose exceeding 80 SEDs will, in most cases, achieve at least an 80% improvement.

Another significant result of this study is the observed high values for the average SCORAD improvement 3 months after completion of DSC, as measured by the dermatologists in Czech Republic. The average SCORAD improvement for all patients 3 months later exceeded 70%, showing a decrease of <20% during this period (Table 3). The average SCORAD improvement after 3 months was about 20% lower for the March 2014 and October 2014 groups and only 10% lower for March

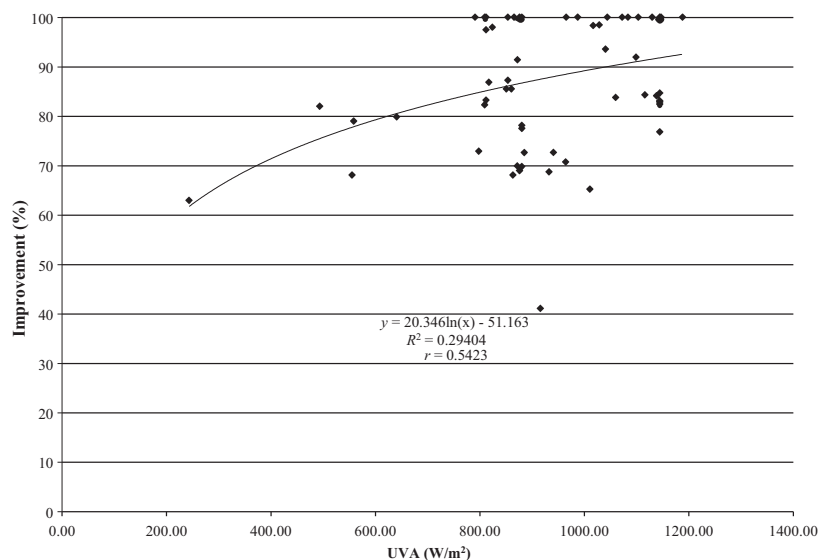


Fig. 1. SCORing Atopic Dermatitis (SCORAD) improvement (in percent) of the individual patients as a function of their cumulative dose of UVA.

2015 group, when compared to that measured after DSC (65% and 83.5%, respectively).

The SCORAD 75 percentages (23), which allow a better overview of the study results, achieved very high values after DSC, that is 70.6, 66.7, and 100 for the groups of March 2014, October 2014, and March 2015, respectively, and decreased to 47.1, 25.0, and 72.2 after 3 months. This emphasizes the differences between the three groups and again highlights that the March 2015 group, with the higher cumulative UV doses, as the most successful one (Table 5).

The same analysis was performed with regard to skin type and it was found that for both skin types II and III, the average SCORAD improvement values decreased by <20% after 3 months (Table 6).

CONCLUSION

The impressive results obtained by DSC in AD patients can be explained by the following: most of the potential triggers and provocative factors are avoided or reduced during this treatment; high cumulative doses of UV can be delivered easily and safely; inducing positive changes in a plethora of cells through immediate and delayed effects (13) and fruitful contacts between patient, parents, and medical team allows for a better control of the disease.

Climatotherapy at the Dead Sea appears as a potent therapeutic option for children suffering from AD. Our findings show a clear correlation between UV cumulative doses and results, while increased amounts are associated with better outcome. However, after reaching an

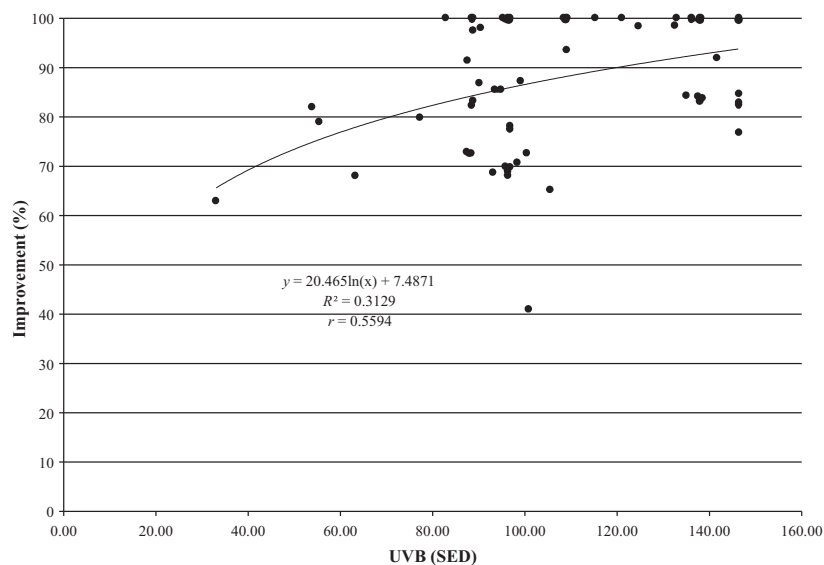


Fig. 2. SCORing Atopic Dermatitis (SCORAD) improvement (in percent) of the individual patients as a function of their cumulative dose of UVB.

Table 5. SCORing Atopic Dermatitis (SCORAD) 75 according to groups

Session	Patients	SCORAD 75 (%) after DSC	SCORAD 75 (%) after 3 months
March 2014	17	70.6	47.1
October 2014	24	66.7	25.0
March 2015	22	100	72.7
All groups	63	79.4	47.6

Table 6. SCORing Atopic Dermatitis (SCORAD) 75 according to skin type

Skin type	Patients	SCORAD 75 (%) after DSC	SCORAD 75 (%) after 3 months
Skin type II	25	80.0	50.0
Skin type III	37	78.4	40.5

optimal cumulative dose for significant improvement (>80%), any further increase in cumulative dose had little positive effect on SCORAD values. This study should encourage physicians to use this option and to propose more frequently phototherapy regimens for their young patients.

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