

Climatotherapy at the Dead Sea: An Effective Treatment Modality for Atopic Dermatitis With Significant Positive Impact on Quality of Life

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Background: Atopic dermatitis (AD) has an appreciable effect on quality of life. Improving the quality of life of AD patients is a priority.

Objective: This study aimed to evaluate the impact of Dead Sea climatotherapy (DSC) as a treatment of AD and its influence on the quality of life of these patients.

Methods: Forty-nine adult patients with AD treated during the years 2009–2010 at the Deutsches Medizinisches Zentrum Medical Center participated in this prospective study. Climatotherapy was administered in accordance with a computer-designed protocol and included gradually increased sun exposure after a sea bath. Severity of AD was evaluated using the Scoring Atopic Dermatitis (SCORAD) index. Patient quality of life was evaluated using Skindex-29. Statistical analysis was performed using a paired *t* test and Wilcoxon and Mann-Whitney *U* tests.

Results: After treatment, the mean SCORAD value improved by 39 points ($P < 0.001$). The overall Skindex-29 score improved by a mean value of 33 points ($P < 0.001$). The pretreatment SCORAD, duration of AD, and maximal daily sun exposure predicted the posttreatment SCORAD values. Pretreatment Skindex-29 and patient age predicted the post-treatment Skindex-29 in a multiple linear regression model.

Conclusions: Dead Sea climatotherapy provides an effective treatment modality for AD by improving the patient's skin condition and quality of life.

ATOPIC DERMATITIS (AD) is a chronic inflammatory skin disease hypothesized to be the product of complex interactions between the host's environment, susceptibility genes, skin barrier dysfunction, and immune system dysregulation.^{1,2} The disease is characterized by pruritus, eczematous lesions, xerosis, and lichenification and bares an alternating relapse and flare-up course.^{1–3} Although AD usually presents during early infancy and up to the age of 5 years, an adult-onset variant is also well recognized.¹ During the last 3 decades, the prevalence of AD in developed and industrialized countries has more than doubled and, in some locations, even tripled, with similar race distribu-

tions and a slight female predominance. Atopic dermatitis is now recognized as the most common childhood skin disorder with a 10% to 20% prevalence among children and a 1% to 3% prevalence in adults.^{3–5}

In light of the chronic nature of the disease, the need for long-term treatment, and the necessity for frequent medical monitoring, AD can significantly impact morbidity and quality of life (QOL). Patients, particularly children, may also experience sleep disturbances, social stigma, loss of school/work days, irritability, daytime tiredness, dependence, fearfulness, and mood changes.^{3,6}

An important part of the overall treatment includes flare-up prevention, with emollients, creams, lubricants, and ointments often being the mainstay of the maintenance therapy.⁷ Other preventive strategies include shortening showers, using warm water, using soap-free preparations, avoiding wearing wool garments, and reducing emotional stress and exposure to triggers and other irritants.

Topical corticoid steroids with variable potency are the cornerstone of treatment in short-term exacerbations.¹ However, prolonged topical application of steroids is associated with steroid rosacea, skin atrophy, striae, acne, purpura, glaucoma, development of allergies, alteration of immune system function, and, more rarely, systemic adverse effects.⁸ As a consequence, corticoid steroid applications should ideally be prescribed for the short-term and restricted to particular and limited areas of the body.

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An alternative therapy to topical steroids is provided by the nonsteroidal immunomodulators calcineurin inhibitors pimecrolimus and tacrolimus,⁹ whereas ultraviolet (UV) phototherapy is also considered as a treatment option for AD.¹⁰ Antihistamines do not usually constitute an important therapeutic aspect and have not been shown to alter the course of the disease.³ Additional systemic therapies for AD include antibiotics, cyclosporine, and other immunosuppressive agents such as mycophenolate mofetil, azathioprine, and methotrexate.¹

Dead Sea climatotherapy (DSC) has been proven to have an excellent healing effect in the treatment of psoriasis.¹¹ Patients with AD have been successfully treated at the Dead Sea since the 1950s.¹² The treatment mainly consists of bathing in the sea (balneotherapy) and exposure to UV natural radiation (phototherapy). Symptom relief comes within 3 to 4 weeks and can last several months. In a previously published study, DSC was shown to be a cost-effective method for AD management of European patients.¹³ An additional German study found that it is possible to treat AD at locations remote from the Dead Sea, provided that patients are immersed in a bath containing Dead Sea salts and are exposed to UV radiation several times a week. The authors demonstrated that the efficacy of this artificial alternative is less impressive than the success rates reported for natural therapy and much more expensive,¹⁴ although a head-to-head comparison has not been conducted, to the best of our knowledge.

The primary objective of the current study was to determine DSC effectiveness on AD by calculating the Scoring Atopic Dermatitis (SCORAD) index¹⁵ before and after DSC. The secondary objective was to evaluate the efficacy of DSC on the QOL of AD patients, using the Skindex-29 questionnaire. To the best of our knowledge, such a prospective study with objective measures of QOL of AD patients treated at the Dead Sea has yet to be carried out.

METHODS

Our study included 49 AD patients in whom AD diagnosis was established using Hanifin and Rajka's criteria.¹⁶ Patients were treated at the Deutsches Medizinisches Zentrum (DMZ) Medical Center, located in the Lot Spa Hotel, Ein Bokek, at the Dead Sea, Israel, from June 2009 to July 2010. They were referred by their health maintenance organization after conventional treatment failed or because of good results during previous stays. All patients underwent a dermatological examination before referral. The dermatologist at the Dead Sea clinic confirmed the diagnosis and was able to modify it as needed.

At the first physician's visit and before entering the study, study goals were explained to the patients, and signed informed consent was received. A preliminary questionnaire (Skindex-29) was filled out and returned to the study team. At the end of stay, after the last physician's visit, the patient received a second questionnaire, which was to be returned before departure. The study procedures followed were approved by the institutional ethical

committee review board of the Hadassah – Hebrew University Medical Center.

Sixty-one patients with AD were eligible for the study. However, 12 patients failed to return either their informed consent or their questionnaires and were therefore excluded. The final study population included 49 patients (80.3% response rate).

Treatment at the DMZ Medical Center included the following:

1. Evaluation by a dermatologist: medical history, sociodemographic details, physical examination, and follow-up during the course of treatment.
2. Personalized climatotherapy program, with gradually increasing sun exposure. The protocol was intended to provide each individual patient with calculated therapeutic UVB radiation doses, while taking into consideration the patient's skin phototype and minimal erythema dose.
3. The attending physician introduced sea bathing for 20 minutes, twice a day, to the treatment protocol, if the patient's skin was free of excoriations. If excoriations were present, we recommended postponing initial contact with Dead Sea water until after the skin condition improved. Improvement was usually seen within a matter of days, at which point the bathing process began.
4. Local treatments: emollients and/or cold and basic creams specifically prescribed to each patient according to his/her skin condition. Steroids were not used during the stay.
5. Guidance by a nurse.
6. Living in a hotel provided the ideal secluded and stress-free environment by relieving patients of any cleaning, cooking, or household responsibilities. In addition, the daily schedule was quite relaxed with very few required activities. Children were supervised by their parents and usually enjoyed a very pleasant stay. Social contacts with other patients were encouraged to promote self-esteem but were never deemed mandatory. The only stress-inducing situations were the clinic appointments and strict treatment guidelines that dictated the duration of sea and sun exposure. In addition, the use of creams, emollients, and lotions was largely controlled by the staff.

The desert and surrounding ecosystem were studied with regard to the evolution of chronic disease.¹⁷ Specifically, the climatic and ecologic conditions at the Dead Sea work synergistically to produce an ecosystem which is dry, unpolluted, mold and allergen free, and with oxygen-rich air in high and stable temperatures.

Previous treatment received at home and the degree of skin involvement were assessed and recorded on arrival at the DMZ Medical Center by a dermatologist. Severity of disease, defined by the SCORAD index, was recorded for patients both on arrival and again (by the same dermatologist) at the end of treatment.

Patient QOL was evaluated using Skindex-29, a previously tested and validated questionnaire, specifically designed to assess QOL in dermatological patients.^{18,19} It consists of 3 scales assessing areas considered essential in QOL evaluation: burden of symptoms, functioning, and emotional state. Patients answered the 30 questions referring to the previous 4-week period, on a 5-point scale from "never" (= 0) to "all the time" (= 4). The score

of each scale was normalized to a scale of 0 to 100 (as a percentage of the maximum score obtainable on that scale). Higher scores reflected a worse QOL.

Our a priori hypothesis was that SCORAD values will decrease by 10 points, from 30 (15) to 20 (15), and that Skindex-29 will similarly decrease from 60 (15) to 50 (15). The sample size needed with a power of 90%, and a significance level of 5% was seen in at least 48 patients.

Baseline characteristics are described using percentages for categorical variables and means (SD) for continuous variables. SCORAD and Skindex-29 scores before and after treatment were compared using Wilcoxon signed-rank tests in all patients, as well as within-patient subgroups. Two outcomes were defined: "SCORAD 75" (improvement of 75% or more in SCORAD, similar to the PASI-75 used for psoriasis) and "SKINDEX 50" (improvement of 50% or more in Skindex-29). The percentages achieved within each outcome were compared using χ^2 tests. Multiple linear regression models were used for multivariate analysis of posttreatment SCORAD and Skindex-29.

RESULTS

A total of 49 patients treated at the DMZ Medical Center for climatotherapy were included in this study. Patients' main characteristics are summarized in Table 1. Mean age was 40.6 years and 51% of the patients were males. Slightly more than 57% (57.1%) of the patients declared having a positive family history of atopic disease. Most patients were treated with topical steroids before arriving to the Dead Sea. The mean onset of disease was at age 8.8 years, and the mean duration of the disease in our population was 31.3 years. Many patients (55.1%) were previously treated at the Dead Sea, and the mean number of previous Dead Sea treatments was 3.2. The Dead Sea protocol delivered, on average, a UVB dose of 1.664 (1.120) J/m², with a mean maximum daily sun exposure of 3.2 (1.6) hours. The mean duration of stay was 31 days (Table 1).

The SCORAD index improved by a mean value of 39 points ($P < 0.001$) from time of arrival to departure (50–11 points; Table 2). Mean SCORAD improvement calculated as the difference between arrival and departure values divided by the arrival value reached 70%. Remarkable improvement was also found for the overall Skindex-29 score. The mean normalized Skindex-29 dropped from 63 to 30—a decrease of 33 points ($P < 0.001$; Table 3). Mean Skindex-29 improvement reached 36%. Significant improvement was noted in all 3 Skindex scales: burden of symptoms (73 vs 33), functioning (59 vs 30), and emotional state (61 vs 31) ($P < 0.001$). A similar degree of improvement was seen in various subgroups of age, sex, onset of disease, and disease duration and previous experience with DSC (Tables 2 and 3). Similarly, no differences were found in the proportion of patients achieving a 75% or higher improvement in SCORAD (SCORAD-75) or a 50% or higher improvement in Skindex-29 (SKINDEX-50). Family

TABLE 1. Baseline Characteristics of the Study Participants (N = 49)

Variable	
Sex, n (%)	
Male	25 (51.0)
Female	24 (49.0)
Age, y	
Mean (SD)	40.6 (12.4)
Median	41
Range	18–71
Family history of AD, n (%)	28 (57.1)
Previous therapy,* n (%)	
Topical steroids	37 (75.5)
Systemic therapy	4 (8.2)
Previous DSC	27 (55.1)
Age at AD onset, y	
Mean (SD)	8.8 (13.9)
Median	1
Range	0–60
AD duration, y	
Mean (SD)	31.3 (13.6)
Median	33
Range	3–59
DSC duration, d	
Mean (SD)	31.5 (7.5)
Median	28
Range	21–42
Total UVB dose, J/m ²	
Mean (SD)	1.664 (1.120)
Median	1450
Range	0–4865
Maximal daily sun exposure, h	
Mean (SD)	3.2 (1.6)
Median	3
Range	0–7

*Some patients had more than 1 previous treatment.

history of AD was negatively associated with SCORAD-75 but not with SKINDEX-50 (Tables 2 and 3).

In a multivariate analysis, the pretreatment SCORAD, maximum daily sun exposure given to the patient, and duration of AD were found to be associated with the posttreatment SCORAD index. Only age and pretreatment Skindex-29 were associated with posttreatment Skindex-29 (Table 4).

DISCUSSION

Atopic dermatitis is a chronic pruritic skin disease characterized by intense itching, dry skin, redness, and inflammation. The disease can lead to personal, familial, and social dysfunction. Both pediatric and adult patients report anxiety disorders, stigmatization, social isolation, sleep disturbances, emotional instability, and depression associated with the disease.^{20–22} Psychological stress and AD symptoms seem to form a vicious cycle.^{23–25}

TABLE 2. SCORAD Values Before and After Therapy and the Proportion Achieving a 75% or Higher Improvement in SCORAD ("SCORAD-75")

Subgroup	SCORAD Before, Mean (SD)	SCORAD After, Mean (SD)	P (After vs Before)	SCORAD-75, n (%)	P (Between Categories)
All	50 (22)	11 (11)	<0.001	34 (69.4)	—
Sex					
Male	53 (23)	14 (13)	<0.001	16 (64.0)	0.404
Female	48 (21)	8 (6)	<0.001	18 (75.0)	
Age					
≤41 y	48 (18)	9 (6)	<0.001	17 (70.8)	0.830
>41 y	53 (25)	13 (14)	<0.001	17 (68.0)	
Duration					
≤31 y	51 (21)	10 (6)	<0.001	17 (65.4)	0.518
>31 y	50 (23)	12 (14)	<0.001	17 (73.9)	
Onset					
≤1 y	54 (20)	13 (13)	<0.001	18 (72.0)	0.686
>1 y	46 (23)	9 (7)	<0.001	16 (66.7)	
Family history					
No	54 (20)	9 (6)	<0.001	18 (85.7)	0.032
Yes	48 (23)	13 (13)	<0.001	16 (57.1)	
Previous DSC					
No	52 (21)	11 (7)	<0.001	15 (68.2)	0.869
Yes	49 (23)	11 (13)	<0.001	19 (70.4)	

It was previously shown that there is a correlation between disease severity and QOL such that the patient's QOL and his/her family's QOL were significantly more disturbed with increasing severity of the disease.^{26,27} In light of these data, improving the QOL of AD patients is of paramount importance and should influence treatment choice.

There are a wide range of treatments for AD including topical, systemic, and phototherapy treatment modalities. Nevertheless, complementary and alternative therapies are commonly used due to concerns regarding potential adverse effects of conventional therapies, along with frustration concerning the lack of response from prescribed medications.²⁸

TABLE 3. Skindex-29 Scores Before and After Therapy and the Proportion Achieving 50% or Higher Improvement in Skindex-29 ("SKINDEX-50")

Subgroup	Skindex-29 Before, Mean (SD)	Skindex-29 After, Mean (SD)	P (After vs Before)	SKINDEX-50, n (%)	P (Between Categories)
All	63 (15)	30 (21)	<0.001	17 (34.7)	—
Sex					
Male	61 (15)	34 (18)	<0.001	6 (24.0)	0.108
Female	65 (14)	27 (23)	<0.001	11 (45.8)	
Age					
<41 y	63 (13)	27 (15)	<0.001	9 (37.5)	0.686
>41 y	63 (16)	34 (25)	<0.001	8 (32.0)	
Duration					
<31 y	63 (15)	29 (18)	<0.001	8 (30.8)	0.539
>31 y	63 (14)	32 (25)	<0.001	9 (39.1)	
Onset					
≤1 y	64 (15)	32 (23)	<0.001	7 (28.0)	0.315
>1 y	62 (15)	29 (19)	<0.001	10 (41.7)	
Family history					
No	59 (15)	28 (20)	<0.001	6 (28.6)	0.436
Yes	66 (14)	33 (22)	<0.001	11 (39.3)	
Previous DSC					
No	63 (15)	28 (18)	<0.001	8 (36.4)	0.825
Yes	63 (15)	32 (23)	<0.001	9 (33.3)	

TABLE 4. A Multivariate Linear Regression Model for Posttreatment SCORAD and Skindex-29

Variable	B	P
Model for posttreatment SCORAD		
Constant	3.46	—
Pretreatment SCORAD (for each additional point)	0.21	0.001
Duration of AD (for each additional year)	0.19	0.039
Maximal daily sun exposure (for each additional hour)	−2.80	0.001
Model for posttreatment Skindex-29		
Constant	−33.02	—
Pretreatment Skindex-29 (for each additional point)	0.66	0.001
Age (for each additional year)	0.54	0.013

B represents the change in the dependent variables (posttreatment SCORAD and Skindex-29) for every unit of change in the independent variable, if all other variables in the model remain unchanged.

P values represent the probability that the association between each independent variable and the dependent variable are due to chance.

Ultraviolet B phototherapy for AD is a useful adjunctive modality in the treatment of chronic recalcitrant cases.²⁹ The DMZ Clinic was the first to document the successful treatment of this disease at the Dead Sea in 1993, correlating the results to the effects of natural UVB phototherapy.³⁰ However, climatotherapy at the Dead Sea is not new. It was first used some 40 years ago, mostly for psoriasis treatment, and has been hailed as a very effective method of treatment.¹¹

Dead Sea climatotherapy has many advantages in the treatment of chronic skin conditions. This treatment modality is relatively safe, induces long-term results, and does not necessitate hospitalization.³¹ Well-known drawbacks of the modality include distance from home, cost (not always covered by medical insurance), and the relatively long period necessary for the disease to clear up.

The effectiveness of salt water baths and subsequent selective UV phototherapy in AD outside the Dead Sea was previously demonstrated by German investigators^{14,32} with one of the studies¹⁴ using the SCORAD index. An additional study of AD patients treated at the Dead Sea, which also demonstrated disease improvement, did not use a valid scoring system.¹³ We present the first prospective study dealing with QOL of AD patients treated with DSC and using the well-validated scoring systems SCORAD and Skindex-29, for assessing DSC effectiveness in AD.

The mean duration of AD in our group of patients was more than 30 years. The patients experienced extensive disease, as presented by their relatively high SCORAD values on arrival at the Dead Sea. At the end of their stay, the overall Skindex-29 score as well as their disease severity was significantly improved. Although approximately half of the patients had previous DSC therapy, selection bias cannot account for the degree of improvement seen because patients without previous DSC experience had similar degrees of improvement both for SCORAD (Table 2) and Skindex-29 (Table 3).

In our protocol, the use of topical corticosteroids was not allowed. This decision was made based on our wishes to significantly alter the patients' regular, and often unsuccessful, treatment regimen. Our results confirm the reported positive outcomes of phototherapy by reduction of use of topical corticosteroids.³³

In a previous study dealing with DSC for AD, Harari et al¹³ showed that contrary to psoriasis, where 4 weeks is an optimal period for DSC treatment, for AD patients stays of up to 6 weeks can achieve better results. This is consistent with our current observation that improvement of disease severity is correlated with a cumulative UVB dose.

Corresponding improvement in both indices of disease severity (SCORAD index) and QOL (Skindex-29 score) is not surprising, as there is a strong relationship between disease severity and QOL. Therefore, improving QOL is expected to lead to skin condition improvement and vice versa.

The strengths of the present study lie in its ability to demonstrate high efficacy of DSC for patients with AD and to describe changes in QOL among AD patients using the Skindex-29 score. However, the present study has some potential limitations. First, the small number of participants ($n = 49$) might have reduced our ability to identify covariates associated with the outcome. Second, to fully evaluate QOL, long-term follow-up of patients is needed. This was not possible within the framework of our present study because patients had left Israel and returned to their country of origin. Finally, one can evoke a potential bias in evaluation of QOL scores as the forms were completed while the patients were essentially "on vacation," without the stressful factors of normal life. Determination of QOL at the end of such a stay could be overestimated. The study was an open-label single-arm study without a control arm. Regression toward the mean cannot be ruled out as a possible explanation to the study's findings, although the remarkable improvement noted cannot be attributed solely to this phenomenon. The intervention included in the present study is a complex one, with multiple components including reduced stress, UVB, salt water immersion, individual physician, nurse care, and others. Therefore, this study was unable to determine which of these aspects is most important to the success seen. It is unknown whether any of these components alone may be providing the benefit or whether benefits can only be seen when all are performed together. Studies that control for the various factors would help to narrow down the most important components of the intervention.

CONCLUSIONS

Dead Sea climatotherapy seems to be an effective therapeutic modality for adult patients experiencing AD. The present study confirms the positive effects of this natural balneophototherapy by demonstrating the significant changes in the QOL of patients, measured through the Skindex-29 score. Follow-up studies are necessary to define the magnitude of the long-term effects of this treatment.

REFERENCES

1. Leung DY, Eichenfield LF, Boguniewicz M. Chapter 14. Atopic dermatitis (atopic eczema). In: Wolff K, Goldsmith LA, Katz SI, Gilchrist B, Paller AS, Leffell DJ, eds. *Fitzpatrick's Dermatology in General Medicine*. 7th ed. New York, NY: McGraw Hill Co, Inc; 2008.
2. Leung DY, Boguniewicz M, Howell MD, et al. New insights into atopic dermatitis. *J Clin Invest* 2004;113:651–657.
3. Buys LM. Treatment options for atopic dermatitis. *Am Fam Physician* 2007;75:523–528.
4. Williams H, Robertson C, Stewart A, et al. Worldwide variations in the prevalence of symptoms of atopic eczema in the International Study of Asthma and Allergies in Childhood. *J Allergy Clin Immunol* 1999;103:125–128.
5. Larsen FS, Hanifin JM. Epidemiology of atopic dermatitis. *Immunol Allergy Clin North Am* 2002;22:1–24.
6. Daud LR, Garralda ME, David TJ. Psychosocial adjustment in preschool children with atopic eczema. *Arch Dis Child* 1993;69:670–676.
7. Ellis C, Luger T, Abeck D, et al. International Consensus Conference on Atopic Dermatitis II (ICCAD II): clinical update and current treatment strategies. *Br J Dermatol* 2003;148:3–10.
8. Hengge UR, Ruzicka T, Schwartz RA, et al. Adverse effects of topical glucocorticosteroids. *J Am Acad Dermatol* 2006;54:1–15.
9. Hultsch T, Kapp A, Spergel J. Immunomodulation and safety of topical calcineurin inhibitors for the treatment of atopic dermatitis. *Dermatology* 2005;211:174–187.
10. Gambichler T, Breukmann E, Boms S, et al. Narrowband UVB phototherapy in skin conditions beyond psoriasis. *J Am Acad Dermatol* 2005;52:660–670.
11. Harari M, Novack L, Barth J, et al. The percentage of patients achieving PASI 75 after 1 month and remission time after climatotherapy at the Dead Sea. *Int J Dermatol* 2007;46:1087–1091.
12. Dostrovsky A, Sagher F. Preliminary report: the therapeutic effect of the hot springs of Zohar (Dead Sea) on some skin diseases [in Hebrew]. *Harefuah* 1959;57:143–145.
13. Harari M, Shani J, Seidl V, et al. Climatotherapy of atopic dermatitis at the Dead Sea: demographic evaluation and cost-effectiveness. *Int J Dermatol* 2000;39:59–69.
14. Schiffner R, Schiffner-Rohe J, Gerstenhauer M, et al. Dead Sea treatment—principle for outpatient use in atopic dermatitis: safety and efficacy of synchronous balneophototherapy using narrowband UVB and bathing in Dead Sea salt solution. *Eur J Dermatol* 2002;12:543–548.
15. European Task Force on Atopic Dermatitis. Severity scoring of atopic dermatitis: the SCORAD index. *Dermatology* 1993;186:23–31.
16. Hanifin JM, Rakja G. Diagnostic features of atopic dermatitis. *Acta Dermatol Venereol* 1980;92:44–47.
17. Carpio-Obeso MP, Shorr M, Valdez-Salas B. Desert ecosystems: similarities, characteristics, and health benefits. *Rev Environ Health* 1999;14(4):257–267.
18. Chren MM, Lasek RJ, Quinn LM, et al. Skindex, a quality-of-life measure for patients with skin diseases: reliability, validity and responsiveness. *J Invest Dermatol* 1996;107:707–713.
19. Chren MM, Lasek RJ, Flocke SA, et al. Improved discriminative and evaluative capability of a refined version of Skindex, a quality-of-life instrument for patients with skin diseases. *Arch Dermatol* 1997;133:1433–1440.
20. Buske-Kirschbaum A, Geiben A, Hellhammer D. Psychobiological aspects of atopic dermatitis: an overview. *Psychother Psychosom* 2001;70:6–16.
21. Howlett S. Emotional dysfunction, child-family relationships and childhood atopic dermatitis. *Br J Dermatol* 1999;140:381–384.
22. Linnet J, Jemec GB. Anxiety level and severity of skin condition predicts outcome of psychotherapy in atopic dermatitis patients. *Int J Dermatol* 2001;40:632–636.
23. Hashizume H, Takigawa M. Anxiety in allergy and atopic dermatitis. *Curr Opin Allergy Clin Immunol* 2006;6:335–339.
24. Arndt J, Smith N, Tausk F. Stress and atopic dermatitis. *Curr Allergy Asthma Rep* 2008;8:312–317.
25. Oh SH, Bae BG, Park CO, et al. Association of stress with symptoms of atopic dermatitis. *Acta Dermatol Venereol* 2010;90:582–588.
26. Balkrishnan R, Housman TS, Carroll C, et al. Disease severity and associated family impact in childhood atopic dermatitis. *Arch Dis Child* 2003;88:423–427.
27. Al Shobaili HA. The impact of childhood atopic dermatitis on the patients' family. *Pediatr Dermatol* 2010;27:618–623.
28. Lee J, Bielory L. Complementary and alternative interventions in atopic dermatitis. *Immunol Allergy Clin North Am* 2010;30:411–424.
29. Jekler J, Larko O. UVA solarium versus UVB phototherapy of atopic dermatitis: a paired-comparison study. *Br J Dermatol* 1991;125:569–572.
30. Seidl V, Harari M, Weinrauch L. Climatotherapy of atopic dermatitis at the Dead-Sea. *Der Deutsch Dermatol* 1993;41:841–884.
31. Kushelevsky AP, Harari M, Kudish AI, et al. Safety of solar phototherapy at the Dead Sea. *J Am Acad Dermatol* 1998;38:447–452.
32. Zimmermann J, Utermann S. Photo-brine therapy in patients with psoriasis and neurodermatitis atopica [in German]. *Hautarzt* 1994;5:849–853.
33. Walling HW, Swick BL. Update on the management of chronic eczema: new approaches and emerging treatment options. *Clin Cosmet Investig Dermatol* 2010;3:99–117.