

INVESTIGATIVE REPORT

Significant Immediate and Long-term Improvement in Quality of Life and Disease Coping in Patients with Vitiligo after Group Climatotherapy at the Dead Sea

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Quality of life in patients with vitiligo is impaired. This study explored the immediate effect of 20 days of climatotherapy at the Dead Sea on quality of life, coping with the disease, general well-being and individual stress levels in a group of 71 patients with vitiligo and 42 matched controls. The long-term effect was assessed after 12 months in 33/71 patients and 12/42 controls. Study instruments were Dermatology Life Quality Index, Beck Depression Inventory and the Adjustment to Chronic Skin Disorders Questionnaire. Stress measurements were based on cortisol and β -endorphin concentrations in saliva samples. Quality of life was significantly improved at day 20 at the Dead Sea compared with day 1, and this was still significant after 12 months. Moreover, social anxiety/avoidance, anxious-depressive mood and helplessness as measured by the Adjustment to Chronic Skin Disorders Questionnaire were significantly reduced. There was no difference in levels of cortisol and β -endorphin between patients and controls, indicating that stress per se is not a significant contributor in vitiligo. In conclusion, therapy in patient groups offers an effective tool for long-lasting improvement in quality of life and patients' well-being. Key words: vitiligo; quality of life; coping; depression; Dead Sea; pseudocatalase PC-KUS.

(Accepted September 20, 2010.)

Acta Derm Venereol 2011; 91: 152–159.

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Vitiligo is a common acquired, idiopathic and often familial depigmentation disorder that affects both sexes equally worldwide. The cause of the disease is unknown (1, 2). Population-based studies involving large numbers of people in several parts of the world have revealed a prevalence of approximately 0.2–1.9% (3–6).

Although not painful or life-threatening, this disfiguring disorder can have a devastating effect on a patient's psychosocial wellbeing and social life (7–9).

Patients often experience stigmatization, including curiosity, by other people, rejection and discrimination at work (8–10), low self-esteem (11, 12), embarrassment (8), impaired quality of life (13, 14) and a higher prevalence of sexual difficulties, especially in women (15, 16). Interestingly, stigmatization was the most influential factor in the variance of Dermatology Life Quality Index (DLQI) measurements (13).

In this context it is noteworthy that stress or certain "life events", including loss of close relations, bereavement, moving home, giving birth or losing a job can be associated with triggering the onset or progression of vitiligo (17–19). A recent study from Italy confirmed a strongly impaired quality of life in these patients (20).

To date, there is no cure for vitiligo, but various treatment approaches are available to reduce the disease burden, including photochemo-therapies with ultraviolet A (UVA) combined with psoralens, khellin or L-phenylalanine (21, 22) and mono-photo-therapies (narrow-band UVB (NB-UVB), UVB-microtherapy, excimer laser) (23–26). Topical therapies include corticosteroids, calcipotriol and calcineurin inhibitors. Other treatments include skin/cell grafting (21, 26), and topical application of narrow-band UVB (311 nm, NB-UVB) activated pseudocatalase PC-KUS (27). The efficacy of the latter treatment has been shown in an initial pilot study and a recent investigation in 71 children (27, 28).

A rather uncommon, but superior, treatment modality is the combination of pseudocatalase (PC-KUS) and balneo/climatotherapy at the Dead Sea (29). Patients' repigmentation has been shown to begin during the 21-day stay at the Dead Sea and, more importantly, continue for up to 3–4 months after returning home (29). Moreover, repigmentation is stable, if patients continue with treatment at home. This successful modality has been used since 1999 in Israel and Jordan under the auspices of the Institute for Pigmentary Disorders (IFPD) in Greifswald, Germany and Bradford, UK, helping many patients from all over the world regardless of skin colour, duration and extent of the disease. The patients spend time together, which creates a supportive environment during their 21-day stay. Most importantly, this

situation provides an excellent basis for any research project related to the disease, due to low variability of multiple factors involved.

Given that several studies have documented altered quality of life and depression in patients with vitiligo, we wanted to learn whether this specific treatment modality had any immediate and long-term effects on patients' well-being besides improvement in skin colour.

MATERIALS AND METHODS

Study design and aim

This prospective non-randomized study was designed to compare baseline data (every new patient with vitiligo attending the clinic) and the influence of one year treatment with NB-UVB-activated pseudocatalase PC-KUS (KUS Dermatologie GmbH, Greifswald, German) (every patient attending for routine follow-up after one year treatment with NB-UVB-activated PC-KUS) with the immediate and long-term effect of combined climatotherapy at the Dead Sea in a patient group utilizing a panel of standardized questionnaires. The aim of the study was to analyse the immediate and long-term effect of combined group climatotherapy on quality of life, coping with a chronic skin condition and depression in patients with vitiligo.

The study took place at IFPD in Greifswald, Germany and at the Dead Sea Medical Centre in Jordan under the auspices of the IFPD from July to December 2006, in May/June 2007 and in April/May 2008. The study was carried out in agreement with the Declaration of Helsinki and was approved by the local ethics committee. All patients and controls provided signed consent. To exclude any biased view, questionnaires were answered before seeing the physician. Due to the international clientele at the IFPD, questionnaires were available in English and German.

Baseline data were obtained from all untreated new patients ($n=116$) who visited the IFPD during July–December 2006. Controls were partners or friends, who accompanied patients. The effect of NB-UVB-activated pseudocatalase PC-KUS on quality of life was assessed in all 51 patients who had already been undergoing this treatment modality at the IFPD for at least one year, attending for a routine follow-up during December 2006.

The immediate influence of combined climatotherapy at the Dead Sea in a patient group was studied in 2007 at day 1 and day 20 using the same panel of questionnaires. All patients ($n=71$) and healthy controls ($n=42$), who came to the Dead Sea, were included. The long-term effect was followed in all patients ($n=33$) and controls ($n=12$) who returned for treatment in 2008. Although the participants came from 16 countries and five continents, all were able to use either German- or English-language questionnaires.

Treatment protocol at the Dead Sea

All patients attended twice daily (08.00 h and 15.30 h) for a 15 min bath in the Dead Sea, followed by rinsing with clear water. Following the application of pseudocatalase PC-KUS to the entire body surface, each body side underwent natural solar exposure (Combineol Climatotherapy) for a maximum of 15 min. This protocol was used for 20 days. After returning home all patients continued treatment at home with low-dose NB-UVB-activated pseudocatalase PC-KUS, as described in detail previously (28, 29).

Study instruments

The Dermatology Life Quality Index (DLQI) has been published in numerous languages and countries and has been used in

many skin diseases (30), allowing a good comparison between different ethnic groups and other skin diseases. It contains 10 items and evaluates the impact of a skin disease of interest on the daily life over the past 7 days. Each question offers four possible answers: *not at all* or *not relevant* (score 0), a *little* (score 1), a *lot* (score 2) and *very much* (score 3). The highest possible score is 30. Hence, a high score correlates with a more impaired quality of life due to the skin disease (31).

The Adjustment to Chronic Skin Disorders Questionnaire (ASC) focuses on coping with chronic skin diseases and consists of 51 items measuring, among others, four main scores (32, 33). Three were used for this project:

- *Social anxiety/avoidance* (15 items)
- *Helplessness* (9 items)
- *Anxious-depressive mood* (8 items).

The *Itch-scratch circle* has been excluded from this study due to its irrelevance for vitiligo. Every item contains a statement and five possible answers: 1: *not at all*, 2: *hardly ever*, 3: *quite right*, 4: *mostly* and 5: *totally*. Each of the single scores is summed up and can be compared with scores provided by the authors of the questionnaire or with the literature (32).

Social anxiety/avoidance refers to fear of situations in which negative reactions to the skin disease are expected by the patient; followed by avoidance of situations, where an exposure of the disease to others is likely. Moreover, it includes the feeling of loss of attractiveness and, in extreme cases it can even reveal the feeling of disfigurement. Experiences of *helplessness* refer to loss of control regarding the course of a skin disease including hypochondriac concerns over a possible worsening of the disease. *Anxious-depressive mood* indicates that the patient is affected by symptoms of an adjustment disorder (33).

Since depression has been reported for patients with vitiligo (8, 34), it seemed appropriate to use the Beck Depression Inventory (BDI). This instrument is long-established and consists of 21 items, each with four different statements, scoring from 0 to 3. The total score can be compared with cut-off scores indicating the severity of the depression. These cut-offs are:

- score 0–9: no depression
- score 10–18: mild to moderate depression
- score 19–29: moderate to severe depression
- score 30–63: severe depression (35).

Collection of saliva samples for analysis of cortisol and β -endorphin levels

Both cortisol and endorphins are well-recognized stress response markers (36, 37). Cortisol and endorphin levels can be followed in saliva samples (37). Compared with other methods it has the advantage of being uncomplicated, recognized and non-invasive (37). Saliva samples were taken from patients and healthy controls at 07.00 h and 19.00 h on day one, day 10 and day 20 at the Dead Sea during the first stay.

Determination of cortisol and β -endorphin levels in saliva

Cortisol levels were determined using a commercially available Salivary Cortisol ELISA kit from DRG Diagnostic (DRG Instruments GmbH, Marburg, Germany).

Briefly, saliva was thawed, centrifuged and aliquoted to 100 μ l samples according to the manufacturer's protocol. Samples and cortisol standards provided were dispensed into the test kit's wells and 200 μ l of conjugate was added to the standard and sample wells and mixed for 10 s, followed by incubation for 60 min. Samples were washed three times with 400 μ l diluted wash solution followed by addition of 200 μ l substrate and further incubation for 30 min. Finally, 100 μ l stop solution was added to each well. Measurements were performed within

10 min at 450 ± 10 nm using a microplate reader (Dyex MRX II, software Revelation 4.02, both from Dyex Technologies, Chantilly, VA, USA). The values of each test run were calculated based on a standard curve employing a power trendline in Excel (Microsoft Office Excel 2003 from Microsoft Inc, Redmond, Washington, USA).

β -endorphin levels were determined in saliva samples utilizing a commercially available specific radio-immuno assay (Bachem Ltd, St Helens, Merseyside, UK) following the manufacturer's protocol.

Statistics

Statistical analysis was based on the independent sample *t*-test (Student's *t*-test) to measure differences between means of two groups within the population. For comparison of two related samples we used the paired-sample *t*-test. The Pearson correlation analysis was utilized for linear correlation between two variables.

All data were analysed with SPSS 14.0 for Microsoft Windows (SPSS Inc., Chicago, IL, USA).

RESULTS

Baseline DLQI, BDI and ASC scores in patients with vitiligo decrease after treatment with NB-UVB activated pseudocatalase PC-KUS

The first stage of this study was to establish baseline data from patients with vitiligo who did not participate in the Dead Sea project. Those data were obtained from 167 patients with vitiligo. Fifty-one patients were already enrolled at the IFPD and undergoing treatment with NB-UVB activated pseudocatalase PC-KUS for at least one year, and 116 patients were attending for the first time to start this treatment modality. The total

group included 64 males and 103 females with a mean age of 42.8 years. Skin phototypes (38) were: II ($n=10$), III ($n=129$), IV ($n=16$), V ($n=9$) and VI ($n=3$).

The results for new patients ($n=116$) revealed a DLQI score of 6.1 (Table I). The data for the ACS showed for *social anxiety/avoidance* 39.8, for *helplessness* 28.1 and for *anxious-depressive mood* 21.0. The data for the BDI revealed 21.0 indicating the presence of depression in the group.

Patients already undergoing treatment with pseudocatalase PC-KUS ($n=51$) showed a significantly lower DLQI score compared with untreated new patients (mean 4.3, $p=0.05$) (Table I). This was also observed for *social anxiety/avoidance* (34.6 vs. 39.8, $p=0.032$) and *anxious-depressive mood* (18.0 vs. 21.0, $p=0.012$). However, for *helplessness* (26.2 vs. 28.1, $p>0.05$) and BDI scores this difference was not significant (5.4 vs. 7.7, $p>0.05$).

Moreover, the baseline data revealed that males ($n=64$) scored significantly lower in the *anxious-depressive mood* subscale (mean 18.1 vs. 21.2, $p=0.006$ *t*-test) and in the BDI (mean 4.5 vs. 8.2, $p=0.003$) compared with females ($n=103$). There were no gender-related differences in the DLQI as well as in the other subscales of the ASC (data not shown).

Significant immediate and long-term improvement in quality of life after combined group climatotherapy at the Dead Sea

The assessment of the immediate effect included 71 patients with 23 males and 48 females. The study took

Table I. Dermatology Life Quality Index (DLQI) scores in the literature compared with data from this study (bold text)

DLQI (mean)	<i>n</i>	Age (mean)	Remarks	Country	References
0.5	100	36.9	Healthy controls	UK	(31)
1.9	71	45.9	After 20 days climatotherapy with PC-KUS at the Dead Sea	Various	This publication
3.7	n.d. ^a	n.d.	Patients with vitiligo of a private dermatological practice	Australia	(39)
3.9	40	n.d.	Patients with stable vitiligo after epidermal cell transplantation	Belgium	(40)
4.3	51	40.9	After treatment with PC-KUS, IFPD Greifswald	Various	This publication
4.8	614	46.6	Patients with vitiligo associated with UK Vitiligo Society	UK	(13)
4.9	102	41.4	Patients with vitiligo	Belgium	(14)
5.0	8	37.8	Patients at the end of an 8-week course of cognitive behavioural therapy	UK	(41)
5.7	30	"Elderly"	Patients with vitiligo	Iraq	(42)
6.1	116	43.6	New patients with vitiligo, IFPD Greifswald	Various	This publication
6.9	78	40.9	Patients after 1 month of using camouflage	Belgium	(7)
6.9	1023	44.4	Patients from self-support organizations	Germany	(43)
6.9	40	n.d.	Stable vitiligo before epidermal cell transplantation	Belgium	(40)
7.0	71	45.9	Before climatotherapy with PC-KUS at the Dead Sea (day 1)	Various	This publication
7.0	70	28.3	Patients with vitiligo	Iran	(44)
9.4	60	n.d.	Patients with vitiligo	Tunisia	(45)
9.4	9	41.2	After treatment (1 year combined NB-UVB/calcipotriol)	Germany	(46)
10.7	141	n.d.	Patients undergoing treatment	India	(47)
13.0	9	41.2	Adults before treatment	Germany	(46)
14.7	109	26.94	Saudi college patients	Saudi Arabia	(48)
15.0	16	39.3	Patients without treatment	UK	(48)

^aTotal number of participants with various skin diseases $n=556$, number of patients with vitiligo not provided.

PC-KUS: narrow-band UVB-activated pseudocatalase; IFPD Greifswald: Institute for Pigmentary Disorders Greifswald; NB-UVB: narrow-band ultraviolet B.

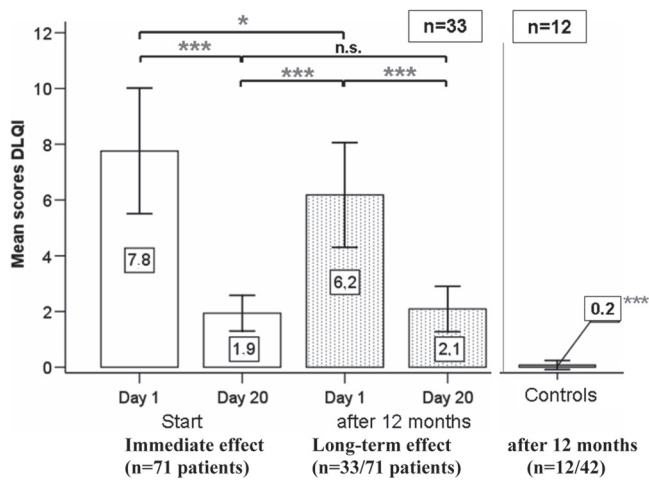


Fig. 1. Immediate effect of combined climatotherapy at the Dead Sea in a group on patients with vitiligo ($n=71$) compared with controls ($n=42$). Significant reduction in patients' Dermatology Life Quality Index (DLQI) scores ($n=71$) on day 20 compared with day 1 in the first year's trip ($***p<0.001$). Long-lasting improvement in quality of life (QoL) after 20 days climatotherapy in a group at the Dead Sea (DLQI) in patients ($n=33$) and healthy controls ($n=12$). $***p<0.001$ day 20/year 1 and year 2 compared with day 1/year 1. $*p<0.05$ day1/year2 compared with day 1/year 1. NB. Reduction is still significant lower after 1 year.

place in 2007. The mean age was 45.9 years. Clinical subtypes of vitiligo were vitiligo *vulgaris* ($n=66$),

vitiligo *totalis* ($n=4$), vitiligo *segmentalis* ($n=1$). The majority of patients had phototype III ($n=55$, followed by phototype V ($n=8$), II ($n=4$), IV ($n=2$) and VI ($n=2$). More than half of the patients ($n=41$, 57.7%) had been to the Dead Sea before. The group of healthy controls ($n=42$) included 26 males and 16 females with a mean age of 48.7 years. Skin phototypes were as follows: I ($n=1$), II ($n=10$), III ($n=27$), IV ($n=1$) and V ($n=3$).

Assessment of the long-term effect was based on 33/71 patients and 12/42 healthy controls who returned to the Dead Sea in 2008. Nine patients were males, 24 were females. The control group included 8 males and 4 females. The mean age of the patients was 45.0 years and of the controls 48.7 years. The majority of the groups were of Caucasian origin with mostly phototype III ($n=24$), followed by IV ($n=4$), II and V (each $n=2$) and V ($n=1$).

Mean DLQI scores of the whole group were significantly decreased at the end of the climatotherapy in the first year, indicating an excellent immediate effect on QoL (Fig. 1). This improvement could be maintained by those patients who participated again one year later ($n=33$, $p<0.05$). Men ($n=9$) scored lower in the DLQI throughout compared with the female patients ($n=24$) (scores of 4.6 vs. 9.0 on day 1 and 0.7 vs. 2.4 on day 20

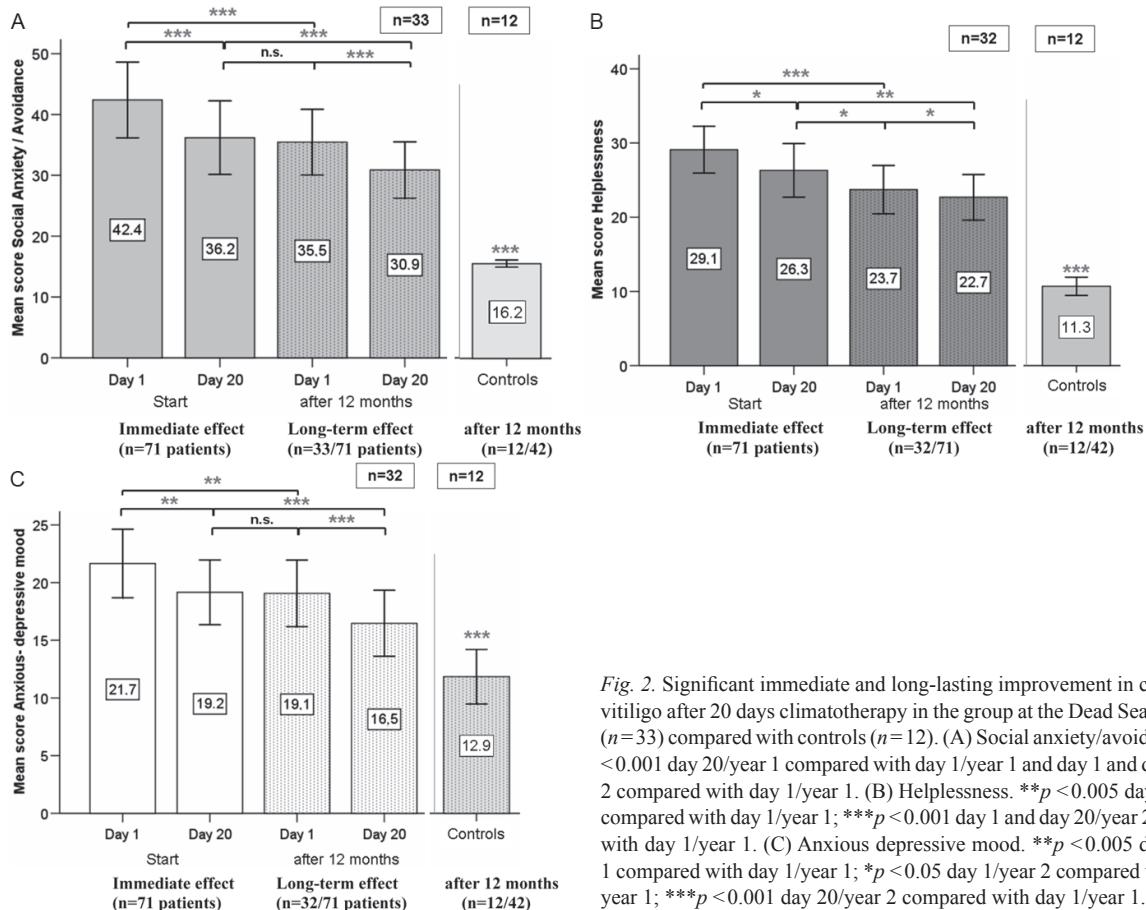


Fig. 2. Significant immediate and long-lasting improvement in coping with vitiligo after 20 days climatotherapy in the group at the Dead Sea in patients ($n=33$) compared with controls ($n=12$). (A) Social anxiety/avoidance. $***p<0.001$ day 20/year 1 compared with day 1/year 1 and day 1 and day 20/year 2 compared with day 1/year 1. (B) Helplessness. $**p<0.005$ day 20/year 1 compared with day 1/year 1; $***p<0.001$ day 1 and day 20/year 2 compared with day 1/year 1. (C) Anxious depressive mood. $**p<0.005$ day 20/year 1 compared with day 1/year 1; $*p<0.05$ day 1/year 2 compared with day 1/year 1; $***p<0.001$ day 20/year 2 compared with day 1/year 1.

Table II. Comparison of immediate and long-lasting effect of climatotherapy on female (n = 24) and male (n = 9) patients with vitiligo

	First year		Second year	
	Day 1 Mean ± SD	Day 20 Mean ± SD	Day 1 Mean ± SD	Day 20 Mean ± SD
<i>Dermatology Life Quality Index</i>				
Men	4.56 ± 4.75	0.67 ± 0.87*	2.67 ± 3.50*	0.89 ± 1.27*
Women	8.96 ± 6.56	2.42 ± 1.84***	7.50 ± 5.30	2.54 ± 2.47***
Significance between gender	p > 0.05	p > 0.05	p > 0.05	p > 0.05
<i>Social Anxiety/Avoidance</i>				
Men	35.78 ± 18.38	25.78 ± 8.76*	25.67 ± 12.22*	23.11 ± 0.01*
Women	44.88 ± 16.95	40.08 ± 15.066**	39.13 ± 14.72***	33.79 ± 13.00***
Significance between gender	p > 0.05	*p = 0.035	*p = 0.028	*p = 0.043
<i>Helplessness</i>				
Men	26.33 ± 10.20	20.44 ± 8.43*	18.44 ± 8.68*	17.56 ± 7.67*
Women	30.17 ± 8.09	28.61 ± 9.79	25.78 ± 8.44***	24.70 ± 8.18***
Significance between gender	p > 0.05	p > 0.05	p > 0.05	p > 0.05
<i>Anxious-depressive mood</i>				
Men	18.11 ± 7.98	13.44 ± 3.21*	13.44 ± 4.95	12.22 ± 5.33*
Women	23.04 ± 8.13	21.39 ± 7.98*	21.26 ± 7.93*	18.13 ± 8.27***
Significance between gender	p > 0.05	*p < 0.05	*p < 0.05	p = 0.057

Mean DLQI and ACS scores in years 1 and 2.

*p < 0.05; **p < 0.005; ***p < 0.001) mark levels of significance of difference to score of day one in the first year, as measured by a paired *t*-test.

SD: standard deviation.

in 2007, compared with 2.7 vs. 7.5 on day 1; 0.9 vs. 2.5 on day 20 in 2008). However, these differences were statistically not significant ($p > 0.05$) (Table II). The mean DLQI scores of healthy controls were significantly lower compared with patients ($p < 0.001$). Based on these results, it can be concluded that a 20-day long climatotherapy in a group at the Dead Sea leads to a dramatic improvement in quality of life. Despite an increase in the DLQI score after 12 months, this improvement was still significant. Moreover, all returning patients from year 1 again experienced a similar improvement after 20 days at the Dead Sea in year 2 (Fig. 1).

Positive immediate and long-term effect on coping with vitiligo

In all 3 subscales of the ASC used for this study (*social anxieties/avoidance*, *helplessness*, *anxious-depressive mood*) there were significant reductions in our patients' scores by the end of each trip compared with day 1 (levels of significance ranging from $p < 0.05$ to $p < 0.001$, Fig. 2). Importantly, this improvement was still significant in those patients who returned for treatment 12 months later (Fig. 2 and Table II). Meanwhile, *social anxieties/avoidance* and *anxious-depressive mood* scores did not change; there was an even further reduction in the mean *helplessness* score at the beginning of the second year compared with the end of the first year's therapy (Fig. 2B). Importantly, all ASC scores for our healthy controls were consistently lower compared with the patient group, emphasizing the fact of impaired coping with the disease. Both male and female patients benefited equally from the stay at the Dead Sea, with only a few exceptions (women regarding *helplessness* in the first year, see Table II).

Men had lower scores compared with female patients, but these differences were statistically significant only in the subscale *social anxieties/avoidance* (Table II). Of all three subscales, the improving effect was stronger in *social anxieties/avoidance* and *helplessness* and weakest on *anxious-depressive mood* (Fig. 2).

Significant immediate and continuous improvement in depression

Thirty percent of all patients ($n = 33$) were mildly to moderately depressed according to the BDI scores on day 1 of the climatotherapy (Fig. 3). Women showed signifi-

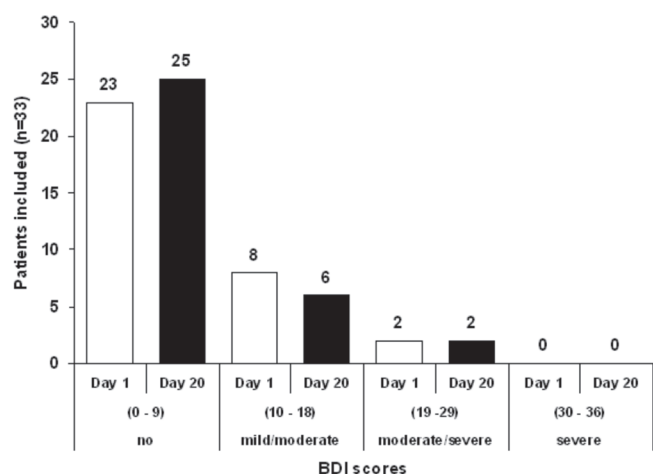


Fig. 3. Prevalence of depression in patients with vitiligo ($n = 33$) before and after climatotherapy in a group at the Dead Sea (Beck Depression Inventory (BDI)). The majority of patients are not depressed. Severe depression was not present. There was no change in moderate/severe depression in two patients between day 1 and day 20, while two patients with mild/moderate depression were no longer affected.

cantly higher BDI scores (mean 8.8) compared with male patients (mean 2.3) on day 1 compared with 6.79 vs. 1.78 on day 20. These improvements had been maintained in those patients who went again to the Dead Sea one year later. A further improvement could be observed on day 20 compared with day 1 in year 2. However, the number in year 2 was too small to conclude (data not shown).

No increase in saliva cortisol and β -endorphin levels in patient with vitiligo compared with healthy controls

Despite the contribution of stress invoked by this disease, evaluation of the classical stress marker did not support any different stress levels between patients and controls (data not shown) (18, 49).

DISCUSSION

Since the evaluation of patient's QoL is based on the DLQI, it should be noted that this questionnaire addresses the past 7 days only. Therefore, only scores obtained at the first appointment in the IFPD can be directly compared with the data published so far (Table I). The mean score of new patients attending our institute was 6.1, whereas patients already undergoing treatment with PC-KUS showed a much lower mean DLQI score of 4.3, one of the lowest published so far (Table I). This result reflects the positive influence of pseudocatalase PC-KUS treatment on QoL of patients with vitiligo. The mean score of 6.95 on day 1 at the Dead Sea is slightly higher compared with baseline data from new patients. This result might indicate that those patients who went to the Dead Sea were more desperate. However, the wide range of scores within this group of patients may also indicate that true feelings were not always expressed through the scores in the questionnaires and may even be more suppressed in many new patients. Once a treatment has begun, many patients are less inhibited about expressing their emotions more honestly. This phenomenon is currently under further investigation.

The very low mean scores of 1.9 and 2.1 (Fig. 1) on day 20 in Jordan reflect patients' well-being. Under those unique conditions they are no longer the centre of unwanted attention, because essential parts of their daily life (clothing, sport, swimming, going out, partnerships) were shared with other patients or people who are used to vitiligo (spouses, partners). Hence, the level of stigmatization is very low.

The DLQI score on day 20 at the Dead Sea is the lowest for any adult group of patients with vitiligo published so far (Table I). There are only two other reports in the literature with low mean scores (3.7 and 3.9) originating from 40 patients with stable vitiligo after epidermal cell transplantation and one group from an Australian dermatological practice (39, 40) (Table I). Importantly, the positive effect from the climatotherapy

at the Dead Sea is still present after 1 year (Figs 1 and 2). However, our data also emphasize that the disease burden is much higher in women compared with men, supporting some reports in the literature (14, 50), despite other authors would not confirm any gender differences (13, 48).

Evaluation of the ASC in our study was based on 3 selected items, and comparable data in the literature are scarce. Schmid-Ott reported a mean *social anxiety/avoidance* score of 34.8 in 363 patients (51), while Stangier et al. (33) documented a score of 35.5 in 33 patients. Both results are significantly lower compared with our data (42.4) on day 1 at the Dead Sea but after completion of climatotherapy at day 20 and during the follow-up appointments our patients revealed similar mean scores (Fig. 2). A comparison between females and males in the literature yielded a significant difference (females: $n=284$, mean score of 35.7; males: $n=79$, mean score 31.3) (51). Our data support this difference.

The scores for *helplessness* in our patient population are in agreement with Schmid-Ott et al. (51) and Stangier et al. (33), whereas their results on *anxious depressive mood* are slightly lower compared with our data.

To the best of our knowledge, we present here for the first time the influence of a treatment modality on *social anxiety/avoidance*, *helplessness* and *anxious-depressive mood* in patients with vitiligo over a longer period of time. All other publications are based on a snapshot evaluation. So far, the ASC has been used only to study the impact of treatment on patients with atopic dermatitis, where it was shown that *social anxiety/avoidance* and *helplessness* were sensitive enough to pick up treatment success, although this was not the case for *anxious-depressive mood* (33). Our results demonstrated a significant improvement in this item (Fig. 2C).

Finally, our data indicate that patients are considerably more depressed compared with healthy controls. However, the published results on this topic are not conclusive. Neither Gieler et al. (52) nor Lee et al. (53) found a difference between patients and controls. Clearly our data are limited because the group that used the BDI after 12 months was too small. However, we found a significant correlation between depression and the *anxious-depressive mood* section of the ASC for patients with vitiligo (2-tailed Pearson correlation, significant at 0.01 level, data not shown). This connection has never been reported for this disease, but correlations with other dimensions, including QoL (13), self-esteem and general disturbance (11), are documented. Hence, the above connection needs further investigation.

Since stress has been implicated in the aetiology of vitiligo (39), it was tempting to monitor the classical stress parameters, cortisol and β -endorphin, under the same conditions. Surprisingly, we could not detect any differences between patients and controls, on day 1, day 20 or 12 months later. This result is puzzling because

the "happiness" hormone β -endorphin has been implicated to increase with exposure to UV (54). Instead we observed a significant decrease in both groups, despite much unavoidable natural light and sun exposure at the Dead Sea.

In summary, the results of this study confirm a significantly impaired QoL together with *social anxiety/avoidance*, *helplessness* and *anxious depressive mood* in patients with vitiligo. One-third of all patients are depressed. Treatment with pseudocatalase PC-KUS leads to a significant improvement in all items. However, a powerful factor influence in all of the above items seems to be therapy in a group. This effect is significant after only 20 days climatotherapy at the Dead Sea and is still present 12 months later.

Based on these results, we suggest that group therapy has a strong and long-lasting positive influence on QoL, coping and general well-being in patients with vitiligo.

ACKNOWLEDGEMENTS

This research was supported by the Deutsche Vitiligo Verein Hamburg/Germany, the American Vitiligo Research Foundation/USA and by private donations to KUS. The results are part of a PhD thesis (CK).

The authors declare no conflict of interest.

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