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INVESTIGATIVE REPORT

Efficacy of Biofeedback and Cognitive-behavioural Therapy in Psoriatic Patients

A Single-blind, Randomized and Controlled Study with Added Narrow-band Ultraviolet B Therapy

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Increasing data suggests that there is a connection between stress and the appearance of psoriasis symptoms. We therefore performed a clinical trial enrolling 40 participants who were randomly allocated to either an 8-week cognitive-behavioural therapy (CBT) (treatment group) plus narrow-band UVB phototherapy or to an 8-week course of only narrow-band UVB phototherapy (control group). We evaluated the clinical severity of psoriasis (PASI), General Health Questionnaire (GHQ)-12, Skindex-29 and State-Trait Anxiety Inventory (STAI) at baseline and by the end of the study. Sixty-five percent of patients in the treatment group achieved PASI75 compared with 15% of standard UVB patients ($p=0.007$). GHQ-12 cases were reduced from 45% to 10% in the treatment group and from 30% to 20% in the control group ($p=0.05$). The Skindex-29 emotional domain showed a significant improvement in the CBT/biofeedback group compared with control patients (–2.8 points, $p=0.04$). This study shows that an adjunctive 8-week intervention with CBT combined with biofeedback increases the beneficial effect of UVB therapy in the overall management of psoriasis, reduces the clinical severity of psoriasis, improving quality of life and decreases the number of minor psychiatric disorders. ***Key words: psoriasis; stress; UVB; cognitive-behavioural therapy; biofeedback.***

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There is increasing evidence that stress or distress may influence psoriasis to such an extent that a significant proportion of patients report stress as one of the principal agents of causation or relapse (1, 2). Additionally, indirect evidence exists that stress may impair the efficacy of systemic treatment (3, 4).

The utility of adjunctive psychological or psychosocial interventions has been investigated in a range of chronic diseases, with varying results. Cognitive-behavioural approaches have been most successfully applied in rheumatic diseases (5), with subsequent improvement in psychosocial variables and clinical indices of disease activity.

However, only a few prospective randomized clinical trials have studied the efficacy of such psychological interventions for psoriasis (3, 6, 7), showing that adjunctive cognitive-behavioural approaches can result in a reduction of clinical psoriasis severity.

We therefore investigated whether patients who underwent a multi-disciplinary management approach that included cognitive-behavioural therapy (CBT) combined with biofeedback plus narrow-band UVB therapy would show improvements in clinical severity of their psoriasis, psychological distress and quality of life (QoL), compared to patients receiving standard narrow-band UVB therapy alone.

PATIENTS AND METHODS

Patients attending a psoriasis specialty clinic at University Hospital of Padova, Italy, were invited to participate in the study. Inclusion criteria were: moderate-severe plaque psoriasis, clinically eligible for narrow-band UVB (TL-01) phototherapy and willing to undergo treatment according to randomisation.

In total, 55 patients (21 males) were recruited by referring dermatologists between October 2013 and February 2015. To minimize the effect of seasonal variation, we did not enrol patients from April to October. Ten declined participation (6 males), citing reluctance to be part of a research protocol. The sex-specific acceptance rate was 88% for female patients and 71% for male patients ($p=$ ns). Overall rates of attrition from the CBT/biofeedback + UVB group were 13% (3 patients). Attrition from the control group was similar (10%, two patients). Forty subjects completed the study.

Baseline descriptive data obtained on all subjects included age, sex, education, years with psoriasis, degree of body surface involvement.

Participants were randomly allocated by an independent researcher to either an 8-week CBT (treatment group) plus concomitant narrow-band UVB phototherapy or to an 8-week course of only narrow-band UVB phototherapy (control group). Order of randomization was determined according to a standard table of random numbers. All assessment were administered and scored by a physician (E.M.) blind to the group to which each participant had been allocated. Patients were asked not to divulge what treatment they were receiving to their study physicians.

While in the study, patients were instructed to avoid any oral or topical psoriasis treatments not specifically prescribed by the physicians, except emollients for skinfold areas not exposed to the light, and this was reinforced by the clinic nurses throughout the study period. Participants were again evaluated at 1-month after the end of the 8-week treatment in order to

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assess maintenance of gains. There was no attrition from the trial between post-treatment and follow-up.

All patients gave informed consent and the study was approved by the local research ethics committee.

Intervention

All subjects were treated with narrow-band UVB 3 times/week for 8 weeks according to standard phototherapy treatment protocols (8). UVB dosage was increased linearly from session to session (by 5 to 15% increments according to skin type). Dosage increases were delayed only if there were signs of burning.

The psychological treatment consisted of weekly one-to-one cognitive-behavioural stress-management assisted with biofeedback. After initial baseline measurements (week 0) the patients participated in 8 individual psychotherapy sessions, each lasting 60 min. The sessions were scheduled to take place on the same weekday and on the same time of day. Treatment sessions were carried out by 2 psychologists (D.C. and A.D.) with post-doctoral training in CBT and biofeedback.

CBT is based on the theory that negative thoughts and behaviours can affect a person's symptoms and be an obstacle to recovery. Where specific fears or negative thoughts can be identified, behavioural fear reduction techniques, such as desensitization, modelling or flooding, may be used. Concomitant use of biofeedback may enhance the therapeutic effectiveness of this technique. Discussions based on the biofeedback imagery aimed at improving the patients' stress-management skills and learning to cope with the particular stressors in the daily life of the patient. With biofeedback, information about the body such as breathing patterns, heart rate and rhythms, muscle tension, sweat gland activity and other measures are seen and heard through colourful graphs, video games and musical tones. The physical measures also reflect emotional states and can help transform anxiety or worry into calm.

We used the following feedback modalities: Electromyographic (EMG); Frontalis, masseter and sternocleidomastoid muscle tension were monitored. Skin Conductance Level (SCL): finger electrodes register sweat gland activity. Thermal: finger thermistors measure vasoconstriction by minute changes in peripheral blood flow. Respiratory: strain gauges measure abdominal and thoracic excursions; a capnometer monitors exhaled CO_2. Heart rate (HR): finger photoplethysmography registers rate and pulse volume.

Outcomes

The severity of psoriasis was evaluated at 4 time-points: baseline (induction to the study), at week 4, at week 8 (end of treatment) and at 1-month follow-up after the end of treatment.

Severity of disease was assessed by a blinded physician (E.M.) experienced in using the Psoriasis Area Severity Index (PASI). The PASI incorporates the clinical extent of psoriasis (surface area of skin affected) and clinical severity of its manifestations (erythema, desquamation and infiltration) using a formula that yields a value between 0 and 72 (9). A 75% reduction in the PASI score was considered a clinically meaningful success (PASI 75). Relapse was defined as loss of 50% of PASI improvement from baseline in patients who achieve a clinically meaningful response.

Moreover, each participant also completed the following, validated, self-report assessments: General Health Questionnaire (GHQ)-12, Skindex-29 and State-Trait Anxiety Inventory (STAI).

The GHQ-12 is a self-administered questionnaire consisting of 12 items, designed to measure psychological distress and to detect current non-psychotic psychiatric disorders, usually depressive or anxiety disorders. The reliability and validity of the Italian version have been documented in many types of patients, including those with dermatological conditions. Answers are given on a 4-point scale. For instance, the answers to the item "in the last weeks, did you feel under strain?" are "no", "no more than usual", "more than usual", and "much more than usual" (10). When scored with the binary method (0-0-1-1), the GHQ-12 can be used as a screening tool to detect minor non-psychotic psychiatric disorders. For instance, to receive a score of 1 on the previously described item, a subject should answer "more than usual" or "much more than usual". In this way, each subject obtains a score from 0 to 12, based on a previous validation study operationally, patients scoring ≥ 4 were considered as "GHQ-12 positive". Thus, for the purpose of this study, patients scoring ≥ 4 have been defined as "cases", while the others have been defined as "noncases" (11).

The Skindex-29 is a reliable and valid instrument that has been specifically designed for measuring health-related QoL in dermatological patients. Skindex-29 consists of 30 items divided in 3 scales, assessing burden of symptoms, social functioning and emotional state. The questions refer to the previous 4-week period, and scores are given on a 5-point scale, from "never" to "all the time" (12). The score of each scale ranges from 0 to 100 (as a percentage of the maximum score obtainable on that scale), and higher scores reflect a worse QoL.

The STAI (Form-Y) is a well-established self-rating scale with high stability and validity, often used in clinical research (13). The first 20 statements assess state anxiety, i.e. anxiety at a particular moment or at a chosen period of time. (The subjects were asked to rate their state anxiety during the last week). The subsequent 20 statements assess trait anxiety, i.e. the relatively stable anxiety proneness. Answers are given on a 4-point Likert scale, and scores on the state and trait scales, respectively, range from 20 to 80 points.

All measures were administered at two time-points: before the intervention and at 8 weeks (end of the UVB and CBT/biofeedback treatment).

Statistical analysis

Means, 95% confidence intervals and descriptive measures were computed for each continuous variable as well as frequencies for categorical variables. Independent *t*-tests and chi-square tests, as appropriate, were used to investigate potential differences between groups at induction of the study or at different time-points. The treatment effect for each outcome was estimated using analysis of covariance (ANCOVA) within a regression framework, controlling for baseline values of the outcome. Significance levels for multiple comparisons were corrected with the Bonferroni method. All analyses were conducted using SPSS software, version 22.0 (SPSS, Chicago, IL, USA) and an α level of 5% was used throughout.

RESULTS

Forty patients completed the study; 20 patients in the interventional arm and 20 patients in the control arm (Table I); their mean age was 49.7 (range 20–76 years), and they had had psoriasis for a mean of 17.7 ± 12.4 years. There were no significant differences in baseline characteristics between the treatment group and the control group.

Psoriasis severity

Patients in the treatment group showed a significant reduction in mean clinical severity of psoriasis (PASI) from 9 at baseline to 3.8 and 2.5 at 4 and 8 weeks, respectively (Fig. 1). The clinical improvement was maintained at one

Table I. *Baseline and post-treatment variables for patients according to the trial arm (20 patients in each group)*

Variables	Trial arm	Baseline	End of treatment	*p*-value
Age, years, mean (95% CI)	Int.	46.4 (38–54.8)		
	C	56.7 (45.7–67.7)		
Duration of psoriasis, years, mean (95% CI)	Int.	12.4 (9.1–15.8)		
	C	21.8 (9.6–33.9)		
Males, *n* (%)	Int.	7 (35)		
	C	5 (25)		
Family history of psoriasis, *n* (%)	Int.	12 (60)		
	C	15 (75)		
PASI, mean (95% CI)	Int.	9 (7.6–10.4)	2.5 (1.6–3.3)	<0.0001
	C	9.1 (7.6–10.7)	3.9 (3–4.8)	0.003
GHQ-12, mean (95% CI)	Int.	14.8 (6.6–21)	7.6 (3.5–10.3)	0.028
	C	10 (6.3–12.5)	6.8 (1–10.8)	0.104
Skindex-29				
Symptoms, mean (95% CI)	Int.	43.2 (35.6–50.3)	30.6 (20.7–40.4)	0.059
	C	39 (27–49.7)	23.5 (2–45.1)	0.715
Emotions, mean (95% CI)	Int.	41.7 (30–58.4)	26.9 (15.6–38.3)	0.015
	C	39.5 (29.3–49.6)	31 (14–46.7)	0.225
Functioning, mean (95% CI)	Int.	28.7 (18–42.4)	18 (6.4–29.5)	0.064
	C	33.5 (20.7–44.8)	23.7 (6.1–42.3)	0.714
STAI-I, mean (95% CI)	Int.	39.7 (34.8–44.6)	34.6 (29.5–39.7)	0.023
	C	39.2 (32.7–45.8)	33.8 (27.4–40.1)	0.225
STAI-II, mean (95% CI)	Int.	43.5 (38.4–48.6)	42.3 (36.2–48.4)	0.366
	C	41.6 (35.8–47.3)	43 (37.1–49)	0.893

Int.: intervention group; C.: control group; STAI: State/Trait Anxiety Index.

month after the end of the treatment (PASI 2.4). Also standard UVB therapy vaused a significant reduction in mean PASI values from 9.1 to 5.4 and 3.9 after 4 and 8 weeks, respectively. However, at one month after the end of the treatment, the mean PASI increased to 6.1.

Similarly, 65% of patients in the treatment group achieved PASI75 compared with 15% of standard UVB patients at 8 weeks ($p = 0.007$). Only one patient (out of 13 achieving PASI75 in the treatment group) relapsed at one month after the end of the therapy, while 2 out of 3 patients in the control group did so ($p = 0.01$).

Repeated-measures ANCOVA with baseline scores showed statistically significant effects of the CBT/biofeedback + UVB intervention compared with standard UVB treatment on PASI score at the end of the 8-week period (–1.47 points, 95% confidence interval (CI) –2.65 to 0.29; $p = 0.016$) (Table II).

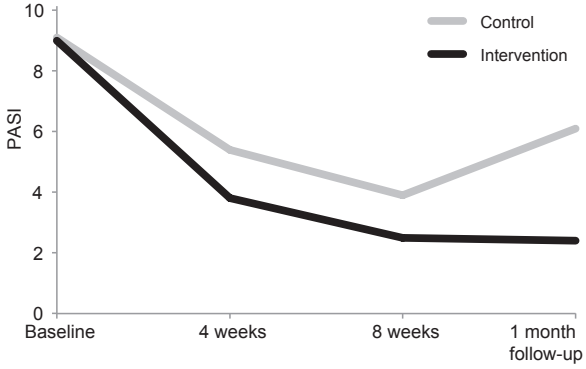

Fig. 1. Efficacy of biofeedback and cognitive-behavioural therapy plus narrow-band UVB phototherapy versus UVB alone (mean PASI values).

Table II. *Estimated treatment effects from ANCOVA analyses*

Outcome	Treatment effect 95% CI	*p*-value
Psoriasis severity (PASI)	–1.47 (–2.65 to –0.29)	0.016
Minor psychiatric disorders (GHQ-12)	–1.8 (–4.34 to 0.81)	0.082
Quality of life		
Skindex-29/Symptoms	–4.9 (–17.283 to 7.451)	0.355
Skindex-29/Emotions	–2.8 (–5.1 to –0.5)	0.041
Skindex-29/Functioning	–1.3 (–10.2 to 7.6)	0.416
Anxiety state (STAI-I)	–0.8 (–6.4 to 7.9)	0.822
Anxiety trait (STAI-II)	–1.8 (–9.1 to 5.3)	0.608

GHQ-12

Both the intervention and the control groups had significant reductions in mean GHQ-12 values (Table I). However, the CBT/biofeedback group showed greater improvement, approaching the statistical significance ($p = 0.08$) (Table II). GHQ-12 cases were reduced from 45% to 10% in the treatment group and from 30% to 20% in the control group ($p = 0.05$).

Quality of life

All 3 scales of Skindex-29 (burden of symptoms, social functioning, and emotional state) reduced significantly both in the treatment and in the control group (Table I). The only domain that showed a significant improvement in the CBT/biofeedback group compared with control patients was the emotional domain (–2.8 points, 95% CI –5.1 to –0.5; $p = 0.04$) (Table II).

Anxiety

STAI-I scores showed significant reductions in both groups by the end of the study, with no significant differences between the psychological intervention and the control groups (Table II). Conversely, STAI-II mean values did not change significantly by the end of the study.

DISCUSSION

This study has shown that an adjunctive cognitive-behavioural symptom management therapy combined with biofeedback is beneficial in the management of psoriasis. Patients who underwent this psychological intervention, in addition to their standard narrow-band UVB treatment, showed significantly greater reductions, in the clinical severity of their psoriasis (PASI), in QoL (emotional domain of Skindex-29) and in number of minor psychiatric disorders (GHQ-12 cases) at 8 weeks, with continued improvement at 1-month follow-up.

The positive effect of the CBT and biofeedback intervention was pronounced, in spite of a small study size, suggesting that the effect is robust and attainable in a significant number of psoriasis patients undergoing the psychological therapy. The lack of differences between the group treated with the psychological intervention and

the control group at baseline indicates that the differences found after intervention are unlikely to stem from differences between the two groups in psoriasis activity or psychological measures before the investigation. Interestingly, the difference between mean PASI values of the two study groups increased one month after the end of treatment. This phenomenon has been previously reported in a similar study by Paradisi et al. (14). In this study, theys showed that patients undergoing a emotional writing disclosure short-term protocol had persistent clinical and psychological benefits even after the end of a 2-months course of narrow-band UVB phototherapy, while patients only treated with phototherapy rapidly relapsed. The observation that skills learnt during participation in the cognitive-behavioural programme can continue to have a significant and beneficial clinical effect for at least one month after the end of the programme underscores the advantage of such an approach.

Our finding that psychological intervention can have important effects on clinical extent of psoriasis, as assessed by the PASI, as well as on QoL and psychiatric morbidity, offers new perspectives on the management of this disease.

This data is in agreement with some previous studies suggesting that psychological interventions including stress-reduction relaxation methods and CBT may reduce psoriasis severity in the absence of systemic treatment (6) or as a complement to it (3, 4).

Moreover, there is some evidence that psychological distress, in particular excessive worrying, is able to significantly reduce the rate of clearance of psoriasis in patients receiving standard phototherapy. Fortune et al. (4) showed that patients with high levels of worry are almost twice as likely not to achieve clearance of their psoriasis within a similar length of time as those with low levels of worry.

Biofeedback combined with CBT has proven effective in improving self-efficacy in people with various disorders and symptoms (15, 16).

Biofeedback characteristically enables a patient to gain voluntary control over covert physiological responses by making these responses explicit through real-time visual or auditory feedback. Patients are typically able to learn how to modify these physiological processes volitionally. Therefore, biofeedback may be able to increase the effectiveness of CBT, making the changes believable and increasing motivation.

The results of this study suggest that the effective management of psoriasis requires that we move beyond simple notions of chronic illness as somatic or functional. Indeed, a substantial number of psychologically distressed patients were identified in the current study. Up to 45% of our study patients had a GHQ-12 $\geq$ 4, indicating minor psychiatric suffering.

Previous studies showed similar data, with a prevalence of psychological distress, as detected by GHQ-12, in 33–46% of psoriatic patients (17, 18). Interestingly, both groups showed a significant reduction in psychiatric morbidity by the end of the study, although this was more apparent in the CBT/biofeedback+UVB group (from 45% to 10%) than the UVB group (from 30% to 20%).

Moreover, we observed that both the intervention and the control groups reported an improvement in all dimensions explored by Skindex-29, indicating better overall health-related QoL, better functioning, lower level of negative emotions. Only the emotional domain, probably more influenced by the psychological intervention, showed a greater improvement in the CBT/biofeedback group. The QoL scores reduction reported in patients only treated with conventional UVB therapy is in agreement with previous study showing that an improvement of psoriasis is associated with a concomitant improvement of QoL (19, 20).

Several factors could have contributed to the significant improvement in the CBT/biofeedback group in clinical severity of psoriasis, measured by the PASI score. Coping with situations that may lead to distress may be associated over time with greater clinical improvement.

There is good evidence that stressful life events can trigger or aggravate psoriasis in a significant number of patients. A clear distinction is made today between two types of stress, acute and chronic stress. From an evolutionary point of view, the acute component is beneficial in that it provides organisms with the mechanisms of the protection from the changeable and threatening environment (21). Both the immune response and the fight-or-flight response provide an adequate protection against infection after the injury occurs. In that context, the relationship between acute stress and immune up-regulation can be viewed as an adaptive trait. In response to acute stressors, T cells in the rat react by redistributing into the skin, which is the organ that is the most likely to be affected in a life-threatening situation when fighting the attackers (22).

This can be beneficial in cases when increased immune-protection is needed, but could also mediate stress-induced exacerbation of inflammatory and autoimmune skin disorders and may also be of relevance to psychodermatology (23).

Despite its relatively promising results, the present study had some limitations. Most importantly, although the sample size was average for CBT intervention studies, a larger sample may have yielded more consistent results across variables.

Furthermore, our study population was unusually composed mostly by women (62%). This differs from the typical sex ratio found in several registries on psoriatic patients. A possible explanation for this disparity might be the reluctance of young male patients to accept to undergo a complete phototherapy course, eventually including a 1-hour weekly session of psychotherapy intervention. Moreover, as a recent study by Hägg et al. (24) demonstrated, although as many women as men are believed to suffer from psoriasis, men seem to be

more severely affected by psoriasis. The asymmetry in allocation of biologic therapy and in international registries thereby probably reflects the differing disease activity between the sexes. In our cohort of patients, mean psoriasis severity was not extremely high (mean PASI 9). So it seems likely that our study was not affected by this phenomenon, showing a more balanced sex ratio (40% of enrolled patients were male).

Another limitation may be an inadequate evaluation of the type and degree of psychological changes induced by the cognitive-behavioural programme. A comprehensive assessment of the psychological impact of this intervention may therefore require further investigation.

Until further studies are performed to control for additional variables, we cannot rule out the possibility that expectancy effects (i.e. enthusiasm and/or disappointment about psychological group assignment) may have played a role in the observed differences.

Since the group of patients in the intervention had received 8 h more attention, a Hawthorne effect may also be present (25). Nevertheless, the results of this study suggest an important psychological influence on the rate of skin clearing related to assignment to the cognitive-behavioural intervention group.

A confirmation of these findings in larger samples, possibly also assessing the cost-effectiveness of this multidisciplinary approach, is warranted to further substantiate the usefulness of a cognitive-behavioural treatment in clinical practice. Finally, future research could usefully investigate the maintenance of psychological intervention effects at longer term and evaluate whether follow-up sessions might help to sustain gains.

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