

Balneotherapy for chronic plaque psoriasis at Comano spa in Trentino, Italy

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ABSTRACT: Thermal therapy is used worldwide in the treatment of psoriasis but few controlled studies have evaluated its efficacy and safety. We studied the efficacy and safety of balneotherapy compared to photobalneotherapy performed at Comano spa in Trentino, Italy, in chronic plaque psoriasis in a prospective, nonrandomized, open study. Three hundred adult patients with mild to severe chronic plaque psoriasis were assigned to either balneotherapy or photobalneotherapy with daily narrow-band ultraviolet B for a mean period of 1 or 2 weeks, reflecting the times that most patients can dedicate to thermal therapy. Patients were evaluated at baseline and end of treatment for psoriasis area and severity index (PASI) and body surface area; self-administered PASI (SAPASI) and Skindex-29 were evaluated at the same times, and also at 4 months by a mailed questionnaire. One-week balneotherapy or photobalneotherapy resulted in a significant reduction in PASI score ($11.54\% \pm 2.76$ and $12.76\% \pm 3.79$, respectively; mean \pm standard deviation; $p < 0.001$). Two-week therapy induced a greater response with photobalneotherapy than with balneotherapy alone, with PASI reduction of $19.8\% \pm 24.5$ and $13.5\% \pm 23.1$ ($p < 0.005$), respectively. These results were confirmed by SAPASI and Skindex-29 evaluation. The therapy was well tolerated. Skin improvement was mostly lost after 4 months. Short-term balneotherapy and photobalneotherapy could thus be offered to patients willing to temporarily discontinue pharmacologic therapy or as adjuvant therapy.

KEYWORDS: Psoriasis, balneotherapy, spa, quality of life

Introduction

Thermal balneotherapy, although not accepted as well-established treatment modality, is used throughout the world in the therapy of psoriasis because it offers a natural, multifactorial, complementary, and nontoxic alternative to traditional pharmacologic treatment (1–3). Indeed, for many patients with psoriasis, the most important attribute of therapy is safety, and many of them accept with enthusiasm the possibility of safe natural treatments even if of limited efficacy.

Thermal balneotherapy at Comano spa in Trentino, Italy, has long been used in the treatment of various skin diseases, with special regard for psoriasis and atopic dermatitis (4–6). In more recent years, balneotherapy has been also associated with ultraviolet B (UVB) narrow-band phototherapy (7).

Comano water is an oligometallic thermal water, containing various microelements, among which calcium and magnesium are more represented; it has a temperature of 27°C in the springs and a pH of 7.5–7.6. Despite the fact that balneotherapy has been used for long time with apparent good clinical results, the mechanism of action is unknown. Recent studies have shown that exposure of cultured human psoriatic keratinocytes to Comano water in vitro significantly down-modulates the

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expression and secretion of vascular endothelial growth factor-A (VEGF-A) isoforms, interleukin (IL)-6, IL-8, and tumor necrosis factor (TNF)- α , as well as of the expression of cytocheratin-16 (8–10), suggesting that Comano water can effectively reduce the production of factors relevant to the pathogenesis of psoriasis.

The aim of this study was to evaluate the efficacy and safety of balneotherapy compared to photobalneotherapy performed at Comano spa in the treatment of chronic plaque psoriasis, with the treatment periods corresponding to the actual staying of most patients at the spa center. The results show that even 1-week balneotherapy can be effective in psoriasis, with only minor side effects. Photobalneotherapy appears to be more effective than balneotherapy alone in the 2-week regimen.

Patients and methods

This was a prospective, nonrandomized, open clinical trial. The primary end point of the study was to compare the efficacy of balneotherapy with photobalneotherapy at Comano spa at 7 and 15 days, by assessing the psoriasis area and severity index (PASI), body surface area (BSA), and self-administered PASI (SAPASI). Secondary endpoints included the evaluation of safety, impact on quality of life, and the patients' outcomes at 4 months. Inclusion criteria were age 18–85 years and diagnosis of chronic plaque psoriasis. Patients younger than 18 years, patients with very severe psoriasis, erythrodermic or sub-erythrodermic and pustular psoriasis, and patients with severe cardiovascular diseases or any other systemic disease judged severe were excluded. Systemic treatments were discontinued at least 4 weeks, and therapy with biologics 3 months before admission to the study.

After informed consent has been signed, patients were alternatively assigned to either balneotherapy or photobalneotherapy. Balneotherapy comprised one to two daily baths (1.63 ± 0.35 bath/day; mean \pm standard deviation (SD)) with total immersion in individual bath tub, lasting 20 minutes each with Comano water heated to 36–37°C. Photobalneotherapy consisted of baths in Comano water (mean 1.64 ± 0.35 bath/day) followed (within 15 minutes) by one daily irradiation with increasing doses of narrow band UVB. The starting dose was 200 mJ/cm^2 , with a daily increase of $150\text{--}200 \text{ mJ/cm}^2$ depending on patient's phototype (cumulative dose: $10.45 \pm 6.03 \text{ J/cm}^2$). The irradiation source was a Waldmann UV 7001 UVB (Waldmann, Villingen-Schwenningen,

Germany) stand-up cabinets fitted with 40 Waldmann F85/100 W UV01 lamps each. During the treatment period, patients were advised not to use topical treatments, with the exception of emollients. Patients were divided into two groups according to the duration of treatments: the 1-week therapy groups had a treatment duration of 7.4 ± 1.6 days (mean \pm SD), whereas the 2-week therapy groups had a treatment duration of 13.8 ± 2.5 days.

At the day of admission (day 0) demographic data, patient medical history (comorbidities), previous treatments for psoriasis as well concomitant therapy for other diseases were collected. Moreover, psoriasis severity was measured by a trained dermatologist using the PASI and BSA involved (11–13), and patients were asked to fill the SAPASI questionnaire, that many studies had demonstrated to be reliable and valid (14–17), and the validated Italian version of the Skindex-29 questionnaire (18). At the end of treatment, patients were evaluated by the same physician for psoriasis severity (PASI and BSA) and adverse events, and asked again to assess SAPASI and answer the Skindex-29 questionnaire. Four months after the end of treatment, each patient received at home a questionnaire inquiring about the course of disease, its severity (SAPASI) and its impact on quality of life (Skindex-29), and treatments used for psoriasis during the 4 months after spa treatment termination.

All data were recorded on electronic support and analyzed with GraphPad Prism 4 program (GraphPad Software, San Diego, CA). The chi-square test was used to compare nominal data (e.g., sex distribution). For ordinal data Student's *t*-test has been utilized with paired *t*-test for the comparison within the same group and unpaired *t*-test for comparison of different groups. All test of significance were two-tailed, and statistical significance was assumed at $p < 0.05$. Results for PASI and BSA are expressed in box and whiskers graphs: the box extends from the 25th to the 75th percentile and the line at the median (50th percentile), while the whiskers show the highest and the lowest values.

Results

Three hundred patients were included in the study during a 2-month period (between 31 August and 30 October 2006); 169 were assigned to balneotherapy alone and 131 to photobalneotherapy. Two hundred and eighty (93.3%) patients completed the study, and 234 (78.0%) sent back the filled

Table 1. Baseline characteristics of patients

	Balneotherapy 1 week (n = 77)	Photobalneotherapy 1 week (n = 40)	Balneotherapy 2 weeks (n = 79)	Photobalneotherapy 2 weeks (n = 84)
Age (years) ^a	55 ± 13	50 ± 15	57 ± 14	52 ± 12
Sex: male/female	49/28	27/13	47/32	53/31
Age of psoriasis onset (years) ^a	32 ± 18	29 ± 15	35 ± 17	29 ± 15
Psoriasis duration (years) ^a	23 ± 16	22 ± 13	22 ± 15	22 ± 12
PASI ^a	7.44 ± 4.97	8.42 ± 4.54	8.21 ± 5.53	9.35 ± 4.89
BSA ^a	14.10 ± 13.78	15.44 ± 12.76	15.69 ± 15.57	18.84 ± 14.23
SAPASI ^a	8.15 ± 5.01	9.46 ± 4.48	9.15 ± 5.15	11.17 ± 6.40
Skindex-29 ^a	35.56 ± 15.59	34.04 ± 20.79	35.24 ± 19.91	37.71 ± 19.05
Psoriatic arthritis	14 (18.2%)	7 (17.5%)	11 (13.9%)	10 (11.9%)
Previous treatments:				
Topical	77 (100%)	40 (100%)	79 (100%)	84 (100%)
nb-UVB	22 (28.6%)	13 (32.5%)	21 (26.6%)	28 (33.3%)
PUVA	13 (16.9%)	13 (32.5%)	11 (13.9%)	19 (22.6%)
Acitretin	15 (19.5%)	2 (5%)	15 (18.9%)	15 (17.8%)
Cyclosporine A	8 (10.4%)	9 (22.5%)	12 (15.2%)	15 (17.8%)
Methotrexate	5 (6.5%)	3 (7.5%)	5 (6.3%)	6 (7.1%)
Fumaric acid	1 (1.3%)	1 (2.5%)	0	0
Etanercept	1 (1.3%)	0	1 (1.3%)	0
Infliximab	1 (1.3%)	0	1 (1.3%)	0
Efalizumab	0	0	1 (1.3%)	0

^aData are expressed as mean ± standard deviation.

BSA, body surface area; PASI, psoriasis area and severity index; PUVA, psoralen plus exposure to ultraviolet A; nb-UVB, narrow-band ultraviolet B; SAPASI, self-administered psoriasis area and severity index.

questionnaire after 4 months, but only for 212 (70.7%) patients all three data points were available. Patients were divided into two groups according to the duration of therapy (1 and 2 weeks) and received either balneotherapy or photobalneotherapy. These treatment periods correspond to the actual staying of most patients at the thermal center. Demographics data of patients and baseline features of psoriasis are shown in Table 1. There were no statistically significant differences between the treatment groups in respect to age and sex, baseline psoriasis severity, duration and age of onset, presence of psoriatic arthritis, and the Skindex-29 values. All patients had received topical or systemic treatments, which were similarly distributed in the patient groups. Table 2 summarizes the most relevant risk factors and comorbidities: about one-third of patients were smokers, one-half were consuming alcohol daily, and more than 60% of patients were overweight or obese. Cardiovascular risk factors were common, particularly hypertension, hyperlipidemia, and diabetes mellitus. These data confirm previous results, showing a higher prevalence of cardiovascular factors in patients with psoriasis (19–21). There were no major differences in skin phototype

between the two photobalneotherapy groups (data not shown).

One-week balneotherapy (12.6 ± 3.1 baths) or photobalneotherapy (13.6 ± 3.5 baths plus 4.9 ± 2.5 J/cm²) was sufficient to obtain statistically significant reduction in the PASI score (FIG. 1a,b), with a PASI improvement of 11.54% ± 2.76 and 12.76% ± 3.79, respectively, with no difference in the efficacy between the two treatment modalities. This improvement was mainly due to reduction in the desquamation as BSA did not change significantly, at least in the balneotherapy group (FIG. 2a,b). In the 2-week therapy groups, both balneotherapy (19.4 ± 3.5 baths) and photobalneotherapy (20.3 ± 4.2 baths plus 12.1 ± 6.1 J/cm²) induced a greater psoriasis amelioration with reduction in both the PASI score and the BSA (FIG. 1c,d; and FIG. 2c,d). In this case, photobalneotherapy performed better than balneotherapy with a PASI reduction of 19.8% ± 24.5 and 13.5% ± 23.1, respectively (*p* < 0.005) (FIG. 1c,d). The efficacy of treatment at both 1 and 2 weeks was confirmed by patients themselves, as shown by the results of the SAPASI and Skindex-29 questionnaires (FIGS. 3 and 4). Disease severity abated and the quality of life was significantly improved with both balneotherapy

Table 2. Risk factors and comorbidities

	Balneotherapy 1 week (n = 77)	Photobalneotherapy 1 week (n = 40)	Balneotherapy 2 weeks (n = 79)	Photobalneotherapy 2 weeks (n = 84)
Nonsmokers	57 (74.0%)	30 (75.0%)	62 (78.5%)	52 (61.9%)
Smokers	20 (25.9%)	10 (25.0%)	17 (21.5%)	32 (38.1%)
Cigarettes/day ^a	18 ± 8	16 ± 11	19 ± 11	14 ± 8
Alcohol consumption:				
Daily	36 (46.7%)	17 (42.5%)	35 (44.3%)	42 (50.0%)
Occasionally	34 (44.1%)	19 (47.5%)	34 (43.0%)	38 (45.2%)
Never	7 (9.1%)	4 (10%)	10 (12.6%)	4 (4.8%)
BMI ^a	26.9 ± 4.8	27.2 ± 5.3	26.8 ± 5.1	27.1 ± 4.5
BMI < 25	27 (35.0%)	12 (30.0%)	29 (36.6%)	29 (34.5%)
BMI 25–30	35 (45.5%)	18 (45.0%)	33 (41.8%)	36 (42.9%)
BMI > 30	15 (19.5%)	10 (25.0%)	17 (21.5%)	19 (22.6%)
Hypertension	26 (33.8%)	14 (35.0%)	25 (31.6%)	29 (34.5%)
Hypertriglyceridemia	7 (9.1%)	3 (7.5%)	13 (16.4%)	18 (21.4%)
Hypercholesterolemia	21 (27.3%)	8 (20.0%)	19 (24.1%)	29 (34.5%)
Diabetes mellitus	7 (9.1%)	2 (5.0%)	14 (17.7%)	11 (13.1%)
Cardiopathy	2 (2.6%)	1 (2.5%)	5 (6.3%)	2 (2.4%)
Cerebrovascular accidents	1 (1.3%)	0	3 (3.8%)	1 (1.2%)

^aData are expressed as mean ± standard deviation. BMI, body mass index.

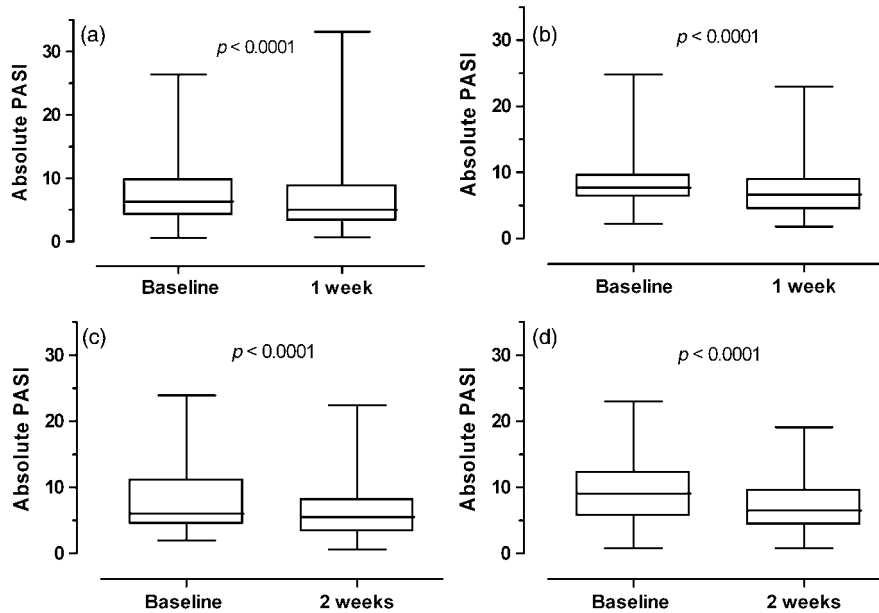


FIG. 1. Psoriasis area and severity index (PASI) variation from baseline to end of treatment (a and c: balneotherapy; b and d: photobalneotherapy). Differences before and after treatment were always statistically significant. Improvement between balneotherapy and photobalneotherapy at week 1 was not different, whereas at week 2 photobalneotherapy was more effective than balneotherapy alone ($p < 0.001$).

or photobalneotherapy both at 1 and 2 weeks ($p < 0.0001$). Again, the efficacy (PASI, BSA, and SAPASI) of balneotherapy was similar to photobalneotherapy at week 1, whereas the latter was superior to the former at week 2 ($p < 0.001$).

According to responses to home-filled questionnaire, 38% (80 of 212) patients noted a further amelioration of their psoriasis at 30 days after, 16% remained stable, and 12% slightly worsened in the absence of any active treatment; 34% of

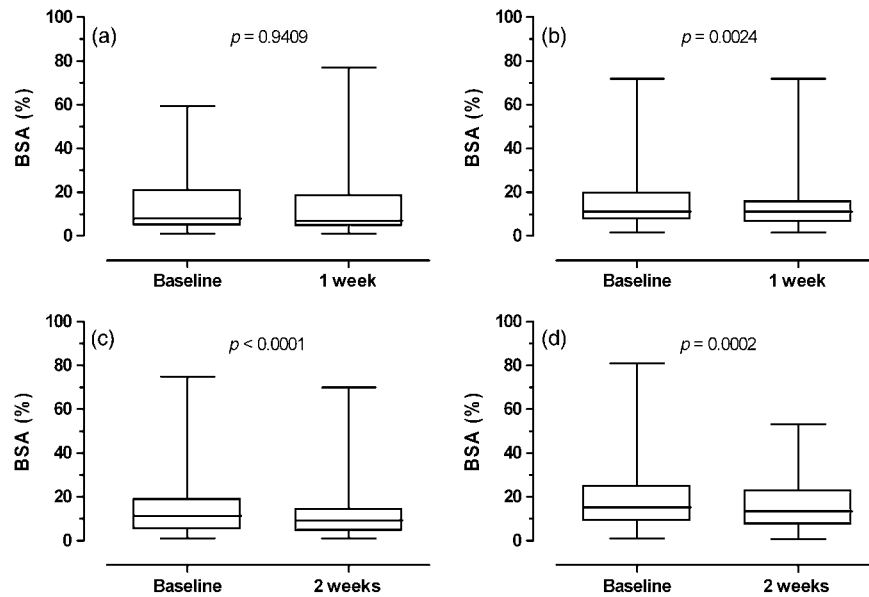


FIG. 2. Body surface area (BSA) variation from baseline to end of treatment. (a and c: balneotherapy; b and d: photobalneotherapy). Differences before and after treatment were not statistically significant at week 1 for balneotherapy. Photobalneotherapy was more effective than balneotherapy alone at week 2 ($p < 0.001$).

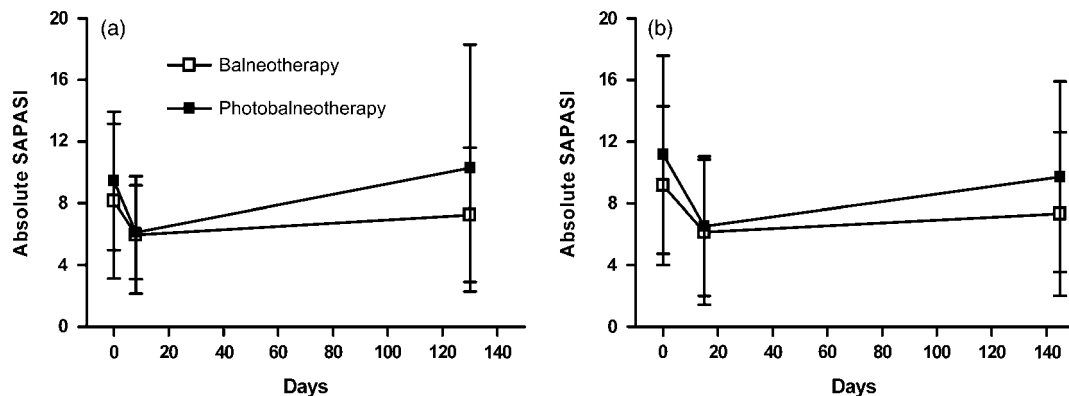


FIG. 3. Self-administered body surface area (SAPASI) at baseline, end of therapy, and after 4 months. (a) 1-week therapy groups; (b) 2-week therapy groups. Differences before and after treatment were statistically significant ($p < 0.001$) at weeks 1 and 2 for both balneotherapy and photobalneotherapy. Differences between baseline and 4 months after end of therapy were not different for balneotherapy, whereas were still significant for patients treated with photobalneotherapy ($p < 0.05$).

patients started a new topical and/or systemic therapy (data not shown). During the following 3 months, many patients experienced a progressive worsening of their skin condition and quality of life with return to the basal situation, with the exception of patients treated with photobalneotherapy for 2 weeks who maintained some beneficial effects ($p < 0.05$) compared to baseline (FIGS. 3b and 4b).

Therapy was, in general, well tolerated with no major side effects. The most common adverse

event related to therapy was mild to moderate cutaneous discomfort (pruritus, burning sensation, and skin dryness) occurring in 13.9% (39 of 280) of patients, irrespective of the type of treatment. These symptoms were self-limiting, and in no case caused changes in the treatment. In the photobalneotherapy groups, about one-third of patients experienced UV-induced erythema, which was, in general, mild to moderate and rarely severe. In about 45% of these patients, the intensity of erythema led to a change in the phototherapy

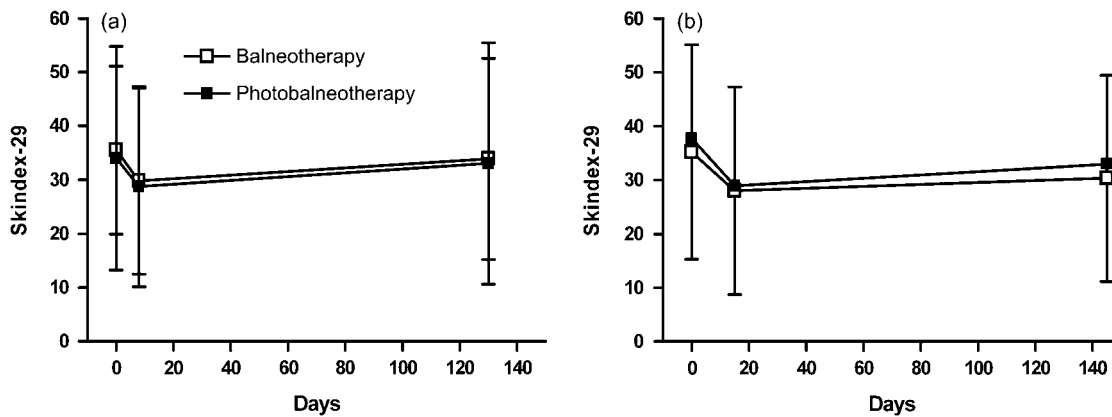


FIG. 4. Skindex-29 at baseline, end of therapy, and after 4 months. (a) 1-week therapy groups; (b) 2-weeks therapy groups. Differences before and after treatment were statistically significant ($p < 0.001$) at weeks 1 and 2 for both balneotherapy and photobalneootherapy. Differences between baseline and 4 months after end of therapy were not different for balneotherapy, whereas were still significant for patients treated with photobalneootherapy ($p < 0.05$).

dose, but only in one case to therapy discontinuation. Five percent of patients reported transient fatigue and 1.1% external otitis.

Discussion

Spa balneotherapy emerged as an important treatment modality in the 1800s, first in Europe and then in the USA; it was subsequently scoffed at by scientists and declined in popularity. Finally it experienced a resurgence of interest over the past two decades, although it has yet to be accepted as a well-established treatment modality for dermatologic conditions (22). Balneotherapy is being practiced in many countries all over the world (22–33), with a variety of mineral springs and muds, considerably different from one another in their hydrogeologic origin, temperature, and chemical composition (22). Although a comparison between different studies is difficult for the heterogeneity of outcome measures and the different modalities of spa therapies (as for chemical composition as for treatment schedule), many authors conclude that balneotherapy alone can gain major benefits to patients after 3–4 weeks of treatment (23,25,26,31). Balneotherapy is frequently associated with phototherapy, because bathing before UV or sun exposure helps to enhance the efficacy of phototherapy (24,29,31), either by reducing desquamation and minimal erythematous dose or enhancing skin hydration, or even eluting UV-absorbing substances or proteolytic enzymes from psoriatic skin lesions (34). Recent and well-designed studies seemed not to completely

confirm these results. In a randomized controlled comparison, pretreatment with Dead Sea salt soaks did result in a slight but not clinically important improvement versus nb-UVB alone (30).

Despite the wide popularity of these therapies, there are only a few controlled clinical trials supporting their use (35). These include studies conducted in the Dead Sea spas (28–30), Blue Lagoon in Iceland (23,24), Comano spa (8), and some spas in western and eastern Europe (25,26,36). Moreover, there are a few biologic studies that have investigated the possible activity of spring water on skin pathophysiology, with particular regard to modification in Langerhans cells (37,38), inflammatory cytokines (39), and other immunologic aspects (40,41). Another study showed skin hydration and histologic effectiveness of bathing with Comano water for psoriasis as compared to common water, beside clinical efficacy (6). More recently, Comano water has been shown to reduce the production of factors relevant to pathogenesis of psoriasis, including vascular endothelial growth factor-A (VEGF-A), IL-6, IL-8, and TNF- α by keratinocytes cultured from psoriatic patients (8–10).

In this study we evaluated the efficacy and safety of balneotherapy compared to photobalneootherapy performed at Comano spa in the treatment of chronic plaque psoriasis. The results show that 1-week balneotherapy was already sufficient to obtain statistically significant improvement in the PASI score, with no differences compared to photobalneootherapy. Although it was administered daily, 1-week phototherapy was obviously not sufficient to see a significant effect. Two-week balneotherapy induced a greater psoriasis

amelioration compared to 1-week therapy, but in this case photobalneo-therapy acted better than balneotherapy alone. These short courses reflect the effective duration of staying at Comano spa of the majority of patients. PASI improvement in the 1-week regimen appeared principally due to reduction of scaling and mild reduction of infiltration, but no changes in BSA involved; in contrast, the 2-week therapy groups showed also a significant reduction of BSA affected. Quality of life, measured by Skindex-29 questionnaire, improved in parallel with disease amelioration and was significant for all treatment groups. Although about one-third of our patients referred a further amelioration at 1 month in the absence of any treatment, another third of patients started a new topical and/or systemic therapy during the same period, either for skin worsening or to maintain or complete the results gained. Furthermore, during the following 3 months, many patients experienced a progressive worsening of their skin condition and quality of life with return to the basal situation, with the exception of patients treated with photobalneo-therapy for 2 weeks who maintained some beneficial effects compared to baseline. This study thus confirms the efficacy of balneotherapy at Comano spa for psoriasis. The study has several limitations, including the absence of randomization and double-blind evaluation, which are very difficult to perform in a spa setting. On the other hand, a previous randomized, double-blind study has shown the higher efficacy of balneotherapy with spring Comano water compared to balneotherapy with tap water (6). The active treatment periods were only of 1 or 2 weeks because these are times most patients can dedicate to thermal therapy. Phototherapy may not be sufficient in these timeframes, but this was partially compensated by the daily administration schedule.

Many patients with psoriasis consider safety as a very important attribute of therapy, sometimes even more important than efficacy, and many of them accept with enthusiasm the possibility of safe natural treatments even if efficacy is not very high. The acceptance of thermal balneotherapy by patients is further increased by the fact that it is performed in a pleasant place, far from every day stressing events and in a setting that favors dialogue and contact with many other people suffering of the same diseases, both spontaneously as in the contest of psychoeducational programs. Moreover, balneotherapy does not interfere with metabolic comorbidities and does not cause drug interactions. Mostly in chronic and not life-threatening diseases, such as psoriasis,

a patient-centered approach is now considered to be the most adequate. Because a definitive cure is still lacking and there is no treatment suitable for all patients, satisfaction of patients' needs should be the first aim for physicians treating psoriasis patients. Therefore, balneotherapy appears an interesting adjuvant or alternative therapy for patients with chronic plaque psoriasis, and can thus be offered to patients willing to discontinue momentarily pharmacologic therapy.

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