Balneotherapy for atopic dermatitis in children at Comano spa in Trentino, Italy

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Balneotherapy for atopic dermatitis in children at Comano spa in

Trentino, Italy

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Abstract

Background No controlled studies have investigated whether balneotherapy is effective in atopic dermatitis (AD).

Objectives To investigate the efficacy and safety of balneotherapy performed at Comano spa (Trentino, Italy) compared to topical corticosteroids (TCS) in the treatment of AD.

Methods Open, randomized clinical trial. 104 children (aged 1-14 years) with mild to moderate AD were assigned either to balneotherapy (n, 54) or TCS (n, 50) once daily for two weeks. AD severity and quality of life were measured using the SCORAD, investigator global assessment (IGA), patients self global assessment (PSGA), children dermatology life quality index (CDLQI) and family dermatitis impact questionnaire (FDIQ). Subjective measures were re-evaluated 4 months after the end of therapy.

Results Balneotherapy and TCS resulted in a significant reduction of all parameters at week 2. TCS were more effective than balneotherapy regarding SCORAD (46% ± 7.71 vs 26% ± 9.4; mean ± SD; p < 0.03). In contrast, IGA, PSGA, CDLQI and FDIQ improvement was similar. At month 4, number and duration of relapses were less in patients treated with balneotherapy compared to those treated with TCS (p <0.0001).

Conclusions Balneotherapy at Comano spa appears to be beneficial in children with mild to moderate AD.
Introduction

Atopic dermatitis (AD) is a chronic relapsing inflammatory skin disease, which is increasingly more frequent especially in infancy and in developed countries (1). In Italian school children, it has been estimated a point prevalence of 5.8% and a lifetime prevalence of 15.2% (2). AD represents a remarkable problem of public health and has a profound effect on quality of life for both children and their parents (3,4). Disease burden is related to the presence of comorbidities (respiratory diseases), complications (skin infections, psycho-affective problems, growth delay), side-effects of therapy, and costs (both direct costs for visits, medicines and medical devices, and indirect costs, such as work days and school days lost and disability), and is comparable to those of other chronic diseases (5,6). The standard of therapy for mild/moderate AD has been and still is in most countries the application of topical corticosteroids (TCS). Topical calcineurin inhibitors are now widely used both in the short and long term (7). TCS are very effective in the short term but long term use can be associated with cutaneous and systemic adverse effects (8). Many parents would wait until AD get worse or apply TCS only as a last resort to avoid their potential side effects; this practice may potentially end in a vicious cycle leading to more extensive inflammation, resulting in a more prolonged course and a larger amount of TCS use (9). The confidence and the adherence to therapy are determinant for treatment success. Among the most commonly reported reasons for poor adherence to topical therapy are lack of efficacy, time required for application and fear of side-effects (corticophobia) (10,11). Therefore, many patients and parents are frustrated with the management of AD and they search for alternative, safe and not much demanding treatments.
Thermal balneotherapy is widely in the treatment of various skin diseases because it offers a natural, pleasant and not-toxic alternative to traditional pharmacological treatment (12). The acceptance of thermal balneotherapy by patients is further increased by the fact that it is performed in pleasant places, far from every day stressing events and in a setting that favors dialogue and contact with many other people suffering of the same disease. Thermal balneotherapy at Comano spa (Trentino, Italy) has long been used in the treatment of various dermatologic conditions, with special regard for psoriasis and atopic dermatitis (13,14). 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 Comano water can effectively reduce the production of factors relevant to the pathogenesis of psoriasis (15-17) and that balneotherapy can represent an interesting adjuvant or alternative therapy for psoriasis patients willing to discontinue pharmacologic therapy (18). Only few studies have evaluated the efficacy of balneotherapy in AD (19-23), and no studies was controlled. The aim of this study was to investigate the efficacy of balneotherapy compared to TCS in two groups of pediatric patients with mild to moderate AD.

Methods
This was an open, randomized, clinical trial. Inclusion criteria were age 1-14 years and diagnosis of mild to moderate AD (investigator global assessment (IGA) < 3; scoring AD (SCORAD) < 40) (24,25). After informed consent had been signed, patients were alternatively assigned to either balneotherapy or topical corticosteroids
treatment (54 patients treated at Comano spa (spa-patients) and 50 patients treated with TCS (TCS-patients), comparable for age, sex and disease severity). Randomization was performed with the use of computer-generated random numbers and block size of 4 patients. Balneotherapy comprised one or two daily baths with total immersion in individual bath tub, lasting 20 minutes each with Comano water heated to 36-37°C. TCS treatment consisted in the use of methylprednisolone aceponate (before the age of two) or mometasone furoate (after the age of two) once daily for two weeks. During the treatment period, any other treatment was prohibited, with the exception of emollients. At admission, demographic data, previous treatments for AD and the presence of respiratory diseases was registered. Moreover AD severity was measured by a trained dermatologist using the IGA (based on a scale ranged from 0 to 5: 0=no disease; 1=almost absent; 2=mild; 3=moderate; 4=severe; 5=very severe) and SCORAD, and patients were asked to express an evaluation of disease severity based on the patients self global assessment (PSGA) and the intensity of pruritus (visual analog scale (VAS): 0-100) and to fill a questionnaire about the quality of life of both patients (children dermatology life quality index, CDLQI) (25) and their families (family dermatitis impact questionnaire, FDIQ) (26). At the end of the treatment, patients were evaluated by the same physician for AD severity, adverse events, treatment adhesion and pleasantness, and asked again to assess PSGA and VAS-pruritus and answer the CDLQI and FDIQ. Four months after the end of the treatment each patient received a telephone interview about the course and severity (PSGA and VAS-pruritus) of AD, the impact on quality of life (CDLQI and FDIQ), and the use of TCS in the last four months.
Statistical analysis

All analyses were performed using the STATA (version 10.0 Stata-Corp LP, College Station, TX) and Graph-Pad (version 4.0, El Camino Real, San Diego, CA) software packages. Data are expressed as means ± SD or percentages. Skewed variables were logarithmically transformed to improve normality for statistical purposes and then back-transformed to their natural units for the presentation in tables and figures. Statistical analyses included the unpaired-t test (for continuous variables), and the chi-squared test with Yates’s correction for continuity (for categorical variables). Values at p<0.05 were considered statistically significant.

Results

Demographics data of study population and baseline features of AD are shown in Table I. A total of 104 children were included in the study during a 1-month period (between 15 August and 15 September 2008), of which 54 were assigned to balneotherapy and 50 to TCS treatment. All patients completed the study and answered the telephone interview after four months. Treatment duration was two weeks, which is the period corresponding to the actual staying of most patients at the thermal center. There where no statistically significant differences between the treatment groups in respect to age and sex, baseline AD severity, baseline intensity of pruritus, the presence of comorbidities, and the impact on quality of life. All patients had received topical or systemic treatments which were similarly distributed in the two groups. Balneotherapy (total number of baths: 13.14 ± 2.63, mean ± SD) or TCS obtained a significant reduction in disease severity after two weeks (Figure 1A), with a higher efficacy of TCS compared to balneotherapy (46% ± 7.71 vs 26% ± 9.4; mean ± SD; p < 0.03). The same results were observed for the IGA (Figure 1B),
pruritus intensity (Figure 2A) and PSGA (Figure 2B), but for these measures the improvement was similar in the two groups. The efficacy of both treatments on quality of life was confirmed by patients themselves and their parents, as shown by the responses to the CDLQI and FDIQ questionnaires (Figure 3A and Figure 3B). Interestingly, quality of life improved better with balneotherapy than with TCS. Four months after the end of the treatment spa-patients noted a further amelioration of their skin disease according to pruritus intensity (Figure 2A) and PSGA (Figure 2B), whereas TCS-patients noted an aggravation of AD. Similar results were observed for quality of life indexes, with the CDLQI and the FDIQ improving further after four months in spa-patients and worsened and unchanged in TCS-patients, respectively (Figure 3). In addition, at four months after the end of the treatment, spa-patients had less relapses and days with disease compared to TCS-patients; disease free time in the absence of any active treatment was longer in spa-patients than in TCS-patient and the need to start a new topical therapy resulted greater in TCS-patients than in spa-patients (Table II). Both balneotherapy and TCS treatment were in general well tolerated with no major side-effects. The most common adverse event related to balneotherapy was mild cutaneous discomfort (erythema and burning sensation) occurring in 42.6% (23 of 54) of patients. These events were self-limiting and in no case caused changes in the treatment.

**Discussion**

Balneotherapy has a relevant place in the therapy of chronic inflammatory skin diseases in many countries, and it obtains patients approval not only for the specific therapeutic property of thermal water but also for the thermal setting dedicated to peace and quiet. Many patients consider safety as a very important attribute of
therapy and many of them accept with enthusiasm the possibility of safe natural
treatments offered by spa balneotherapy, that allows patients to take care of their
psyco-physical wellbeing, slowing down daily frenetic activities and enjoying a natural
environment (27). This is true especially for pediatric patients because the thermal
setting favors a positive parents-children relationship and it overcomes the discomfort
caused by AD. Despite the wide popularity of thermal therapies there are only few
studies supporting their use and investigating the possible activity of thermal water
on skin pathophysiology. A retrospective analysis of literature shows that spring water
low in mineral content, like Comano spa water, is blessed with decongestant effect
and it is able to reduce erythema, pruritus and burning sensation and to improve skin
hydration (28); the same water has been shown to reduce basophil degranulation, to
suppress inflammatory cytokines production by Langerhans cells, to prevent mast
cells activation and to improve membrane fluidity, negatively modulating the
activation of lymphocytes subsets involved in the induction and maintenance of
eczema lesions (15-17).

Our study evaluated the efficacy and safety of balneotherapy performed at
Comano spa compared to TCS in the treatment of pediatric AD. The results showed
that TCS were more rapidly effective in the short-term compared to balneotherapy.
However, at 4 months balneotherapy induced a greater AD amelioration than TCS,
not only in terms of disease severity but also in terms of frequency and duration of
relapses, days with disease and disease free time. Quality of life improved in parallel
with disease amelioration in both groups but later on it resulted better in spa-patients
than in TCS-patients. This study thus confirms the efficacy and safety of
balneotherapy at Comano spa for pediatric AD. The study has several limitation,
including the absence of double-blind evaluation, which however is very difficult to
perform in a spa setting. Patients were recruited on a voluntary basis; this limits any generalization of the results. Therefore balneotherapy appeared an interesting adjuvant or alternative therapy for management of mild to moderate AD.
References


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<th>SPA patients</th>
<th>TCS patients</th>
<th>p value</th>
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<tr>
<td><strong>n</strong></td>
<td>54</td>
<td>50</td>
<td></td>
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<tr>
<td>Gender (male/female)</td>
<td>21/33</td>
<td>26/24</td>
<td>0.2</td>
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<tr>
<td>Age (years)</td>
<td>7.8 ± 3.3</td>
<td>7.2 ± 2.9</td>
<td>0.7</td>
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<tr>
<td>Positive family history for atopic disease (asthma, dermatitis, rhinitis or conjunctivitis) (%)</td>
<td>77.8</td>
<td>73.3</td>
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<tr>
<td>Concomitance of atopic diseases:</td>
<td></td>
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<tr>
<td>Rhinitis (%)</td>
<td>33.3</td>
<td>16.7</td>
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<td>Conjunctivitis (%)</td>
<td>20.4</td>
<td>10.0</td>
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<tr>
<td>Asthma (%)</td>
<td>31.5</td>
<td>16.7</td>
<td>0.1</td>
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<td>Previous therapy:</td>
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<td>Emollients (%)</td>
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<td>0.1</td>
</tr>
<tr>
<td>Topical steroids (%)</td>
<td>55.6</td>
<td>56.7</td>
<td>0.1</td>
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<td>Topical calcinuerin inhibitors (%)</td>
<td>22.2</td>
<td>10.0</td>
<td>0.1</td>
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<tr>
<td>Systemic steroids (%)</td>
<td>16.7</td>
<td>33.3</td>
<td>0.1</td>
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<tr>
<td>SCORAD</td>
<td>26.6 ± 7.9</td>
<td>25.6 ± 7.6</td>
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<td>IGA</td>
<td>2.0 ± 0.8</td>
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<td>PSGA</td>
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<td>2.4 ± 0.6</td>
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<td>VAS pruritus</td>
<td>43.9 ± 24.5</td>
<td>43.7 ± 21.9</td>
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<tr>
<td>CDLQI</td>
<td>7.0 ± 5.8</td>
<td>5.1 ± 2.0</td>
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<tr>
<td>FDIQ</td>
<td>8.5 ± 5.8</td>
<td>8.2 ± 3.3</td>
<td>0.7</td>
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Data are expressed as means ± SD or percentages.
Table II Results after 4 months from the end of treatment

<table>
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<th>SPA patients</th>
<th>TCS patients</th>
<th>p value</th>
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<tbody>
<tr>
<td>Relapses</td>
<td>0.5 ± 0.5</td>
<td>1.8 ± 0.9</td>
<td>0.001</td>
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<tr>
<td>Days of disease</td>
<td>6.9 ± 9.7</td>
<td>17.6 ± 10.2</td>
<td>0.001</td>
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<tr>
<td>Disease free time (months)</td>
<td>3.1 ± 1.1</td>
<td>1.6 ± 0.8</td>
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<tr>
<td>TCS (%)</td>
<td>29.63%</td>
<td>93.33%</td>
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</table>

Data are expressed as means ± SD or percentages.
Legend to figures

Figure 1. (A) SCORAD (mean ± SD) at baseline and after 15 days. Column in white represents spa-patients and column in black represents TCS-patients. (B) IGA (mean ± SD) at baseline and after 15 days. Column in white represents spa-patients and column in black represents TCS-patients.

Figure 2. (A) VAS PRURITUS (mean ± DS) at baseline, after 15 days and after 4 months. Column in white represents spa-patients and column in black represents TCS-patients. (B) PSGA (mean ± DS) at baseline, after 15 days and after 4 months. Column in white represents spa-patients and column in black represents TCS-patients.

Figure 3. (A) CDLQI (mean ± DS) at baseline, after 15 days and after 4 months. Column in white represents spa-patients and column in black represents TCS-patients. (B) FDIQ (mean ± DS) at baseline, after 15 days and after 4 months. Column in white represents spa-patients and column in black represents TCS-patients.
Farina et al. Figure 2

PRURITUS (VAS)

PSGA

BASELINE 15 DAYS 4 MONTHS

BASELINE 15 DAYS 4 MONTHS