**Diet and Weight Loss as a Treatment for Psoriasis**

Joel M. Gelfand, MD, MSCE; Katrina Abuabara, MA; Department of Dermatology, and Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania School of Medicine, Philadelphia

**Commentary on:** Weight loss improves the response of obese patients with moderate-to-severe chronic plaque psoriasis to low-dose ciclosporine therapy: A randomized, controlled, investigator-blinded clinical trial

Gisondi P, Del Giglio M, Di Francesco V, Zamboni M, Girolomoni G


**Question:** Does moderate weight loss induced by a calorie-restrictive diet improve the therapeutic response to low-dose ciclosporine in obese patients with moderate to severe psoriasis?

**Design:** A 24-week randomized controlled investigator-blinded clinical trial.

**Setting:** Psoriasis outpatient clinic of the University Hospital of Verona, Verona, Italy.

**Patients:** Patients were 18 years or older, had active but clinically stable plaque psoriasis involving at least 10% of their body surface area (BSA) and a Psoriasis Area and Severity Index (PASI) score of at least 10, and had a body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) of at least 30 but less than 45. Patients were excluded if they had other variants of psoriasis, had uncontrolled medical disorders, active or chronic infections, previous malignant diseases, any history treatment with ciclosporine, or had received phototherapy or any systemic or topical therapy for psoriasis in the 4 weeks before enrollment.

**Intervention:** All patients were treated with ciclosporine, 2.5 mg/kg/d. Patients were randomized to receive a dietary intervention (low-calorie diet administered by a dietician) vs no dietary intervention. The dietary intervention was a caloric restriction of 500 kcal below the calculated resting energy expenditure involving a diet of 60% carbohydrates, 25% fat, and 15% protein. All of the patients were encouraged to exercise at least 40 minutes 4 or more times per week.

**Main Outcome Measures:** The primary end point was an improvement in PASI from baseline of at least 75% (hereinafter, PASI 75) at week 24. Secondary end points were an improvement in PASI from baseline of at least 50% (hereinafter, PASI 50) at week 24 and premature withdrawal from the study at week 24.

**Results:** Sixty-one patients were enrolled in the study. The baseline characteristics of the patients in terms of age, sex, BMI, waist circumference, PASI, and BSA affected were similar in both groups. The authors performed an intention-to-treat analysis. The mean (SD) weight loss and reduction in waist circumference were 7.0 (5.7) kg and 3.5 (2.3) cm, and 0.2 (0.9) kg and no reduction in waist size in the diet intervention group and the nonintervention group, respectively. At week 24, PASI 75 and PASI 50 were achieved by significantly larger percentages of patients in the diet intervention group (*P* < .001) (Table). The number of patients needed to treat (NNT) with the dietary intervention plus ciclosporine to achieve 1 additional PASI 75 responder compared with using low-dose ciclosporine alone was 3. In the intervention group, 4 patients (13.3%) dropped out owing to adverse events associated with ciclosporine, whereas 14 patients (45.1%) dropped out in the nonintervention group (10 because of lack of efficacy and 4 owing to ciclosporine-associated adverse events; *P* < .001). Patients switched to other treatments but were encouraged to maintain their diet after the study ended. At the 1-year follow-up, 24 patients (80%) had returned to their baseline weight and experienced relapses in their psoriasis.

**Conclusions:** Gisondi et al conclude that obese patients with moderate to severe psoriasis increase their response to low-dose ciclosporine if a calorie-controlled diet is included in the treatment regimen.

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Cyclosporine and Low-Calorie Diet (n=30)</th>
<th>Cyclosporine Alone (n=31)</th>
<th>Difference (95% CI)a</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>PASI 75 response, No. (%)b</td>
<td>20 (67)</td>
<td>9 (29)</td>
<td>0.38 (0.15 to 0.61)</td>
<td>3</td>
</tr>
<tr>
<td>PASI 50 response, No. (%)c</td>
<td>26 (87)</td>
<td>15 (48)</td>
<td>0.38 (0.16 to 0.60)</td>
<td>3</td>
</tr>
<tr>
<td>Weight loss, mean, kg (95% CI)</td>
<td>7.0 (5.7 to 8.3)</td>
<td>0.2 (−0.1 to 0.5)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Reduction in waist circumference, mean, cm (95% CI)</td>
<td>3.5 (2.3 to 4.5)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; NA, not applicable; NNT, number needed to treat; PASI, Psoriasis Area and Severity Index.

a Calculated 95% CIs assume a normal distribution (PASS 2008 statistical software; NCSS LLC, Kaysville, Utah).

b An improvement in PASI from baseline of at least 75%.

c An improvement in PASI from baseline of at least 50%.

d Reported as “no reduction.”
Comment

Obesity promotes systemic inflammation, is an independent risk factor for the development of psoriasis, and is associated with psoriasis severity.14 Moreover, case reports suggest that psoriasis may improve with weight loss, as evidenced by patients undergoing bariatric surgery.7,8 Based on these data, rigorous clinical trials are indicated to determine if weight loss can improve psoriasis. Gisondi et al should be congratulated for conducting an important randomized controlled clinical trial (RCT) to ascertain if moderate weight loss induced by a calorie-restrictive diet improves the therapeutic response to low-dose cyclosporine in obese patients with moderate to severe psoriasis. A useful resource for clinicians in interpreting therapeutic clinical trials is the JAMA Evidence Web site (http://www.jamaevidence.com/), which provides a set of users’ guides to evidence-based practice.7 Central issues in trial evaluation include determining if the results are valid (internal validity) and if the results will be helpful in caring for your patients (external validity). To be internally valid, a clinical trial must attempt to resolve an explicitly specified uncertainty “by isolating both the control variable (i.e., treatment) and the outcome from extraneous influences.”8(p10) To achieve this goal, RCTs typically use such methods as randomization, placebos, and masking of treatment arm from the patients and investigators (ie, double-blinding).

Several methodological problems raise concerns about the internal validity of the results from this trial. First, although the study was randomized, we cannot conclude whether the groups were indeed similar because the intervention itself may have led to increased cyclosporine exposure in the low-calorie diet group that lost weight during the study. Cyclosporine blood levels are essential to address this uncertainty, but unfortunately they were not measured. Similarly, the intervention may have led to differences in other potential confounding factors between treatment groups such as alcohol use, exercise and time spent outdoors, and diet composition.9-11 Attempts to minimize and report any differences between the groups would help to isolate the control variable and improve interpretation of the results. Second, it is possible that bias was introduced in the assessment of the outcome (PASI). For example, patients were not blinded to the dietary intervention, and it is likely that the investigators became aware of the intervention assignment as patients achieved noticeable weight loss. To gain insight into the extent of this bias, one could survey the evaluators at the end of the study to see which patients they believed were in the intervention group. Third, there was substantial loss to follow-up in the non-intervention arm, which may have further affected the validity of the results.12 Finally, without a diet-only group, we cannot differentiate whether the improvement in psoriasis was due to the combined effect of cyclosporine and diet or to the diet alone. The authors note that a diet-only control group would have been unethical. However, there is considerable uncertainty about the impact of weight loss alone on psoriasis severity, suggesting that the principal of equipoise would be satisfied, and thus it would be ethical to randomize patients to a diet-only intervention.

If, despite these limitations, the results are internally valid, we then need to determine if the findings are externally valid. That is, are the outcomes clinically important, are they achievable in clinical practice, and do they generalize to treatment populations outside the clinical trial? The NNT of 3 for the primary outcome compares favorably with other psoriasis treatments (ie, the NNT for biologic agents ranges from 8 for alefacept to 2 for infliximab13) and suggests that the dietary intervention provides a clinically meaningful improvement in objective measures of psoriasis such as PASI 75. Unfortunately, the objective benefits were short lived. Despite impressive weight loss at 24 weeks in this trial, at 52 weeks of follow-up, 80% of patients had returned to their baseline weight. This finding is consistent with studies investigating dietary counseling that found that, on average, patients experience progressive weight loss for about 6 months but eventually return to their baseline weight after 1 year.14 In addition, to more fully understand and confirm the clinical usefulness of this intervention, patient-reported outcomes such as measures of health-related quality of life would have been particularly useful. More data are needed to estimate the long-term effectiveness and whether the treatment benefits outweigh potential costs for patients.

After evaluating whether the results are clinically useful, we need to determine if the results are feasible and generalizable. Feasibility refers to whether the results can be achieved in settings outside of the trial. For example, in many dermatological practices, it may be challenging to implement a successful dietary intervention because it requires comprehensive counseling by a nutritionist and highly motivated patients. A meta-analysis concluded that the major commercial and self-help weight-loss programs alone generally show disappointing results.15 In addition, clinical trials often have narrow inclusion and exclusion criteria, resulting in trial populations that may not represent the general patient population and do not reflect real-world clinical practice settings. The concept of generalizability refers to whether patients are likely to benefit from the intervention outside of the rigorous clinical trial setting. Based on the design of this study, we do not know if the dietary intervention would improve psoriasis in patients with a BMI less than 30 or higher than 45, nor do we know if the dietary intervention would be useful to augment response to other psoriasis therapies such as topical agents; phototherapy; traditional oral medications, such as acitretin and methotrexate; and biologic agents.

Bottom Line: Obesity is a risk factor for multiple comorbidities, including psoriasis, and most patients should be counseled on the importance of healthy eating habits and an active lifestyle. Weight-loss interventions for patients with severe psoriasis who are obese may be particularly critical because severe psoriasis itself seems to be an independent risk factor for heart attack, stroke, and all-cause mortality.16-21 Well-designed, long-term, placebo-controlled studies comparing dieting alone with dieting with systemic treatment are necessary.
search may help elucidate the impact of different types of diets and whether these results will extrapolate to other psoriasis therapies. Although the therapeutic and long-term impact of diet and weight loss on psoriasis remains unclear, the net benefit of moderate weight loss is likely to be positive and is therefore recommendable for most patients with psoriasis who are not at their ideal body weight.

Accepted for Publication: October 22, 2009.

Correspondence: Joel M. Gelfand, MD, MSCE, Department of Dermatology and Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania, One Convention Avenue, 1471 Penn Tower, Philadelphia, PA 19104 (Joel.Gelfand@uphs.upenn.edu).

Author Contributions: Both authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Gelfand. Acquisition of data: Gelfand and Abuabara. Analysis and interpretation of data: Gelfand and Abuabara. Drafting of the manuscript: Gelfand and Abuabara. Critical revision of the manuscript for important intellectual content: Gelfand and Abuabara. Statistical analysis: Gelfand. Obtained funding: Gelfand and Abuabara. Administrative, technical, and material support: Abuabara. Study supervision: Gelfand.

Financial Disclosure: Dr Gelfand receives grant support or is an investigator for Amgen, Centocor, Novartis, Abbott, and Pfizer. He is a consultant for Pfizer, Genentech, Celgene, Amgen, Astellas, and Centocor.

Funding/Support: This study was supported by an unrestricted grant to the Trustees of the University of Pennsylvania from the Psoriasis Research Foundation in Honor Herman Beerman (Dr Gelfand), grant No. RO1HL089744 from the National Heart Lung Blood Institute (Dr Gelfand), and the Doris Duke Charitable Foundation Clinical Research Fellowship (Ms Abuabara).

Role of the Sponsors: The sponsors had no role in the design and conduct of the study; in the collection, analysis, and interpretation of data; or in the preparation, review, or approval of the manuscript.

EVIDENCE-BASED DERMATOLOGY: RESEARCH COMMENTARY

Effects vs Improvement of Photoaged Skin

Daihung Do, MD; Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts

Commentary on: A cosmetic “anti-ageing” product improves photoaged skin: a double-blind, randomized controlled trial

Watson RS, Ogden LF, Cottrell LF, et al

Question: Does treatment with No7 Protect & Perfect Intense Beauty Serum (Alliance Boots Ltd, Nottingham, England) improve facial wrinkles for photoaged patients?

Design: The first part of this study consisted of an in vivo patch test examining fibrillin-1 levels in response to test product. The second part of the study was a 6-month double-blind, randomized controlled trial (RCT) followed by a 6-month open phase.

Setting: Industry-sponsored study conducted at a university-based academic clinical and basic science research center.

Patients: Healthy volunteers with photoaged skin.