

Lifestyle intervention in psoriasis: a new avenue for treatment?

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Psoriasis is a chronic immune-mediated disorder that has a substantial impact on quality of life (1). It is characterized by systemic inflammation and cytokine dysregulation. In particular, alterations in T helper (Th)¹, Th17, and Th22 cells drive this disease with elevated serum concentrations of multiple proinflammatory cytokines, including TNF, IL-6, and IL-8 (1). Thus, monoclonal antibodies directed against TNF and other implicated cytokines are highly effective in its management. Similarly, obesity has been characterized as a proinflammatory state, with visceral adiposity generating adipocytokines, including TNF (1). Given that psoriasis has long been associated with metabolic syndrome and obesity, it is plausible that shared biological mechanisms could drive the systemic inflammation underlying psoriasis.

The first suggestions of a possible association of obesity with psoriasis came from bariatric surgery patients in whom there was documented substantial and sustained remission of psoriasis with weight loss postoperatively (2). Later, an investigator-blinded randomized trial showed that cyclosporine, an immunosuppressant used to treat psoriasis, was significantly more effective when combined with a hypocaloric diet [Psoriasis Area Severity Index (PASI) of 75: 66.7% compared with 29.0%; $P < 0.0001$] (3). Similarly, a large cohort of patients who received systemic antipsoriatic therapy reported that the odds of treatment failure were higher among obese patients than among nonobese patients (OR: 1.61; $P < 0.0001$) (4). The logical next step would be a long-term clinical study evaluating the effect of weight loss on psoriasis severity.

In this issue of the Journal, Jensen et al. (5) report a prospective cohort of low-energy-diet (LED) patients with mild psoriasis. This is an extension of a 16-wk randomized controlled trial that examined an LED of 800–1000 kcal/d for 8 wk followed by 1200 kcal/d for 8 wk (6). Unfortunately, in the original trial, they did not reach their primary endpoint of a significant reduction in psoriasis severity (PASI = -2.0 ; 95% CI: $-4.1, 0.1$; $P = 0.06$). This long-term observational study followed $n = 32$ patients for 67 wk. Although there was some weight regain, the mean loss remained impressive at -10.1 kg (95% CI: $-12.0, -8.1$ kg). By the end of the study period, PASI and Dermatology Life Quality Index scores were maintained (PASI = -2.9 ; 95% CI: $-3.9, -1.9$; Dermatology Life Quality Index = -1.9 ; 95% CI: $-3.0, -0.9$). This would suggest that psoriasis severity and quality of life improved with weight loss and were maintained despite some weight regain.

This study does have several important limitations. First, all of the patients had mild psoriasis (mean PASI: 4.8–4.9), which would limit the external validity. Also, it is unclear whether the reduction in PASI would be proportional in patients with severe psoriasis or whether a 2.9 score reduction is the absolute benefit conferred by weight loss. If the latter is true, then it would not likely be clinically meaningful in patients with severe disease. In addition, the outcome assessor was the lead author, who was unblinded, potentially introducing significant observer bias. Furthermore, although PASI is commonly used in clinical trials, it is subjective and based on a visual assessment of psoriatic lesions (7). The intervention itself was an intensive LED regimen including formula products and frequent dietitian follow-up. It is unrealistic that such an intervention would be feasible on a large scale among busy clinicians. It would be prudent to test rapid lifestyle interventions in a population that includes patients with moderate to severe psoriasis to further extend the generalizability. Just over half (53.3%) of participants from the original study completed the long-term follow-up, thereby introducing attrition bias. No sensitivity analysis that assumed a “worst-case scenario” was reported or discussed. One can speculate that the stringent requirements of the diet made it unsustainable for many participants.

There are several reasons to be optimistic, however. To my knowledge, this is the first long-term cohort on the effect of weight loss on psoriasis severity and it suggests that benefits can endure over 1 y. This study showed reduced psoriasis severity and, perhaps more importantly, improved quality of life. It adds to a recent randomized trial by Naldi et al. (8), which showed improvements in PASI with dietary and exercise counseling over 20 wk. By using intention-to-treat analysis, they reported greater reductions in PASI in the intervention group than in the control group (48% compared with 25.5%; $P = 0.02$).

Evidence suggests that multiple metabolic comorbidities are associated with psoriasis, including dyslipidemia, hypertension, and diabetes (9). A recent large ($n = 99,386$) population-based study in patients with psoriasis reported the OR of myocardial infarction to be 1.34 (95% CI: 1.07, 1.69) (10). In the United States, psoriasis is estimated to be responsible for 11,000 excess

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¹Abbreviations used: LED, low-energy-diet; PASI, Psoriasis Area Severity Index; Th, T helper.

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cardiac events annually and for up to 1200 deaths (10). Given that obesity is a major modifiable risk factor for cardiac disease, the sustained weight loss shown in this study is encouraging and suggests that lifestyle intervention may be another important tool in the primary prevention of heart disease in patients with psoriasis.

What has become abundantly clear is the need to widely disseminate the impact of metabolic comorbidities among patients with psoriasis. Both dermatologists and primary care physicians are often the only point of contact for such patients and should be taking the lead in risk factor reduction. A collaborative approach with dietitians and exercise specialists is needed to maximize the benefits for patients. Compared with many psoriasis treatments, lifestyle interventions are relatively inexpensive and have minimal harms. We now have a growing body of convincing evidence that such interventions may be effective in reducing psoriasis severity and comorbidities associated with psoriasis. Ultimately, a multimodal and holistic approach may improve the long-term health and quality of life in our patients with psoriasis.

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