delivered intervention to enhance both patient satisfaction with care and UV protective behaviors in a dermatologic setting. Future studies will examine the efficacy of the ABC method on enhancing patients’ sun-protective behaviors to assess how physicians’ use of the intervention positively influences patients’ actions over time.

Kimberly A. Mallett, PhD
Rob Turrisi, PhD
Elizabeth Billingsley, MD
Carly D. Comer, BS
Aimee Read, BS
Lindsey Varvil-Weld, MS
Rikki Gaber, BS
Sarah Favero, MS
Kelly Guttman, BS
June K. Robinson, MD

Accepted for Publication: March 18, 2012.

Author Affiliations: Prevention Research Center, Department of Biobehavioral Health (Drs Mallett and Turrisi and Mss Comer, Read, Varvil-Weld, Favero, and Guttman), and Department of Dermatology (Dr Billingsley), Milton S. Hershey Medical Center, The Pennsylvania State University, State College; Department of Dermatology, Feinberg School of Medicine, Northwestern University, Chicago, Illinois (Ms Gaber and Dr Robinson).

Correspondence: Dr Mallett, Prevention Research Center, The Pennsylvania State University, 204 E Calder Way, Ste 208, State College, PA 16801 (kmallett@psu.edu).

Author Contributions: Drs Mallett and Turrisi 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: Mallett, Turrisi, and Billingsley. Acquisition of data: Mallett, Turrisi, Comer, Read, Varvil-Weld, Gaber, Favero, Guttman, and Robinson. Analysis and interpretation of data: Mallett, Turrisi, and Comer. Drafting of the manuscript: Mallett, Comer, Read, and Favero. Critical revision of the manuscript for important intellectual content: Mallett, Turrisi, Billingsley, Comer, Varvil-Weld, Gaber, Guttman, and Robinson. Statistical analysis: Mallett and Turrisi. Obtained funding: Mallett and Turrisi. Administrative, technical, and material support: Comer, Read, Favero, Guttman, and Robinson. Study supervision: Turrisi.

Financial Disclosure: None reported.

Funding/Support: This study was supported in part by National Cancer Institute grant R03 CA144435 (Dr Mallett).

Epidemiologic studies have shown an association between psoriasis and cardiovascular diseases. An interesting but unproven hypothesis ascribes this association to the psoriatic march, the process by which inflammatory mediators released in the course of the psoriatic autoimmune reaction cause insulin resistance, which ultimately leads to atherosclerosis.1 Tumor necrosis factor (TNF) is a proinflammatory cytokine that impairs response to insulin in adipocytes and muscle cells via inhibition of tyrosine kinase activity of the insulin receptor, activation of perosisome proliferator–activated receptor-δ, and changes in secretion of adipokines.2 For the present study, we investigated the effect of anti–TNF treatment on insulin resistance and body composition in patients with psoriasis.

Methods. Eligible participants were anti–TNF–naïve male patients with psoriasis recalcitrant to other systemic treatments and UV-B therapy. They also had a PASI (Psoriasis Area and Severity Index) or a DLQI (Dermatology Life Quality Index) of 10 or higher. The selection of the TNF agent was left to the treating dermatologist. Patients were asked to maintain their usual physical activity and to stay on their usual diet during the 12-week study period. Approval was granted by the scientific ethical committee (approval No. H-D-2009-040).

Insulin sensitivity was determined by a 2-hour hyperinsulinemic euglycemic clamp. Body composition was estimated by dual-energy x-ray absorptiometry. Peak oxygen uptake was assessed during a progressive exercise test. Patients completed the International Physical Activity Questionnaire. A sample size of 18 was required to detect an increase of 15% or more in insulin sensitivity (1-sided α = 0.05 and power=0.91). An interim analysis after 9 completed patients was performed to indicate a trend for a difference. A P<.20 was needed to justify study continuation. A more detailed description of methods is available in the eAppendix (http://www.archdermatol.com).

Results. The interim analysis did not indicate a trend; therefore, the study was terminated. Baseline patient characteristics are summarized in Table 1. Truncal fat percentage was negatively correlated with insulin sensitivity (r=-0.78; P<.01) and positively correlated plasma leptin (r=0.88; P=.002). After 12 weeks of therapy (infliximab=5, adalimumab=4), there were no significant changes in insulin sensitivity or levels of fasting glucose, hemoglobin A1c, or C-peptide. Body fat increased by 6.5%, and truncal fat increased by 11.4%. Leptin concentrations significantly decreased after anti–TNF treatment (Table 2).

Comment. It is known that anti–TNF therapy increases body weight in patients with psoriasis. In line with our results, Renzo et al3 observed a gain in the body fat of 8.6% in patients with psoriasis after 24 weeks of anti–TNF therapy. It is known that TNF stimulates lipolysis...
in human adipocytes; thus, anti-TNF may reduce lipolysis and thereby accumulation of fat in adipocytes.

We confirmed an inverse correlation between truncal fat percentage and insulin sensitivity, but anti-TNF therapy had no significant influence on insulin sensitivity. Martínez-Abundis et al reported no effect on insulin sensitivity measured using a hyperinsulinemic clamp during 2 weeks of etanercept treatment, but Marra et al reported a decrease in insulin resistance assessed by homoeostatic model assessment after 24 weeks of etanercept treatment. The clamp primarily measures insulin-mediated glucose disposal by skeletal muscles. To investigate insulin sensitivity in adipose tissue, other methods should have been used.

Epidemiologic evidence indicates a lower risk of developing diabetes mellitus for patients with psoriasis who are treated with a TNF inhibitor compared with several other drugs. Leptin is a fat-tissue hormone. Reduction in plasma leptin level indicates that anti-TNF treatment reduces insulin sensitivity measured using a hyperinsulinemic clamp. The clamp primarily measures insulin-mediated glucose disposal by skeletal muscles. Therefore, an inverse correlation between truncal fat percentage and insulin sensitivity suggests that anti-TNF therapy reduces lipolysis and thereby accumulation of fat in adipocytes.

We confirmed an inverse correlation between truncal fat percentage and insulin sensitivity, but anti-TNF therapy had no significant influence on insulin sensitivity. Martínez-Abundis et al reported no effect on insulin sensitivity measured using a hyperinsulinemic clamp during 2 weeks of etanercept treatment, but Marra et al reported a decrease in insulin resistance assessed by homoeostatic model assessment after 24 weeks of etanercept treatment. The clamp primarily measures insulin-mediated glucose disposal by skeletal muscles. To investigate insulin sensitivity in adipose tissue, other methods should have been used.

Epidemiologic evidence indicates a lower risk of developing diabetes mellitus for patients with psoriasis who are treated with a TNF inhibitor compared with several other drugs. Leptin is a fat-tissue hormone. Reduction in plasma leptin level indicates that anti-TNF treatment reduces insulin sensitivity measured using a hyperinsulinemic clamp. The clamp primarily measures insulin-mediated glucose disposal by skeletal muscles. Therefore, an inverse correlation between truncal fat percentage and insulin sensitivity suggests that anti-TNF therapy reduces lipolysis and thereby accumulation of fat in adipocytes.

We confirmed an inverse correlation between truncal fat percentage and insulin sensitivity, but anti-TNF therapy had no significant influence on insulin sensitivity. Martínez-Abundis et al reported no effect on insulin sensitivity measured using a hyperinsulinemic clamp during 2 weeks of etanercept treatment, but Marra et al reported a decrease in insulin resistance assessed by homoeostatic model assessment after 24 weeks of etanercept treatment. The clamp primarily measures insulin-mediated glucose disposal by skeletal muscles. To investigate insulin sensitivity in adipose tissue, other methods should have been used.

Epidemiologic evidence indicates a lower risk of developing diabetes mellitus for patients with psoriasis who are treated with a TNF inhibitor compared with several other drugs. Leptin is a fat-tissue hormone. Reduction in plasma leptin level indicates that anti-TNF treatment reduces insulin sensitivity measured using a hyperinsulinemic clamp. The clamp primarily measures insulin-mediated glucose disposal by skeletal muscles. Therefore, an inverse correlation between truncal fat percentage and insulin sensitivity suggests that anti-TNF therapy reduces lipolysis and thereby accumulation of fat in adipocytes.

We confirmed an inverse correlation between truncal fat percentage and insulin sensitivity, but anti-TNF therapy had no significant influence on insulin sensitivity. Martínez-Abundis et al reported no effect on insulin sensitivity measured using a hyperinsulinemic clamp during 2 weeks of etanercept treatment, but Marra et al reported a decrease in insulin resistance assessed by homoeostatic model assessment after 24 weeks of etanercept treatment. The clamp primarily measures insulin-mediated glucose disposal by skeletal muscles. To investigate insulin sensitivity in adipose tissue, other methods should have been used.

Epidemiologic evidence indicates a lower risk of developing diabetes mellitus for patients with psoriasis who are treated with a TNF inhibitor compared with several other drugs. Leptin is a fat-tissue hormone. Reduction in plasma leptin level indicates that anti-TNF treatment reduces insulin sensitivity measured using a hyperinsulinemic clamp. The clamp primarily measures insulin-mediated glucose disposal by skeletal muscles. Therefore, an inverse correlation between truncal fat percentage and insulin sensitivity suggests that anti-TNF therapy reduces lipolysis and thereby accumulation of fat in adipocytes.

We confirmed an inverse correlation between truncal fat percentage and insulin sensitivity, but anti-TNF therapy had no significant influence on insulin sensitivity. Martínez-Abundis et al reported no effect on insulin sensitivity measured using a hyperinsulinemic clamp during 2 weeks of etanercept treatment, but Marra et al reported a decrease in insulin resistance assessed by homoeostatic model assessment after 24 weeks of etanercept treatment. The clamp primarily measures insulin-mediated glucose disposal by skeletal muscles. To investigate insulin sensitivity in adipose tissue, other methods should have been used.

Epidemiologic evidence indicates a lower risk of developing diabetes mellitus for patients with psoriasis who are treated with a TNF inhibitor compared with several other drugs. Leptin is a fat-tissue hormone. Reduction in plasma leptin level indicates that anti-TNF treatment reduces insulin sensitivity measured using a hyperinsulinemic clamp. The clamp primarily measures insulin-mediated glucose disposal by skeletal muscles. Therefore, an inverse correlation between truncal fat percentage and insulin sensitivity suggests that anti-TNF therapy reduces lipolysis and thereby accumulation of fat in adipocytes.

We confirmed an inverse correlation between truncal fat percentage and insulin sensitivity, but anti-TNF therapy had no significant influence on insulin sensitivity. Martínez-Abundis et al reported no effect on insulin sensitivity measured using a hyperinsulinemic clamp during 2 weeks of etanercept treatment, but Marra et al reported a decrease in insulin resistance assessed by homoeostatic model assessment after 24 weeks of etanercept treatment. The clamp primarily measures insulin-mediated glucose disposal by skeletal muscles. To investigate insulin sensitivity in adipose tissue, other methods should have been used.
Weaknesses of the present study include the limited number of patients, the fact that only men were included, the uncontrolled study design, and the use of 2 different anti-TNF antibodies. Using the gold-standard methods, we found that the increase in body weight in patients with psoriasis treated with anti-TNF is due to an increase in the amount of truncal fat, but we were unable to demonstrate any significant effect of anti-TNF therapy on insulin sensitivity. Future studies should investigate the mechanism behind the increase in body fat.

Kristian Kofoed, MD, PhD
Anders Clemmensen, MD, PhD
Ulla R. Mikkelsen, MSc, PhD
Lene Simonsen, MD, DMSc
Ove Andersen, MD, PhD
Robert Gniadecki, MD, DMSc

Accepted for Publication: April 27, 2012.

Author Affiliations: Department of Dermatology (Drs Kofoed, Clemmensen, and Gniadecki), Institute of Sport Medicine, Department of Orthopedic Surgery (Dr Mikkelsen), and Department of Clinical Physiology (Dr Simonsen), Copenhagen University Hospital, Bispebjerg, Denmark; Center for Health Aging (Dr Mikkelsen), Faculty of Health Sciences (Drs Mikkelsen and Gniadecki), University of Copenhagen, Copenhagen, Denmark; and Clinical Research Center, Copenhagen University Hospital, Hvidovre, Denmark (Dr Andersen).

Correspondence: Dr Kofoed, Department of Dermatology, Copenhagen University Hospital, Bispebjerg, Bispebjerg Bakke 23, DK2400 Copenhagen NV, Denmark (kkkofoed@hotmail.com).

Author Contributions: Drs Kofoed, Clemmensen, and Gniadecki had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Kofoed and Gniadecki. Acquisition of data: Kofoed, Clemmensen, Mikkelsen, Simonsen, and Andersen. Analysis and interpretation of data: Kofoed and Gniadecki. Drafting of the manuscript: Kofoed and Gniadecki. Critical revision of the manuscript for important intellectual content: Kofoed, Clemmensen, Mikkelsen, Simonsen, Andersen, and Gniadecki. Statistical analysis: Kofoed. Obtained funding: Kofoed. Administrative, technical, and material support: Kofoed, Mikkelsen, Simonsen, and Andersen. Study supervision: Kofoed, Clemmensen, and Gniadecki.

Financial Disclosure: Drs Kofoed has received fees as a speaker from Abbott, Janssen-Cilag, and Pfizer and has served as an advisory board member for Abbott. Dr Gniadecki has obtained research grants from Abbott and Merck Sharp & Dohme, and Pfizer.

Funding/Support: This study was supported by unrestricted research grants from Abbott and Serono Nordic and by the Danish Psoriasis Research Foundation.

Previous Presentations: This study was presented in part, at the Third International Congress on Psoriasis; July 2, 2010; Paris, France; and at 41st Annual Meeting of the European Society for Dermatology Research; September 7-10, 2011; Barcelona, Spain.


COMMENTS AND OPINIONS

Pitfalls of Evidence-Based Medicine Revisited

I enjoyed greatly the article in the Archives by Gilchrest and Martin1 about some of the pitfalls of evidence-based medicine. The article was insightful and nuanced, so much so that I cannot but believe that their first sentence was written with a degree of irony. The authors state that “No one can argue about the merit of evidence-based medicine.”1(p528) Well, of course, the medical literature is full of cogently argued expressions of doubts about the epistemology of evidence-based medicine (for a recent review, see Goldenberg et al2 and all articles in that same volume of Perspectives in Biology and Medicine devoted to this subject).

Most physicians have always claimed that they practice medicine on the basis of evidence, but what they have disagreed about is what types of knowledge constitute this evidence. Central to these concerns today is how we integrate evidence from randomized controlled trials (RCTs) with other sorts of knowledge.

First, we need to be cautious about our metaphors.3 Gold standard originally referred to the currency policy in which a given unit of (say) paper currency is exchangeable for a defined amount of gold. For this standard to

ARCH DERMATOL/VOL 148 (NO. 9), SEP 2012 WWW.ARCHDERMATOL.COM

©2012 American Medical Association. All rights reserved.