Systemic treatment and narrowband ultraviolet B differentially affect cardiovascular risk markers in psoriasis

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Background: Psoriasis is associated with a systemic inflammation and an increased frequency of the metabolic syndrome, both of which are believed to link psoriasis to an increased risk of cardiovascular disease.

Objective: The study aimed to investigate the systemic expression of markers of cardiovascular risk and determine their response to ultraviolet B therapy and treatment with the tumor necrosis factor-alfa inhibitor, etanercept.

Methods: Six markers of cardiovascular risk were measured in 28 patients with psoriasis and 28 control subjects.

Results: Five of the 6 investigated markers were elevated in patients with psoriasis. Four of these correlated to the body mass index and waist-hip ratio, suggesting a link to the metabolic syndrome. Total plasminogen activator inhibitor-1 remained elevated independently of these factors. The levels of the investigated risk markers decreased considerably after tumor necrosis factor-alfa inhibitor treatment but remained unaffected by ultraviolet therapy.

Limitations: A relatively limited study population and nonrandomization are limitations.

Conclusion: These findings suggest that the choice of treatment in psoriasis may influence the cardiovascular risk in patients with psoriasis and the metabolic syndrome. (J Am Acad Dermatol 2014;70:1067-75.)

Key words: cardiovascular risk; matrix metalloproteinase-9; myeloperoxidase; psoriasis; soluble E-selectin; soluble intercellular adhesion molecule-1; soluble vascular cell adhesion molecule-1; total plasminogen activator inhibitor-1; tumor necrosis factor-alfa inhibitor; ultraviolet B.

Psoriasis is a chronic, immune-mediated inflammatory skin disease that affects 2% to 3% of the population worldwide. In addition to running an increased risk of psoriatic arthritis, patients with psoriasis run a higher risk of developing obesity, dyslipidemia, hypertension, and diabetes, all components of the metabolic syndrome.[1,2] Psoriasis may also confer an elevated risk of

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Supported by Ingrid Asp Foundation, Welander Foundation, Medical Research Council of Southeast Sweden.

Disclosure: Dr Ståhle has had speaking and/or advisory board engagements for Pfizer, Abbott, Novartis, and Janssen, and received honoraria for this. She has also served as investigator for Pfizer and Janssen and received grants for this. Drs Sigurdardottir, Ekman, Bivik and Enerbäck have no conflicts of interest to declare.

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Accepted for publication December 21, 2013.

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Published online March 21, 2014.
0190-9622/$36.00

http://dx.doi.org/10.1016/j.jaad.2013.12.044

cardiovascular disease, such as myocardial infarction and stroke, independently of major risk factors for these diseases. An increase in mortality is observed in patients with severe disease and is most pronounced in young patients.[3-8]

Specific biomarkers aid in detecting disease, determining the activity and the severity and evaluating the response to therapy and monitoring disease progression. Cardiovascular biomarkers, many of which are also mediators of inflammation, have previously been studied in patients with psoriasis. These studies have mainly focused on cardiovascular markers related to the obesity-associated systemic inflammation. The expression of the adipokine leptin and the soluble leptin receptor is higher in the serum of patients with psoriasis[9] and is most pronounced in severely affected individuals. Systemic psoriasis treatment decreases the levels of the adipokine resistin and increases the levels of the anti-inflammatory cardioprotective adipokine adiponectin.[10]

CAPSULE SUMMARY

- Patients with psoriasis have an increased risk of cardiovascular disease.
- Markers of cardiovascular risk that are increased in patients with psoriasis are reduced by tumor necrosis factor-alfa inhibitor treatment but not by ultraviolet B therapy.

In a former study, we investigated circulating chemokines in psoriasis as a sign of an ongoing systemic inflammation. Five chemokines of a T helper (Th)1-, Th2-, or Th17-associated phenotype were elevated in psoriasis plasma but not in healthy control subjects.

The expression of the chemokine (C-C motif) ligand (CCL) 20 correlated strongly with disease severity.[11] However, although these chemokines were highly expressed in patients with psoriasis, they were not affected by narrowband (NB) ultraviolet (UV)-B treatment, despite the relief of disease symptoms in the skin. In this study, selected risk-associated molecules implicated in the process of cardiovascular disease, soluble vascular cell adhesion molecule (sVCAM)-1, soluble intercellular adhesion molecule (sICAM)-1, soluble E (sE)-selectin, matrix metalloproteinase (MMP)-9, myeloperoxidase (MPO) and total plasminogen activator inhibitor (tPAI)-1, were analyzed. The aim of the study was 2-fold: firstly, to assess the plasma levels of the selected cardiovascular risk molecules in patients with psoriasis compared with age-, gender-, body mass index (BMI)-, and waist-hip ratio (WHR)-matched control subjects; and, secondly, to investigate the effects of local (NB-UVB therapy) and systemic (tumor necrosis factor [TNF]-alfa inhibitor) treatment.

METHODS

Study design

All patients and control subjects included in the study were examined and the diagnosis of psoriasis was verified by a dermatologist at the departments of dermatology at Linköping University Hospital, Sahlgrenska University Hospital in Gothenburg, or Karolinska University Hospital in Stockholm, Sweden. Disease severity was assessed with the Psoriasis Area and Severity Index (PASI). The study was approved by the local ethics committee and every participant gave his/her written informed consent.

Six cardiovascular risk markers were analyzed in plasma from 28 patients with psoriasis and 28 age- and gender-matched control subjects. This study group was complemented with additional patients and control subjects to enable the matching of 26 age-, gender-, and BMI-matched and 13 age-, gender-, and WHR-matched pairs. The patients had not received systemic TNF-alfa inhibitor treatment for at least 4 weeks before the study.

The BMI matching was performed within the range of ± 1.0 kg/m^2 and the WHR matching within the range of ± 0.05, where both individuals in a matched pair either had WHR values within the normal range or could be defined as having abdominal obesity.[12]

Finally, the systemic expression of selected risk markers was quantified in 21 patients with psoriasis before and after 12 weeks of treatment with NB-UVB and in 20 patients with psoriasis before and after treatment with the TNF-alfa inhibitor etanercept (Enbrel, Pfizer, Morris Plains, NJ). The patients had not received UV therapy or TNF-alfa inhibitor treatment for at least the previous 4 weeks. The study was nonrandomized and the evaluations of markers were performed unblinded.

Blood samples

Blood was collected in cell preparation tubes (CPT) (Becton Dickinson, Stockholm, Sweden) coated with sodium heparin anticoagulant, or in serum tubes with clot activator (Terumo Europe, Västra Frölunda, Sweden) for the isolation of plasma and serum, respectively. The CPT tubes were centrifuged at 1400 rcf for 25 minutes, separating the leukocytes from the plasma. The serum tubes were allowed to sit for 30 minutes before separating the