New Adjunctive Treatment Option for Venous Stasis Ulcers

Adding simvastatin to standard wound care improves ulcer healing rates and times, as well as the patient's quality of life.

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PRACTICE CHANGER

Consider adding simvastatin (40 mg/d) to standard wound care and compression for patients with venous stasis ulcers.[1]

STRENGTH OF RECOMMENDATION

B: Based on a high-quality randomized controlled trial (RCT).[1]

ILLUSTRATIVE CASE

A 74-year-old woman with chronic lower extremity edema seeks treatment for a nonhealing venous stasis ulcer. For the past nine months, she's been wearing compression stockings and receiving intermittent home-based wound care, but nothing seems to help. She asks if there's anything else she can try.

Venous stasis ulcers affect 1% of US adults and lead to substantial morbidity and more than $2 billion in annual health care expenditures.[1,2] Edema management—generally limb elevation and compression therapy—has been the mainstay of therapy. Treatment can be lengthy, and ulcer recurrence is common.[2,3]

Statins have been found to aid wound healing through their diverse physiologic (pleiotropic) effects. Evidence indicates they can be beneficial in treatment of diabetic foot ulcers,[4] pressure ulcers,[5] and ulcerations associated with systemic sclerosis and Raynaud phenomenon.[6] Evangelista et al[1] investigated whether adding a statin to standard wound care and compression could improve venous stasis ulcer healing.

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STUDY SUMMARY

Ulcers more likely to close when statin added

This randomized, double-blind, placebo-controlled trial was performed at a large medical center in the Philippines. It was designed to assess the efficacy and safety of simvastatin (40 mg/d) for venous ulcer healing when combined with standard treatment (compression therapy, limb elevation, and standard wound care).[1]

Study subjects were 66 patients, ages 41 to 71, who'd had one or more venous ulcers for at least three months. They were randomly assigned to receive either simvastatin (40 mg/d; n = 32) or an identical-appearing placebo (n = 34). Patients were excluded if they were pregnant, had an ulcer that was infected or > 10 cm in diameter, or were taking any medication that could interact with a statin. Patients were stratified according to ulcer diameter (≤ 5 cm and > 5 cm). There was no statistically significant difference between the two groups in the duration of venous ulceration (3.80 y in the placebo group vs 3.93 y in the simvastatin group) or incidence of diabetes (5% vs 3%, respectively).

The primary outcome was the proportion of patients whose ulcers completely healed at 10 weeks. Secondary outcomes were measures of the total surface area healed, healing time, and Dermatology Life Quality Index (DLQI) scores. Baseline ulcer diameter and surface area and DLQI scores were obtained prior to therapy initiation. The same dermatologist, who was blinded to the patients' group assignments, evaluated all patients every two weeks until wound closure or for a maximum of 10 weeks.

Overall, 90% of the patients who received simvastatin had complete ulcer closure at 10 weeks, compared with 34% of patients in the control group (relative risk [RR], 0.16; number needed to treat [NNT], 2).

Among patients with ulcers ≤ 5 cm, 100% of the ulcers healed in the simvastatin group, compared to 50% in the control group (RR, 0.10; NNT, 2). Perhaps more importantly, in patients with ulcers > 5 cm, 67% in the simvastatin group had

closure with a mean healing time of nine weeks, whereas none of the ulcers of this size closed in the control group (RR, 0.33; NNT, 1.5), and the mean healed area was significantly larger in patients who received simvastatin (28.9 cm^2 vs 19.6 cm^2).

In addition, in the simvastatin group, healing times were significantly reduced (7.53 ± 1.34 wk vs 8.55 ± 1.13 wk) and quality of life (as evaluated by DLQI scoring) significantly improved compared to the control group.

Study dropouts were minimal (8%; two in the placebo group and three in the intervention group). Using intention-to-treat analysis and worst-case scenarios for those who dropped out did not affect the primary outcome. There were no withdrawals due to adverse reactions.

WHAT'S NEW

Statins offer significant benefits for treating venous stasis ulcers

This is the first human study to investigate the use of a statin in venous stasis ulcer healing. This intervention demonstrated significant improvements in healing rate and time, a very small NNT for benefit, and improved patient quality of life compared to placebo.

CAVEATS

Carefully selected patients

Many wounds will heal with compression therapy alone, as occurred in this study, in which 50% of ulcers ≤ 5 cm treated with standard therapy healed, albeit at a somewhat slower rate. Adding another medication to the regimen when target patients generally have multiple comorbidities should always prompt caution.

The study by Evangelista et al[1] was performed in a select population, and the exclusion criteria included the use of some commonly prescribed medications, such as ACE inhibitors. No data were collected on patient BMI, which is a risk factor for delayed healing.

The prevalence of obesity is lower in the Philippines than in the US. It is uncertain what role this difference would have in the statin's effectiveness.

Further studies, especially those conducted with a less selective population, would better clarify the generalizability of this intervention.

Nontheless, we found the results of this study impressive. The methods reported are rigorous and consistent with standard RCT methodologies.

This is the only study of a statin in human venous stasis disease, but studies in animals—and studies of statins for other types of ulcers in humans—have consistently suggested benefit. It seems hard to argue against adding this low-cost, low-risk intervention.

CHALLENGES TO IMPLEMENTATION

There are no known barriers to implementation of this practice. **CR**

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