FOOT ULCERS
Investigating Options For Reducing Risk

Sheri Colberg, PhD

Occupation
Associate Professor of Exercise Science
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Professional Focus
Exercise science and diabetes

Outside Interests
Swimming, exercising, playing with her kids, reading, writing

Research Funding
ADA Clinical Research Award

If you have diabetes, decreased blood flow in your feet can increase your risk of developing foot ulcers. When wounds don’t get enough oxygen-rich blood, they don’t heal properly. They can become infected and, if left untreated, lead to foot ulcers and amputation.

What causes this decreased blood flow? High blood glucose can damage your blood vessels and keep your blood from flowing freely. But Sheri Colberg, PhD, associate professor of

Sheri Colberg, PhD, believes a deficiency in a substance released by blood vessels can raise foot ulcer risk—but that exercise can counteract the deficiency.
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exercise science at Old Dominion University in Norfolk, Va., thinks there may be another culprit: low levels of a substance called endothelium-derived hyperpolarizing factor (EDHF) in the blood vessels just below the skin’s surface.

EDHF is a vasodilator released by the endothelium, or lining, of your blood vessels. Vasodilators open and relax your blood vessels so that blood can flow freely. Other vasodilators include nitric oxide and hormone-like substances called prostaglandins.

Colberg is using funds from an American Diabetes Association Clinical Research Award to study the interplay between EDHF and decreased blood flow in people who have type 2. Her interest in this topic stems from prior work in which she and her colleagues discovered that people with type 2 often have altered blood flow in the tops of their feet. (Their work also suggests that nitric oxide and prostaglandins don’t play a large role in this phenomenon.)

Colberg wants to go beyond defining EDHF’s role, however. She also hopes to offer ways that people with diabetes can maintain healthy circulation in their feet even if there’s a deficiency in their EDHF. To that end, her research will have a second phase in which the team will study the effects of two diabetes drugs, glimepiride (Amaryl) and glyburide (Diabeta, Glynase, Micronase), and regular aerobic exercise on blood flow in the feet.

**EDHF**

Colberg’s study will include four groups: 15 sedentary people with type 2 and 15 sedentary people who don’t have diabetes (as a control group). The researchers will also study 15 people with type 2 who exercise regularly and 15 exercisers who don’t have diabetes. Comparing these groups will help shed light on the differences between people with and without diabetes as well as between regular exercisers and people who are sedentary.

In the first phase of the study, participants will make four visits to the clinic to have the blood flow in their feet measured. The researchers will attach painless sensors to the tops of the participants’ feet. The sensors will measure blood flow for 45 minutes. Then the team will apply heat near the sensors, slowly raising the temperature and then keeping the feet warm for another 30 to 45 minutes. This will help stimulate the production of vasodilators and increase blood flow, as long as no defect is present.

The purpose of the first visit will be to establish each participant’s natural blood flow and response to heat. Colberg anticipates that some participants with type 2 may have diminished blood flow, but that it probably won’t be severe because these participants are otherwise healthy.

During the second visit, the researchers will confirm that nitric oxide and prostaglandins aren’t substantially contributing to any diminished blood flow found during the first visit. They will apply a special compound to the participants’ feet to inhibit the release of nitric oxide, and the participants will take aspirin to inhibit the release of prostaglandins. Then the participants will undergo the heat stimulus tests again.

“Because of the compound and the aspirin, we’ll know by process of elimination that any remaining defect in blood flow is because of a problem with the release or action of EDHF,” Colberg says.

During the third visit, all the participants will take glimepiride and undergo the tests. On the fourth visit, participants will take glyburide and undergo the tests.

“There’s some very preliminary evidence in other research we’ve done indicating that glimepiride may increase blood flow and glyburide may decrease...
blood flow in the feet,” Colberg says. If her research bears this out, it could help doctors make treatment decisions for their patients with diabetes who have risk factors for foot ulcers, such as severe nerve damage.

It may seem risky for people without diabetes to take diabetes drugs, but because participants will take only one dose of each drug per test, the only possible side effect is temporarily lower blood glucose levels, says Colberg. The team will check all participants’ blood glucose during and after the tests and treat any lows as well.

Throughout the first phase, the researchers will note the differences in test results between participants with and without diabetes, those who are regular exercisers and those who are sedentary, and those with and without decreased blood flow.

**Exercise**

After the first phase, the sedentary participants (both with and without diabetes) will enroll in a 6-month aerobic exercise program at the local YMCA. They’ll choose which forms of exercise they’d like to do, like walking on a treadmill or riding stationary bicycles. They’ll start slowly, at three 20-minute sessions per week, and gradually work up to 45 minutes per session at a higher intensity.

After 3 months they’ll come back for all of the tests they took during the first phase to see if the blood flow in their feet has improved. After 3 more months of exercise, they’ll come back for more tests.

“We know that regular exercisers have better blood flow than people who are sedentary, regardless of diabetes status,” Colberg says. “Now we want to know if 3 months of exercise will be enough for an improvement, or if 6 months are necessary.

“We’d like to be able to tell people that becoming a regular exerciser can help them avoid problems with their feet, and how long it will take to see benefits.”