

Biologics for Diabetic Foot Ulcers Often Delayed

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FROM ARCHIVES OF DERMATOLOGY

The earlier an advanced biologic therapy is initiated in a patient with a diabetic foot ulcer, the sooner the wound is likely to heal, with first use of engineered skin resulting in the fastest healing, findings from a large retrospective cohort study suggest.

First use of an advanced biologic therapy occurred at a mean of 28 days in 2,517 patients who presented with a diabetic neuropathic foot ulcer between Jan. 1, 2001, and Dec. 31, 2004, and who were treated with at least one such therapy. Healing occurred at a median of 100 days, Dr. Robert S. Kirsner of the University of Miami and his colleagues reported.

The advanced biologic therapies reviewed included bilayered living skin substitute (Apligraf), recombinant human platelet-derived growth factor (becaplermin [Regranex]), and platelet releasate (Procurin). Human fibroblast-derived dermal substitute (Dermagraft) was not commercially available at the start of the study and so was not included.

VITALS

Major Finding: First use of an advanced biologic therapy in a cohort of patients with diabetic foot ulcers occurred at a mean of 28 days, and healing occurred at a median of 100 days.

Data Source: A retrospective cohort study of 2,517 patients.

Disclosures: This study was supported in part by Organogenesis, makers of Apligraf. Coauthor Laure Stasik reported that she was employed by Diversified Clinical Services during the study and is now employed by Organogenesis.

A total of 1,892 patients (75%) were treated with recombinant growth factor, 446 (18%) with bilayered living cell therapy, 125 (5%) with platelet releasate, and 54 (2%) with platelet releasate or recombinant growth factor followed by bilayered living cell therapy.

Healing was faster in those who received engineered skin as the first advanced biologic therapy used (median of 84 days vs. 101 days for recombinant growth factor therapy and 108 days for platelet releasate, after adjustment for confounding factors). In addition, healing was 31.2% more likely than when topical recombinant growth factor was

used first, and 40% more likely than when platelet releasate was used first, the researchers found. The differences were statistically significant (Arch. Dermatol. 2010;146:857-62).

However, the median time to use of engineered skin was 6 weeks, compared with 4 weeks for platelet releasate and 3 weeks for recombinant

growth factor, and 25% of wounds treated with engineered skin were not treated until after 24 weeks.

The delay in using engineered skin vs. the other biologic treatments might be related to cost concerns, they suggested, but they also cited studies that have found that use of advanced biologic therapies reduced costs.

Longer time to healing after the first advanced biologic therapy was used was significantly associated with larger wound area, more severe wound grade, longer duration prior to first visit, and longer time from first visit to use of advanced biologic therapy. These associa-

tions were present across all treatment groups, the researchers said.

Foot ulcers are a major complication of diabetes, affecting up to 15% of diabetic patients and accounting for 20% of all diabetes-related hospital admissions in the United States. Faster foot healing can reduce the incidence of amputation in diabetic patients, the investigators said.

Although the findings underscore the importance of appropriate treatment for the management of chronic diabetic foot ulcers, this study focused on usage patterns with advanced biologic therapies and did not compare outcomes with these therapies and with standard therapy. Because of this and other limitations of the study—including its retrospective nature and the lack of detail on wound history and therapy for some patients—the results “should not be used in isolation when making decisions regarding when to use adjuvant therapy in combination with standard care,” the investigators wrote.

Nonetheless, proper treatment is critical, and delays in providing that treatment will lengthen time to healing, they concluded. ■

Prevention Approach Tried

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to deliver Montana's lifestyle coaching.

Staff at all sites—another four were added in 2009—attended a 2-day training in the DPP program that was adapted for group sessions, in contrast to the individual sessions delivered in the original trial, according to Karl K. Vanderwood, M.P.H., of the Montana Diabetes Project.

Goals Spring From DPP

The weight loss and exercise goals were the same as in the DPP. A total of 16 classes were delivered over 16 weeks, compared with the DPP, where 16 sessions occurred over 16-24 weeks. Participants also had the option of attending twice-weekly physical activity sessions. Between 8 and 30 participants attended the classes, and there was no variation in outcome by group size, said Mr. Vanderwood.

Eligible adults were referred by primary care providers. Participants had to have a body mass index of 25 kg/m² or greater, along with one or more other risk factors for diabetes or cardiovascular disease such as a diagnosis of impaired glucose tolerance (IGT) or impaired fasting glucose (IFG), hypertension, dyslipidemia, or a history of gestational diabetes mellitus. (Unlike the DPP, a strict diagnosis of IGT or IFG was not required.)

Of 1,003 patients recruited, 801 completed the initial 16-week program. Of those, 563 were followed up again at 10 months.

At 16 weeks, there were significant reductions from baseline in weight (99 to 92 kg, a 7% drop), systolic blood pressure (134 to 127 mm Hg, a 5% drop), diastolic blood pressure (82 to 79 mm Hg, a 4% drop), HDL cholesterol (49 to 46 mg/dL, a 6% drop), LDL cholesterol (125 to 115 mg/dL, an 8% drop), and fasting blood glucose (102 to 97 mg/dL, a 5% drop).

Weight reduction often brings an initial drop in HDL cholesterol, which tends to level out with weight maintenance, Mr. Vanderwood noted.

Indeed, at the 10-month follow-up, the mean HDL cholesterol had risen to 51 mg/dL, a statistically significant increase from baseline. At 10 months, the improvements in systolic and diastolic blood pressure, LDL cholesterol, and fasting blood glucose remained statistically different from baseline. Mean weight was 90 kg, down from 97 kg at baseline among the 563 participants analyzed. This did not achieve statistical significance.

At baseline, 70% of participants had three or more cardiometabolic risk factors, whereas by 10 months more than half had just 0-2 such risk factors, he added.

These outcomes are similar to those seen in the DPP. Because the only evaluation after 10 months has been a mailed survey, there are no conclusive data regarding progression to diabetes. However, that's not really the aim of this pilot project, which was designed to see whether a DPP-based program could be implemented in the community, Mr. Vanderwood said in a follow-up interview.

“Our focus is on implementing the DPP and using our resources (money) to do so. Our thought is that it is more important to get people ‘inoculated’ with intervention than to expend time and resources following up on them,” he said, adding that the health department may decide to monitor diabetes conversion rates long term.

Referrals Lead to Success

An important key to success of the program was that it utilized experienced staff at facilities with established referral mechanisms from community providers. “Health care providers welcomed this project into their community. I think they were jumping for joy to have a place to send these folks,” said certified diabetes educator Marcene K. Butcher, R.D., also of the Montana Diabetes Project.

Future plans include a telehealth option contracted with rural sites, the addition of four additional new physical sites, and a possible demonstration

project with the state Medicaid program.

Diabetes Educators Are Key

A major question has been whether the intensive lifestyle intervention provided in the optimal DPP clinical trial setting could be implemented in the real world. At the meeting, Ms. Butcher and Mr. Vanderwood described how the adapted version of the DPP lifestyle intervention was delivered in the state of Montana via group sessions conducted within established diabetes education programs. They also offered advice on how other parts of the country might follow suit.

Diabetes educators were key. “Diabetes educators are uniquely qualified and uniquely situated to provide diabetes prevention,” said Ms. Butcher, quality diabetes education initiative coordinator with the Montana Department of Public Health and Human Services in Helena.

“Here in Montana, we’re providing the evidence that is needed for reimbursement for diabetes educators doing prevention,” she added.

Mr. Vanderwood, who served as the Montana project's program manager but is now a PhD student in epidemiology at the University of Pittsburgh, said that the concept initially came from the state's medical officer, who recognized the burden of diabetes in the state and the importance of prevention. In 2006, he urged the state health de-

partment to request available tobacco settlement funding for chronic disease programs, including diabetes prevention.

A subsequent bill that provided funding for asthma, cancer, cardiovascular disease, and diabetes was signed into law in April 2007. The keys to securing funding were the strong evidence base of the DPP, the leadership within the health department, the fact that the proposed program had measurable objectives, and a supportive legislative subcommittee that “understood the importance of diabetes prevention,” Mr. Vanderwood said.

Seeking support through state legislation is one way to obtain funding. Other sources include existing wellness programs or having participants themselves pay.

In addition, a new partnership between UnitedHealth Group and the Centers for Disease Control and Prevention is launching diabetes prevention programs that will be delivered to covered employees through Walgreen's pharmacies and local YMCAs around the country. Hopefully, that will spur coverage from other insurers, he commented.

In addition to diabetes prevention programs, other proven options might include work sites, churches, and YMCAs, Ms. Butcher said.

Both Ms. Butcher and Mr. Vanderwood stated that they had no financial disclosures. ■