

## AMERICAN PROFESSIONAL WOUND CARE ASSOCIATION NATIONAL CLINICAL CONFERENCE 2005

The meeting was held from April 1 to 2, in Philadelphia.

### Create a Balance to Heal Diabetic Feet

When diabetic feet refuse to heal, the most likely cause is a dysregulation in synthesis, said Robert Frykberg, DPM.

"The important thing is, very basically, we need to realize that there is a finely-tuned balance between collagen, deposition or synthesis and degradation," said Dr. Frykberg, during a presentation. "When [diabetic] wounds don't heal, it is because there is a dysregulation, or an upset in that balance."

Biochemical imbalances, which are caused by the abnormal regulation of synthesis, are the largest factor of wound nonhealing. An unnatural healing response – such as prolonged inflammation – is the result of such imbalances, Dr. Frykberg said. Increases in proinflammatory cytokines, upregulation of destructive proteases and inflammation are major factors of the imbalance. Bacteria also sustain inflammation and cause a dysregulation in fibroblasts and matrix metalloproteases (MMPs).

"The problem is when we have too many MMPs, too much inflammation, too many proinflammatory cytokines in the wound, and decreases in the tissue inhibitors," he said. "We have too much destruction going on."

When infection is present, strain on cellular function, bioburden and inflammation occur. This causes an increased risk of a nonhealing wound. Inadequate offloading, inadequate debridement, repeated trauma and patient noncompliance also affect healing in diabetic feet, Dr. Frykberg said.

"When we can bring [collagen, deposition or synthesis and degradation] back in to balance, we see that there can be a healing wound, with high mitogenic activity and low inflammatory cytokines," he said. "It is critically important that we understand the balance is tipped – it is dysregulated – and we need to bring that back in to regulation if we are going to let these wounds heal."

Diabetic neuropathic foot ulcers are prevalent, with 800,000 new cases annually. To promote wound healing, physicians must find a way to retain a biochemical balance. One way to ensure a proper balance is through nutrition. "We must realize the importance of maintaining ... a high protein and calorie count," Dr. Frykberg said. "You can't heal these wounds in a debilitated patient without added nutrition."

Proper assessment and management of the patient is a key component of diabetic wound healing. In most cases, Dr. Frykberg said, diabetic feet do not heal because of inadequate patient assessment.

### Stabilize Glycemic Levels to Manage DPN

A number of drugs may potentially treat diabetic peripheral neuropathy (DPN), however, managing the complication should begin with glycemic control.

Andrew J.M. Boulton, MD, FRCP suggested that maintaining normal glycemic levels from the onset of diabetes is the best line of defense to prevent DPN. Patients with acute painful diabetic neuropathy can also benefit from improving their glycemic levels because pain usually decreases when glycemia is stabilized. The pain threshold of a patient with DPN is reduced during hyperglycemia, he explained.

"Hyperglycemia is the major cause of [DPN]," said Dr. Boulton, during a presentation. "Stable normoglycemia should be the first step in [DPN] management."

Other factors contributing to painful DPN are poor diabetes control, high blood glucose readings and increased fluctuation of blood glucose. Controlling triglyceride and cholesterol levels and abstaining from smoking – three other neuropathy risk factors – will also decrease incidence to DPN. Diabetic patients should also have an annual screening to combat the condition, and the American Diabetes Association has recently published a position statement in regards to DPN and tight glycemic control. (See related article on page 18).

There are two groups of treatments for painful DPN, Dr. Boulton said. The first group – disease-based therapies – influences the history of DPN. Such drugs work to prevent or slow the progression of DPN. However, most drugs in this category are investigational, he said. The other treatment group reflects the history of DPN, and these drugs work to treat DPN symptoms.

"We've come a long way, but we still have a long way to go in terms of finding a truly pathogenic treatment that will prevent the development or slow the progression of neuropathy once it is formed," Dr. Boulton concluded.

## THE 24TH ANNUAL SCIENTIFIC MEETING OF THE AMERICAN PAIN SOCIETY

The meeting was held from March 30 to April 2 in Boston.

### TCA's Commonly Prescribed To Older Patients

As a therapy for treating painful DPN, tricyclic antidepressants (TCAs) are a common prescription for diabetic patients. However, the side effects from the therapy may compromise patients' overall health.

During a presentation, investigators said that the treatment may cause cardiac arrhythmias, myocardial infarction, stroke, orthostatic hypotension and psychosis. To determine the frequency of TCA prescriptions in an older population, they used a health care claims database to enroll patients who were placed on the DPN treatment between January 1999 and June 2001. All patients (n=296) were aged

≥65 years at time of prescription, which was either amitriptyline (23.5 mg/day for an average 147.6 days) or nortriptyline (25.9 mg/day for an average 117.3 days).

Coronary heart disease, cardiac arrhythmias or other cardiovascular disorders were present in 34.1% of patients who received amitriptyline and 24.4% of patients who received nortriptyline. About 44.7% of amitriptyline patients and 48.8% of nortriptyline patients used the treatment inappropriately, the investigators said.

A small percentage of patients were also receiving treatment for a thyroid condition, which investigators considered to be a contraindication. They concluded that the prescription of TCAs is common in older patients with DPN.

### **DPN, Chronic Pain May Inhibit Sleep Patterns**

Sleep impairment in DPN patients is affected by the severity of the condition, according to meeting presenters.

The level of sleep impairment of 255 patients with painful DPN was compared to two other patient populations to determine how the disease affected sleep. Investigators said that impairment was higher in the DPN population than in the healthy control population, and it was also higher than a chronic disease population. The amount of sleep patients received was calculated with the MOS Sleep Scale, which produces a summary sleep problem score on a scale of six sleep attributes. The mean age of patients with painful DPN was 61 years.

Investigators adjusted scores for age and duration of painful DPN and found that pain still predicted the level of sleep impairment. In fact, the combination of anxiety symptoms and pain accounted for 46% of sleep problems. They concluded that painful DPN does bear a tie to sleep impairment, and the tie is also related to neuropathic pain conditions and chronic medical conditions.

### **2005 ANNUAL SCIENTIFIC CONFERENCE OF THE AMERICAN COLLEGE OF FOOT AND ANKLE SURGEONS**

The meeting was held from March 9 to 13 in New Orleans.

### **Foot Surgery Method Eases Nerve Pressure, Prevents Amputations**

The presentation of a new surgical technique during the meeting showed results that suggest it relieves nerve compression and may prevent lower-leg amputation.

In addition to foot reconstruction procedures and plastic surgery to heal diabetic foot ulcers, the new approach relieves nerve pressure that causes loss of feeling and foot ulceration.

Kent R. DiNucci, DPM, a Chicago-area foot and ankle surgeon, showed that this procedure restored nerves, helped regain sensation and prevented foot ulcers development.

"It's a new way of looking at the old problem of diabetic neuropathy (DN)," said Dr. DiNucci, in a news release.

"Most nerve problems in the lower extremities are considered to be neuropathy in diabetic patients. Many, however, actually can be described as carpal tunnel syndrome of the feet because the nerves swell and are compressed by surrounding ligaments."

Dr. DiNucci explained that some nerves pass through tarsal tunnels. In diabetes patients, nerves in the lower extremity enlarge from water build-up caused by elevated blood sugar levels. As this happens, blood flow is impeded and nerves deteriorate.

"The new surgical approach is to release the tarsal tunnel to decompress the nerve and allow it to regain circulation and regenerate," said Dr. DiNucci. "For the best outcomes, diabetic patients should be evaluated as soon as they feel tingling or burning in their toes, well before extensive nerve damage occurs. This procedure isn't a cure for diabetic neuropathy, but it can delay eventual nerve degeneration."

A study published late last year showed that 50 diabetic patients who underwent the nerve decompression surgery on one leg did not develop foot ulcers or require foot or lower-leg amputations. On the opposite leg of 15 patients, foot ulcers developed. Three patients underwent amputations.

### **AMERICAN COLLEGE OF CARDIOLOGY'S 54TH ANNUAL SCIENTIFIC SESSION**

The ACC annual meeting was held in Orlando, from March 6 to 9.

### **Oral Agent Shows Anti-atherogenic Effects**

Investigators of a randomized, placebo-controlled trial presented information showing that pioglitazone, an oral drug used to treat patients with type 2 diabetes, reduced neointima formation after stent implantation in nondiabetic patients.

The formation of new tissue within the stented area occurred without altering blood glucose or other metabolic parameters, they said.

Previous animal studies revealed that glitazones have anti-atherogenic properties, and clinical trials in type 2 diabetic patients undergoing percutaneous interventions (PCI) showed they reduced restenosis. Based on these results, investigators decided to see whether these effects could be achieved in nondiabetic patients, said Nikolaus Marx, MD, from the University of Ulm, Germany.

A total of 50 nondiabetic patients were randomly assigned to receive either 30 mg pioglitazone/day or placebo. All patients also received standard treatment after coronary stent implantation. After 6 months, patients

were examined by intravascular ultrasound to locate new tissue within the stented area.

Patients treated with pioglitazone showed a significant reduction in neointima formation and significantly lower plaque volume versus controls. The restenosis rate was significantly reduced by pioglitazone. Fasting blood sugar, insulin and lipid profiles were not affected.

## **Sirolimus Stent Superior to Paclitaxel Stent in Diabetic Patients**

The sirolimus-eluting stent is superior to the paclitaxel-eluting stent to prevent restenosis in diabetic patients, according to a presentation by Adnan Kastrati, MD.

After allocation to angioplasty with the sirolimus or paclitaxel stent, 250 diabetic patients had an angiogram at 9 months to measure late lumen loss, or the degree of renarrowing after stent implantation. Lumen loss, restenosis and the need for target vessel revascularization were all greater in the paclitaxel group, said Dr. Kastrati, from Deutsches Herzzentrum, Munich.

“Diabetic patients are the most problematic patients for interventional cardiology,” he said. “Many believe that percutaneous coronary intervention is not the right thing to do with diabetic patients. Many, especially in the United States, go to surgery because PCI is associated with a very high risk of restenosis in this population. So their need for appropriate percutaneous therapy is great, and we must learn which is the best device for them at present.”

## **Hypertension Study Nixes Conventional Beta-Blockers**

A large randomized trial comparing newer antihypertensive treatment strategies to conventional ones has recommended that beta-blocker-based treatment be withdrawn “where appropriate” and substituted with newer antihypertensive therapy with calcium channel antagonists and angiotensin-converting enzyme (ACE) inhibitors.

It is debatable that newer antihypertensive strategies using calcium channel antagonists and ACE inhibitors are superior to older treatments with beta-blockers and diuretics. Peter S. Sever, MD, Imperial College, London, presented information from ASCOT-BPLA.

Approximately 20,000 hypertensive patients aged 40 to 79 years were randomized to amlodipine (a calcium channel antagonist) with or without perindopril (an ACE inhibitor), or atenolol (a beta blocker) with or without bendroflumethiazide (a diuretic). Target blood pressures were <140/90 mm/Hg (<130/80 mm/Hg for patients with diabetes), and the primary endpoint was nonfatal myocardial infarction and fatal coronary heart disease.

The reduction in stroke, coronary events, cardiovascular death and all-cause mortality was significantly greater

in the amlodipine/perindopril arm, and it was recommended that the trial be stopped because it was unsafe for patients in the beta blocker-diuretic arm to continue, Dr. Sever said.

In addition, there was a substantial excess of new diabetes in the beta blocker/diuretic arm, he noted. “This has been reported in quite a few studies now. It’s clear that patients on any regimen containing a beta-blocker, and even worse, if it also contains a diuretic, are 30% more likely to develop diabetes. Something about this drug combination induces diabetes, and this is not good news at all, given the worldwide epidemic of diabetes.”

## **Bypass Grafting Surgery Helpful for High-Risk Patients**

During a presentation highlighting the benefits of coronary artery bypass grafting (CABG) surgery, researchers noted that the procedure extended survival time in diabetic patients with several narrowed heart arteries.

Diabetic patients who undergo CABG surgery are more likely to die within 8 years of surgery versus patients without diabetes. Heart disease is more likely the cause of death in these patients. To examine these factors, investigators looked at the medical records of 3,600 patients participating in the Bypass Angioplasty Revascularization Investigation (BARI) study, 46% of which died during the long-term follow-up. Thirty-two percent of the patients were diabetic.

Cardiac disease deaths accounted for 51% of diabetic patients and 43% of nondiabetic patients. Investigators noted that the largest difference between diabetic and nondiabetic deaths was from heart failure, which caused death in 16% of diabetic patients and only 9% of nondiabetic patients. In all patients, the risk of sudden death was reduced with CABG.

Investigators of a separate study concluded that the surgery improved long-term survival rates in diabetic patients versus other treatment options. The patients had narrowed arteries of the heart.

Survival rates were tracked using the Medicine Angioplasty or Surgery Study (MASS); rates were calculated for patients treated with CABG, angioplasty and stenting, or medical therapy. Although the overall 5-year death rate was higher in diabetic patients, investigators said that CABG surgery benefited diabetic patients who had more than one diseased artery.

Using stents coated with sirolimus in patients who need three or more stents may produce an increased risk, they said. When compared with patients who received one stent, patients needing multiple stents were more likely to experience complications, heart attack or cardiovascular illness. In these cases, CABG should be the considered treatment option. ■