

AMERICAN SOCIETY OF NEPHROLOGY'S 37TH ANNUAL MEETING AND SCIENTIFIC EXPOSITION

The 2004 meeting was held from October 27 to November 1 in St. Louis.

Kidney Disease Patients May Have Worse Health with a Very Low-protein Diet

A very low-protein diet may not be a healthy alternative to the harmful effects of a high-protein diet on patients with kidney disease.

Researchers used data from the Modification of Diet in Renal Disease (MDRD) study – a long-term, randomized, controlled trial conducted from 1988 to 1993. They conducted a 10-year follow-up on the 255 patients with predominantly nondiabetic kidney disease and severe reduction in kidney function enrolled in the study. Low protein intake in these patients reduced the build up of waste in their blood and delayed the onset of kidney failure symptoms.

Follow-up results indicated that the mortality of patients who consumed a very low-protein diet was increased versus patients who consumed a low-protein diet. The diet also slowed the progression of kidney disease, researchers reported. A companion study showed that a possible benefit to a low-protein diet versus a usual-protein diet exists because it does not have a detrimental effect on mortality and does not slow the progression of kidney disease.

“Although the results remain inconclusive, the studies echo concerns of investigators that very low-protein diets may be detrimental to the health of patients with kidney disease. Further research is warranted, but in the meantime, patients are best advised to work with their nephrologists and dieticians to create the best diet for their condition,” said Andrew S. Levey, MD, chief of the division of nephrology at Tufts-New England Medical Center, Boston.

Results from Landmark 4D Trial Presented

International researchers of the Deutsch Diabetes Dialyse Study (4D) said that atorvastatin (Lipitor, Pfizer) provides significant cardiovascular benefits for type 2 diabetic patients.

The 4D trial is the first study to examine the use of statins in type 2 diabetic patients with kidney failure or end stage renal disease. The study examined the effectiveness and safety of atorvastatin. Researchers said that study findings helped to show that the use of atorvastatin is

beneficial in type 2 diabetic patients who have progressed to kidney failure where hemodialysis is the only option for survival.

Researchers studied the cardiovascular outcomes in dialysis of 1,255 patients from 178 dialysis centers in Germany. All were on maintenance hemodialysis and had diabetic complications including diabetic nerve disease, diabetic gangrene, retinopathy or blindness. A majority of patients also had diseases including hypertension, congestive heart failure, peripheral artery disease and cardiac disease. All patients took 20 mg atorvastatin or placebo between 1998 and February 2004.

“The findings contribute to the understanding of the mechanisms of cardiovascular disease in type 2 diabetic [patients] on hemodialysis treatment and will help to guide treatment options,” said Christoph Wanner, MD, lead author and professor of medicine and chief of the nephrology division at the University Clinic, Wuerzburg, Germany.

Other studies have shown that atorvastatin provided significant cardiovascular benefits in type 2 diabetic patients who do not have significant kidney disease. The studies suggested that patients should have early preventive therapy to lower their cardiovascular risk.

Landmark Trial Initiative Announced

Researchers announced the design of a multicenter, randomized, double-blind placebo-controlled study that will determine if Aranesp (Amgen Inc) is an effective treatment of anemia.

A common complication of kidney disease, anemia becomes more common as kidney function declines.

The Trial to Reduce cardiovascular Events with Aranesp Therapy (TREAT) will evaluate the cardiovascular outcomes of 4,000 patients with kidney disease and type 2 diabetes who are undergoing treatment for anemia. Patients will receive Aranesp, a recombinant erythropoietic protein, once monthly during the landmark trial, and the endpoint will be a composite index of time to mortality or nonfatal cardiovascular event including myocardial infarction, myocardial ischemia, stroke or heart failure.

“Current research suggests that anemia is an augmenter of cardiovascular risk in individuals with kidney disease and type 2 diabetes,” said Marc Pfeffer, MD, PhD, lead TREAT investigator, and chief of medicine at Brigham and Women's Hospital, and professor at Harvard Medical School, in a news release. “TREAT will be the definitive study to determine if treating anemia with Aranesp does, in fact, lower the risk of death and nonfatal cardiovascular events in individu-

als with [kidney disease] and type 2 diabetes.”

Hemoglobin Levels Stabilized with New Agent

Researchers reported that a new antianemia agent sustained and stabilized the correction of anemia in patients with kidney disease.

Results from two study populations showed that Continuous Erythropoietin Receptor Activator (CERA), a subcutaneous injection, delivered rapid and stable anemia correction at dosings up to 4 weeks.

“CERA has a unique activity at the receptor and has been designed to provide sustained stimulation of erythropoiesis with long dosing intervals,” said Robert Provenzano, MD, chair, division of nephrology, St. John Hospital and Medical Center, Detroit, in a news release. “This more closely mimics the body’s natural control of red blood cell production.”

Populations from two phase 2, dose-finding, open-label, randomized, multicenter studies consisted of erythropoiesis stimulating agent (ESA) naïve patients with kidney disease not on dialysis, and patients previously treated with epoetin on dialysis. Both populations benefited by using CERA, researchers reported. The benefits included the stabilized maintenance of hemoglobin levels in the dialysis patients taking CERA; and rapid anemia correction in the ESA naïve patients.

2004 JOINT MEETING OF THE AMERICAN ACADEMY OF OPHTHALMOLOGY AND THE EUROPEAN SOCIETY OF OPHTHALMOLOGY

The AAO/SOE was held from October 22 to October 27 in New Orleans.

Ruboxistaurin May Benefit Diabetes-induced Eye Disease

The investigational compound ruboxistaurin (Eli Lilly and Company) may reduce diabetes-related vision loss, according to presented information.

Two phase III placebo-controlled trials, one with a 30-month minimum duration and one with a 3-year minimum duration, assessed the effects of ruboxistaurin on over 900 patients with diabetic retinopathy or diabetic macular edema (DME). Visual acuity and extent of DME were measured in both trials.

Researchers concluded that patients receiving a daily 32-mg dose of ruboxistaurin whose center macula showed levels of DME involvement (n=67) had better vision than those treated with placebo (n=61). Patients also experi-

enced a slower progression of DME from outside of 500 µm to the center of the macula (n=168) versus patients treated with placebo (n=176), they said. However, these differences were not significant in patients treated with lower doses of ruboxistaurin, researchers noted.

Findings from previous analyses showed that ruboxistaurin is generally well tolerated among patients, and it did not increase the incidence of side effects versus patients who received placebo.

“A key to preventing vision loss from diabetic eye disease is to prevent macular edema from involving the center of the macula, where it affects the part of the retina that is most important for detailed vision,” Lloyd Paul Aiello, MD, PhD, associate director of the Beetham Eye Institute at the Joslin Diabetes Center, said in a news release. “These data suggest that ruboxistaurin may have the potential to decrease the progression of DME to involve the center of the macula. A phase III clinical trial is underway to further explore these preliminary findings.”

Drug Delivery System Promising for Macular Edema

A dexamethasone-containing intravitreal biodegradable implant (Posurdex, Allergan) worked for treating macular edema occurring after cataract surgery or due to uveitis.

George A. Williams, MD, presented data from a subset of 39 patients from the larger cohort of the multicenter phase II clinical trial for macular edema. Twelve patients were randomized to Posurdex 300 µg, 13 to Posurdex 700 µg and 14 to observation, Dr. Williams reported. “Significantly more patients achieved a 3-line or greater improvement in visual acuity in the Posurdex 700-µg group (54%) than in the observation group (7%) $P=0.013$ at day 90,” he said. Dr. Williams concluded that Posurdex is effective for the treatment of inflammatory macular edema. He has a financial interest in the product.

Treatment of DME: Corticosteroids With, Without Vitrectomy

Steroids are a reasonable treatment for DME because they are potent inhibitors of vascular endothelial growth factor, said Ramin Sarrafzadeh, MD, PhD. “Steroids are angiostatic, primarily due to upregulation of extracellular matrix protein plasminogen activator inhibitor in vascular endothelial cells,” he said. Steroids inhibit activation of plasmin; and plasmin activated collagenases, which are critical in the dissolution of capillary basement membrane cells. Dr. Sarrafzadeh is with Associated Retinal Consultants in Williamsburg, Mich.

Steroids are useful in DME, Irvine Gass disease, branch retinal vein occlusion with cystoid macular edema (CME), central retinal vein occlusion with CME, macular pucker with CME, vitreomacular traction syndrome with CME and neovascular age-related macular degeneration, Dr. Sarrafizadeh said.

A trial of steroids in macular disease included 143 eyes of 129 patients, 65 were female. Patients ranged in age from 23 to 93 years and follow-up ranged from 6 to 30 months (mean 17 months). Of the 143 eyes, 88 had DME and 55 had nondiabetic macular edema; 68 had prior focal laser, 24 had vitrectomy with intravitreal triamcinolone acetonide (Kenalog, Allergan). Forty-nine (34%) had vitrectomy with membrane peeling with intravitreal triamcinolone; intravitreal triamcinolone dosage of 4 mg or 20 mg.

"Results were measured by final visual outcome, macular thickness on OCT [optical coherence tomography], incidence of raised intraocular pressure (IOP), hypopyon or fibrinoid uveitis, and retinal detachment," Dr. Sarrafizadeh said. Half of the eyes developed raised IOP, 5% developed hypopyon or fibrinoid uveitis and no retinal detachments occurred, he said.

"Intravitreal triamcinolone acetonide can result in a modest improvement in visual acuity and in macular thickness in eyes with DME," Dr. Sarrafizadeh said.

"Improvement was also noted in eyes that had vitrectomy in association with intravitreal triamcinolone use. However, a relatively high incidence of raised IOP may be associated with this treatment. As a group, the final visual outcome may be worse in eyes that develop uveitis."

HEART FAILURE ASSOCIATION OF AMERICA 8TH ANNUAL SCIENTIFIC MEETING 2004

The HFSA meeting was held from September 12 to 15 in Toronto, Ontario.

Diabetes Worsened Prognosis of HF in Black Patients

Diabetes contributed to the development and progression of heart failure (HF) – and lead to a worse outcome – in black patients.

Judith Mitchell, MD, of the department of medicine/ cardiology at the State University of New York, Brooklyn, said that coronary artery disease is the most common cause of HF, and diabetes may be an independent cause. The prevalence of diabetes among patients with HF is thought to be around 25%, based on large clinical trials. In this study, researchers determined the prevalence/impact of diabetes in 286 patients with HF, 92% of whom are black.

Forty-seven percent of the patients had diabetes. Of these, 91 were classified as noninsulin dependent and 44 insulin dependent. Sixty-four percent of the total population had impaired systolic function and 36% had preserved systolic function. Patients with HF and diabetes were more likely to have elevated serum creatinine (>1.5 mg/dL) versus those who had HF only. Diabetes did not affect the length of hospital stay and had little bearing on the treatment drugs.

Investigators said the study was important because 98% of the enrollees were black. Because close to 50% of the patients had diabetes, other studies may have underestimated the prevalence of diabetes among the black population with HF. The percentage of black patients with HF and insulin resistance or the metabolic syndrome is largely unknown and therefore could also be underestimated.

Poorly Controlled Diabetic Patients With Chronic Heart Failure Have Longer Hospital Stays

Patients with poorly controlled diabetes who are admitted to the hospital with chronic heart failure exacerbation are likely to stay in the hospital longer. Researcher Vishal Bhatia, MD, said that admission blood sugar values can help identify this subset of patients who might have poor in-hospital glycemic control and may stay longer.

Researchers said that diabetes is a risk factor for chronic heart failure and increases the prevalence and incidence of chronic heart failure. The condition is independently associated with clinical and subclinical left ventricular systolic and diastolic function. Hyperglycemia, with or without diabetes, is associated with worse symptomatic status in chronic heart failure patients.

Researchers attempted to correlate glycemic control in diabetic patients who were admitted to the hospital with acute exacerbation of chronic heart failure with the number of hospital days of admission. They included 100 chronic heart failure patients with a mean age of 76.5 years and an average hospital stay of 4.8 days. They found a strong correlation between HbA1c and hospitalization. Patients with uncontrolled diabetes stayed in the hospital for 6.3 days versus diabetic patients with blood glycemic control who stayed for 3.2 days.

Diabetic patients with uncontrolled baseline glycemic status had worse glycemic control in the hospital, and a strong correlation between average fasting blood sugar while in the hospital and number of days of hospitalization ($P<.001$) existed. Higher blood sugar values at admission also correlated with in-hospital days ($P<.001$). ■