Drug Combo May Help Cut CV Risks in Diabetics

More patients achieve the goals set by the American Diabetes Association with fibrates plus statins.

BY PATRICIA L. KIRK
Contributing Writer

GRAPEVINE, TEX. — A combination of fibrates and statins to target different lipids may provide the best protection against cardiovascular events in diabetics and patients with metabolic syndrome, said Dr. Alistair I. Fyfe at the annual convention of the American College of Osteopathic Family Physicians.

The incidence of metabolic syndrome and type 2 diabetes is increasing because of the "fattening of America," he said, noting that on average, Americans have gained 30 pounds since 1985.

Metabolic syndrome is a research term that refers to a combination of related health factors that together increase the risk for heart disease, including insulin resistance, obesity, unhealthy lipid levels, high blood pressure, and signs of kidney disease.

A hallmark of metabolic syndrome is the accumulation of visceral adipose fat, leading to disturbances in various cardiometabolic risk factors, which can increase insulin resistance and risk for both type 2 diabetes and heart attack.

The rationale for a combination treatment has evolved from a number of clinical trials that evaluated the efficacy of statins and fibrates in reducing cardiometabolic risk factors alone and together, said Dr. Fyfe, director of primary and secondary cardiac prevention at Medical City Hospital in Dallas.

"More patients achieve American Diabetes Association goals with combined drug therapy," he said.

Diabetic subanalyses of four major placebo-controlled clinical trials that evaluated the efficacy of statins, a class of lipid-lowering drugs, to treat hypercholesterolemia, concluded that statins alone do not reduce cardiovascular risk in diabetic patients, said Dr. Fyfe. Cardiac risk in diabetics and people with metabolic syndrome is associated with elevated triglycerides and low HDL cholesterol, he explained.

'Diabetics need to be treated differently. With the combination therapy, 'the fibrate makes LDL available for the statin to clean out of the blood.'

Statins cured hypercholesterolemia in about one-third of study participants, but had no effect on the other 70%, he said. "Diabetic patients need to be treated differently [than other high-risk patients]. There is no doubt that statin therapy is here to stay; it is the right drug for 30% of people."

Niacin and fibrates, another class of lipid-lowering drugs, improve triglycerides and increase HDL cholesterol. However, niacin is contraindicated for diabetics because it worsens insulin resistance. Fibrates have been used clinically since the 1970s to treat unhealthy lipids, but their mechanism of action was unclear until the 1990s, when researchers discovered that they activate peroxisome proliferator-activated receptors, which modulate carbohydrate and fat metabolism and adipose tissue differentiation.

By lowering triglycerides and raising HDL cholesterol levels, fibrates decrease the concentration of very-low-density lipoprotein (VLDL), resulting in a lower concentration of LDL cholesterol particles and increased particle size, which makes it easier for them to be eliminated from blood compared with small particles, Dr. Fyfe said, adding that elevated triglycerides are the result of an increase in VLDL.

Statins reduce hepatic cholesterol synthesis, which lowers intracellular cholesterol, which in turn stimulates upregulation of LDL cholesterol receptors and increases the uptake of non–HDL cholesterol particles from the blood. With the combined therapy, "the fibrate makes LDL available for the statin to clean out of the blood," he said.

The results of several studies have verified the efficacy of combined therapy in diabetics. In one study, 120 patients were given 20 mg of atorvastatin or 200 mg of fenofibrate alone or a combination of the two drugs (Diabetes Care 2002;25:1198-202). The researchers recorded a 46% drop in LDL, a 50% reduction in triglycerides, and a 22% increase in HDL for participants who were given the combination therapy, compared with a 40% decline in LDL, a 30% drop in triglycerides, and a 9% increase in HDL for those who were given atorvastatin alone and a 15% decline in LDL, 41% reduction in triglycerides, and 15% increase in HDL in those who were given fenofibrate alone.

In another study, involving 618 participants, a combination of 20 mg of simvastatin and 160 mg of fenofibrate lowered LDL by 31%, VLDL by 48%, and triglycerides by 43% and raised HDL by 19%, compared with reductions of 26% in LDL, 24% in VLDL, and 20% in triglycerides and an increase of 10% in HDL in those who received 20 mg of simvastatin alone (Am. J. Cardiol. 2005;95:462-8). ■

Anemia in Diabetics May Flag Kidney Disease, Heart Risks

BY PATRICIA L. KIRK
Contributing Writer

GRAPEVINE, TEX. — The presence of anemia in older adults often signals a serious illness such as cancer, infection, or chronic inflammatory disease, but in diabetics, anemia may be an indication of chronic kidney disease, Dr. Naushira Pandya said at the annual meeting of the American College of Osteopathic Family Physicians.

This link in diabetics between anemia and chronic kidney disease (CKD) arises because, as diabetes progresses, the kidneys become damaged and there is a decrease in the production of erythropoietin, which can also cause anemia, said Dr. Pandya.

He recommended routinely checking diabetics for anemia and noted that the severity of anemia correlates with the severity of underlying disease, which often exists along with other causes of anemia, particularly iron deficiency.

In stressing the importance of checking high-risk patients, Dr. Pandya cited the findings in a study of Medicare patients, which suggested that anemia is a mortality multiplier when combined with another disease.

Anemia of CKD is now also considered a nontraditional risk factor for cardiovascular disease. Erythropoietin deficiency and the resulting reduction in the concentration of hemoglobin causes tissue hypoxia and increased cardiac work, which results in left ventricular hypertrophy and ischemic heart disease.

That, in turn, increases the risk for heart failure, angina pectoris, heart attack, and poor health–related outcomes, explained Dr. Pandya, chair of the department of geriatrics at Nova Southeastern University's College of Osteopathic Medicine in Fort Lauderdale, Fla.

Study findings indicate that anemia doubles the risk for hospitalization for a comorbid condition and significantly increases the risk of premature death in older adults with diabetes, CKD, and heart failure, as well as the risk of stroke in patients with CKD, he noted.

Anemia of CKD is defined by a hemoglobin level of less than 12 g/dL in men and postmenopausal women, and a glomerular filtration rate of 60 mL/min per 1.73 m^2 of body surface area for 3 months with or without kidney damage, or kidney damage for 3 months as shown by pathologic abnormalities or markers such as proteinuria.

Dr. Pandya said that anemic adults experience a decline in functioning because of lower exercise tolerance, muscle wasting, decreased mobility and cardiovascular fitness, greater physical instability and frailty, and an increase in the number of falls. CKD patients, however, have even lower functioning scores than do patients with other comorbid conditions. For example, CKD patients have a mean physical functioning score of 41.2 (0 denotes total disability and 100 denotes full functioning), compared with a mean score of 47.5 in heart failure patients, 67.7 in diabetics without CKD, and 73.4 in hypertensives.

Anemia is effectively a diagnosis of exclusions, because its signs and symptoms, such as weight loss, erectile dysfunction, and often feeling cold, are nonspecific, said Dr. Pandya.

The National Kidney Foundation advises assessing for anemia when the glomerular filtration rate is less than 60 mL/min per 1.73 m^2. The evaluation consists of checking hemoglobin and/or hematocrit, red blood indices, reticulocyte count, and iron parameters, and for occult blood. A test for iron, total iron-binding capacity, percentage saturation of iron-binding capacity, ferritin and soluble transferrin receptor levels will distinguish anemia of chronic disease (ACD) from iron-deficiency anemia (IDA). A high ferritin level is the hallmark of ACD, whereas ferritin is normal in IDA; transferrin is normal in ACD but elevated in IDA.

A more extensive work-up, dictated by clinical and laboratory circumstances, and which may include bone marrow aspiration or biopsy, may be needed to determine the cause of anemia.

Dr. Pandya emphasized that it is imperative to identify the cause, because cause directs therapy.

ACD is treated with erythropoietic stimulatory proteins, which are peptide hormones and their derivatives, manufactured by recombinant DNA technology.

The two major products are epoetin alfa (Eprex, Ortho Biologics) and darbepoetin alfa (Aranesp, Amgen Inc.). Darbepoetin's half-life is three times longer than epoetin's half-life. Epoetin alfa is given subcutaneously or intravenously one to three times weekly, whereas 0.45 mcg/kg, given once every 2 weeks, usually maintains a target hemoglobin level of 11-12 g/dL. ■

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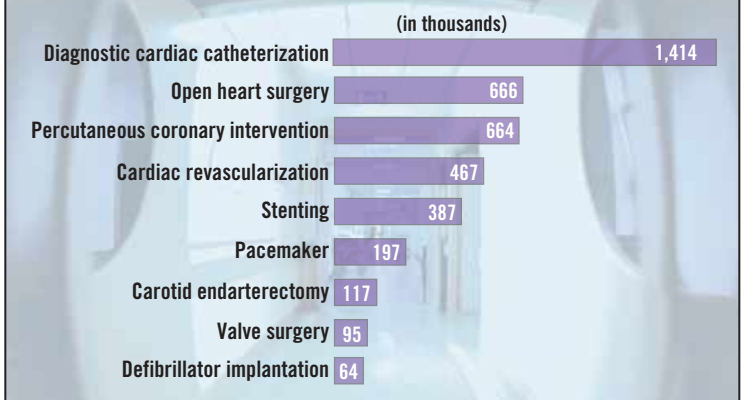

Note: Based on 2003 estimates from the National Center for Health Statistics.
Source: American Heart Association

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