ACCORD eye study finds 2 therapies slow diabetic eye disease progression

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In high-risk adults with type 2 diabetes, researchers have found that two therapies may slow the progression of diabetic retinopathy, an eye disease that is the leading cause of vision loss in working-age Americans.

Intensive blood sugar control reduced the progression of diabetic retinopathy compared with standard blood sugar control, and combination lipid therapy with a fibrate and statin also reduced disease progression compared with statin therapy alone. However, intensive blood pressure control provided no additional benefit to patients compared with standard blood pressure control.

Results of the Action to Control Cardiovascular Risk in Diabetes (ACCORD) Eye Study, supported by the National Institutes of Health, are published online June 29 in the New England Journal of Medicine (NEJM) and will be presented June 29 at the 70th Scientific Sessions of the American Diabetes Association.

"The ACCORD Eye Study clearly indicates that intensive glycemic control and fibrate treatment added to statin therapy separately reduce the progression of diabetic retinopathy," said Emily Chew, M.D., chair of the Eye Study and chief of the Clinical Trials Branch of the Division of Epidemiology and Clinical Applications at the National Eye Institute (NEI). "The main ACCORD findings showed that fibrate treatment added to statin therapy is safe for patients like those involved in the study. However, intensive blood sugar control to near normal glucose levels increased the risk of death and severe low blood sugar, so patients

and their doctors must take these potential risks into account when implementing a diabetes treatment plan."

The ACCORD study was a landmark clinical trial that included 10,251 adults with type 2 diabetes who were at especially high risk for heart attack, stroke or cardiovascular death. The study evaluated three intensive strategies compared with standard treatments for lowering cardiovascular risks associated with diabetes.

Intensive treatments included control of blood sugar to near normal levels, control of blood pressure to normal levels, and combination treatment of multiple blood lipids with fenofibrate and simvastatin compared to standard treatment with simvastatin alone. Fenofibrate treatment lowers triglycerides and raises the "good" high density lipoprotein (HDL) cholesterol levels, while simvastatin lowers the "bad" low density lipoprotein (LDL) cholesterol levels. All participants were enrolled in the blood sugar trial and in either the blood pressure or lipid trial.

The ACCORD Eye Study involved a subset of 2,856 participants. Researchers analyzed the effects of the treatment strategies on blood vessels in the eye by identifying diabetic retinopathy progression over four years. Diabetic retinopathy is a disease in which blood vessels in the eye's light-sensitive retinal tissue are damaged by diabetes. Blood vessels can begin to leak, causing swelling in the retina, and abnormal new blood vessels can develop, both causing vision loss. In the study, disease progression was identified through retinal photographs that indicated blood vessel changes or by the need for laser or eye surgery to treat abnormal blood vessels.

Compared with standard blood sugar control, intensive control decreased the progression of diabetic retinopathy by about one-third, from 10.4 percent to 7.3 percent, over four years. Participants in the intensive

control group had a median blood sugar level of 6.4 percent hemoglobin A1c—a level close to values in people without diabetes. The standard blood sugar control group maintained a median level of 7.5 percent.

"Previous clinical trials have shown the beneficial effects of intensive blood sugar control on slowing the progression of diabetic retinopathy in people with type 1 diabetes or newly diagnosed type 2 diabetes," said NEI director Paul A. Sieving, M.D., Ph.D. "The ACCORD Eye Study expands these findings to a larger population of adults who had type 2 diabetes for an average of 10 years, and demonstrates that the eye benefits from the reduction of glucose below previously established levels."

In addition, compared with simvastatin treatment alone, combination lipid therapy with fenofibrate plus simvastatin also reduced disease progression by about one-third, from 10.2 percent to 6.5 percent, over four years. No prior clinical trial has shown that the combination of fenofibrate and simvastatin reduces diabetic eye disease progression.

There were no differences in diabetic retinopathy progression among participants treated to an intensive systolic blood pressure (top number in a reading) target of less than 120 mm Hg compared with those treated to a standard target of less than 140 mm Hg.

In the main ACCORD study, none of the three treatment strategies resulted in a significant decrease in the combined rates of heart attack, stroke or cardiovascular death compared with standard treatments. However, over about three-and-a-half years of follow up, participants in the intensive blood sugar group had a 22 percent higher risk of death (5.0 percent versus 4.0 percent) and a three times higher risk of seriously low blood sugar (10.5 percent versus 3.5 percent) compared with participants in the standard blood sugar control group.

The ACCORD study began in 2001, and participants were treated and monitored for an average of five years. Results of the blood sugar clinical trial were reported in 2008, when the intensive blood sugar therapy was stopped 18 months early due to an increased risk of death in that treatment group compared with the standard blood sugar control group. Findings from the blood pressure and lipid clinical trials appeared in the April 29, 2010 edition of NEJM.

"A key question in the main ACCORD study was whether intensive glucose control, previously demonstrated to reduce risk of microvascular disease—including eye problems—in diabetes, would reduce large vessel disease that causes problems like heart attacks. Investigators are continuing to evaluate the risks and benefits of the treatment strategies in these high-risk patients with type 2 diabetes," said Susan B. Shurin, M.D., acting director of the National Heart, Lung, and Blood Institute, the primary sponsor of the ACCORD study. "Clinicians should individualize treatment for each patient to prevent complications, also incorporating information about conditions such as cardiovascular or visual problems. Lifestyle interventions, including physical activity, weight loss and healthy diets, can improve diabetes control and reduce onset of diabetes."

More information: Find more information about this trial (NCT00542178) at www.clinicaltrials.gov. Visit www.nei.nih.gov/health/diabetic for more information about diabetic retinopathy.

Provided by NIH/National Eye Institute

diabetic-disease.html