Diabetes Drug Metformin Prevents Worsening of Calcium Deposits in Arteries

March 9, 2012 By Tim Horn

Treatment with the diabetes drug metformin prevented the progression of coronary atherosclerosis (hardening of the arteries) in a study of people living with HIV presented Wednesday, March 7, at the 19th Conference on Retroviruses and Opportunistic Infections in Seattle.

According to lead presenter Kathleen Fitch, a research nurse practitioner at Massachusetts General Hospital and her colleagues, study volunteers receiving daily doses of metformin had essentially no progression of coronary artery calcification (CAC) during the yearlong study period, while those receiving a placebo had calcium increases of up to 50 percent.

The study also found that lifestyle modification—participation in regular exercise and dietary counseling sessions—did not have a significant effect on calcification, though there was some evidence of actual improvements in CAC scores among those who combined metformin with lifestyle modifications.

In her introduction remarks, Fitch noted that rates of metabolic problems, notably cardiovascular disease (CVD) and diabetes, are elevated in people living with HIV. CAC—a process in which the interior lining of the arteries develops a layer of hard substance known as plaque—has been found to be a strong predictor of cardiovascular disease, at least in HIV-negative individuals. CAC has also been found to be common among people living with HIV and metabolic syndrome, notably abdominal obesity and insulin resistance (a diabetes precursor).

A long-established treatment for type 2 diabetes, metformin is proved to reduce the incidence of cardiovascular disease associated with diabetes. And though metformin has also been shown to reverse insulin resistance in people living with HIV, the drug's effects on specific cardiovascular risks—such as artery calcification—have not been explored in detail.

Also of importance is lifestyle modification. Whether or not this, too, improves CAC scores in people living with HIV hasn't been tested in a prospective clinical trial until now.

The trial conducted by Fitch and her colleagues enrolled 50 people living with HIV, all of whom were receiving antiretroviral therapy and had been diagnosed with metabolic syndrome. They were randomized to four groups: One group received standard daily doses of metformin and lifestyle modification classes; another received metformin only; a third received a placebo and

lifestyle modification; and the fourth, placebo only.
Eighty-four percent of the volunteers completed six months of the study; 72 percent completed 12 months of the study.

Compliance was high. Fitch reported that 88 percent adhered to daily metformin dosing, determined by pill counting, and that 84 percent showed up regularly for their lifestyle modification trainings.

After 12 months, participants taking metformin showed little change in CAC, while those receiving neither intervention had an average calcium increase of 56 percent. There was also a slight decrease in CAC among those who received metformin plus lifestyle modification, though this reduction did not appear to be statistically significant.

As for lifestyle modification alone, there did appear to be a trend in favor of less pronounced CAC increases among those who received exercise and nutritional guidance but not metformin, compared with those who didn't receive any intervention, but the observed difference was not statistically significant. However, lifestyle modification did improve physical fitness, dietary choices and several cardiovascular-associated metabolic measures.

Not surprisingly, metformin also improved insulin resistance in the study.
Side effects of metformin, notably gastrointestinal side effects, occurred in six patients. There were, however, no reports of lactic acidosis—a serious side effect that can be caused by metformin. Among those who received lifestyle modification, muscle strains in two volunteers were the only problems reported.

Fitch put the encouraging metformin findings into clinical context. Based on the data reported, she looked at a hypothetical case involving a 47-year-old non-smoking male with a total cholesterol level of 180 milligrams per deciliter (mg/dL), a "good" HDL cholesterol level of 35 and a systolic blood pressure reading of 120. Daily metformin, she said, reduced his 10-year risk of a serious cardiovascular event by 13 percent—from 25 percent in the absence of metformin to 12 percent with daily metformin therapy.

She concluded that further studies are "clearly needed" to understand the mechanisms of metformin in the prevention of CAC progression. "Larger, longer-term studies using metformin in HIV-infected patients with metabolic syndrome and insulin resistance will be useful to determine whether this strategy will prevent CVD events," she said, referring to life-threatening heart attacks and strokes.

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