

Diabetes drug halts atherosclerosis progression in HIV-infected patients

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Treatment with the common diabetes drug metformin appears to prevent progression of coronary atherosclerosis in patients infected with HIV. In a presentation today at the 19th Conference on Retroviruses and Opportunistic Infections, Massachusetts General Hospital (MGH) researchers reported that study participants receiving daily doses of metformin had essentially no progression of coronary artery calcification during the year-long study period, while participants 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, although it did improve several cardiovascular risk factors.

"HIV-infected patients are known to have higher rates of cardiovascular disease and elevations in traditional risk factors – such as insulin resistance, abdominal obesity, high triglyceride levels and hypertension," says Steven Grinspoon, MD, director of the Program in Nutritional Metabolism in the MGH Neuroendocrine Unit, the study's principal investigator. "This is the first demonstration of a therapy that is effective in preventing progression of coronary [calcium](#) in patients infected with [HIV](#)."

Several large epidemiologic studies have found that HIV-infected individuals have approximately twice the rate of cardiovascular disease as non-infected individuals in the same demographic groups. Between 20 and 40 percent of HIV-infected patients meet the diagnostic definition for metabolic syndrome – a cluster of symptoms including abdominal

obesity, abnormal HDL cholesterol and triglyceride levels, insulin resistance and abnormal glucose levels, and elevated blood pressure – which is known to increase the risk of heart attack, stroke and type 2 diabetes. Factors behind these symptoms probably include side effects of antiviral medications and the effects of HIV itself on fat distribution, cholesterol levels and inflammatory factors.

A long-established treatment for type 2 diabetes, metformin is proven to reduce the incidence of cardiovascular disease associated with diabetes and is also used to treat insulin resistance caused by polycystic ovary syndrome. In 2000, Grinspoon led a pilot study finding that metformin reduced insulin levels in HIV patients with insulin resistance, abnormal fat distribution, and elevated cholesterol and triglyceride levels. The current study enrolled 50 participants – receiving antiviral therapy for HIV infection and diagnosed with metabolic syndrome – who were randomized into 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.

At the end of the 12-month study period, participants taking metformin showed little change in [coronary artery calcification](#) – a standard measure to assess atherosclerosis – while those receiving neither intervention had an average calcium increase of 56 percent. Metformin treatment also reduced a standard measure of insulin resistance. Participation in the lifestyle modification sessions improved participants' physical fitness, dietary choices, and several cardiovascular-associated metabolic measures, but did not have a significant impact on coronary artery calcification.

"A recent report from a long-term study of cardiovascular risk factors in a non-HIV-infected population found that doubling of coronary artery calcium – a 100 percent increase – increased cardiac events by 26

percent," explains Grinspoon, who is a professor of Medicine at Harvard Medical School. "The more than 50 percent increase in coronary calcium in our participants who did not receive metformin supports the urgent need to develop strategies to slow the progression of atherosclerosis in HIV-infected patients with metabolic abnormalities. This study was small and needs to be confirmed in larger studies, but our results suggest that physicians caring for HIV patients might want to consider prescribing [metformin](#) for those with significant insulin resistance and multiple metabolic abnormalities."

Provided by Massachusetts General Hospital

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