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Novel lipid lowering medication improves blood sugar control in type 2 diabetes

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High triglycerides—a type of fat, or lipid, in the blood—increase the risk of heart disease and perhaps type 2 diabetes. For the first time, it has been shown that profoundly lowering triglycerides in diabetics improves their insulin sensitivity over time, which helps them maintain healthy glucose - blood sugar—levels. Volanesorsen, an experimental lipid-lowering medication, improved insulin sensitivity and glucose control by significantly decreasing patients' overall hemoglobin A1c—the standard clinical measurement of blood glucose levels for diabetics—in a new study reported by researchers from the Perelman School of Medicine at the University of Pennsylvania. The results are published online this month in *Diabetes Care*.

Researchers enrolled 15 adult patients with type 2 diabetes and hypertriglyceridemia who had been taking metformin - an oral medication that helps control blood sugar levels - for their diabetes. Patients were randomly assigned to two groups: one to receive volanesorsen and the other a placebo. After taking the medication for 12 weeks, researchers found that patients on volanesorsen experienced a 69 percent reduction in triglycerides, and a 57 percent improvement in whole-body insulin sensitivity. Several tests of glucose control, including hemoglobin A1c, were also significantly improved. Researchers concluded that the drop in triglycerides was strongly related to improved insulin sensitivity and improved hemoglobin A1c.

"These results prove volanesorsen to be an effective treatment method for improving insulin sensitivity, but what's most interesting, and

perhaps most encouraging, is that this drug also significantly improved patients' hemoglobin A1c levels," said the study's lead co-author, Richard Dunbar, MD, an assistant professor of Cardiovascular Medicine at Penn. "In most cases, it takes many months of therapy to improve the hemoglobin A1c, so to move the needle so significantly in a fairly short time is very promising. Scientifically, these results provide important proof that profoundly lowering triglycerides improves insulin sensitivity. And clinically, the results go a step further and show that doing so improves the underlying metabolic problems enough to actually improve diabetes."

To quantify the effects of the drug, researchers used a very sophisticated test of insulin sensitivity, the hyperinsulinemic-euglycemic clamp or "the clamp," which is largely regarded as the gold standard in insulin sensitivity measurement. This technique infuses insulin at fixed rates, and infuses glucose at a varying rate to keep blood glucose constant, in order to determine how well a patient responds to insulin.

For many years, researchers had suspected that high triglycerides worsened diabetes, but there had not been powerful tool to prove this concept.

"While we were able to determine the effectiveness of this medication in a very specific group of diabetic patients, it will be important to evaluate this drug in a broader diabetic population," Dunbar said. "The next phase will be to determine clinical success in patients with type 2 diabetes on the whole range of diabetic medications or perhaps with less severe lipid problems. It will also be important to conduct longer studies, as glucose control may improve even further with longer exposures to the drug."

Several other classes of medications that profoundly lower triglycerides are also in development. If improved insulin sensitivity and improved glucose control are truly the result of lowering triglycerides, researchers

suggest these other novel drugs should show the same effect.

Dunbar added, "after a long dry spell, there is a lot of activity right now for triglyceride-lowering therapies. Penn Medicine has been conducting several clinical trials evaluating this and other novel triglyceride-lowering drugs. Not only do we have a variety of very potent options emerging, we may be able to help improve glucose at the same time. Both of these developments would be great news for our patients with high triglycerides, including diabetics."

Provided by University of Pennsylvania School of Medicine

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