

# Combination therapy for type 1 diabetes improves blood glucose control

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A combination of three medications—dapagliflozin, liraglutide and insulin—helped people with Type 1 diabetes improve blood sugar control and lose weight, according to a new study published in the *Endocrine Society's Journal of Clinical Endocrinology & Metabolism*.

Type 1 diabetes is an autoimmune disease in which the immune system destroys the insulin-producing cells of the pancreas. As a result, blood sugar builds in the bloodstream and cells cannot get the energy they need to function. Long-term increases in blood sugar levels lead to complications, which include blindness, kidney failure, nerve damage, heart attack and stroke.

More than 29 million Americans have diabetes, but only a fraction of them have Type 1 diabetes. Out of every 1,000 American adults, between one and five adults has Type 1 diabetes, according to the Endocrine Society's Endocrine Facts and Figures Report. People who have Type 1 diabetes can experience serious health problems such as heart attacks and strokes, kidney problems and vision problems.

"A majority of patients who have Type 1 diabetes do not have their [blood glucose](#) levels sufficiently controlled and monitored, and then they are left vulnerable to more complications of the disease," said the study's senior author, Paresh Dandona, MD, PhD, SUNY Distinguished Professor and Chief of endocrinology, diabetes and metabolism in the Department of Medicine at the Jacobs School of Medicine and Biomedical Sciences at the University at Buffalo in Buffalo, NY. "Our research found a [triple therapy](#) (insulin, liraglutide and dapagliflozin) approach led to impressive improvements in blood glucose control as well as weight loss. This strategy advances our previous work showing improvements in blood glucose management with the use of liraglutide in combination with insulin".

Thirty people who had Type 1 diabetes participated in the randomized, placebo-controlled clinical trial. The phase IV study's [participants](#) were between the ages of 18 and 75, and they were already taking liraglutide and insulin to manage their [diabetes](#). Twenty participants were randomly assigned to receive 10 milligrams of dapagliflozin daily for 12 weeks, and the other 10 received a placebo during that period.

During the study, the participants used continuous glucose monitors (CGMs) to track their blood glucose levels. The researchers downloaded weekly reports from the CGMs to monitor the participants' ability to manage their average blood glucose levels from the past three months, a measurement called HbA1c. The researchers also tracked the participants' weight during the study.

HbA1c declined by 0.66% among participants who received the triple therapy, while there was no significant change in the placebo group. Participants who received the triple therapy lost 1.9 kilograms, on average, and 14 of the 17 people on the triple therapy lost weight. In comparison, the placebo group's body weight remained unchanged.

Twenty-six participants completed the study. Two of the participants receiving the triple therapy developed diabetic ketoacidosis, a dangerous complication that occurs when acids and substances called ketones build up in the blood due to lack of insulin. This occurred within two days of researchers increasing the daily dapagliflozin dose to 10 milligrams from 5 milligrams. Both people were withdrawn from the study.

"Our data also show for the first time that all patients on dapagliflozin experience an increase in ketones," Dandona said. "This may predispose people to developing diabetic ketoacidosis, particularly among those who have a marked reduction in insulin from taking liraglutide together with dapagliflozin and who have consumed too few

carbohydrates. On the basis of the data, the dose reduction of insulin should be minimized and the higher dose of dapagliflozin should not be used in such patients. Our study sheds light on potential strategies for preventing diabetic ketoacidosis, but more research is still needed in this area."

**More information:** The study, "Dapagliflozin as Additional Treatment to Liraglutide and Insulin in Patients with Type 1 Diabetes," will be published online at [press.endocrine.org/doi/10.1210/jc.2016-1451](https://press.endocrine.org/doi/10.1210/jc.2016-1451) , ahead of print.

Provided by The Endocrine Society

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