

Common diabetes drug may trigger rare complications for COVID-19 patients

28 December 2020

DIABETES



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Diabetes is a known risk factor for morbidity and mortality related to COVID-19. In diabetes patients, rare but severe complications, like the potentially lethal condition diabetic ketoacidosis (DKA), can arise when illness or certain conditions prevent cells from receiving enough glucose to fuel their functioning. An uptick in a particular type of DKA called euDKA at Brigham and Women's Hospital during the COVID-19 pandemic has led researchers to hypothesize that diabetes patients on glucose-lowering drugs may be at increased risk for euDKA when they contract COVID-19. The observational case series was published in *The American Association of Clinical Endocrinologists Clinical Case Reports*.

EuDKA is a subset of the diabetes complication known as DKA, which occurs when the body's cells fail to absorb enough glucose and compensate by metabolizing fats instead, creating a build-up of acids called ketones. EuDKA differs from DKA in that it is characterized by lower blood sugar levels, making it more difficult to diagnose. The U.S. Food and Drug Administration has warned that the risk of DKA and euDKA may be increased for individuals who use a popular class of diabetes

drugs called sodium-glucose cotransporter 2 inhibitors (SGLT2i), which function by releasing excess glucose in the urine. Underlying nearly all euDKA cases is a state of starvation that can be triggered by illnesses that cause vomiting, diarrhea, and loss of appetite and can be compounded by the diuretic effect of SGLT2i drugs.

Brigham researchers studied five unusual euDKA cases brought to the diabetes inpatient services within the span of two months, three of which occurred in one week, at the height of the pandemic in Boston in the spring of 2020. The five cases represented a markedly heightened incidence of euDKA compared to that of the previous two years, when inpatient services saw fewer than 10 euDKA cases. All five of the recent euDKA cases were observed in COVID-19 patients who were taking SGLT2i; three patients were discharged to rehabilitation facilities, one was discharged home, and one, a 52-year-old male with [acute respiratory distress syndrome](#), died.

"We have the background knowledge of recognizing that SGLT2 inhibitors can cause DKA and euDKA," said corresponding author Naomi Fisher of the Division of Endocrinology, Diabetes, and Hypertension. "Our report reinforces that if patients are ill or have loss of appetite or are fasting, they should pause their medication and not resume until they are well and eating properly."

The authors of the study also suspect that COVID-19 may particularly exacerbate euDKA risks. When the virus infects a patient, it binds to cells on the pancreas that produce insulin and may exert a toxic effect on them. Studies of the earlier SARS-CoV-1 virus found that many infected patients had increased blood sugar. "It's been posited through other models that the virus may be preferentially destroying insulin-producing cells," Fisher said.

Moreover, the maladaptive inflammatory response

associated with COVID-19, which produces high levels of immune-response-related proteins called cytokines, may increase DKA risks. "These high levels of cytokines are also seen in DKA, so these inflammatory pathways may be interacting," Fisher said. "It's speculative, but there may be some synergy between them."

Though these findings are observational, rather than the results of a randomized controlled trial, similar reports of heightened euDKA incidence have emerged from other institutions. The authors encourage patients and physicians to halt SGLT2i-use in the event of illness, which is already standard practice for the most common [diabetes](#) drug, metformin.

"Patients should continue to monitor their blood sugar, and if the illness is prolonged or if their blood sugar is very high, they can speak to their doctor about other forms of therapy," Fisher said. "But often it's a very short course off of the drug. We're hopeful that with widespread patient and physician education, we will not see another cluster of euDKA cases amid the next surge in COVID-19 infections."

More information: Vitale, RJ, Valtis, YK, et al. "Euglycemic Diabetic Ketoacidosis with Covid-19 Infection in Patients with Type 2 Diabetes Taking SGLT2 Inhibitors," The American Association of Clinical Endocrinologists Clinical Case Reports. [DOI: 10.4158/ACCR-2020-0551](https://doi.org/10.4158/ACCR-2020-0551)

Provided by Brigham and Women's Hospital
APA citation: Common diabetes drug may trigger rare complications for COVID-19 patients (2020, December 28) retrieved 18 January 2021 from <https://medicalxpress.com/news/2020-12-common-diabetes-drug-trigger-rare.html>

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