

DSEN ABSTRACT

SGLT2 Inhibitors and the Risk of Diabetic Ketoacidosis

A study conducted by the Canadian Network for Observational Drug Effect Studies (CNODES)

Summary

- SGLT2 inhibitor use was associated with an increased risk of DKA compared to DPP-4 inhibitors among patients with type 2 diabetes.

Key messages

- These findings provide evidence of an increased risk of DKA with SGLT2 inhibitors in a real-world setting.
- Physicians should be aware of DKA as a potential adverse effect when prescribing SGLT2 inhibitors.

Project Lead & Team

- Pierre Ernst, MD, MSc, FRCP(c)
- Team members [available here](#)

Link to publication

- Douros et al. Ann Intern Med. 2020. [doi: 10.7326/M20-0289](#).

What is the issue?

- Sodium-glucose cotransporter 2 (SGLT2) inhibitors are newer classes of antidiabetic drugs used as second- or third-line treatments in the management of type 2 diabetes.
- However, several safety concerns related with the use of SGLT2 inhibitors have been raised including a potentially increased risk of diabetic ketoacidosis (DKA).

What was the aim of the study?

- This study, conducted by the Canadian Network for Observational Drug Effect Studies (CNODES), evaluated the risk of DKA associated with the use of SGLT2 inhibitors compared to the use of dipeptidyl peptidase-4 (DPP-4) inhibitors, another class of antidiabetic drugs used as second- or –third line treatment.

How was the study conducted?

- CNODES investigators conducted eight population-based cohort studies with electronic health records of over 400,000 patients with type 2 diabetes from seven Canadian provinces and the United Kingdom.
- Cohorts included patients aged 18 years and older who received a prescription for an SGLT2 inhibitor or a DPP-4 inhibitor between 2013 and 2018.
- The risk of DKA was compared in users of SGLT2 inhibitors and a matched group of DPP-4 inhibitors. Results were combined across studies using a statistical approach called meta-analysis.

What did the study find?

- The use of SGLT2 inhibitors was associated with an almost three-fold relative increase in the risk of DKA compared with DPP-4 inhibitors. This increased risk was observed for each of the three SGLT2 inhibitor molecules (canagliflozin, dapagliflozin, empagliflozin) available during the study period.
- Given the rapidly increasing use of SGLT2 inhibitors in patients with type 2 diabetes, physicians should be aware of DKA as a potential adverse effect.
- CNODES has the ability to analyze a large amount of anonymous patient data to reliably assess questions of drug safety and effectiveness. The results of this study are an important addition to previous research.

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For more information, please contact info@cnodes.ca.