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Correspondence

SGLT2 inhibitors: An answer to diabetes or a question to its complications?

Dear Editor,

SGLT2 inhibitors (SGL2i) such as canagliflozin, dapagliflozin, and empagliflozin are relatively newer additions to the class of oral drugs used in the treatment regimen of Type 2 Diabetes Mellitus. Their primary mode of action involves blocking glucose reabsorption in the proximal renal tubules by targeting the sodium-glucose transporter, inducing glycosuria. They are frequently reported to cause hypotensive states but they have a very minimal risk of drug-induced hypoglycemia which in addition to its ability to cause modest weight loss explains the increased preference for this class in today's era. In addition to this, few SGLT2i have also displayed advantageous effects for the heart and kidneys. The current literature reports this class to have a favorable tolerability profile and is also authorized by the US Food and Drug Administration (FDA). However, SGLT2i also have a few well-known adverse effects that should be taken into consideration to scale their risk-benefit ratio before prescribing them to the patients. Vaginal fungal infections, urinary tract infections, and polyuria are the most frequently reported side effects of this class [1]. One rare but potentially fatal outcome of this drug that should not be overlooked is Diabetic Ketoacidosis (DKA). The pathophysiology of SGLT-2-associated DKA has received little attention.

A study conducted by Hamblin et al. concluded that SGLT2i users were more prone to develop DKA as an inpatient in comparison to non-SGLT2i users [2]. Furthermore, a meta-analysis conducted by Liu et al. also reported that SGLT2 inhibitors increase the risk of DKA when compared to the control population i.e., patients who are not consuming SGLT2i [3]. SGLT2 inhibition results in excessive lipolysis and the subsequent rise of free fatty acid levels contributes to the pathogenesis of ketogenesis. This mechanism becomes more accountable for DKA in an insulin-deficient state. Moreover, inhibiting SGLT2 channels in the renal tubules results in increased Na + concentration in the tubular fluid which is responsible for the electrostatic attraction for anions such as ketone bodies. Ketonuria disturbs the body's physiology and results in excessive ketone production to compensate for the lost ketone; thus, resulting in diabetic ketoacidosis [4].

SGLT2 inhibition works to lower insulin secretion and increases the secretion of glucagon; which in turn promotes an ideal environment for ketogenesis. This strong association of SGLT2i with DKA warranted the need for the FDA to issue a warning about the risk of this vicious outcome [5].

In light of the aforementioned statistics, physicians must take important precautions for their patients before prescribing this drug. They should rule out the possibility of DKA in every patient to avoid potentially fatal complications. Patients should be informed about DKA symptoms such as fruity-smelling breath, muscle aches, headache, lethargy, and deep breaths and glucose levels should be monitored regularly in high-risk patients. Strong adherence to these precautions can increase the safety profile of SGLT2i and they can still be safely prescribed for Type II Diabetes.

Ethics statement

The present study includes printed and published information; therefore, the formal ethical clearance was not applicable for this study.

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Declaration of competing interest

The authors declare that there is no conflict of interests.

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Not applicable.

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