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Letter to the Editor

Unveiling the occurrence of diabetic ketoacidosis with SGLT2 Inhibitors: need for vigilance and careful monitoring

Sir,

With great interest, we have read the case report titled "Euglycemic diabetic ketoacidosis (DKA)-a rare side effect of sodium-glucose co-transporter-2 inhibitor in a patient of type 2 diabetes mellitus with left ventricular dysfunction: a case report" published in the international journal of advances in medicine.[1]

The report emphasises the potential risk of developing euglycemic DKA in patients with type 2 diabetes on sodium-glucose cotransporter 2 inhibitor (SGLT2i) therapy. SGLT-2 inhibitors lower glucose independently of insulin. Hypoglycemia is rare when used as monotherapy or in conjunction with non-insulin secretagogue oral agents.[2] They are also known to have cardio-renal benefits.[3] The downside of using them is the occurrence of DKA due to the decrease in circulating insulin levels that increase the rate of lipolysis in adipose tissue and ketogenesis in the liver, which would increase circulating ketone body levels and precipitate DKA.[4] A slightly conflicting possible mechanism was proposed by Ogawa et al. that a decline in circulating insulin levels results in a lowering of the antilipolytic activity of insulin and consequent stimulation of the production of free fatty acids, which are converted to ketone bodies by β-oxidation in the liver.[5]

The incidence of DKA in patients on SGLT2i therapy is 0.1-0.5% per patient-year.[6] The complications of DKA include hypokalemia, cerebral edema, rhabdomyolysis (though more common with HHS) leading to acute kidney injury, ARDS, TTP, and acute myocarditis and may also result in death.[7] Therefore, it is essential to look out for the signs and symptoms of DKA in patients on SGLT2i therapy and predisposition to DKA, such as organic pancreatic insufficiency, carbohydrate restriction, and withdrawal of insulin secretagogues at the beginning of the treatment with the SGLT2 inhibitors shown in the Figure 1.[5]

Several case reports and articles have reported similar cases of DKA in patients on SGLT2i therapy, indicating the potential risks associated with this treatment.[4-5,8] A recent systematic review and meta-analysis of randomised controlled trials reported a higher incidence of DKA in patients with type 2 diabetes on SGLT2i therapy compared to those on placebo (odds ratio 3.39; 95% CI 1.51-7.62; p=0.003).[9]

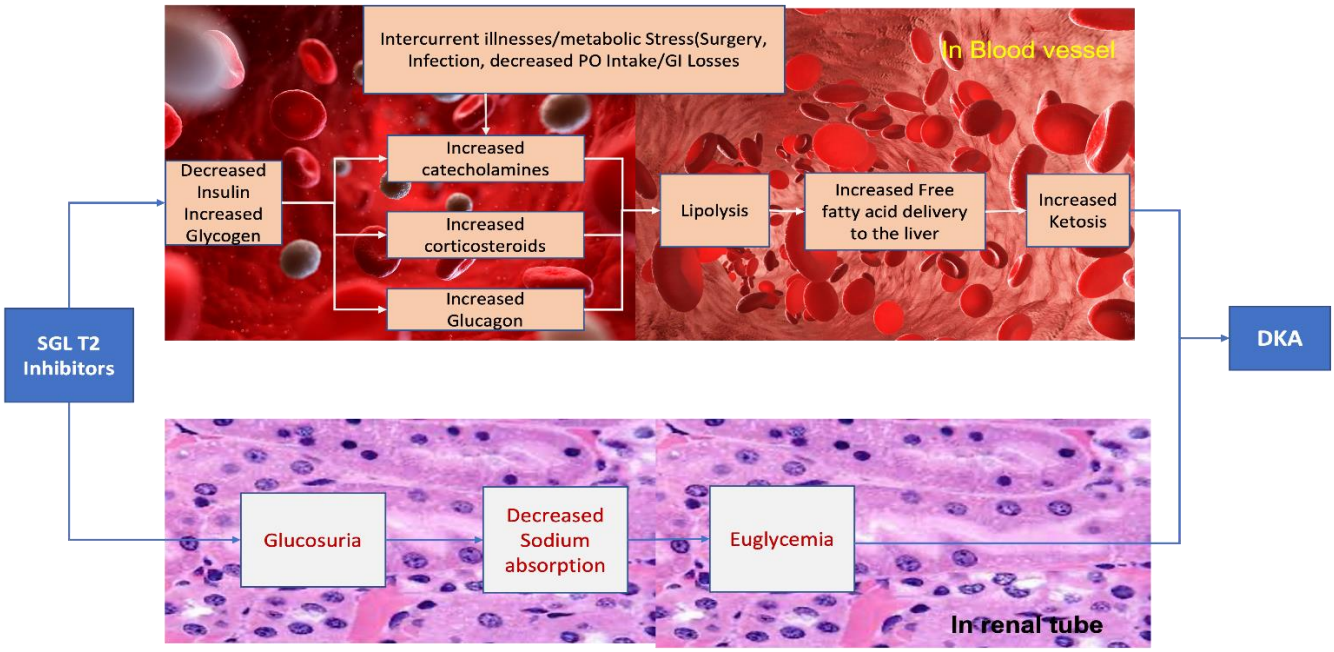

Figure 1: Mechanism behind development of DKA with SGLT2 (sodium glucose transporter 2) inhibitors.

To minimise the risk of DKA, regular monitoring of blood glucose and ketone levels is recommended in patients on SGLT2i therapy.[7] Additionally, it is essential to educate patients on the potential risks associated with SGLT2i therapy and to look out for Signs and symptoms such as vomiting, abdominal pain, deep gasping breathing, increased urination, weakness, confusion, and occasionally loss of consciousness. A person's breath may develop a specific "fruity" smell.[10] Patients should contact their healthcare professional if they have any of these symptoms.

According to the pharmacovigilance risk assessment committee (PRAC), if DKA is suspected or confirmed, treatment should be stopped immediately and should not be re-started unless another cause for the ketoacidosis is identified and resolved. Healthcare professionals should exercise caution in patients with risk factors for ketoacidosis and inform patients of the risk factors. These include low reserves of insulin-secreting cells, conditions that restrict food intake or can lead to severe dehydration, a sudden reduction in insulin, or an increased requirement for insulin due to illness, surgery, or alcohol abuse.

In addition, the PRAC recommended temporarily stopping SGLT2-inhibitor treatment in patients in the hospital for major surgical procedures or due to serious illness.

In conclusion, while using SGLT2i therapy in the management of type 2 diabetes, it is crucial to assess the risks and benefits of the therapy for that particular individual and personalise the treatment according to the individual's preferences, predisposing factors, and the benefits the treatment provides. Regular monitoring of blood glucose and ketone levels and prompt recognition and management of DKA are essential to ensure safe and effective treatment. In the initial stages, frequent follow-ups are required, which can be spaced out gradually as both the patient and doctor are more confident with the compliance and results of the treatment plan. Clinicians must constantly update themselves regarding the potential risks and benefits and alter their treatment plans accordingly.

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