CANAGLIFLOZIN INDUCED EUGLYCEMIC KETOACIDOSIS IN TYPE II DIABETES MELLITUS

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Introduction

Diabetic ketoacidosis (DKA) generally occurs in patients with diabetes mellitus (DM) and is a common cause of metabolic acidosis requiring ICU admission. Although classically associated with type I DM, multiple cases of DKA have been reported in type II DM and can occur without any precipitating cause. The use of selective sodium glucose cotransporter-2 (SGLT2) inhibitors, such as canagliflozin, has recently been associated with DKA without significant hyperglycemia in patients with DM type II. Here we present a case of canagliflozin precipitated euglycemic DKA (euDKA) in a patient with type II DM.

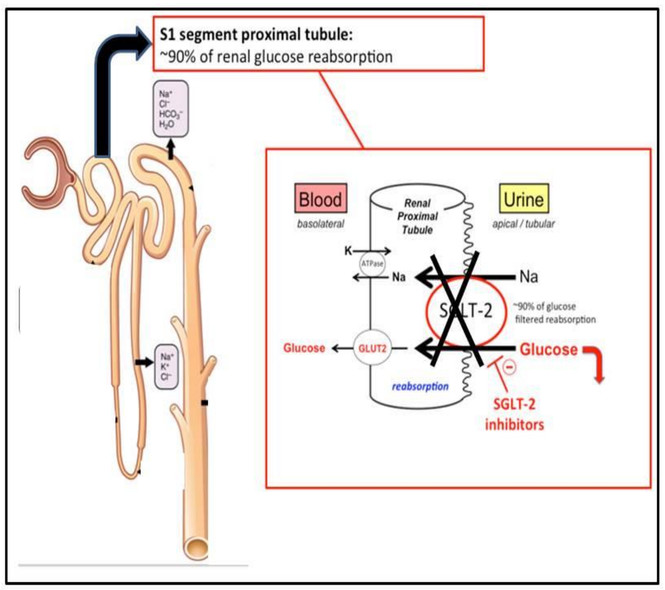

Figure 1: Effect of SGLT-2 inhibitors at the nephron

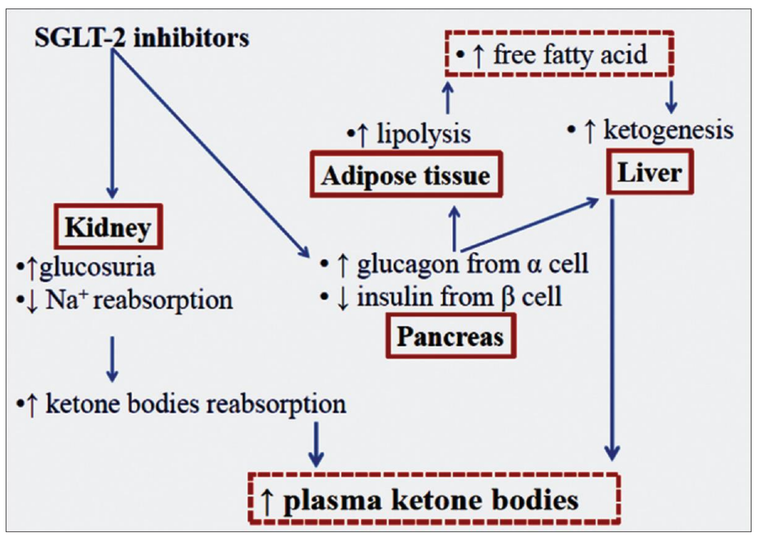

Figure 2: Mechanism by which SGLT-2 inhibitors lead to euDKA

Clinical Case

A 34-year-old male with history of type II DM, was referred to the hospital by his primary care physician (PCP) for nausea, non-bilious vomiting, and increasing symptoms of polyuria and polydipsia of 1 day prior to admission (PTA). Patient was diagnosed with type II DM a year ago and was prescribed metformin. He took metformin for six months and decided to discontinue the medication due to adverse reaction. Since then, he was non-compliant with his medication and diet. Two weeks PTA, the patient experienced worsening polydipsia and polyuria for which he visited his PCP two days PTA. His blood sugar was found to be elevated (419 mg/dL) and was prescribed a combination canagliflozin and metformin. The patient took this medication for two days during which he developed presenting symptoms.

Vitals revealed HR of 122/min, BP of 134/74 mmHg, temperature of 97.8ºF, and pulse oximetry 100%. Physical examination was benign except for dry mucous membranes. Labs showed hemoconcentration without leukocytosis, serum glucose of 159 mg/dL, normal renal function, mild hyperkalemia (5.6 mEq/L), and high anion gap metabolic acidosis. Urine analysis revealed glucosuria and ketonuria. Serum β-hydroxybutyrate was 13.9 mmol/L and venous blood pH was 7.06. Urine toxicology was negative. Patient was admitted to the medical ICU for management of ketoacidosis and was treated with IV fluids and IV insulin. His condition eventually improved over the next two days. He was discharged home on metformin and glipizide with education of his underlying condition.

Discussion

SGLT2 inhibitors decrease glucose reabsorption at the proximal tubule, thereby inducing glycosuria. This leads to a fall in insulin levels which increases lipolysis and ketogenesis. With increasing number of euDKA cases being reported, the FDA has issued a warning to patients and clinicians to look for symptoms of ketoacidosis with SGLT2 inhibitor use.

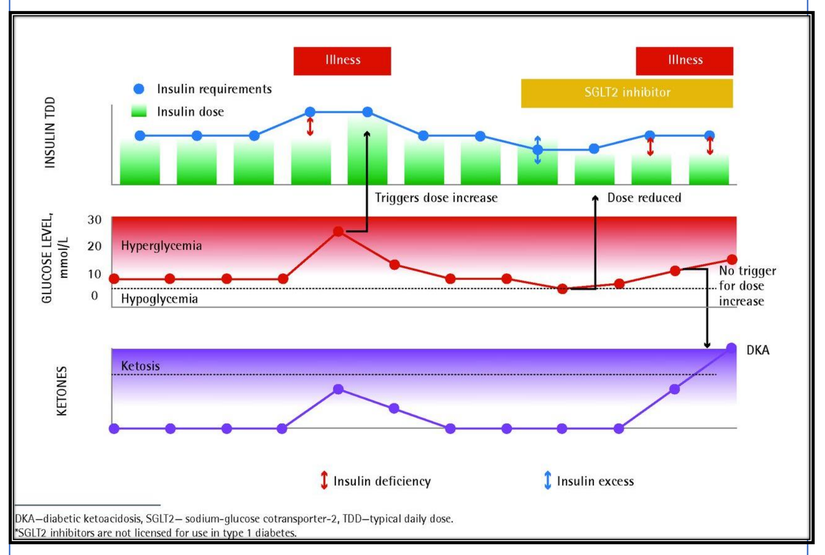

Figure 3: SGLT2 inhibitors provide an insulin-independent route for glucose disposal. Intercurrent illness in the setting of an SGLT2 inhibitor will lead to an insulin deficit, leading to ketonemia without hyperglycemia, because of ongoing renal glucose excretion, thus resulting in a delayed diagnosis of DKA.

Conclusion

Recognizing euDKA in patients taking SGLT2 inhibitors is crucial for timely and appropriate management of this condition.

Patient should be educated about symptoms of DKA even when blood sugars are within normal limits.

References

1. Singh AK. Sodium-glucose co-transporter-2 inhibitors and euglycemic ketoacidosis: Wisdom of hindsight. Indian J Endocr Metab 2015;19:722-30

2. Maureen C Euglycemic diabetic ketoacidosis with canagliflozin: Canadian Family Physician Sep 2016, 62 (9) 725-728;