

Dapagliflozin Causing Euglycemic Diabetic Ketoacidosis

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ABSTRACT

Background: Diabetic ketoacidosis (DKA) is one of the serious acute complications of diabetes. Euglycemic diabetic ketoacidosis (EDKA) is one of the side effects associated with sodium-glucose cotransporter 2 (SGLT2) inhibitors. It is very difficult to diagnose due to the absence of hyperglycemia, thereby leading to delayed diagnosis and treatment.

Case: The author did a case of a diabetic patient who underwent coronary artery bypass grafting (CABG) and developed EDKA during the intraoperative period, most likely due to the use of dapagliflozin.

Keywords: Dapagliflozin, Euglycemic diabetic ketoacidosis, Sodium-glucose cotransporter 2 inhibitors.

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INTRODUCTION

Euglycemic diabetic ketoacidosis is associated with euglycemia, metabolic acidosis, and ketonemia. Its incidence has increased with the treatment of diabetes by SGLT2 inhibitors and it is difficult to diagnose, which results in delayed diagnosis and treatment.

CASE DESCRIPTION

A 61-year-old male patient with a known case of ischemic heart disease and type 2 diabetes mellitus (DM) was admitted to the hospital for a CABG.

He was a known diabetic for >20 years on tab. metformin 500 mg BD and tab. dapagliflozin 10 mg OD (recently started 1 month ago.)

Patient labs were within normal limits apart from serum creatinine, potassium, and hemoglobin A1C, which were 1.8 mg/dL, 5.4 mmol/L, and 6.5%, respectively. His ejection fraction was 50–55% with coronary angiogram suggestive of triple vessel disease [left anterior descending artery (LAD) 80%, left circumflex artery, dominant vessel 90%, and right coronary artery 80%].

A nephrology opinion was taken preoperatively for high potassium and creatinine levels. Patient's oral hypoglycemic agents were stopped 24 hours prior to surgery.

The patient underwent CABG with five arterial grafts [left internal mammary artery (LIMA) --right internal mammary artery (RIMA) Y, LIMA to LAD & first diagonal artery, RIMA to ramus, obtuse marginal and posterior descending artery.

The patient's intraoperative serial arterial blood gas (ABG) showed a picture of metabolic acidosis [pH <7.3, bicarbonate (HCO₃) <17, anion gap 18.5]. Serum lactate was normal. The patient's intraoperative blood sugars were in the range of 110–181 mg/dL. Urine tested positive for ketones, and thus

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EDKA diagnosis was made, and the patient was shifted to the intensive care unit on a ventilator with minimal inotropic support, 2 mL of noradrenaline (4 mg/50). He was started on intravenous fluids and insulin therapy as per the sliding scale.

Over a period of time, ketoacidosis got corrected, and the patient was extubated uneventfully. The patient was advised a permanent cessation of dapagliflozin at the time of discharge.

DISCUSSION

Diabetic ketoacidosis is a very serious complication of diabetes characterized by metabolic acidosis, hyperglycemia, and high levels of ketones in the blood and urine. High blood glucose is one of the diagnostic features of DKA.¹

Few patients have normal serum glucose levels, the condition called EDKA.

Munro et al. first described EDKA where few patients had normal sugar and low plasma HCO₃ level.²

Euglycemic diabetic ketoacidosis is characterized by high anion gap metabolic acidosis and increased ketones in blood or urine with normal blood glucose levels.

The pathogenesis of EDKA is due to the reduced production of glucose by the liver or its increased urinary excretion caused by an excess of counter-regulatory hormones.

The common causes of EDKA are inadequate food intake, fasting, excessive starvation, pregnancy, pancreatitis, drug intoxication, vomiting, diarrhea, and drugs like insulin and SGLT2 inhibitors.³

Food and Drug Administration has approved the use of SGLT2 inhibitors to treat DM. They reduce blood glucose levels by blocking SGLT2 protein, causing increased excretion of glucose in urine.⁴

The mechanism of EDKA with SGLT2 inhibitors is due to inadequate insulin production with increased glucagon secretion, thereby leading to an increase in fat metabolism, causing ketogenesis.^{3,5}

Since SGLT2 inhibitors' half-life ranges from 11 to 17 hours, these medications should be discontinued for at least 2–3 days before major surgical procedures to prevent EDKA.

Diagnosis of EDKA is very difficult in the perioperative and immediate postoperative periods. The management includes aggressive correction of dehydration with glucose-containing intravenous fluids,⁶ along with insulin until ABG normalizes.⁷ Regular urine and ABG analysis for ketone bodies and anion gap, respectively, are required till the values normalize.

Diagnosis and treatment of EDKA should be made early to minimize morbidity and mortality.

CONCLUSION

- Sodium-glucose cotransporter 2 inhibitors are associated with EDKA, a very serious complication.

- Euglycemic diabetic ketoacidosis diagnosis requires a high degree of clinical suspicion.
- Monitor ABG, blood, or urine ketones and sugar levels in critically ill diabetic patients.
- Monitor blood and urine ketone levels in patients on SGLT2 inhibitors.

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