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Case Report
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Preoperative Use of Sodium Glucose Transporter 2 Inhibitors and Life-Threatening Euglycemic Diabetic Ketoacidosis in Immediate Cardiac Postoperative Care

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Abstract

One of the major focuses of immediate postoperative cardiac care is the acid-base status of the patient, as it can be a reflection of inadequate perfusion secondary to poor cardiac function. Significant effort is being made to maintain ideal blood pH as it allows for optimization of cardiac function in the early cardiac postoperative period. In this case report we describe association of sodium glucose transporter 2 inhibitors used in the treatment of diabetes with euglycemic diabetic ketoacidosis postoperatively despite being held 72 h prior to surgery. As is demonstrated in our case, early recognition and treatment are essential in prevention and treatment of acidosis in this vulnerable group of patients.

Keywords: Euglycemic ketoacidosis; Cardiac surgery; Sodium glucose transporter 2 inhibitor; SGLT2i; Diabetic ketoacidosis

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Introduction

Diabetic Ketoacidosis (DKA) is a serious and well-studied complication of Diabetes Mellitus (DM). Euglycemic DKA (eu-DKA) is characterized by milder degrees of hyperglycemia with blood glucose values often under 200 mg/dL. After introduction of Sodium Glucose Transporter 2 inhibitors (SGLT2i) for treatment of DM, several reports were published describing eu-DKA following treatment with SLGT2i [1,2]. Even though eu-DKA can be easily missed given subtle clinical signs, it can result in potentially life-threatening metabolic acidosis [3]. In the immediate postoperative period, acid-base status is followed rigorously in patients undergoing cardiac surgery as it can often be a sign poor cardiac function. Early recognition and treatment of significant acidosis is essential to support and maintain optimal cardiac function postoperatively. In this report we describe a successful timely diagnosis and treatment of eu-DKA and provide a review of pertinent literature.

Case Presentation

The patient is a 62-year-old male with past medical history of hypertension, diabetes mellitus with hemoglobin A1c of 7.9%, who presented to the hospital with sudden onset of palpitations, chest pain and dizziness while exerting himself. Upon arrival to emergency room, the patient's electrocardiogram revealed wide complex tachycardia. Due to evidence of hemodynamic compromise the patient was cardioverted electrically to normal sinus rhythm. Laboratory analysis revealed hyperglycemia with serum glucose of 307 mg/dL, anion gap of 22 mEq/L, and beta-hydroxybutyrate of 1.3 (upper normal is 0.4 mmol/L) which was suggestive of mild DKA. Patient was treated for DKA with intravenous fluids and insulin. Anion gap quickly normalized with correction of serum glucose and intravenous insulin. On Hospital Day (HD) 2 and 3 patient's anion gap trended down to 15 mEq/L and 12 mEq/L, respectively. Patient's acidosis was attributed to use of SGLT2i (empagliflozin). The patient underwent cardiac ischemic workup and was found to have on HD 3 multi-vessel coronary artery disease. Patient underwent off-pump coronary artery bypass grafting on HD 4. Postoperatively patient within hours developed significant acidosis with pH of 7.28, Base Deficit (BD) of 11 mEq/L, serum glucose of 150 mg/dL, anion gap of 21 mEq/L, and lactate of

0.8 mg/dL. Despite aggressive fluid resuscitation, acidosis worsened with pH decreasing to 7.26, BD of 14.5 mEq/L, serum glucose of 159 mg/dL, anion gap of 25 mEq/L, and lactate of 0.8 mg/dL. Patient's hemodynamics were excellent with cardiac index ranging from 2.6 L/min/m^2 to 3.1 L/min/m^2 without pressors or inotropes. Both normal lactate and excellent hemodynamics suggested a non-cardiac cause of acidosis. Diagnosis of eu-DKA was suspected, and beta-hydroxybutyrate was noted to be 7.1 mg/dL. At this point treatment with intravenous insulin and fluids, along with multiple sodium bicarbonate boluses was instituted with normalization of anion gap and correction of pH to 7.41 and BD to 4.9 mEq/L. Patient recovered well after surgery and was discharged home on postoperative day five.

Discussion

There are relatively few reports correlating use of SLGT2i with eu-DKA in patient undergoing cardiac surgery [4-6]. SGLT2i were introduced in 2013 and within several years both US and European regulatory agencies issued a warning related to use of SGLT2i [1,2]. Multiple triggering factors were connected to DKA, including infections, trauma, reduced insulin use, pregnancy, decreased caloric or fluid intake, heavy alcohol use, chronic liver disease and cocaine abuse. Not surprisingly, cardiac surgery, being a major physiologic stress, was also associated in multiple reports as cause of eu-DKA in patients who were on SGLT2i preoperatively. Many of the precipitating factors that were associated with eu-DKA after SLGT2i are present in patients undergoing cardiac surgery: many days of poor PO intake due to ongoing workup, fluid shifts often associated with hypovolemia, stress of surgery and cardiopulmonary bypass.

Life-threatening processes such as DKA can be especially injurious to cardiac surgery patients in vulnerable perioperative period. Maintenance of normal acid-base status is paramount in the immediate postoperative period, where worsening acidosis may be a marker of inadequate cardiac function resulting in poor perfusion. Optimal cardiac function is strongly dependent on normal milieu and a strong effort is made to maintain normal acid-base status.

It is important for the cardiac community to be aware of the potential for eu-DKA in the setting of previous treatment with SLGT2i. This is especially relevant considering recent approval of this class of drugs by US Food and Drug Administration in treatment of heart failure patients with Type 2 DM. This approval will lead to higher prevalence of SLGT2i use in patients undergoing cardiac surgery.

In this case report, the patient who was treated with empagliflozin (SGLT2i) three days prior to cardiac surgery. In previous reports describing eu-DKA in patients undergoing cardiac surgery previously on SLGT2i were held 1 to 2 days prior to surgery. Although, there are no currently established guidelines on how long SGLT2i should be held before surgery [7], most recent recommendations are to wait at least 3 days to allow for drug elimination. Most recent report by Smyth et al. recommends waiting 5 days prior to elective cardiac surgery, which is in agreement with our observation. Given presence of many triggers of eu-DKA in these patients, it probably reasonable, if possible, to wait longer than 3 days prior to surgery and also avoid other triggers mentioned above.

Authors' Contribution

Author I.G., A.S., and F.R. have given substantial contributions to the conception or the design of the manuscript, authors I.I., I.G., A.L., Y.F. and F.R. to acquisition, analysis, and interpretation of the data. All authors have participated to drafting the manuscript, author I.G. revised it critically. All authors read and approved the final version of the manuscript.

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