Intraoperative Diagnosis of SGLT-2 Inhibitor Associated Euglycemic Diabetic Ketoacidosis, a Case Report

Hanning Xing, BS[1], Christian D. Seger, MD[2], Libing Wang, MD[2], John S. Shin, MD[2]

[1]David Geffen School of Medicine at UCLA, [2]UCLA Department of Anesthesiology & Perioperative Medicine

INTRODUCTION

- Euglycemic diabetic ketoacidosis (EDKA) is a rare subtype of DKA that presents with a normal glucose level (<250 mg/dL) along with the usual metabolic acidosis and ketonemia.
- Sodium glucose co-transporter 2 (SGLT2) inhibitors are known to be associated with EDKA.
- The incidence of perioperative EDKA associated with SGLT2 inhibitors is unknown.
- We present one of the first cases of intraoperative diagnosis of SGLT2 inhibitor-associated EDKA in a patient presenting from home for scheduled surgery.

CASE DESCRIPTION

Pre-operative history:

A 55-year-old male with history of hypertension and poorly controlled T2DM (HgBA1c: 9.4%) presented for a scheduled left lateral craniotomy and infratentorial brain resection. Medications included saxagliptin, metformin, and an SGLT2 inhibitor, empagliflozin. He had also started taking dexamethasone 2 months prior to surgery.

On the day of surgery, he had fasted since midnight. Of note, he took his SGLT2 inhibitor in the morning. Preoperative blood glucose (BG) was 130 mg/dL.

Intraoperative course:

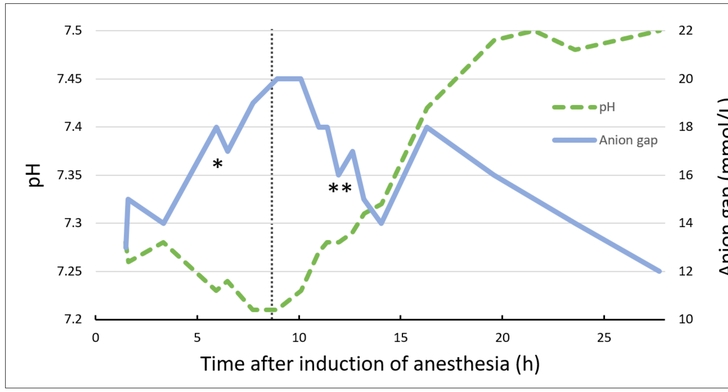
Induction and intubation were uncomplicated. Arterial and peripheral IV lines were placed. A balanced crystalloid maintenance infusion was at 75 mL/h. The patient received 12 mg of dexamethasone and 100 g of mannitol before surgical incision. Pertinent labs are shown in Figure 1 and the Table.

Successive blood samples continued to show a worsening metabolic acidosis with widening anion gap despite fluid administration. Lactate and urea nitrogen were within normal limits. A serum beta-hydroxybutyrate (BHOB) was elevated. Patient was suspected to be in EDKA and management was started appropriately (Table). The anion gap and acidosis started to improve and serum BHOB started to decrease by the end of surgery.

Postoperative course:

Patient care continued in the ICU. Insulin and dextrose infusions were titrated to maintain euglycemia and to close the anion gap, which was consistently closed after postoperative day (POD) 4. The patient was transitioned to enteric feeding, and the insulin and dextrose infusions were both held after POD 6. He was not restarted on an SGLT2 inhibitor. The patient was eventually discharged on oral metformin and subcutaneous long-acting insulin.

Figure 1. Trend of Pertinent Laboratory Values



Vertical dotted line indicates when insulin + glucose therapy was initiated.

(*) indicates when the first beta-hydroxybutyrate (BHOB) of 88.8 mg/dL was obtained.

(**) indicates when the second BHOB of 66.8 mg/dL was obtained.

Table. Pertinent Laboratory Values and Medications During Hospital Course

	Glucose, mg/dL	pH	Anion gap, mmol/L	Total CO_2, mmol/L	BHOB, mg/dL	D10 0.45% NaCl, mL/h	Insulin, u/h	DM, mg
Hour from induction of anesthesia								
-2	130	NA	NA	NA	NA	NA	NA	NA
1	107	7.28	13	20.6	NA	NA	NA	6
6	142	7.24	17	16.7	88.8	NA	NA	6
8	148	7.21	19	14.9	NA	NA	NA	NA
9	162	7.21	20	13.4	NA	150[a]	5	NA
11	140	7.27	18	14.7	NA	150	5	NA
12	148	7.29	17	18.8	66.8	150	10	NA
14	153	7.42	18	19.9	NA	175	12	NA
Post-operative day[b]								
1	121	7.5	12	24.2	NA	175	12	8
2	190	7.42	15	20.9	15.6	200	3	4
3	181	7.47	16	23.3	30.5	125	3	4
4	190	7.49	12	29.2	5.2	125	5	1
5	162	7.46	12	29.2	NA	0	3	0

Abbreviations: BHOB, beta-hydroxybutyrate; DM, dexamethasone.

[a] Dextrose was initially started at 5% but switched to 10% at hour 11.

[b] Values listed in this section are approximately from noon of each postoperative day.

DISCUSSION

- Perioperative risk factors for EDKA in our patient included preoperative starvation, physiological stress from a major surgery, and SGLT2 inhibitor use in the morning of surgery (despite being told not to).
- Intraoperative presentation of EDKA differs significantly than if it were in clinic or non-anesthetized settings, especially given how anesthetics obscure classic symptoms of ketoacidosis.
- A broad differential should be considered for intraoperative anion gap metabolic acidosis (AGMA) (Figure 2).
- Ketonuria may not be useful for diagnosis given fluctuations in perioperative renal function. Serum ketones assisted the diagnosis of EDKA in our patient.
- Treatment of EDKA is like that of classic DKA, but dextrose infusion is critical given the ongoing renal glucose loss with SGLT2 inhibitors.

Figure 2. Intraoperative Testing for Anion Gap Metabolic Acidosis

Arterial Blood Gas (ABG) with Co-oximetry

- Lactic acidosis*
  - Hypoperfusion / shock*
  - Sepsis*
  - Carbon monoxide toxicity*
  - Methemoglobinemia*
  - Iron toxicity
  - Isoniazid toxicity
  - Methanol (or other alcohol) toxicity*

Require Specialized Testing

- Ketoacidosis
  - DKA (including EDKA)*
  - Alcoholic ketoacidosis
  - Starvation ketoacidosis
- Ingestions
  - Acetaminophen toxicity
  - Aspirin toxicity
  - Glycolic acid toxicity

Serum Chemistry

- Uremic acidosis

*characteristically acute in onset

CONCLUSION

- EDKA is a rare adverse effect of SGLT2 inhibitor use.
- The intraoperative period has many potential precipitating factors for EDKA.
- EDKA should be considered on the differential of AGMA, especially with preoperative SGLT2 inhibitor use.
- We recommend holding SGLT2 inhibitors for >24 hours preoperatively to obtain adequate clearance.