Euglycaemic ketoacidosis after abdominal surgery: Implications of SGLT2 inhibitors for anaesthesiologists - A case study

Dear Editor,

Management of surgery in a diabetic patient poses a challenge for the anaesthesiologist. While metformin has been associated with lactic acidosis, the impact of newer antidiabetic medications is yet to be well recognised. We present the case of a 55-year-old lady, diabetic for 15 years on multiple medications and insulin, who presented with euglycaemic diabetic ketoacidosis (eDKA) following surgery for carcinoma rectum.

This lady presented to the hospital with abdominal pain that was diagnosed as moderately differentiated adenocarcinoma of the rectum with liver metastasis. She was scheduled for open low anterior resection with liver metastatectomy. Her medications at this time were oral metformin 1 g twice daily, teneligliptin 5 mg once daily, dapagliflozin 5 mg once daily and inj. insulin mixtard 15 units subcutaneously once daily. As per standard preoperative protocols, her oral hypoglycaemic medications were withheld the day before surgery, and blood sugars were managed with short-acting insulin, while two-thirds of the long-acting insulin was administered before her night meal before surgery. Her blood sugar level on the morning of

surgery was 138 mg/dL, and intraoperatively, her blood sugar level was between 140 and 200 mg/dL, without the need for insulin. Following an uneventful surgery, she was extubated on the table. On postoperative day (POD) 1, her blood gas showed pH 7.43, partial pressure of carbon dioxide (pCO $_2$) 39.6 mmHg, bicarbonate (HCO $_3$) 26 mEq/L, lactate 1.4 mmol/L and blood sugar 126 mg/dL. Later, she was shifted to the ward on POD2 and subsequently allowed orally.

On the fourth POD, she developed tachycardia and tachypnoea with mild hypotension. Her blood gases showed a pH of 7.22, pCO $_2$ 22 mmHg, bicarbonate of 9 mEq/L, anion gap of 22, lactate 1.1 mmol/L and blood sugar 178 mg/dL. Her creatinine was 0.5 mg/dL, and urine ketones was found to be significantly high (3+).

A diagnosis of eDKA induced by dapagliflozin was made. The patient was managed with an infusion of bicarbonate, non-invasive ventilation and insulin for the management of blood sugars. The ketosis settled after withholding dapagliflozin, and she was discharged after a week of hospitalisation and remains well on follow-up.

A rare but potentially life-threatening complication of SGLT2 (sodium-glucose co-transporter) inhibitors, eDKA, is characterised by metabolic acidosis, ketonuria and blood glucose levels within the normal range. [1] SGLT2 inhibitors are widely used in the treatment of diabetes with the advantage of the reduction in cardiovascular mortality, but the risk of developing eDKA is higher among surgical patients. [2,3]

Dapagliflozin, an SGLT 2 inhibitor, inhibits kidney glucose reabsorption and promotes glucose excretion but increases the risk of eDKA.^[4] Dapagliflozin's effect on urinary glucose in our patient may have persisted during surgery. Reduced oral intake can increase gluconeogenesis and insulin deficiency, resulting in lipolysis producing acetyl CoA.^[5] Beta oxidation of acetyl CoA in hepatocyte mitochondria generates acetoacetic acid, which breaks down into beta-hydroxybutyric acid and acetone. Ketoacid accumulation contributes to acidosis with a large anion gap.

The near-normal blood sugars confounded the diagnosis in our patient. The effects of fasting and limited feeding in the postoperative period created the milieu for the manifestation of eDKA. Further delay may have increased the morbidity and could have been fatal if unrecognised.

This case report highlights the need for vigilance in monitoring patients on SGLT2 inhibitors for the development of eDKA in the postoperative period. With increasing use of this group of medications amongst diabetic patients, anaesthesiologists involved in perioperative care should be aware of this complication and discontinue these medications 48 h before surgery. In addition, attention to reinstating oral feeding or the use of intravenous glucose with insulin postoperatively can avoid the detrimental effects of starvation. It may reduce or prevent the occurrence of this feared complication.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient consented to her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

Financial support and sponsorship Nil.

Conflicts of interest

There are no conflicts of interest.

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> Submitted: 22-Mar-2023 Accepted: 08-Apr-2023 Published: 06-Sep-2023

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Access this article online	
Quick response code	
	Website: https://journals.lww.com/ijaweb
	DOI: 10.4103/ija.ija_232_23

How to cite this article: Kartha AP, Irimpan J, Thomas DE, Kumar L. Euglycaemic ketoacidosis after abdominal surgery: Implications of SGLT2 inhibitors for anaesthesiologists – A case study. Indian J Anaesth 2023;67:840-1.

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