

# Euglycemic Diabetic Ketoacidosis After Robotic-Assisted RYGB in a Patient Taking an SGLT-2 Inhibitor: A Re-Examination of Guidelines

**AUTHORS:**

Johnson KR; Kuhn JE; Daouadi M

**CORRESPONDING AUTHOR:**

Kelly R. Johnson, DO  
New York Breast Health  
805 Northern Boulevard  
Great Neck, NY 11021  
Email: kelly.r.johnson9@gmail.com

**AUTHOR AFFILIATION:**

Geisinger Medical Center, Danville, PA 17822

## Case Description

A 37-year-old morbidly obese female presented for elective bariatric gastric bypass surgery with a BMI of 43.6. The contributing comorbidities related to her obesity include diabetes mellitus type 2, hypercholesterolemia, hypertension, and obstructive sleep apnea requiring CPAP. Her preoperative hemoglobin A1C was 5.9, and her diabetic medication regimen included empagliflozin 25 mg oral daily, metformin 1000 mg orally twice daily, and regular insulin 50 units with lunch and 60 with dinner. For 14 days preoperatively, she was maintained on a high-protein liquid diet. It was discussed with the patient preoperatively that her insulin requirements would decrease while on the high-protein liquid diet. She did not require any insulin correction during these two weeks. She was instructed to stop her lisinopril 48 hours prior to surgery and metformin and empagliflozin 24 hours before surgery. On the morning of surgery, her preoperative blood glucose (BG) was 129 mg/dL.

The patient underwent an uneventful robotic-assisted laparoscopic Roux-en-Y gastric bypass, liver biopsy, and upper endoscopy. Throughout the surgery, she remained hemodynamically stable, and her blood glucose levels exceeded 150 mg/dL; therefore, she was started on an insulin infusion intraoperatively per Geisinger protocol.

Immediately postop, her pain was controlled, she was tolerating a stage 1 bariatric diet by POD 0 without nausea or vomiting, her vitals were stable, and she was independently ambulating. She was seen by our bariatric medicine specialist postop, who did not anticipate having to restart any of her oral diabetic medications and noted that her insulin requirements would likely decrease.

On POD 0, her blood glucose ranged from 132–164 mg/dL. She required 0–1 unit of insulin/hour (u/hr) POD 0–1. In the early morning of POD 1, she was feeling well overall and was independently ambulating.

On POD 2, her tachycardia improved to 90–106 beats/min, and her respiratory rate improved by 17–24 breaths/min, remaining on room air and CPAP at night. Her insulin requirements decreased from 5 u/hr to 1 u/hr. Her anion gap closed, electrolytes replaced and monitored, started on a stage 1 diet, and she was transitioned to dextrose and started on Plasma-Lyte maintenance fluid.

On POD 3, her anion gap opened again, her blood glucose levels were low, and she was restarted on dextrose. The insulin drip was titrated to 1–2 u/hr, her vital signs were stable, and she was advanced to a stage 2 diet. Zosyn was discontinued as cultures were negative. She was deemed stable for transfer to the med-surg floor.

From POD 4 to 6, the patient's vital signs remained stable, and the insulin infusion was titrated to 1 u/hr. She was transitioned to an insulin sliding scale, and her blood glucose levels remained within normal range. She was followed by bariatric medicine, endocrinology, and the diabetes educator during her stay. She was discharged on POD 6 to home and instructed to stop metformin and empagliflozin and continue Lantus 25 units daily and 1:15 carb coverage with sliding scale insulin with meals.

## Discussion

SGLT-2 inhibitors are among the newest medications for managing diabetes mellitus type 2 (T2DM). This drug binds to sodium-glucose cotransporter-2 (SGLT2) receptors found in the proximal convoluted tubule. It inhibits glucose reabsorption, causing glycosuria and the excretion of glucose and sodium in the urine.<sup>1-3</sup> This drug is very effective in promoting glycemic control without an increased risk of hypoglycemia, has renal and cardiovascular benefits and promotes weight loss, and comes in an oral formulation.<sup>1</sup> Nevertheless, during the perioperative period, this drug has been increasingly reported to cause the life-threatening adverse effect of euDKA.<sup>4-8</sup>

SGLT-2 inhibitors have a rapid onset with a time-to-peak (TTP) of 1-2 hours and a long half-life of 10.6-16.6 hours.<sup>1</sup> Empagliflozin specifically has a TTP of 1.5 hours and a half-life of 12.5 hours.<sup>1</sup> The current perioperative guidelines recommend that SGLT-2 inhibitors be stopped 24 hours before surgery. The half-life of these medications extends past this 24-hour window and has been shown to have serious adverse effects in the perioperative period.

During the perioperative period, the human body experiences increased metabolic demand, stress, dehydration, and limited oral intake, which can contribute to a ketogenic state.<sup>1</sup> SGLT-2 inhibitors contribute to this ketogenic state by increasing renal absorption of ketones and enhancing ketogenesis, which can lead to worsening ketoacidosis.<sup>1</sup> Over the last few years, there has been an increasing number of case reports of euDKA associated with SGLT-2 inhibitors in post-surgical patients and, even more specifically, bariatric patients.<sup>4-8</sup>

Euglycemia DKA is a rare condition. It differs from DKA because blood glucose levels do not usually exceed 250 mg/dL.<sup>2</sup> Common symptoms of euDKA include abdominal pain, nausea, vomiting, and altered mental status. In this case, the patient presented with abdominal pain, nausea, vomiting, and altered mental status.

## Conclusion

The use of SGLT-2 inhibitors in diabetic type 2 and reports of euDKA in surgical patients requiring extensive workup and ICU admission before the diagnosis are on the rise. We advocate for revising the current guidelines regarding the perioperative management of SGLT-2 inhibitors. Due to the prolonged half-life, we advise stopping these medications at least three days or 72 hours before major surgery. We recommend closely monitoring blood glucose levels and insulin requirements within two weeks of surgery for bariatric patients on a low-carbohydrate or high-protein diet. These levels can drastically change during this time, pre-disposing patients to euDKA. We urge surgeons, endocrinologists, and anesthesiologists to be mindful of the preoperative hyperglycemic agents their patients are prescribed and to be able to recognize the precipitating risk factors as well as the signs and symptoms of euDKA.

*Update: As of March 20, 2020, the FDA has revised labels for SGLT-2 inhibitors, recommending that these medications be stopped at least 3-4 days prior to scheduled surgery due to the risk of developing ketoacidosis.<sup>9</sup>*

## Lessons Learned

euDKA is a life-threatening and difficult-to-diagnose complication known to be associated with SGLT-2 inhibitors.

This case demonstrated the importance of reducing the risk for euDKA in our bariatric (and likely all surgical patients) by discontinuing SGLT-2 inhibitors 72 hours prior to elective surgery.

## References

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