

# Euglycaemic Ketoacidosis Due to Extremely Low-Calorie Intake and Dehydration After Laparoscopic Sleeve Gastrectomy in a Patient with Type 2 Diabetes

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**Background:** Bariatric surgery is an effective therapy for type 2 diabetes mellitus (T2DM) and obesity. Euglycaemic ketoacidosis (EKA) has been reported in patients taking sodium-glucose cotransporter 2 (SGLT2) inhibitors after bariatric surgery. Cases of T2DM complicated with EKA without SGLT2 inhibitors after bariatric surgery are rarely reported.

**Purpose:** To present a case report of a T2DM patient (without SGLT2 inhibitor use) who developed EKA soon after laparoscopic sleeve gastrectomy.

**Methods:** Clinical records and interviews were used.

**Results:** A 35-year-old female patient was diagnosed with T2DM and obesity. The patient underwent laparoscopic sleeve gastrectomy to lose weight and control her blood glucose levels. Her daily fluid intake was 800–1000 mL, and her daily caloric intake was less than 500 kcal during the first days after the surgery. She was prescribed degludec insulin, metformin and dulaglutide and her blood sugar was lower than 13.9 mmol/L. On postoperative Day 6, the patient complained of fatigue and vomiting. Blood gas analysis and urine analysis supported the diagnosis of ketoacidosis. Fluid resuscitation, insulin and glucose were administered to the patient immediately. On postoperative Day 8, the patient recovered without any symptoms.

**Conclusion:** We report an extremely rare case of T2DM in which the patient developed EKA after laparoscopic sleeve gastrectomy owing to extremely low-calorie intake and dehydration. Physicians should be on alert for ketoacidosis in patients with T2DM after bariatric surgery with an euglycaemic status, even without the use of SGLT2 inhibitors or the presence of stresses, such as infection.

Level V: Opinions of respected authorities, based on descriptive studies, narrative reviews, clinical experience, or reports of expert committees.

**Keywords:** bariatric surgery, euglycaemic ketoacidosis, type 2 diabetes mellitus

## Introduction

For patients with type 2 diabetes mellitus (T2DM) and clinically severe obesity, bariatric surgery has been proven to be an effective treatment. Remission of diabetes or medication reduction is an established benefit of bariatric surgery.<sup>1</sup> There has been increasing evidence of the cardiovascular and renal protective effects of sodium-glucose cotransporter 2 (SGLT2) inhibitors, and their use has also resulted in moderate weight reduction. These inhibitors are widely used in T2DM patients, especially in those with obesity and multiple risk factors for cardiovascular disease and chronic kidney disease.<sup>2</sup> Recently, it was reported that SGLT-2 inhibitor use may lead to euglycaemic ketoacidosis (EKA) in patients with sleeve gastrectomy.<sup>3</sup> However, cases of T2DM with EKA after bariatric surgery are rarely reported without SGLT2 inhibitor use.<sup>4</sup> Herein, we report a T2DM patient who developed EKA soon after laparoscopic sleeve gastrectomy without SGLT2 inhibitor use.

## Case Report

A 35-year-old female patient had a history of T2DM for 6 years. The patient had a body weight of 87 kg and body mass index of 31 kg/m<sup>2</sup>. Liraglutide was once prescribed to the patient (less than 3 months) for controlling blood glucose and losing weight. She reported no obvious adverse reactions and stopped taking it 1 year ago. She was taking metformin (1000 mg bid) and did not develop diabetic ketoacidosis (DKA). She was admitted to our hospital for poor blood glucose (glycated hemoglobin 8.8%) and poly-morbidities (hypertension, dyslipidemia, hyperuricemia and non-alcoholic fatty liver disease). The insulin release test showed delayed insulin secretion without insulin deficiency (Table 1). Pancreatic islet autoantibodies were negative. Her father was also diagnosed with T2DM. Laparoscopic sleeve gastrectomy was carried out and the procedure went well. Metformin was discontinued the day before surgery. Short-acting recombinant human insulin was used to control perioperative hyperglycaemia and was discontinued immediately after the surgery.

On postoperative Day 1, the patient's blood glucose level fluctuated between 13.4 mmol/L and 16.8 mmol/L. Degludec insulin 20 IU qn plus metformin 500 mg tid and dulaglutide 1.5 mg weekly were prescribed for controlling blood sugar after the surgery. During the 4 days following surgery, the patient started sipping water and enteral nutritional suspension. The patient felt bloated and full. Thus, the total daily fluid intake was 800–1000 mL, and the total daily calorie intake was less than 500 kcal. Abdominal CT showed no abnormal signs such as anastomotic fistula. The patient lost 5 kg in 5 days. Her fasting blood glucose levels during that period were between 7 and 8 mmol/L, and the postprandial blood glucose levels were between 8 and 12 mmol/L.

On postoperative Day 6, the patient complained of fatigue, sweating, nausea and vomiting 30 times. The blood gas analysis demonstrated metabolic acidosis with a blood sugar level of 16.1 mmol/L (Table 2). Urine ketone was over 4+ while glucose was also over 4+. Fluid resuscitation as well as glucose and insulin were administered immediately to the patient. Degludec insulin, metformin and dulaglutide were discontinued. The crystalloid fluid plus water intake was more than 4000 mL every day. Recombinant human insulin was initiated at a rate of 0.05 units/kg/h and adjusted according to the blood glucose levels. On postoperative Day 8, the general state of the patient improved significantly. No nausea or vomiting occurred, the ketones in the urine were negative, and the random blood glucose level was less than 11.1 mmol/L. We discontinued insulin and fluid infusion and advised her to ensure fluid and energy intake in the following days. The patient was discharged on postoperative Day 10.

**Table 1** Pancreatic  $\beta$  Cell Function of the Patient (Insulin Releasing Test)

	0min	30min	60min	120min	180min
Blood glucose (mmol/L)	15.11	20.35	22.6	20.48	14.88
Insulin level (mU/L)	50.62	53.49	58.64	49.52	37.78
C peptide (ng/mL)	1.72	2.22	2.56	3.04	2.51

**Table 2** Laboratory Studies from Postoperative Day 1 to Day 8

	POD1	POD6	POD7	POD8
Serum glucose level (mmol/L)	13.9	16.1	11.8	10.9
PH	7.389	7.265	7.333	7.385
pCO <sub>2</sub> (mmHg)	35.8	23.7	27.2	34.2
Bicarbonate (mmol/L)	24.2	10.5	14.1	21.6
Anion gap	14	21.8	22	16
ABE (mmol/L)	-2.9	-14.5	-10.1	-3.0
SBE (mmol/L)	-3.0	-14.5	-10.3	-3.3
Lactate (mmol/L)	1	0.5	0.4	0.7
Urine ketone	+-	++++	+++	-

**Note:** pH, potential of hydrogen; pCO<sub>2</sub>, partial pressure of carbon dioxide.

**Abbreviations:** ABE, actual base residue; SBE, standard base residue.

## Discussion

DKA often occurs in diabetes with absolute or relative insulin deficiency. Patients with DKA are usually complicated with significant hyperglycemia ( $\geq 13.9$  mmol/L). It was reported that patients with T1DM undergoing bariatric surgery could develop postoperative DKA in 20–25% of the cases.<sup>5</sup> Recently, mild hyperglycaemia or even a euglycaemic status with ketoacidosis, which is defined as euglycaemic ketoacidosis (EKA), has also been reported in patients with diabetes.<sup>6</sup> Dowsett et al<sup>7</sup> reported a case of T1DM in which the patient developed EKA after bariatric surgery. Poor food intake, specifically reduced carbohydrate intake, was suggested to be related to the onset of EKA.

EKA is also reported in T2DM patients. Any underlying condition resulting in decreased glucose availability or production, reduced insulin secretion, and increased counterregulatory hormone production may result in EKA. Such conditions include infection, trauma, prolonged fasting, pregnancy, alcohol intake and SGLT2 inhibitor use.<sup>8</sup> Several T2DM cases were reported to be complicated with EKA after bariatric surgery with combination of SGLT2 inhibitors, and presentation time varied from a few hours up to 6 weeks after the operation.<sup>9</sup> However, EKA rarely occurs in patients with T2DM without SGLT2 inhibitor use. Yu-Ting Lo et al<sup>4</sup> reported immediate EKA after gastric bypass in a T2DM patient. The patient experienced fever, an attack of chronic gouty arthritis, and acute exacerbation of chronic kidney disease but eventually made a full recovery.

There are two major types of bariatric surgery. Generally, postoperative malnutrition is prone to occur after malabsorptive surgery (bypass) due to the restriction of food intake and the change in absorption. However, postoperative malnutrition is extremely rare after restrictive surgery (sleeve gastrectomy).<sup>10</sup> Hence, EKA in T2DM with obesity may be more common when undergoing gastric bypass.<sup>4</sup> In fact, patients with T2DM complicated with EKA after sleeve gastrectomy have been reported. However, the patients in these cases were using SGLT2 inhibitors.<sup>3</sup>

This patient was diagnosed with T2DM without the use of SGLT2 inhibitors, and the laparoscopic sleeve gastrectomy procedure was successful. There were no infections and no alcohol intake. During the days before she began vomiting, her blood glucose level was less than 13.9 mmol/L. When she felt sick and nauseated and vomited 30 times, she denied consuming extra calories. The blood gas and urine ketone body results supported the diagnosis of ketoacidosis. The glucose level determined by the blood gas analyzer was 16.1 mmol/L, which was presumed to be caused by stress from excessive vomiting. Nausea and vomiting are clinical manifestations of ketoacidosis. The patient recovered quickly with fluid resuscitation, glucose and a small dose of insulin infusion. Taken together, the clinical findings support that this patient met the diagnosis of EKA, and the direct cause of this condition was extremely low-calorie intake and dehydration. Excessive ketones induced by low-carbohydrate diets may predispose patients to EKA, and dehydration caused by inadequate fluid intake exacerbates it. The patient was treated with 1.5 mg dulaglutide on postoperative Day 1 (0.75 mg dulaglutide not available in China). Without titration of a low dosage and gastrointestinal side effects, long-acting GLP1-A (dulaglutide) may also be a predisposing factor for EKA. There were some limitations in our paper. First, case reports may not be representative, and the frequency and timing of EKA need further observation. Second, low carbohydrate levels may send the body into a state of starvation in which high glucagon and low insulin levels lead to the activation of other counter-regulatory hormones, such as catecholamine, cortisol and growth hormone. These counter-regulatory hormones play a role in the production of ketone bodies by raising the level of free fatty acids. Unfortunately, we did not test the counter-regulatory hormone level when our patient showed obvious vomiting, and more detailed screening is needed when we encounter similar patients in the future. It was presumed that counter-regulatory hormone levels would be elevated in response to starvation and stress.

## Conclusion

We report an extremely rare case of T2DM in which the patient developed EKA after laparoscopic sleeve gastrectomy owing to extremely low-calorie intake and dehydration. Physicians should be on alert for ketoacidosis in patients with T2DM after bariatric surgery with an euglycaemic status, even without the use of SGLT2 inhibitors or the presence stresses such as infection. The diagnosis of EKA may be missed because of atypical presentation. Patients need to be educated on the potential complications of operations and ensure adequate calorie and fluid intake after the surgery. In addition, long-acting GLP1-A should be carefully used immediately after bariatric surgery.

## Data Sharing Statement

All the data are fully available without restriction. All data generated or analyzed during this study are included in this published article.

## Ethics Approval and Informed Consent

All procedures performed in this study involving human participants were in accordance with the ethical standards of the ethics committee of Tsinghua Changgung Hospital, and with the 1964 Helsinki declaration and its later amendments. Informed consent was obtained from the patient included in the study. Publication of case report does not need ethical review in our institution.

## Consent for Publication

Written informed consent for publication was obtained from the patient. A copy of the written consent is available by request.

## Acknowledgments

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## Disclosure

The authors have no relevant financial interests to disclose.

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