Annals of Thyroid Research

Open Access

Austin Publishing Group

Case Report

Euglycemic Diabetic Ketoacidosis in COVID-19 Patient Caused by Empagliflozin: A Case Report from Intensive Care Unit

Al-Taie N[1]*, Fuchs W[2], Waechter H[2], Wagner M[1] and Stingl H[1]

[1]Department of Internal Medicine, Melk General Hospital, Austria

[2]Department of Anaesthesia and Intensive Care, Melk General Hospital, Austria

***Corresponding author:** Nawras Al-Taie, Department of Internal Medicine, Melk General Hospital, Austria

Received: April 13, 2021; **Accepted:** May 08, 2021; **Published:** May 15, 2021

Abstract

The novel coronavirus - Severe Acute Respiratory Syndrome coronavirus 2 - is responsible for mainly respiratory disease (COVID-19). On the other hand, Diabetic Ketoacidosis (DKA) is a life-threating complication. The usual form of DKA is caused by insulin deficiency and is characterized by high blood glucose (usually more than 250mg/dl or 14mmol/L), ketonemia, low pH, and low serum bicarbonate. The other form of DKA is the euglycemic DKA, which occurs in patients with blood glucose lower than 250mg/dl (14mmol/L). This case report describes a patient that presented to the intensive care unit with Covid-19 pneumonia and euglycemic DKA.

Keywords: Severe Acute Respiratory Syndrome coronavirus 2; COVID-19; Diabetic Ketoacidosis

Case Presentation

A 67-year-old male with a history of diabetes type 2 for 7 years presented to our emergency department in Melk general hospital in Austria with 5 days of fever, dyspnea, and sore throat. The patient's diabetes medications before hospital admission were metformin and empagliflozin. Other medications were atorvastatin, aspirin, and bisoprolol. The patient had also had a stroke and hypertension.

Due to the Covid-19 outbreak, we conducted PCR assays for Covid-19 detection, and the result was positive. His vital signs on admission were: blood pressure, 140/85 mmHg; temperature, 38.0°C; respiratory rate, 26/min; pulse, 90/min; and oxygen saturation, 96% (breathing room air). The patient's initial blood test results were: HbA1c, 7.0% (53mmol/l); creatinine, 0.77mg/dl (0.70-1.20); CRP, 139.9mg/l (0.0-5.0); sodium, 138mmol/l (136-145); potassium, 4.2mmol/l (3.5-5.1) mild lymphopenia; and initial procalcitonin, 0.2ng/ml (0.0-0.5).

Twenty-four hours later, the patient's condition deteriorated, and he was admitted to the intensive care unit with the diagnosis of severe viral pneumonia, which was also confirmed by chest x-ray. In intensive care, the patient's blood glucose was 180mg/dl, with serum pH of 7.25, pCO_2 of 33mmHg (base excess -12mmol/l), serum bicarbonate of 13mmol/l, increased anion gap of 27mmol/l, and creatinine of 0.95mg/dL (0.70-1.20). Initially, it was not clear why the patient had metabolic acidosis. Metformin associated lactic acidosis was considered, but the patient had normal lactate of 1.0mmol/L and normal creatinine, and so this diagnosis was ruled out. After reviewing the medications of the patient, a diagnosis of euglycemic DKA was confirmed with blood ketones of 4.4mmol/l (<0.6 using the ketone meter).

The patient was started on Intravenous (IV) insulin with an infusion rate of 2-3 unit/h and dextrose 5% to keep the blood glucose at ~150mg/dl, in addition to a conservative IV fluid regime as per Covid-19 local guidelines. It is essential to mention that we did not use our DKA insulin infusion protocol (which needs hourly assessment) to minimize the medical staffs' exposure to the virus. Twenty-four hours later, the pH improved (7.38), with 22mmol/l bicarbonate, and 0.7mmol/L blood ketones. Unfortunately, the patient developed a secondary bacterial infection as a complication of Covid-19 and was intubated and ventilated, and an ampicillin/sulbactam IV antibiotic was started, as per local Covid-19 guidelines. The patient was extubated after 9 days, and recovered well.

Discussion

Sodium-Glucose Cotransporter 2 (SGLT2) inhibitors have many advantages, such as lowering blood glucose, blood pressure, and improved cardiovascular outcomes [1], but they also have many disadvantages, such as increased risk of urinary tract infection, genital fungal infections, and DKA [2]. DKA can be induced by SGLT inhibitors through a reduction in the carbohydrate availability, with a decrease in insulin dose, increased lipolysis, increased delivery of the free fatty acid to the liver, increased production of ketone bodies, and high glucagon level in the blood [3].

In March 2020, the World Health Organization declared Covid-19 as a pandemic that has infected over 100 million of patients worldwide, and unfortunately, nearly three millions of patients have died from this viral infection [4]. The virus that causes Covid-19, SARS-CoV-2, infects patients' cells through binding to the Angiotensin-Converting Enzyme 2 (ACE2) receptor, which is found in epithelial cells (mainly in the lung but also in the intestine, blood vessels, and kidney) [5]. Studies have suggested that the expression of ACE2 is significantly increased in patients with both types of diabetes and treated with ACE inhibitors and angiotensin II type I receptor blockers (ARBs) [5,6], but this hypothesis needs to be confirmed.

Many studies conducted in China - where the Covid-19 outbreak started - show that about 13-16% of patients admitted to the hospital

Citation: Al-Taie N, Fuchs W, Waechter H, Wagner M and Stingl H. Euglycemic Diabetic Ketoacidosis in COVID-19 Patient Caused by Empagliflozin: A Case Report from Intensive Care Unit. Annals Thyroid Res. 2021; 7(2): 333-334.

with Ccovid-19 had diabetes [7,8]. In another study from the intensive care unit of the Wuhan Jin Yin-tan hospital, about 20% of the non-survivors had diabetes [9].

It is well known that hyperglycemia increases susceptibility to various infections [10,11] and that hyperglycemia leads to immune dysfunction through decrease lymphocyte response, decrease neutrophil dysfunction, dysfunction of the humoral immunity, and reduction of inflammatory cytokines secretion [10,11]. It is well documented that diabetes is associated with various respiratory infections similar to the Covid-19 infection, such as influenza and swine flu and SARS-CoV-1 [10-12].

A recent review showed that the Covid-19 virus could damage the pancreatic β cells and leading to DKA due to insulin deficiency, and many diabetic patients infected with Covid-19 may need higher insulin doses than usual [13].

The importance of this case is to emphasize the need for reasonable blood glucose control in such an outbreak and to consider severe, and life-threating adverse effects, such as SGLT2 inhibitor-induced DKA, even in difficult cases, such as COVID-19 infection, which might explain the acidosis in such patients.

References

1. Davies MJ, D'Alessio DA, Fradkin J, et al. Management of Hyperglycemia in Type 2 Diabetes, 2018. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care. 2018; 41: 2669-2701.
2. US Food and Drug Administration. FDA Drug Safety Communication: FDA warns that SGLT2 inhibitors for diabetes may result in a serious condition of too much acid in the blood. Bethesda, MD: US Food and Drug Administration. 2015.
3. Goldenberg RM, Berard LD, Cheng AYY, et al. SGLT2 Inhibitor-associated Diabetic Ketoacidosis: Clinical Review and Recommendations for Prevention and Diagnosis. Clinical Therapeutics. 2016; 38: 2654-2664.e1.
4. World Health Organization. Coronavirus disease 2019 (COVID-19): situation report. 2020: 66.
5. Wan Y, Shang J, Graham R, Baric RS, Li F. Receptor Recognition by the Novel Coronavirus from Wuhan: an Analysis Based on Decade-Long Structural Studies of SARS Coronavirus. Journal of Virology. 2020; 94: e00127-20.
6. Fang L, Karakiulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? The Lancet Respiratory Medicine. 2020.
7. Zhang J-j, Dong X, Cao Y-y, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy. 2020.
8. Guan W-j, Ni Z-y, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. New England Journal of Medicine. 2020.
9. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. The Lancet Respiratory Medicine. 2020.
10. Casqueiro J, Casqueiro J, Alves C. Infections in patients with diabetes mellitus: A review of pathogenesis. Indian J Endocrinol Metab. 2012; 16: S27-S36.
11. Geerlings SE, Hoepelman AIM. Immune dysfunction in patients with diabetes mellitus (DM). FEMS Immunology & Medical Microbiology. 1999; 26: 259-265.
12. Yang JK, Feng Y, Yuan MY, et al. Plasma glucose levels and diabetes are independent predictors for mortality and morbidity in patients with SARS. Diabetic Medicine. 2006; 23: 623-628.
13. Stefan R Bornstein, Francesco Rubino, Kamlesh Khunti, Geltrude Mingrone, David Hopkins, Andreas L Birkenfeld, et al. Practical recommendations for the management of diabetes in patients with COVID-19. Lancet Diabetes Endocrinol. 2020; 8: 546-550.