ISSN 1948-9358 (online)

World Journal of *Diabetes*

World J Diabetes 2022 March 15; 13(3): 129-281

Published by Baishideng Publishing Group Inc

World Journal of Diabetes

Contents

Monthly Volume 13 Number 3 March 15, 2022

REVIEW

MINIREVIEWS

ORIGINAL ARTICLE

Case Control Study

Retrospective Cohort Study

Retrospective Study

World Journal of Diabetes

Monthly Volume 13 Number 3 March 15, 2022

Contents

World Journal of Diabetes

Monthly Volume 13 Number 3 March 15, 2022

Contents

ABOUT COVER

Editorial Board Member of *World Journal of Diabetes*, Djordje S Popovic, MD, PhD, Assistant Professor, Clinic for Endocrinology, Diabetes and Metabolic Disorders, Clinical Center of Vojvodina, Department of Internal Medicine, Medical Faculty, University of Novi Sad, 21000 Novi Sad, Serbia. djordje.popovic@mf.uns.ac.rs

AIMS AND SCOPE

The primary aim of *World Journal of Diabetes* (*WJD*, *World J Diabetes*) is to provide scholars and readers from various fields of diabetes with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJD mainly publishes articles reporting research results and findings obtained in the field of diabetes and covering a wide range of topics including risk factors for diabetes, diabetes complications, experimental diabetes mellitus, type 1 diabetes mellitus, type 2 diabetes mellitus, gestational diabetes, diabetic angiopathies, diabetic cardiomyopathies, diabetic coma, diabetic ketoacidosis, diabetic nephropathies, diabetic neuropathies, Donohue syndrome, fetal macrosomia, and prediabetic state.

INDEXING/ABSTRACTING

The *WJD* is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Current Contents/Clinical Medicine, Journal Citation Reports/Science Edition, PubMed, and PubMed Central. The 2021 Edition of Journal Citation Reports® cites the 2020 impact factor (IF) for *WJD* as 3.763; IF without journal self cites: 3.684; 5-year IF: 7.348; Journal Citation Indicator: 0.64; Ranking: 80 among 145 journals in endocrinology and metabolism; and Quartile category: Q3.

RESPONSIBLE EDITORS FOR THIS ISSUE

NAME OF JOURNAL
World Journal of Diabetes

ISSN
ISSN 1948-9358 (online)

LAUNCH DATE
June 15, 2010

FREQUENCY
Monthly

PUBLICATION DATE
March 15, 2022

World Journal of Diabetes

Submit a Manuscript: https://www.f6publishing.com

World J Diabetes 2022 March 15; 13(3): 272-274

DOI: 10.4239/wjd.v13.i3.272

ISSN 1948-9358 (online)

LETTER TO THE EDITOR

Sodium-glucose co-transporter 2 inhibitors induced euglycemic diabetic ketoacidosis within four days of initiation

Almurtada Razok, Fateen Ata, Sara Mohamed Ibrahim Ahmed, Dabia Hamad S H Al Mohanadi

Specialty type: Endocrinology and metabolism

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Papazafiropoulou A

Received: September 6, 2021
Peer-review started: September 6, 2021
First decision: December 4, 2021
Revised: December 5, 2021
Accepted: February 10, 2022
Article in press: February 10, 2022
Published online: March 15, 2022

Almurtada Razok, Fateen Ata, Sara Mohamed Ibrahim Ahmed, Dabia Hamad S H Al Mohanadi, Department of Internal Medicine, Hamad Medical Corporation, Doha 3050, Qatar

Dabia Hamad S H Al Mohanadi, Department of Endocrinology, Hamad Medical Corporation, Doha 3050, Qatar

Corresponding author: Fateen Ata, BSc, MBBS, MD, Doctor, Department of Internal Medicine, Hamad Medical Corporation, Al Rayyan Street, Bin Omran Area, Al Rayyan, Doha 3050, Qatar. docfateenata@gmail.com

Abstract

Euglycemic diabetic ketoacidosis (EDKA) is a well-known complication of sodium-glucose co-transporter 2 inhibitors, and many cases with variable onset following the initiation of these agents are reported before, with a median onset of approximately 2 wk. This letter discusses a 45-year-old lady who initially presented with ischemic stroke but developed EDKA 4 d after starting empagliflozin, a rare occurrence. The patient had severe metabolic acidosis that necessitated admission into the intensive care unit. Prompt discontinuation of empagliflozin and DKA management resulted in clinical recovery.

Key Words: Euglycemic diabetic ketoacidosis; Sodium-glucose co-transporter 2 inhibitors; Type 2 diabetes mellitus; Empagliflozin

Core Tip: With a steady surge in the prescription of sodium-glucose co-transporter 2 inhibitors (SGLT2-i) in medical conditions including type 2 diabetes mellitus (DM), type 1 DM, and heart failure, there are increasingly reported cases of euglycemic diabetic ketoacidosis (EDKA) with their use. EDKA in the context of SGLT2-i use is reported in various patients with different precipitating factors, some even with no inciting event. One of the rarely reported inciting events is stroke. Another aspect of SGLT2-i induced EDKA which remains relatively less understood is the time of initiation of the drug to the development of EDKA. In our patient, severe EDKA developed within 4 d of empagliflozin initiation, necessitating intensive care and discontinuation of empagliflozin, resulting in complete recovery regarding the EDKA.

Citation: Razok A, Ata F, Ahmed SMI, Al Mohanadi DHSH. Sodium-glucose co-transporter 2 inhibitors induced euglycemic diabetic ketoacidosis within four days of initiation. *World J Diabetes* 2022; 13(3): 272-274
URL: https://www.wjgnet.com/1948-9358/full/v13/i3/272.htm
DOI: https://dx.doi.org/10.4239/wjd.v13.i3.272

TO THE EDITOR

With great interest, we read the recent article "Euglycemic diabetic ketoacidosis: A missed diagnosis" by Nasa *et al*[1]. The authors have described various factors that can potentiate euglycemic diabetic ketoacidosis (EDKA) in sodium-glucose co-transporter 2 inhibitor (SGLT2-i) use. There is a steady increase in EDKA reports secondary to SGLT2-i. Most of the articles mention a precipitating factor behind the development of EDKA in patients taking SGLT2-i. More extensive studies mention no or unknown precipitating factor in 16%-51% of cases[2,3]. This creates a need to explore a possible direct link of SGLT2-i in the development of EDKA in an otherwise healthy patient with diabetes. Acute vascular events such as stroke are infrequent inciting events for EDKA in the setting of SGLT2-i use.

We recently encountered an interesting case of a patient with type 2 diabetes mellitus (T2DM) who was admitted with acute stroke and developed EDKA within 4 d of initiation of empagliflozin.

A 45-year-old woman presented with sudden onset left arm weakness and slurred speech with facial droop. Magnetic resonance imaging revealed a right basal ganglia acute infarction, in addition to left parietal subcortical microangiopathic changes. The patient had a history of breast carcinoma, treated with mastectomy and maintenance tamoxifen. She also had T2DM and was prescribed sitagliptin/metformin 50/1000 mg two tablets daily. However, the patient was non-compliant with the medication and was not checking her blood sugar regularly.

The patient was started on dual antiplatelet therapy (aspirin 100 mg and clopidogrel 75 mg once daily) after establishing the diagnosis of an acute stroke. Her HbA1c was 14%, confirming a poor control of her diabetes. To manage her poorly controlled diabetes mellitus, sitagliptin/metformin was continued, with the addition of insulin glargine 12 units at bedtime and empagliflozin 10 mg once daily.

Four days later, the patient developed vomiting and generalized fatigue. Arterial blood gas showed severe metabolic acidosis with a pH of 6.9 and bicarbonate level of 3 mEq/L (reference range: 22-26 mEq/L). Serum B-hydroxy butyrate was higher than the reported threshold of 9.60 mmol/L (reference range: 0.03-0.3). Her blood glucose level at the time was 10.3 mmol/L (reference range: 3.3-5.5), and her urine dipstick showed +4 ketone. She was diagnosed with severe EDKA and was shifted to the medical intensive care unit for further management and treatment.

Regular insulin infusion and intravenous fluids were initiated, and a right internal jugular line was inserted for monitoring and resuscitation. Her arterial blood gas was measured every 2 h, and serum ketones were measured daily. Forty-eight hours later, the patient's condition improved, and she started tolerating oral feed. Her ABG results showed significant improvement with the closure of the anion gap (Table 1). She was started on subcutaneous glargine 20 units daily and insulin as part 7 units three times a day.

The patient was consequently shifted back to the care of the general medicine team, where her glycemic control was monitored closely. After ensuring the patient's fitness and stability, she was transferred to a physical and occupational therapy rehabilitation facility.

Our case highlights that in the presence of a precipitating factor, SGLT2-i drugs can cause an early and severe EDKA. We recommend that wherever other choices are available, initiation of SGLT2-i should be delayed until patients are otherwise healthy and not admitted with an acute event. SGLT2-i medications should ideally be started in an outpatient setting, and the patients should be counseled not to rely on blood glucose and seek immediate medical attention when experiencing symptoms of DKA.

Table 1 Laboratory investigations of the patient during euglycemic diabetic ketoacidosis

Investigation	Onset	24 h	48 h	Reference
PH	6.9	7.32	7.42	7.35-7.45
HCO_3 (mmol/L)	3	12.5	20.6	22-29
Glucose (mmol/L)	10.3	10.8	6.4	3.3-5.5
Sodium (mmol/L)	140	137	139	133-146
Potassium (mmol/L)	3.8	3.2	3.4	3.5-5.3
Chloride (mmol/L)	101	111	110	95-108
Anion Gap	36	13.5	8.4	10-12
Lactate (mmol/L)	1.3	0.7	0.9	0.36-1.6
B-hydroxybutyrate (mmol/L)	> 9.60	1.22	0.11	0.03-0.3

FOOTNOTES

Author contributions: Razok A, Ata F, and Ahmed SMI wrote the letter; Al Mohanadi DHSH revised the letter.

Conflict-of-interest statement: The authors have no actual or potential conflict of interest to declare.

Country/Territory of origin: Qatar

ORCID number: Almurtada Razok 0000-0001-9430-0220; Fateen Ata 0000-0001-7121-8574; Sara Mohamed Ibrahim Ahmed 0000-0003-4499-5006; Dabia Hamad S H Al Mohanadi 0000-0002-6967-6047.

Corresponding Author's Membership in Professional Societies: American College of Physicians, 03770816.

S-Editor: Zhang H
L-Editor: Wang TQ
P-Editor: Zhang H

REFERENCES

1 **Nasa P**, Chaudhary S, Shrivastava PK, Singh A. Euglycemic diabetic ketoacidosis: A missed diagnosis. *World J Diabetes* 2021; **12**: 514-523 [PMID: 33995841 DOI: 10.4239/wjd.v12.i5.514]
2 **Clark A**, Mohammed AS, Raut A, Moore S, Houlden R, Awad S. Prevalence and Clinical Characteristics of Adults Presenting With Sodium-Glucose Cotransporter-2 Inhibitor-Associated Diabetic Ketoacidosis at a Canadian Academic Tertiary Care Hospital. *Can J Diabetes* 2021; **45**: 214-219 [PMID: 33046401 DOI: 10.1016/j.jcjd.2020.08.100]
3 **Ata F**, Yousaf Z, Khan AA, Razok A, Akram J, Ali EAH, Abdalhadi A, Ibrahim DA, Al Mohanadi DHSH, Danjuma MI. SGLT-2 inhibitors associated euglycemic and hyperglycemic DKA in a multicentric cohort. *Sci Rep* 2021; **11**: 10293 [PMID: 33986421 DOI: 10.1038/s41598-021-89752-w]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com