VOLUME - 11, ISSUE - 03, MARCH - 2022 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Internal Medicine

# DAPAGLIFLOZIN ASSOCIATED EUGLYCEMIC DIABETIC KETOACIDOSIS: A CASE REPORT

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**ABSTRACT** SGLT2 inhibitors are a new class of drugs for lowering blood sugar levels in type 2 diabetics. They have been shown to reduce cardiovascular risk along with improving glycemic control. Some of the SGLT2 inhibitors are Canagliflozin, Dapagliflozin, Empagliflozin, Ertugliflozin, Remogliflozin. We are presenting a case of a 60-year-old female patient who is a known case of Type 2 Diabetes Mellitus presented to the emergency room with loss of responsiveness for 1 day gradual in onset. Her history revealed she is type 2 diabetic for the past 10yrs and was hospitalized 20days back when her RBS was 889mg/dl & urine ketones were positive with a diagnosis of type 2 DM with DKA. since then, she was put on Tab Dapagliflozin 10mg OD along with other OHA's. On presentation, the patient was unconscious GCS-E1, V2, M2-5/15, pulse-100/min, BP-80mm of hg systolic, glucometer RBS-211 mg/dl, ABG showed severe metabolic acidosis pH-6.86, $HCO^3$-2.9mmol/L, $PCO^2$-24mm hg, PaO2-58mm hg, urine ketones came positive, and the patient was managed conservatively. The patient responded well, and her GCS improved with stabilization in her condition. Dapagliflozin and other SGLT2 inhibitors can cause Euglycemic DKA, and these can be missed out in the emergency room as they have not so high blood sugar levels making the diagnosis of DKA difficult in emergency conditions.

**KEYWORDS :** SGLT2 inhibitors, gliflozin, euglycemic diabetic ketoacidosis (eu-DKA), diabetes mellitus (DM).

## INTRODUCTION

Sodium-glucose cotransporter-2 (SGLT-2) inhibitors inhibit renal SGLT-2 receptors responsible for glucose reabsorption thus promoting glycosuria [1]. The use of Sodium-glucose cotransporter-2 (SGLT-2) inhibitors are oral hypoglycemic agents as monotherapy or with other hypoglycemic agents for treating type 2 diabetes mellitus (DM) is increasing.

The most common adverse side effect of SGLT2 inhibitors are genital infections, high concentrations of glucose in the urine can predispose to mycotic infections, because of the osmotic diuresis induced by glycosuria resulting from SGLT2 inhibition, volume depletion can lead to increased urinary frequency, thirst, and rarely orthostatic hypotension. A rare complication of Euglycemic diabetic ketoacidosis has been reported in diabetes patients on SGLT2 inhibitors [2].

SGLT-2 inhibitors reduce blood glucose levels, thereby decreasing the secretion of endogenous insulin by pancreatic b-cells. This in turn stimulates pancreatic a-cells, leading to increased glucagon secretion. SGLT-2 inhibitors also directly stimulate a-cells, thereby increasing plasma glucagon concentration and promoting hepatic ketogenesis. SGLT-2 inhibitors increase the reabsorption of acetoacetate in the renal tubules, which increases the blood level of ketone bodies. Thus SGLT-2 inhibitors can lead to euglycemic diabetic ketoacidosis (eu-DKA)[3].

Here, we are presenting a case of a 60-year-old female patient who developed euglycemic diabetic ketoacidosis (eu-DKA) with hypernatremia following dapagliflozin administration.

### Case Report

A 60-year-old female presented to our emergency room with a chief complaint of loss of responsiveness for 1 day. Her history revealed she is Diabetic and hypertensive for 10 years and was hospitalized 20 days back, that time her random blood sugar was 889mg/dl & urine ketones was positive with a diagnosis of type 2 DM with DKA since then she was put on oral Dapagliflozin 10mg OD along with her previous Oral Hypoglycemic Agents on discharge. On physical examination patient was unconscious, GCS-E1V2M2-5/15, pallor was present, skin turgor was decreased, the tongue was dry, Pulse-100/min, SBP-80mm of Hg, glucometer RBS-211 mg/dl,

### Investigations:

ABG-severe metabolic acidosis of pH-6.86, $HCO_3$-2.9mmol/L, $PCO_2$-24mm of Hg, $PO_2$-58mm of Hg, Urine ketones-positive, ECG- Normal study with sinus rhythm.

The patient was resuscitated with intravenous fluids, inotropic support, and insulin infusion. The patient responded well, GCS improved, and the patient became stable.

Laboratory data of the patient during hospitalization.

| Parameter | Reference range | DAY 1 | DAY 3 | DAY 6 |
|---|---|---|---|---|
| Blood glucose (mg/dL) | 70–115 | 211 | 165 | 144 |
| Creatinine (mg/dL) | 0.6–1.2 | 1.1 | 0.8 | 0.7 |
| Sodium (mEq/L) | 135–145 | 162 | 151 | 143 |
| Potassium (mEq/L) | 3.5–5.0 | 2.5 | 3.5 | 4.1 |
| pH | 7.35 –7.45 | 6.86 | 7.4 | 7.41 |
| PaCO2 (mmHg) | 35–45 | 12.0 | 33.2 | 36.1 |
| HCO3 - (mEq/L) | 22–26 | 2.9 | 21.1 | 23.4 |
| Serum lactate (mmol/L) | 0.7–2.1 | 1.1 | 1.0 | 0.8 |
| Serum ketone (mmol/L) | <0.6 | 2.7 | 0.6 | 0.4 |
| U. Osm (mOsm/kg H2O) | 50–1400 | 713 | 624 | 541 |

## DISCUSSION

Diabetic ketoacidosis is a fatal complication of diabetes mellitus and an emergency condition that should be identified and treated timely. In this condition, there is insulin deficiency leading to hyperglycemia, volume loss, fatty acid oxidation, and the formation of ketone bodies with resultant metabolic acidosis.

Eu-DKA is an uncommon form of DKA that is characterized by metabolic acidosis (pH< 7.3), a decreased level of serum bicarbonate, and a relatively low blood glucose level [3].

SGLT-2 receptors are transporters responsible for the reabsorption of approximately 90% of filtered glucose in the S1 segment of the proximal tubule of the kidney. Selective SGLT-2 inhibitors inhibit the SGLT-2 transporters, thereby preventing the reabsorption of glucose and reducing blood glucose levels by inducing glycosuria. Various other clinical benefits of SGLT-2 inhibitors include improved insulin sensitivity by decreasing visceral and subcutaneous fat, decreasing the risk of cardiovascular mortality, and decreasing hypoglycemic episodes [4].

SGLT2 inhibitors lower blood sugar levels by excessive urinary glucose excretion, which reduces insulin secretion from pancreatic beta-cell. This results in lowering of antilipolytic activity of insulin and stimulation of free fatty acids synthesis, which are converted to ketone bodies in the liver. SGLT2 inhibitors are also associated with an increase in glucagon production. The lowering of the insulin-to-glucagon ratio further stimulates lipolysis and increases circulating free fatty acids and lipid oxygenation. SGLT2 receptors have been identified on pancreatic α-cells where their inhibition promotes glucagon secretion, and this provides a strong drive to increase ketone body production. Enhanced ketogenesis is seen in nondiabetic patients receiving SGLT2 inhibitor medications. Additionally, the fluid loss associated with SGLT2-induced glycosuria may compound the hypovolemic state of DKA and further increase counter-regulatory hormone secretion[5].

## CONCLUSION

Dapagliflozin and other SGLT2 inhibitors can cause Euglycemic DKA, and so can be missed out in the emergency room as these patients may not have high blood sugar levels, hence making the diagnosis of DKA difficult.

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