Mind the gap!

Euglycemic DKA in the setting of SGLT2 inhibitor use: a rare but preventable complication

Kathie Zhang, MD and Meenakshi Sambharia, MD

Department of Internal Medicine, University of Iowa, Iowa City, IA

Introduction

- SGLT2 inhibitors are becoming increasingly popular for the treatment of DM2 due to cardiac and renal benefits.
- Euglycemic diabetic ketoacidosis (euDKA) is a rare adverse effect of SGLT2 inhibitors characterized by a triad of ketosis, anion gap metabolic acidosis, and normoglycemia (BG < 250).
- euDKA may go unrecognized due to normoglycemia, resulting in delayed diagnosis, treatment, and even death.

Case Presentation

- 41-year-old female presented with a two-day history of nonspecific symptoms (malaise, body aches, nausea, vomiting, and headache)
- History of type 2 diabetes mellitus managed with empagliflozin for the past 1.5 years
- Saw her PCP four days prior and was told her sugars were too high (A1C 10.9%)
- Made sure to decrease her carbohydrate intake after her PCP appointment—went back to “keto” diet

Vital signs: BP 153/93 mmHg, HR 99 bpm, RR 17, temperature 36.7°C, and BMI: 31.15 kg/m2. Physical examination notable only for mild tachycardia.

Initial Workup:

135	106	14	152
3.9	9	0.5	

	15.1	
16.1		384
	45	

Anion gap 20
VBG: 7.11/29
Lactic acid 1.2
Serum acetone positive

Urinalysis:
Glucose 2+, ketones 3+,
protein 2+, spec grav >1.030

Case Presentation

She was diagnosed with euDKA, started on an insulin drip, and transferred to the MICU for further management.

She was treated with intravenous insulin until resolution of DKA.

Hospital Course:

	Admission	HD 2	HD3	HD4	HD5
Na	137	134	137	135	140
K	3.9	3.2	3.3	3.3	3.3
Cl	111	110	110	104	104
CO2	7	13	14	19	23
BUN	12	5	7		6
Cr	0.5	0.5	0.6		0.4
Glucose	119	120-201	128-194	125-286	167-184
Anion gap	19	11	13	12	13
pH	7.15	7.29	7.34	7.34	7.44
pCO2	24	23	35	39	32
β-hydroxybutyrate	5.5	2.1	3.6	2.0	0.8

She was discharged home on an insulin regimen briefly. She later transitioned to monotherapy with a GLP-1 agonist (dulaglutide). A1C of 7.9% at last check.

Discussion

- SGLT2 inhibitors block reabsorption of filtered glucose. The resulting glycosuria and lowered blood glucose levels increases **glucagon**-insulin ratio, resulting in increased **lipolysis** and **ketogenesis**—predisposing patients to ketosis.
- Further ketosis in the setting of relative **insulin-deficient states** (e.g. acute illness, decreased caloric intake, or abrupt insulin reductions) may then result in progression to DKA.
- In our patient, the euDKA was likely triggered by her abrupt decrease in carbohydrate intake.

Discussion

It is crucial to recognize the appropriate hold parameters for these medications to prevent this potentially life-threatening complication.

Precautions to Reduce Risk:

- Discontinue in the setting of acute illness
- Discontinue 3-4 days prior to elective surgery
- Avoid >20% reductions in insulin dose
- Avoid very low-carbohydrate diets (e.g. ketogenic diet)
- Avoid use in patients with alcohol use disorder

Conclusions

1. Recognize that euDKA may develop even in patients who have been on SGLT2 inhibitors for a long period of time.
2. Normal or minimally elevated glucose levels may lead to a delay in diagnosis or treatment of euDKA.
3. Recognize appropriate hold parameters for SGLT2 inhibitors.

References

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