

House of Carbs: the path to euglycemic DKA in patients with Diabetes on SGLT2 inhibitors

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Aim:

To bring awareness to a newer line of oral medication which can increase risk euglycemic diabetic ketoacidosis (eDKA) in Type 1 and Type 2 Diabetes patients on carb restrictive diets.

Background:

The Ketogenic "Keto" or "Carnivore" has come into mainstream focus for patients trying to lose weight. The aim is to induce "ketosis" by catabolizing fat into ketone bodies. Using these as fuel rather than carbohydrates. This shift can occur over the course of several days when carbohydrate intake is restricted to 20-50 g daily. This is effective for short-term weight loss but may lead to life-threatening euglycemic diabetic ketoacidosis in those with Diabetes Mellitus (DM) on SGLT2 inhibitors.

Case 1:

71 year-old Caucasian woman with controlled Type 2 DM on sitagliptin, metformin and canagliflozin was admitted for eDKA after she presenting with worsening symptoms of shortness of breath for 3 days. Three days prior to admission, she had been experiencing shortness of breath and was started on prednisone for a presumed COPD exacerbation and discharged home. The next day, she returned in respiratory distress and mild nausea.

On presentation in the ER, her anion gap was 31 with a serum bicarbonate level of <5 mmol/L. Beta hydroxybutyrate was critically elevated 118mg/dl (ref. 0.2-2.8mg/dl). Serum glucose level is 265 mg/dl. She was also noted to have pre-renal acute kidney injury.

On physical examination, she was noted to be tachypneic, with dry mucous membranes with ill appearance.

Upon questioning, she recently started a "carnivore diet" in which she severely restricted carbohydrate intake to near zero a few weeks prior. eDKA was treated in the ICU with an IV insulin and bicarbonate drip. Once stabilized, she was transitioned to the medical floor. She was discharged home on sitagliptin and metformin. Canagliflozin was discontinued and moderate carbohydrate intake was recommended with her diet.

Labs:

Urinalysis was showed small amount ketones without evidence of infection. EKG, chest x-ray were unremarkable.

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		ange: 36 - 4	46								li	O2 Sat, Arterial	97.5		88.4	
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	Range: 3.5 - 5.1															
	mmol'L															
cride	Ref	102	109	110 (H)	107	106	103	105	103	102						
	Range: 95 - 107															
	mmol'L															
O2, otal	Latest Ref	45 (CL)	6 (CL)	10 (L)	15 (L)	17 (L)	19 (L)	23	22	24						
	Range: 22 - 30															
	mmolt															
inion iap	Ref		19 (H)	12	12	12	12	8	9	8						
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irea Etrogen	Ref		10	13	11	y		,	6 (L)	5 (L)						
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reatini o	Latest Ref	1.0	0.7	0.6	0.5	0.5	0.5	0.5	0.4 (L)	0.4 (L)						
	Rance:															
	0.5 - 1.0 mg/dL															
	Latest Ref	287	254	279 (L)	251	251	279 (L)	283	282	281						
alculat				(L)			(L)									
4	280 - 30 mOs/Kg	3														
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alculati	Latest Ref	55 (L)	>60	>60	>60	>60	>50	>50	>50	>50						
n, Non- ifrican	Range: H50															
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	Latest	265	159	195	161	143	150	122	214	195						
	Ref	(11)	(11)	(H)	(H)	(11)	(11)		(H)	(H)						

Case 2:

51 year-old Caucasian woman with uncontrolled Type 1 DM and Obesity class 2 on continuous subcutaneous insulin infusion treatment and empagliflozin was admitted for eDKA. She had started a ketogenic diet 4 months prior, restricting her carb intake to 30 g daily. She was also on continuous glucose monitoring.

She reported that she had become progressively fatigued, anorexic with shortness of breath. Her BS however, were around 200s on both CGM and glucometer readings. Her symptoms progressed to having nausea, vomiting and diarrhea.

Upon evaluation, she too appeared ill looking, speaking in short sentences with tachycardia of 116 bpm. Her blood glucose was measured to 276 mg/dl with anion gap of 32. Serum bicarbonate of <5 mmol/L, beta hydroxybutyrate was found to be 138 mg/dl.

Upon admission to the ICU, her was 8.1%. She was treated as per DKA treatment protocol again with insulin and bicarbonate drip. She responded well and discharged with increase in her basal doses.

Labs:

	Ref. Range	6/10/2018 14:26
WBC (auto)	Ref Range: 3.8 - 11.0 K/mcL	13.0 (H)
RBC	Ref Range: 4.0 - 5.2 M/mcL	4.73
HGB	Ref Range: 12.0 - 16.0 g/dL	14.8
HCT	Ref Range: 36 - 46 %	45.0
MCV	Ref Range: 80 - 100 fL	95
MCH	Ref Range: 26 - 34 pg	31
MCHC	Ref Range: 31 - 36 g/dL	33
RDW	Ref Range: 10.5 - 13.5 %	12.6
Platelet Count	Ref Range: 150 - 450 K/mcL	276

	Hemoglobin A1C			
Ref. Range	Latest Ref Range: 0 - 5.6 %			
6/10/2018 1426	8.4 * 📤			
6/10/2018 1800	8.1 * 📤			
7/11/2018 1802	8.4 * △			

	Ref. Range	6/10/2018 18:00	6/10/2018 22:45	6/11/2018	6/12/2018 65:07
Sodium	Raf Range: 137 - 145 mmolt.	142	137	130	141
Potassium	Ref Range: 3.5 - 5.1 mmolt.	4.1	3.9	3.3 (L)	3.1(L)
Chloride	Ref Range: 98 - 107 mmolt.	100 (H)	100 (H)	111 (H)	112 (H)
CO2, Total	Ref Range: 22 - 30 mmoit.	<5 (CL)	10 (L)	15 (L)	22
Anion Gap	Ref Range: 6 - 14 mmolt.	24 (H)	19 (H)	12	7
Urea Nitrogen	Ref Range: 7 - 17 mg/dL	15	15	14	11
Creatinine	Ref Range: 0.5 - 1.0 molds.	1.2 (H)	1.1 (H)	1.1 (H)	0.7
Osmolality Calculated	Ref Range: 290 - 305 mOs/Kg H2O	300	290	290	294
GFR Calculation , Non- African American	Ref Range: >60 mL/mn/1.73 m2	47 (L)	52 (L)	52 (L)	Nati
GFR Calculation , African American	Ref Range: >60 mL/mn/1.73 m2	57 (L)	>60	>60	>60
Glucose	Ref Range: 20 - 105	191 (H)	182 (H)	153 (H)	147 (H)

ARTERIAL BG		
pH, Arterial	7.01	1
pCO2, Arterial	8	9
pO2, Arterial	173	4
HCO3, Arterial	2	9
Base Deficit	27	-
O2 Sat, Arterial	98.5	4
FIO2	4LNC	
Allen test	Y	
Site of draw	RRAD	
Total Hgb	13.8	

Post Discharge Follow-Up:

Both patients had SGLT-2 inhibitors discontinued and followed up in clinic within 4 weeks. The first patient's A1c remained stable on moderate carbohydrate intake. Our second patient struggled with achieving euglycemia is still requiring high doses of basal and prandial insulin.

Discussion:

These two cases demonstrate serious negative consequences that can occur with SGLT-2 inhibitor use. Prior to this, one case has been reported of eDKA associated with Dapagliflozin[1] as well as two other a cases of eDKA associated with T1DM.[2] We postulate the common thread of carbohydrate restriction was essential in tipping the balance into DKA without the cardinal feature of hyperglycemia seen in the classical presentations of DKA.

Conclusion:

We present our case series in efforts to raise awareness regarding risk of low carbohydrate diets in patient's prescribed SGLT-2 inhibitors. A detailed history regarding patient's dietary habits and appropriate discussion between the provider and patient is important to prevent serious adverse outcomes in both Type 1 and Type 2 diabetes.

References

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