SGLT2 Inhibitors block the renal resorption of glucose and sodium in the proximal tubules to lower blood sugars. When some are paired with other diabetic medications, like Metformin, this can lead to 2% of people developing hypoglycemia.[1] Hyponatremia is rarer though due to the compensation of the distal tubules by their redundant resorption of sodium.[2] However, during prerenal azotemia the distal tubules resorption of sodium can be impaired.[3] The combination of SGLT2 inhibitors and acute kidney injury (AKI) could be a mechanism for hyponatremia. The purpose of this case study is to review where a patient in diabetic ketoacidosis (DKA) developed a hyponatremia refractory to saline until the SGLT2 inhibitor was discontinued.

A 47-year-old male was admitted to the ICU on DKA protocol. Insulin drip and fluid hydration were started with the intent of lowering the patient's anion gap, resolving his prerenal azotemia and improving his hyponatremia [130]. Initially, the patient began to improve as his anion gap closed. However, during this time the patient was given 3 separate IV saline boluses, but remained hyponatremic. To correct the sodium the patient's SGLT 2 inhibitor was discontinued and it returned to normal [137] without the need for an additional saline bolus. The patient was subsequently discharged home with resolution of his AKI and DKA.

Recognition of refractory hyponatremia secondary to SGLT2 inhibitor prescriptions during AKI is critical to improve outcomes and minimize patient risk. Future studies and monitoring should focus on hyponatremia as a side effect SGLT2s specifically during episodes of prerenal azotemia.

1. Acheson, E.E, Bexagliflozin: Drug Information. In: *UpToDate*, Waltham, MA. (Accessed on July 20, 2023.)
2. Dantzler WH. Regulation of renal proximal and distal tubule transport: sodium, chloride and organic anions. Comp Biochem Physiol A Mol Integr Physiol. 2003 Nov;136(3):453-78. doi: 10.1016/s1095-6433(03)00135-1. PMID: 14613778.
3. Vallon V. Tubular Transport in Acute Kidney Injury: Relevance for Diagnosis, Prognosis and Intervention. Nephron. 2016;134(3):160-166. doi: 10.1159/000446448. Epub 2016 May 31. PMID: 27238156; PMCID: PMC5089910.