The Prevalence and Clinical Characteristics of Adult Patients Presenting with Sodium-Glucose Co-Transporter-2 Inhibitor (SGLT-2i) Associated Euglycemic Diabetic Ketoacidosis

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Background
Sodium-Glucose Co-Transporter-2 Inhibitors (SGLT-2i) have been associated with euglycemic diabetic ketoacidosis (EuDKA). The pathophysiology is related to decreased insulin secretion given glucosuria and a lower insulin- to-glucagon ratio, resulting in enhanced lipolysis and ketogenesis at reduced glucose levels. SGLT-2i may unmask underlying undiagnosed type-1 diabetes, including Latent Autoimmune Diabetes of the Adult (LADA).

Objective
(1) To describe the frequency and clinical characteristics of SGLT-2i associated EuDKA at Kingston Health Sciences Centre. (2) To identify the most common underlying diabetes-type associated with EuDKA.

Methods
A chart review identified patients with SGLT-2i-associated EuDKA from June 2015 to May 2019 who presented to Kingston Health Sciences Centre. Clinical characteristics including age, gender, diabetes type, SGLT-2i drug prescribed, laboratory results at the time of EuDKA and possible precipitants were reviewed. Pancreatic autoantibodies (anti-GAD-65, anti-islet cell, IA-2, and insulin antibodies) were measured to screen for the possibility of undiagnosed Type-1 Diabetes.

Results
There were 647 DKA events of which 43 were related to SGLT-2i (Prevalence 6.64%). Of these events, there were 25 events (58.1%) with euglycemia. In all DKA events, Canagliflozin was the most common SGLT-2i (53.5%) followed by Empagliflozin (34.9%). The most common precipitant was infection (16.3%), followed by surgery (14%). At presentation, average blood glucose was 14.95±12.51 mmol/L, pH 7.23±0.16, HCO3 12.86 ± 5.51 mmol/L, potassium 4.40±0.86 mmol/L and anion-gap 22.05±5.51 mmol/L. Average HbA1c was 9.2%±2.10 and BMI was 29.34±4.49. Twenty patients had pancreatic autoantibodies testing and seven were positive (35%); most commonly anti-GAD-65 (71.4%). As a result, seven patients were diagnosed with LADA who were previously diagnosed with type-2 diabetes. Out of the 7 patients with LADA, 2 had a positive family history of Type-1 Diabetes.

Conclusion
SGLT-2i associated DKA could unmask underlying LADA. Further studies are warranted to determine if routine pancreatic antibodies should be drawn for diabetes typing prior to prescribing or at presentation of SGLT-2i associated DKA.