bcdiabetes.ca
Patient Care + Research + Clinical Trials

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SGLT2 inhibitors & DKA in Type 1 diabetes

There is an increase in the incidence of the life-threatening diabetes complication DKA (diabetic ketoacidosis) in individuals with Type 1 diabetes who are receiving SGLT2 inhibitors (SGLT2i). SGLT2i on the Canadian market include canagliflozin (Invokana), dapagliflozin (Forxiga), empagliflozin (Jardiance). Sotagliflozin is currently not approved for use in Canada in either Type 1 or Type 2 but is before Health Canada for Type 1 diabetes at the time of writing.

In clinical trials of SGLT2i in Type 1 diabetes the incidence of DKA in subjects randomized to SGLT2 is roughly double that of those who receive placebo, equivalent to one additional episode of DKA per 100 patients (see Dandona 2017 for dapagliflozin & Garg 2018 for sotagliflozin). Physician readers may find the review article of the use of SGLT2i in Type 1 diabetes by McCrimmon 2018 of interest.

Note the only SGLT2i currently prescribed by Dr. Elliott in Type 1 diabetes are dapagliflozin in a dose of 5 mg daily and empagliflozin 2.5 mg daily (¼ 10 mg tab). These prescriptions are "off-label" meaning that their use is not approved by Health Canada.

The earliest stage of DKA can be detected & treated before the need for hospitalization using a blood ketone meter. Blood ketone meters measure beta-hydroxybutyrate (BHB). BCDiabetes recommends using either the Freestyle Precision Neo meter or the Freestyle Libre continuous glucose meter both of which double as glucose meters.

To prevent DKA, and if necessary treat DKA in the early stages BHB levels should be measured in all Type 1 diabetes prescribed SGLT2i who feel unwell (unable to maintain oral intake, or who have generalized weakness, excessive thirst, abdominal pain, nausea, vomiting, weight loss, fever, frequent urination, fruity-scented breath, confusion, acute illness) & have sugars consistently > 9 mM (163 mg/dL). Note, the normal range of BHB is < 0.6. A ketone value of 0.6 or higher is abnormal* and requires immediate action - action is "sick day" management.

Sick day management includes
1) temporarily stopping SGLT2 inhibitor (if applicable); and
2) pushing salty fluids: take 1 cup of beef, chicken or vegetable broth every 30 minutes (or make up your own salt solution by adding ½ teaspoon salt per cup or 2 teaspoons per litre); and
3) taking extra insulin if sugar > 10. An hourly bolus of rapid insulin equivalent to 15% of the average total daily insulin dose is recommended (example: if you take Lantus 34 units once daily and rapid insulin 12@ breakfast, 12@ lunch and 14@ dinner total daily dose = 34+12+12+14=70 units. Fifteen percent of 70 = 10.5 units so take 10 or 11 units every hour).

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4) if sugar < 10.0 take 30 grams of glucose or simple starch every 30 minutes; and
5) remeasuring ketones every 2 hours until <0.6 twice consecutively. If ketones remain > 0.6 or sugar > 15 after 4 hours the patient should go to hospital. Any individual unable to keep fluids down with sugar > 15 should go to hospital immediately.

Note it is normal for BHB levels to rise into the 0.6-4.0 range after periods of fasting for >24 hours or during "ketogenic" diets (very low carbohydrate, restricted protein, high fat diets) whether or not they have Type 1 diabetes. Providing individuals feel well and their sugar is <10 elevated BHB levels in the 0.6-4.0 range is of no concern.

This document can also be accessed using https://goo.gl/cR8VKk
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