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Patient Care + Research + Clinical Trials

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SGLT2 inhibitors

Dr. Elliott has prescribed a drug from the SGLT2-inhibitor class to more than 1000 patients with Type 2 diabetes and 50 patients with Type 1 diabetes. There are three drugs in this class on the Canadian market: canagliflozin (Invokana),dapagliflozin (Forxiga) & empagliflozin (Jardiance). In September 2016 he blogged on this extraordinary class of drugs (see http://www.bcdiabetes.ca/empa-reg-outcome-renal/).

BC remains the only Canadian province not to cover this life-saving class of medication (see below). On 2016-Nov-10 Dr. Elliott launched a petition to lobby BC Pharmacare to cover the SGLT2 inhibitor class. As of today 1100 individuals have signed the petition - the goal is 20,000. If you haven't already signed the petition please do so now. For more up-to-date information on this campaign and diabetes in general please like the BCDiabetes Facebook page.

The most important benefits of SGLT2 inhibitors are that they lower sugar and weight without causing hypoglycemia (low sugar). Most diabetes medications are associated with weight gain. SGLT2 inhibitors reduce mortality by 32% in individuals with Type 2 diabetes at high risk (those with a past history of heart attack, bypass or stent or stroke): for the evidence follow this link. In addition there is strong evidence that SGLT2 inhibitors improve outcomes for individuals with Type 2 diabetes & kidney disease (for the evidence follow these two links study1 and study2; see further discussion below under "Reduction of eGFR".

The ability of these drugs to lower blood sugar and to cause weight loss is proportional to the elevation of blood sugar. For patients with fasting sugar > 10 they are remarkable effective but they remain effective even for patients with sugar in the 6-8 range before breakfast. All individuals treated with SGLT2 inhibitors will have an increase in urine flow - this is an indirect effect of the drug, not a side-effect. Blood sugar and weight decrease with the SGLT2 inhibitors because these drugs cause wasting of sugar in the urine, the additional sugar in the urine drags water with it by a process called osmosis resulting in increased urine volumes. The higher the blood sugar the greater the urine flow - in some patients this will cause excessive nighttime urination which may necessitate stopping therapy.

There is only one common side-effect, the development of genital yeast infections: in women this is experienced as vaginal thrush (also known as candida, commonly experienced as itch and white discharge). Approximately 6% of women will get one infection during a year of therapy. In men balanoposthitis (soreness & redness on the tip of the penis/glans and under the foreskin) may occur. For both men and women treatment with anti-fungal agents is generally effective. Dr. Elliott usually provides a prescription for anti-fungal therapy at the time of prescription. The standard treatment for both sexes is oral fluconazole: take three 50 mg tablets by mouth in one go. This is usually curative within 3 days. The dose may be repeated once within two weeks. If not effective patients should see their family physician. *Note fluconazole interacts adversely with two commonly used medications: the blood-thinner warfarin*

"Coumadin" & the blood pressure pill sotalol. Individuals taking either of these agents should not receive fluconazole. For men an alternative treatment is to apply ketoconazole 2% cream to the affected area twice daily as necessary. It may be repeated frequently or even used on a daily basis.

There are two serious potential side-effect which fortunately are rare: these are 1) serious reduction in kidney (renal) function and 2) diabetic ketoacidosis (DKA)

reduction of eGFR (kidney function)

SGLT2 inhibitors exert numerous beneficial effects upon the diabetic kidney. The net effect is an overall improvement in kidney prognosis. A drop in kidney function, as measured by eGFR (normal >60) is common and expected during the first 10-30 days of therapy. In most cases eGFR returns to normal by 3 months. In some patients eGFR remains lower than pre-treatment. Paradoxically this drop in eGFR is considered by kidney experts to be a positive sign. The background reasoning is complex: in simple terms diabetic kidney disease is associated with hyperfiltration; hyperfiltration leads to a higher GFR than would normally be expected but damages the kidney in the long term. SGLT2 inhibitors, through their many effects, stop hyperfiltration, lower the eGFR and thus protect the kidney.

Most patients prescribed these drugs have normal kidney function (eGFR is a value >60). Dr. Elliott routinely uses SGLT2 inhibitors in individuals with eGFR >30; he is involved in research examining the safety and efficacy of SGLT2 inhibitors in patients with eGFR 15-30.

SGLT2 inhibitors occasionally cause significant volume contraction (loss of salt and water, a form of dehydration) that excessively reduces eGFR. To anticipate the development of this side-effect Dr. Elliott routinely measures kidney function in all patients before starting these medications & 10-14 days after starting these medications using a requisition such as this. Note, eGFR is calculated from the serum creatinine using a formula that corrects for age & gender. Reported eGFR values assume the patient to have a standardized body surface area of 1.73 m2 (for example: height 5'7", weight 140). Thus reported eGFR tends to be underestimated in larger individuals and overestimated in smaller individuals.

A reduction in eGFR of >30% 10-14 days after commencing SGLT2 inhibitor requires attention - patients with a reduction in eGFR of >30% should take a high salt diet such as chicken or vegetable broth twice daily for 4-5 days then repeat the eGFR. If the eGFR is still >30% below the baseline value it should be stopped.

Diabetic ketoacidosis (DKA)

DKA is a rare complication with SGLT2 inhibitors but is seen more commonly in Type 1 diabetes - thus for individuals with Type 1 diabetes receiving SGLT2 inhibitors a routine screening program for serum ketones (BHB) is strongly recommended (see https://goo.gl/cUfPHs). For individuals with Type 2 diabetes the risk is very low; no routine screening for DKA is either recommended or required. In the rare circumstance that ketosis is a concern the measurement of serum ketones is recommended on a one-off basis.

This document can also be accessed using https://goo.gl/J6pc5C
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