

Helping Your Patients Stay on Their SGLT2 Inhibitor

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Within Canada, the prevalence of type 2 diabetes (DM2) and pre-diabetes is increasing. Sodium-glucose cotransporter-2 inhibitors (SGLT2i) have demonstrated benefits in these patient populations who also have cardiac and renal risk factors. In our practice as Cardiovascular Nurse Practitioners (NP), some people who were started on a SGLT2i report that they stopped therapy because of what were described as adverse events. A poor experience makes it challenging for NPs to reinstate therapy due to patient hesitancy; to avoid this situation and improve compliance, prescribers should screen patients for potential problems and address these issues prior to initiating SGLT2i therapy.

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Diabetes is a chronic endocrine disease that manifests via inadequate insulin production or utilization resulting in elevated blood glucose levels. The poor delivery of glucose to cells for energy synthesis leads to potential complications, including cardiovascular disease, neuropathy, nephropathy and retinopathy (Leblanc et al., 2019). It is estimated that among Canadians ages 20 to 79 years, 12.4% have pre-diabetes and 7.5% have DM2. The prevalence of both pre-diabetes and DM2 increases with age (Hussein et al., 2019).

The Diabetes Canada Clinical Practice Guidelines were updated in 2020 to include SGLT2i in the first line of medication, after metformin, for patients whose glycated hemoglobin (HgbA1c) is greater than 1.5% above target, and in patients who have one or more of the following; atherosclerotic cardiovascular disease (ASCVD), chronic kidney disease (CKD), or heart failure (HF); and in patients over the age of 60 years with two cardiovascular risk factors (Lipscombe et al., 2020). The updated guidelines reflect the cardiovascular (CV) benefits SGLT2i provide to patients who have cardiac risk factors but are not yet diagnosed with ASCVD. SGLT2i also are effective in slowing the progression of CKD, reducing the risk of hospitalization for patients with HF and their use has been associated with weight loss, which can be of further benefit to some patients with DM2 (Lipscombe et al., 2020).

Addressing Common Issues that Prevent Compliance with SGLT2i Use

Urinary Tract and Yeast Infections

SGLT2i function by inhibiting the reabsorption of glucose in the proximal tubule of the loop of Henle, which results in the excretion of excessive glucose in the urine. The resulting higher glucose concentration in the perineum increases proliferation of both bacteria and yeast, especially in women (Khan et al., 2020). Therefore, people who are already at risk of urinary tract infections (UTI) may report more frequent UTI after starting SGLT2i therapy (Khan et al., 2022). Recent studies have demonstrated, however, that for patients who do not already suffer from frequent UTI issues, the risk of developing an infection while using a SGLT2i was no higher than the placebo group (Sarafidis & Ortiz, 2020). The onus therefore, falls on the prescriber to identify all pre-existing UTI risk factors and address/provide health teaching to reduce the occurrence of UTI (Table 1) prior to initiating SGLT2i therapy.

Hypotension and Dehydration

SGLT2i are effective in heart failure management primarily due to the diuretic effect, decrease in intravascular volume, and the promotion of natriuresis (Lopaschuk & Verma, 2020). Studies have also identified a 4.9% to 10.4% reduction in systolic blood pressure for patients on SGLT2i (Kario et al., 2021; Weber et al., 2015). Both mechanisms of action, however, can lead to volume depletion, dizziness, and an increased risk of accidents, such as falls (Pittampalli et al., 2018; Lopaschuk & Verma, 2020). SGLT2i therapy, therefore, should not be initiated on patients with pre-existing hypotension or hypovolemia. Prescribers must be aware of this action and be cautious when starting a SGLT2i, closely monitoring the effect on BP as the patient reaches their target and then decreasing or eliminating other anti-hypertension agents and diuretics as needed (Lam & Shaikh, 2021). The objective is a slow and consistent improvement in BP and blood glucose management in order to help the patient establish and maintain confidence in the SGLT2i agent. Patients should receive health teaching regarding the potential for dizziness, the importance of adequate fluid intake and monitoring their BP.

Hypoglycemia

Due to the mechanism of action; eliminating excess glucose from the blood stream via the kidneys and excreting it in urine; the risk of hypoglycemia for patients on SGLT2i is very low. However, this risk increases for patients using insulin or insulin secretagogues (Lipscombe et al., 2020) and the guidelines from Diabetes Canada suggest caution when adding a SGLT2i to these patients' treatment regime. If the SGLT2i is being added for its renal and cardiovascular benefits, other medications that increase the risk of hypoglycemia should be stopped or their dose reduced (Lam & Shaikh, 2021; Lipscombe et al., 2020). Patients should also be educated about blood glucose monitoring, and preventing, detecting, and treating

Table 1: Addressing Common Issues that Prevent Compliance to SGLT2i Therapy

Issue	Possible Solution
Urinary Tract Infection	<ul style="list-style-type: none"> • Improve washroom hygiene, including wiping front to back for women • Increase water intake • Urinate regularly; avoid holding urine for long periods of time • Improve peri-care and encourage voiding after sex • Correct use of antibiotics • UTI prevention plan (i.e. cranberry juice daily)
Yeast Infection	<ul style="list-style-type: none"> • Choose loose fitting cotton garments instead of synthetic fabrics • Keep genital areas dry and maintain good hygiene • Treat with over-the-counter products such as clotrimazole at the first sign of infection
Dehydration	<ul style="list-style-type: none"> • Awareness of signs of dehydration • Awareness of dizziness and actions to minimize effect • Adequate oral intake of water • Limited intake of coffee, tea, and soda drinks • Monitor output and increase fluid intake • Awareness of effect of increased activities in hot, humid environment
Hypotension	<ul style="list-style-type: none"> • Monitor blood pressure • Awareness of dizziness and act to minimize its effect • Frequent follow up with practitioner
Hypoglycemia	<ul style="list-style-type: none"> • Prescriber caution when adding to a medication regimen with risk of hypoglycemia (i.e. risk medication such as insulin or sulfonylureas) • Glucose monitoring • Hypoglycemia health teaching (signs, symptoms, and treatment) • Frequent follow up with practitioner
EDKA	<ul style="list-style-type: none"> • SADMANS health teaching • Sick day management health teaching • Importance of telling care providers you are on a SGLT2i, especially if having surgery or have an infection • Patients who have had bariatric surgery are at greater risk

hypoglycemia. If mealtime insulin is added, begin with one meal injection per day and consider stopping any sulfonylureas (Lipscombe et al., 2020).

Euglycemic Diabetic Ketoacidosis (EDKA)

EDKA is a clinical syndrome whereby a patient presents with euglycemic (normal) blood glucose levels, however, is suffering severe metabolic acidosis. In patients taking SGLT2i, the general state of carbohydrate deficiency results in a decrease of serum insulin while simultaneously having

excessive counter-regulatory hormones such as glucagon, epinephrine, and cortisol. The increased glucagon to insulin ratio leads to elevated lipolysis and increased free fatty acids resulting in ketoacidosis (Plewa et al., 2020). Serum glucose levels remain normal and do not elevate as would be seen in typical cases of diabetic ketoacidosis however, because glucose is secreted by the kidneys and eliminated in the urine, which is the normal mechanism of action of SGLT2i. Upon patient presentation to a care provider or in the emergency department, the signs of the resulting anion gap and metabolic acidosis presents as nausea, vomiting and respiratory compensation, with a normal blood glucose level, making an accurate diagnosis of EDKA easy to miss (Plewa et al., 2020).

Education about sick day management is paramount and needs to be reviewed at every patient encounter. SADMANS, which is an acronym identifying medications that should be temporarily stopped when a patient has an illness that puts them at risk of dehydration; for example high fever, vomiting, and/or diarrhea; includes SGLT2i class on its list. (Table 2) Patients therefore, should be instructed to hold administration if they feel unwell. Despite any nausea the patient may feel, fluid intake should be stressed and patients should continue to monitor blood glucose levels; if within normal range they should continue to take in carbohydrates as liquids or food (Lipscombe et al., 2020).



Patients should also be educated about blood glucose monitoring, and preventing, detecting, and treating hypoglycemia.





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Table 2: SADMANS medications	
S	= Sulfonylureas, other secretagogues
A	= ACE inhibitors
D	= Diuretics direct renin inhibitor
M	= Metformin
A	= Angiotensin receptor blockers
N	= Nonsteroidal anti-inflammatory drugs
S	= SGLT2 inhibitors

SGLT2i have demonstrated benefits for patients with ASCVD, HF, and renal complications who also have diabetes, as well as assisting people in managing their chronic disease through weight loss. An assessment of the potential side effects prior to initiating SGLT2i therapy, followed by proactive medication changes and patient health teaching, offers increased therapy compliance, which in turn, provides the greatest value for patients who would benefit from SGLT2i treatment.

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