My First Medical Writing

Editorial

In this release of My First Medical Writing, we welcome one of the first articles written by Robin Sachdeva. Robin finished his PhD at Heidelberg University in Germany, and he is passionate about reading and writing about diabetes. Fortunately, since we started working together on this article, he transitioned from being an "aspiring medical writer" to being hired as a research scientist in Canada. He is now involved in designing clinical trials, preparing comprehensive final reports, and writing manuscripts. It has been a great pleasure to share this journey with him, seeing him grow in his writing skills, and now publishing his first article in *Medical Writing*.

One drug, many benefits:
Promising outcomes from a new class of antidiabetic drugs

SECTION EDITOR

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Can you imagine how much damaging power a glucose molecule possesses? In patients with diabetes, long-term high blood glucose levels can lead to limb amputation, blindness, kidney dysfunction, or cardiovascular disease. Such an uncontrolled increase in blood glucose can be due to the autoimmune destruction of pancreatic ß cells (type 1 diabetes) or insulin deficiency combined with insulin resistance (type 2 diabetes).

There have been many approaches to treat diabetes and its associated complications. The first-ever commercially available antidiabetic agent was insulin.[1] Most antidiabetic drugs seek to lower blood glucose levels by increasing either insulin secretion by the pancreas or insulin sensitivity and, therefore, can lead to potentially fatal hypoglycaemia.

Sodium glucose co-transporter-2 (SGLT2) inhibitors, the most recently developed class of antidiabetic drugs, act independently of the insulin pathway. SGLT2 inhibitors include empagliflozin, canagliflozin, dapagliflozin, and ertugliflozin. Canagliflozin was the first to be approved in 2013 and, as of 2019, four drugs of this class have been approved by the FDA. These molecules act in the kidneys where they block SGLT2 proteins, which are the prime mediators of renal glucose reabsorption in the proximal tubules (Figure 1). Consequently, by removing excess glucose from the blood, SGLT2 inhibitors maintain normal blood glucose levels.[2]

The most stunning result from clinical studies is that SGLT2 inhibitors confer cardiovascular benefits to patients with diabetes.[3,4] In contrast to other antidiabetic drugs, the use of SGLT2 inhibitors reduce cardiovascular-related mortality risk in patients with type 2 diabetes.[5] Because SGLT2 inhibitors do not affect insulin secretion or action, unlike other antidiabetic drugs (e.g., sulfonylureas), they have low risk of inducing hypoglycaemia. In clinical trials, SGLT2 inhibitors reduced fasting blood glucose and HbA1c levels that are the markers most commonly used for diagnosing diabetes.[6] Interestingly, SGLT2 inhibitors can cause weight loss and blood pressure reduction, probably by increasing glucose and sodium secretion.[7]

Although these clinical studies are promising, SGLT2 inhibitors may cause urogenital tract infections by increasing urinary glucose levels. SGLT2 inhibitors may also increase the risk of stroke and diabetic ketoacidosis (i.e., high blood ketone levels), although the mechanisms are not fully understood.[8,9] SGLT2 inhibitors can be prescribed alone (monotherapy) or in combination with other antidiabetic agents (e.g., metformin) for patients who cannot substantially reduce their glucose levels with only one drug.[10]

SGLT2 inhibitors act *via* a novel mechanism to control blood glucose levels. Although SGLT2 inhibitors can cause diabetic ketoacidosis and urinary tract infections, they can still be used in carefully selected patients. In the future, these inhibitors may be utilised for diabetic patients with hypertension, but more clinical studies will be needed to verify benefits other than their ability to normalise glucose levels.

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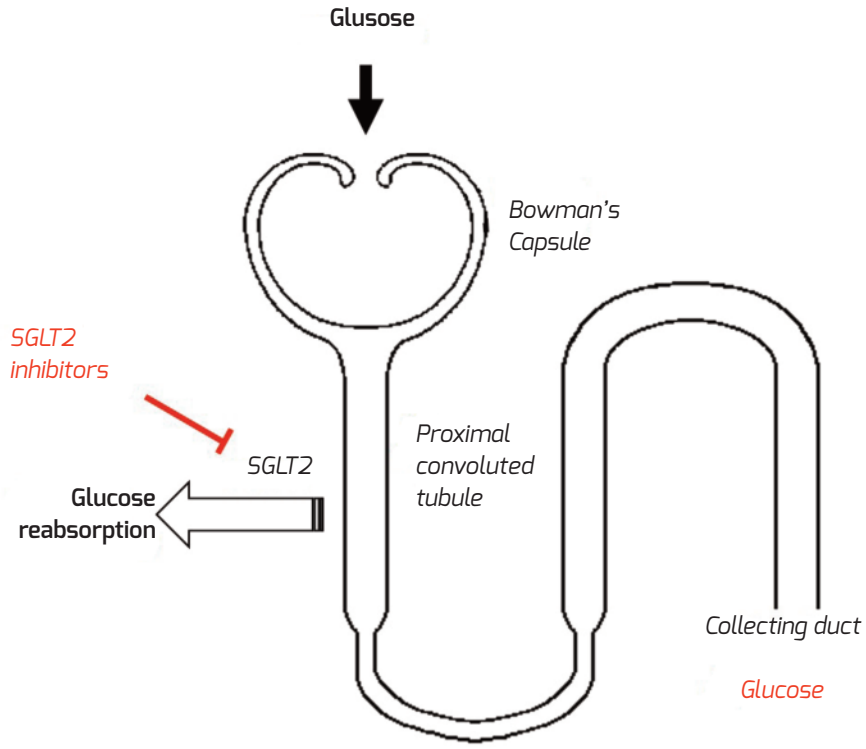

Figure 1. Mechanism of action of sodium glucose co-transporter-2 (SGLT2) inhibitors in a nephron. Under physiological conditions, most of the glucose in the blood is filtered through the Bowman's capsule and reabsorbed by SGLT2 proteins present in the proximal convoluted tubule. SGLT2 inhibitors normalise blood glucose levels by blocking glucose reabsorption and inducing the elimination of glucose through urine.

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