Acute pancreatitis in the use of canagliflozin: A rare side-effect of the novel therapy for type 2 diabetes mellitus

Abstract

Canagliflozin (Invokana) is an innovative treatment for type 2 diabetes mellitus (DM) approved in a new class acknowledged as sodium-glucose co-transporter 2 inhibitors. Acute pancreatitis is a very rare side effect with an incidence <1%. a 50-year-old white male with DM type 2 presented to the emergency department with acute onset of abdominal pain after 4 days treatment with canagliflozin. He was successfully diagnosed with diabetic ketoacidosis induced by acute pancreatitis. Canagliflozin was discontinued. His diabetic ketoacidosis was improved after aggressive intravenous fluid along with intravenous insulin infusion. Our case demonstrates very rare but serious side effect, acute pancreatitis in the use of canagliflozin. As the utility of canagliflozin expands, physicians must be aware of this potentially fatal adverse effect. More specific details on potential candidates for this novel therapy are urgently needed.

Key words:
Canagliflozin, diabetes ketoacidosis, diabetes mellitus, pancreatitis

Introduction

Canagliflozin (Invokana) is a novel therapy for type 2 diabetes mellitus (DM) approved in a new class acknowledged as sodium-glucose co-transporter 2 (SGLT2) inhibitors. Canagliflozin inhibits the glucose reabsorption by the kidney, increasing glucose elimination and reducing blood glucose levels in diabetic patients. Acute pancreatitis is a very rare but severe side effect with an incidence <1%. We report a case of a 50-year-old man who received a few doses of canagliflozin and developed pancreatitis-induced diabetic ketoacidosis requiring hospitalization in the intensive care unit.

Case Report

A 50-year-old white man presented to the emergency department with malaise, weakness, abdominal pain, and loss of vision that progressively worsened over 3 days. He has a history of a long-standing well-controlled type 2 DM treated with insulin, glyburide, and metformin. 4 days before admission his endocrinologist stopped his Lantus (insulin glargine) and prescribed him on canagliflozin 100 mg oral daily along with glyburide and metformin. After 10 days of treatment, he developed malaise, weakness, abdominal pain that progressively worsened. On the day of the presentation, he developed blurry vision.

Physical examination in the emergency department was remarkable for dry lip and epigastric tenderness. Blood test showed blood glucose of 506 mg/dL; sodium of 125, potassium 6.8, chloride of 94, total carbon dioxide <5 and anion gap of 26 mEq/L; creatinine 2.0 mg/dL, trop I was negative; amylase 643, lipase 982 U/L, aspartate aminotransferase 18 U/L; total bilirubin 0.9 mg/dL; atrial blood gas pH 6.85, partial pressure of carbon dioxide 11 mmHg, partial pressure of oxygen 149 mmHg, bicarbonate 1.9 mmol/L, and electrocardiogram showed normal sinus rhythm but no ST-T change. He was diagnosed diabetic ketoacidosis induced by acute pancreatitis along with acute kidney injury from dehydration. Computed tomography of abdomen demonstrated the evidence of acute inflammation of pancreas. Abdominal ultrasound revealed no gallstones or bile duct dilatation. The patient denied any history of recent alcohol use and his serum triglyceride level was normal at 95 mg/dL (normal range, <150 mg/dL). Therefore, canagliflozin was likely the cause of acute pancreatitis in this case. The patient was treated with aggressive intravenous fluid along with intravenous insulin infusion. His serum creatinine,
sodium, potassium, lipase, and amylase level returned to normal after 3 days, and we could stop insulin infusion after the anion gap returned to the normal range. His visions returned to baseline after his blood glucose was well controlled. Canagliflozin was completely discontinued and subcutaneous glargine insulin was restarted. The patient continues to do well at 2-month follow-up visit without any recurrent symptoms.

**Discussion**

Canagliflozin is one of SGLT2 inhibitors and has been approved by the Food and Drug Administration for type 2 DM by inhibiting SGLT2 in the proximal renal tubules. Canagliflozin reduces the reabsorption of filtered glucose from the tubular lumen and lowers the renal threshold for glucose (RTG). SGLT2 is the main site of filtered glucose reabsorption; reduction of filtered glucose reabsorption and lowering of RTG result in increased urinary excretion of glucose, thereby reducing plasma glucose concentrations. Its safety and effectiveness were assessed in nine clinical trials involving over 10,285 patients with type 2 DM. The trials demonstrated improvement in fasting plasma glucose and glycosylated hemoglobin levels.[1]

The most common adverse effects described in the clinical trials were genital yeast infections, urinary tract infections, and increased urination.[4] Anaphylaxis,[5] acute respiratory distress syndrome,[4] or significant electrolyte abnormalities[5] have not been demonstrated in the literature review. An ongoing trial, CANagliflozin cardioVascular Assessment Study,[6] will provide us more information on risks of malignancies, serious cases of pancreatitis, and other adverse events.

In summary, our case demonstrates very rare but serious side-effect, acute pancreatitis in the use of canagliflozin. As the utility of canagliflozin expands, physicians must be aware of this potentially fatal adverse effect. More specific details on potential candidates for this novel therapy are urgently needed.

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