

Dapagliflozin: A new drug for treatment of type 2 diabetes mellitus

Sir,

Type 2 diabetes mellitus is a complex and progressive disease characterized by elevated blood glucose which is frequently associated with other co-morbidities such as obesity, hypertension, and dyslipidemia. Significant unmet needs exist as nearly half of the patients of diabetes mellitus remain uncontrolled on their current treatment regimen.^[1]

The kidneys play a key but underappreciated role in the overall regulation of blood glucose levels in the body. Normally, in healthy individuals, the kidneys filter a large volume of glucose and actively reabsorb virtually all of it. Glucose reabsorption is necessary to retain calories, but becomes counterproductive in type 2 diabetes mellitus. In patients with hyperglycemia, a greater amount of glucose is filtered and reabsorbed by

the kidneys, which contributes to sustained hyperglycemia in diabetes.^[2] Over time, sustained hyperglycemia worsens insulin resistance and contributes to dysfunction in the beta cells of the pancreas further undermining control of the disease. Sustained hyperglycemia is also directly related to diabetic microvascular complications such as blindness and may also contribute to macrovascular complications.^[2]

Dapagliflozin a new drug for treatment of diabetes mellitus type 2 aims to lower the blood glucose, by improving glycemic control independent of insulin action. The drug reduces renal glucose reabsorption and increases the elimination of glucose in the urine. Dapagliflozin is intended for treatment of diabetes mellitus type 2.^[3]

Sodium-glucose transport proteins (SGLT2) is responsible for at least 90% of the glucose reabsorption in the kidney. Dapagliflozin

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is a selective sodium-glucose cotransporter-2 inhibitor and works by preventing reabsorption of glucose in the kidneys and promotes the excretion of glucose in the urine. The drug thereby reduces high levels of blood glucose without affecting insulin-dependent systems.^[3]

In a recent phase 3, multicentric study, 534 adults with type 2 diabetes mellitus were selected. All the volunteers were receiving at least 1500 mg of metformin per day but still had poor glycemic control. The participants were randomly assigned to receive one of three doses of dapagliflozin or placebo (n = 134) orally once daily, in addition to receiving their prestudy metformin dosing. The primary outcome measure was to measure the change in levels of hemoglobin A1c (HbA1c) at 24 weeks. The study found that mean HbA1c decreased significantly (statistically) in the groups receiving dapagliflozin.^[2]

Dapagliflozin causes hypoglycemia and genital infections in 8% to 13% of patients who are on this drug. However, it has also been noted in various clinical trials that the adverse drug reactions are not life threatening and the drug is generally considered safe for patients with type 2 diabetes mellitus.^[4]

Given with metformin, dapagliflozin represents a new therapeutic option for the treatment of patients with type 2 diabetes who have inadequate glycemic control with metformin alone.^[2]

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