SGLT2 inhibitor use in adult GSD1a - a case report of improved glucose homeostasis without worsening of hypoglycemia

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Background:
GSD1a, also known Glucose 6 Phosphatase(G6Pase) deficiency, results from inability of the hydrolase subunit (G6Pase-α) to hydrolyze Glucose6-phosphate (G6P), impairing last step of gluconeogenesis with resultant hypoglycemia, hyperuricemia and hyperlipidemia.

G6Pase is encoded by G6PC gene (OMIM#613742) located on chromosome 17q21.31.

Management often requires frequent feeding including use of cornstarch to prevent hypoglycemia. And, predispose many GSD1a patients to have increased BMI into adulthood.

Purpose:
To describe clinical outcomes of SGLT2 inhibitor, empagliflozin use in a adult GSD1a patient of Mexican descent born of consanguineous union, diagnosed with G6PC homozygous c.379_380dup (p.Y128Tfs*3) frameshift mutations in the third decade of life.

Findings:
Clinical presentation included history of recurrent hypoglycemia and hyperglycemia, hepatosplenomegaly, hepatocellular adenomas, lactic acidosis, hyperlipidemia, chronic kidney disease, hearing loss and borderline to extremely low cognitive ability, increased BMI and type 2 diabetes, and use of cornstarch 3-4 times a day.

Treatment /Intervention:
After trial of lifestyle modifications, nutritional compliance with Q4-6 hours of low-glycemic-index foods, exercise, gluco-monitoring, patient’s corn starch use was limited to bedtime due to early morning hypoglycemia. These had minimal impact to daytime hyperglycemia, HbA1c levels and GSD1a metabolic complications despite some weight loss with exercise and improved nutritional compliance.

SGLT2 inhibitor, empagliflozin, used for Type 2 diabetes, used once daily (0.08mg/kg/day) showed rapid alleviation of hyperglycemia and improved glucose homeostasis within a month of treatment, with one episode of asymptomatic hypoglycemia (resolved with oral intake) during a bacterial infection.

Conclusion:
SGLT2 inhibitors can help treat glucose intolerance without worsening of hypoglycemia in GSD1a.

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