Abstract #209371

Impact of Sglt-2 Inhibitors on Sickle Cell Disease Patients with Type 2 Diabetes: A Retrospective Matched Cohort Study

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Introduction: Sickle cell disease (SCD) is associated with an increased risk of chronic kidney disease (CKD), with 12% of patients developing CKD by a median age of 37 years in one large 40 year longitudinal study. Glucagon-like peptide-1 (GLP-1) agonists and sodium-glucose cotransporter-2 (SGLT-2) inhibitors have demonstrated reno-protective benefits in type 2 diabetes mellitus (T2DM) and CKD, but their efficacy in SCD nephropathy is not well studied. A retrospective analysis of 7 SCD patients with T2DM found observed treatment with GLP-1 agonists or SGLT-2 inhibitors improved estimated glomerular filtration rate (eGFR) slope, but increased the rate of vaso-occlusive pain episodes (VOEs). Additionally, a large placebo-controlled study showed that empagliflozin increased hemoglobin (Hgb) levels in patients with T2DM, but no SCD. In the previous study, serum erythropoietin (EPO) levels were found to be inappropriately normal or increased in all 27 patients with EPO tested, with a median of 10.3 mIU/mL (6.1-37.3 mIU/mL)

Methods: Using a large federated network database, we identified 75 patients with SCD and T2DM. Less than 20 patients had CKD. For our control group, we had 2,366 patients with SCD and T2DM, who were not on SGLT2 inhibitor therapy. There were 1,754 patients with CKD in this group. In this retrospective study, we matched 65 patient in SGLT2 cohort to 65 control group patients based on sex assigned at birth, age and co-morbidities including stage of CKD (if present), hypertension, obstructive lung disease and heart failure.

Results: We did not observe statistically significant differences in the risk of progression or development of CKD. Similarly, we observed no significant difference in proteinuria, A1c and microalbuminuria between the two groups when comparing mean lab-values on student t-test. However, patients on SGLT-2 inhibitors had significantly higher mean Hgb levels (12.459 g/dL) compared to controls (10.358 g/dL; $p<0.0001$).

Discussion: Putative mechanisms for this erythrocytosis include increased erythropoietin production, modulation of iron metabolism, and hemoconcentration. The inappropriately normal or increased EPO levels observed in previous study support the role of EPO in the erythrocytosis associated with SGLT-2 inhibitor therapy. The observed increase in Hgb levels in SCD patients with T2DM treated with SGLT-2 inhibitors could potentially increase the risk of VOEs, as seen in a previous small study. Further research is needed to elucidate the risks and benefits of SGLT-2 inhibitor therapy on SCD-related nephropathy.

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