DIABETIC COMPLICATIONS ASSOCIATED WITH SGLT2 AND DPP4 INHIBITORS: A REAL WORLD APPROACH

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OBJECTIVES
Prior studies have investigated and shown an association between use of sodium glucose co-transporter 2 (SGLT2) inhibitors with serious adverse events (SAEs), including lower limb amputation, acute kidney failure, diabetic keto-acidosis and acute pancreatitis (1, 2). This study aimed to investigate whether there is any difference in the risk for these SAEs when comparing sodium glucose co-transporter 2 (SGLT2) inhibitors, to dipeptidyl peptidase-4 (DPP4) inhibitors in a real world setting.

METHODS
Real world data, composed of electronic medical records, pharmacy records and insurance claims, from approximately 190 million U.S. patients were analyzed using TriNetX Analytics. Type 2 diabetes patients were defined with the ICD-10 code, E11 and two unique cohorts were defined for patients treated with SGLT2 inhibitors and DPP4 inhibitors (figure 1). In both cohorts, medication adherence was specified as having a second documentation of either SGLT2 inhibitors or DPP4 inhibitors in the SGLT2 and DPP4 cohorts respectively two years after the initial documentation. Patients who took drugs from the other anti-diabetic classes including thiazolidinediones, sulfonylureas or metformin were excluded from the analysis. Those who may have switched from taking SGLT2 inhibitors to DPP4 inhibitors or vice-versa were also excluded from the respective cohorts. The index event was defined as initiation of either SGLT2 or DPP4 inhibitors for type 2 diabetes. Medical diagnosis (ICD-10), lab (LOINC) and procedural (CPT) codes were used to define primary outcomes, which included acidosis (ICD-10 codes: E87.2, and LOINC codes: 9021, 584-8), acute kidney failure (ICD-10 codes: N17, N18, N19), acute pancreatitis (ICD-10 codes: K84.9, K85.9) and lower limb amputation (ICD-10 codes: Z84.9, Z85.5, Z86.6 and CPT codes: 1005524, 1005529, 1014590, 28820, 27880, 28810, 1001146, 1014580, 27950, 28825, 1005525, 28805, 27882, 27886), with an observation period between 7 days to 5 years after medication initiation. Risk ratios (RR) with 95% confidence intervals (95% CI) were calculated and propensity score matching used to balance cohorts and adjust for 22 most likely confounders (table 1). Propensity scores were matched 1:1 using a nearest neighbor matching (caliper of 0.25 times the standard deviation).

RESULTS
In the balanced cohort of 10,538 patients, use of SGLT2 inhibitors, compared to DPP4 inhibitors was associated with a lower risk for acidosis RR (95% CI) 0.51 (0.43,0.60), amputation RR (95% CI) 0.56 (0.42,0.74), acute kidney failure RR (95% CI) 0.26 (0.20,0.31), but not with acute pancreatitis RR (95% CI) 1.5 (0.88,2.57) (table 3). In this real world analysis, use of SGLT2 inhibitors was associated with a lower risk for acidosis, acute kidney failure and lower limb amputation, but not acute pancreatitis as compared with DPP4 inhibitors.

CONCLUSIONS

Figure 1. Study population

Figure 2. Baseline co-morbidities and medications (before and after propensity score matching)

Table 1. Baseline demographics (before propensity score matching)

Table 2. Propensity score matching characteristics

Table 3. Risks and risk ratios (SGLT2 inhibitors vs DPP4 inhibitors)

1.Ueda et al. Sodium glucose cotransporter 2 inhibitors and risk of serious adverse events: nationwide register based cohort study. 2018; 363: k4365
2. Chang et al. Association Between Sodium-Glucose Cotransporter 2 Inhibitors and Lower Extremity Amputation Among Patients With Type 2 Diabetes. JAMA Internal Medicine. 2018; 178:9