Safety analysis of sodium-glucose co-transporter 2 inhibitor administration in an inpatient setting

Melinda Johnson, PharmD; Chip Hayes, PharmD, BCPS, BCCP; Theresa Lockwood, PharmD, BCACP; Taiyeb Khumri, MD; Michael Nassif, MD

Background:

Sodium-glucose co-transporter 2 inhibitors (SGLT2i) have shown to improve outcomes and offer a favorable safety profile for multiple comorbidities but are often held in hospitalized patients. Clinical trials for SGLT2i have primarily focused on outpatient metrics with little emphasis on implications in acute settings. There is limited data available investigating the administration of SGLT2i concerning safety and tolerability in hospitalized patients which poses to be a barrier to initiation. The purpose of this study was to quantify the incidence of adverse drug reactions (ADR) due to SGLT2i administration in an inpatient setting and determine ADR that led to order discontinuation during admission.

Methods:

This research was granted approval by the entities' Institutional Review Board (IRB) and was a descriptive retrospective study. An informatics report was generated to include all inpatients that were 18 years and older and were administered an SGLT2i across four hospitals during a 17-month period (June 1, 2019 – October 31, 2020). The population was comprised of patients from one academic medical center and three community hospitals. The exclusion criteria were admitted for one day and administered one dose of SGLT2i and admitted to a rehabilitation institution. Data was collected via an informatics report in combination with retrospective chart review. Adverse events that were reviewed included DKA, UTI, AKI, genital mycotic infection, hypoglycemia, hypotension, hypovolemia/dehydration, and other. The Naranjo Score and Likert Scale were used to assess all ADR to standardize and validate conclusions that an event was due to the drug or other confounders. The primary endpoint was the composite occurrence of adverse event(s) during admission attributed to SGLT2i administration in the inpatient setting. The secondary endpoint was the proportion of SGLT2i-related ADR that led to inpatient order discontinuation.

Results:

Data collection is ongoing. There were 174 encounters reviewed that included 154 patients in this analysis due to patients with multiple admissions. The primary endpoint of composite occurrence of adverse event(s) during admission attributed to SGLT2i administration resulted in 114 ADRs. The most common adverse drug reactions in order from most common to least common were hypotension 61/174 (35.1%), hypoglycemia 29/174 (16.7%), AKI 11/174 (6.3%), hypovolemia/dehydration 7/174 (4.0%), UTI 5/174 (2.9%), and other 1/174 (0.6%). There were no reported cases of DKA or genital mycotic infections. The secondary endpoint of the proportion of SGLT2i-related ADR that led to inpatient order discontinuation occurred in 7/174 (4.0%) encounters. Likert Scale results from a single reviewer indicated that 112/114 (98.2%) of ADRs received a score of 1-3, indicating that the ADR was more likely due to disease or other causes than treatment. The Naranjo Probability Score results from a single reviewer were $\leq$0 (doubtful) in 23/114 (20.2%), 1-4 (possible) in 86/114 (75.4%), 5-8 (probable) in 5/114 (4.4%), and no ADRs received a score of $\geq$9 (definite). The kappa value was 0.93 for Naranjo and Likert scores.

Conclusion:

Hypotension and hypoglycemia occurred more frequently in this patient population in comparison to outpatient SGLT2i safety data, however ADR causation was rarely attributed to SGLT2i administration based on Likert Score and Naranjo Probability Scale results. Discontinuation of inpatient SGLT2i orders due to an ADR was rare and occurred at a similar frequency as outpatient discontinuations due to an ADR. Results from this study indicate that SGLT2i are safe to use in patients admitted to the hospital, however additional data and prospective trials are needed to further validate these findings.