Adverse Effects in Older Patients with Type 2 Diabetes Mellitus Treated with SGLT2 Inhibitors

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Background/Introduction

Sodium glucose co-transporter 2 inhibitors (SGLT2 inhibitors) are recommended as initial treatment in patients with type 2 diabetes mellitus (T2D) with cardiovascular and renal disease.[1]These oral antidiabetic agents inhibit the proximal renal tubular reabsorption of glucose, coupled with sodium, leading to osmotic diuresis and natriuresis. Based on this mechanism of action, SGLT2 inhibitors are known to cause common adverse effects (AEs), including genital infections and diabetic ketoacidosis.

Several reasons exist for discontinuing SGLT2 inhibitors in the ambulatory care setting, including AEs. A post-marketing review by Donnan et al. found there was no increased risk of harm with SGLT2 inhibitors, as a class, when compared to placebo for urinary tract infections, diabetic ketoacidosis, acute kidney injury (AKI) or fracture.[2] The review found that the class was significantly protective against AKI.

Patients treated in ambulatory practice may have different characteristics than patients recruited for clinical trials, such as older age, making them more susceptible to AEs. The occurrence of AEs, leading to discontinuation of therapy with a SGLT2 inhibitor, in an older patient population has not been well reported in the literature.

Methods

In this retrospective analysis, data was extracted from Northeast Georgia Health System electronic health records for adult patients with T2D who discontinued using an SGLT2 inhibitor between January 1, 2018, to January 31, 2023. The primary outcome was the presence of AEs in older patients. This study was approved by the institutions Investigation Review Board.

Results

Of the 745 patients with T2D who discontinued treatment with a SGLT2 inhibitor, 80 patients (52.5% male, 47.5% female) stopped treatment due to experiencing AEs. The average age for this patient population was 62.6 ± 8.4 years and 22.5% (n=18) of these patients were diagnosed with chronic kidney disease.

The most common AE reported was yeast infection (11.3%, n=9). An AE occurred in 31% (n=25) of patients age < 65 and 15.8% (n=13) of patients age ≥ 65, p = 0.11. Within the CKD patient population that discontinued treatment due to AEs, 20% (n=4) were < 65 and 16.3% (n=3) of patients were ≥ 65, p = 0.82.

Mean A1c at discontinuation was 7.96 and Mean A1c at follow-up was 7.8 (mean difference = -0.16, p = 0.5548).

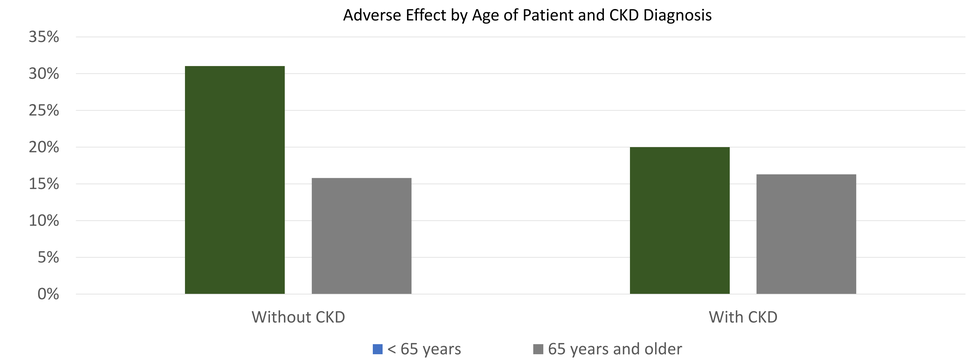

Figure 1: Reported total adverse effects by age of patient and diagnosis of CKD. Data are n(%) of patients.

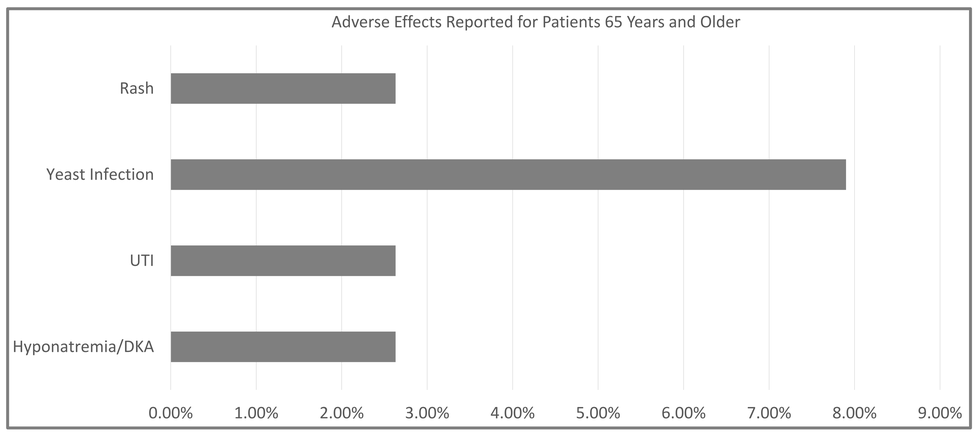

Figure 2: Reported total adverse effects for all patients age 65 years and older. Data are n(%) of patients.

Discussion

Based on these retrospective findings, treatment with SGLT2 inhibitors in older patients with T2DM is generally well tolerated and AEs were consistent with the known safety profile. Additionally, there was no significant difference in AEs between patients < 65 or ≥ 65 in the subgroup with and without CKD. Therefore, age may not be a contributing cause leading to discontinuation of SGLT2 inhibitor therapy in patients with or without CKD. These results are consistent with a previous study by Kaku et al.[3] The investigators found that the safety and effectiveness of empagliflozin in older patients was consistent with the medication's safety profile from clinical trials.

This study has certain limitations, including a small sample size. The patients included were older, and on many different medications that could lead to development of AEs. Confounding factors include concomitant medications, comorbidities and healthcare access.

Conclusions

Based on these retrospective findings, treatment with SGLT2 inhibitors in older patients with T2DM is generally well tolerated and AEs were consistent with the known safety profile for this class of medications.

References

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