CKJ REVIEW

Sodium-glucose cotransporter 2 inhibitors for diabetic kidney disease: a primer for deprescribing

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ABSTRACT

Chronic kidney disease (CKD) is a critical global public health problem associated with high morbidity and mortality, poorer quality of life and increased health care expenditures. CKD and its associated comorbidities are one of the most complex clinical constellations to manage. Treatments for CKD and its comorbidities lead to polypharmacy, which exponentiates the morbidity and mortality. Sodium-glucose cotransporter 2 inhibitors (SGLT2is) have shown remarkable benefits in cardiovascular and renal protection in patients with type 2 diabetes mellitus (T2DM). The pleiotropic effects of SGLT2is beyond glycosuria suggest a promising role in reducing polypharmacy in diabetic CKD, but the potential adverse effects of SGLT2is should also be considered. In this review, we present a typical case of a patient with multiple comorbidities seen in a CKD clinic, highlighting the polypharmacy and complexity in the management of proteinuria, hyperkalemia, volume overload, hyperuricemia, hypoglycemia and obesity. We review the cardiovascular and renal protection effects of SGLT2is in the context of clinical trials and current guidelines. We then discuss the roles of SGLT2is in the management of associated comorbidities and review the adverse effects and controversies of SGLT2is. We conclude with a proposal for deprescribing principles when initiating SGLT2is in patients with diabetic CKD.

Keywords: chronic kidney disease, deprescribing, diabetic kidney disease, polypharmacy, sodium-glucose cotransporter 2

CASE PRESENTATION

A 67-year-old morbidly obese male with a history of hypertension, type 2 diabetes mellitus (T2DM), systolic heart failure and hyperuricemia was followed in the renal clinic for chronic kidney disease (CKD) Stage 3a with nephrotic-range proteinuria. He had a recent kidney biopsy for increasing proteinuria and serum creatinine, which revealed diabetic nephropathy with chronic active interstitial nephritis. He was previously taken off a blocker of the renin–angiotensin–aldosterone system (RAAS) because of multiple episodes of hyperkalemia. Despite being on a low potassium diet, furosemide and patiromer, his potassium remained >5 mEq/L, which precluded reintroduction of the RAAS blockade medications. Also, his endocrinologist had recently intensified his diabetic regimen with insulin due to poor hemoglobin A1c control, and since then he has experienced...
weight gain and more frequent episodes of hypoglycemia. He also required up-titrated of furosemide due to fluid retention in the lower extremities. The higher dose of furosemide precipitated a gout attack in his right knee, for which he took a course of steroids and was started on allopurinol. He reported persistent right knee pain from the gout attack, which severely limited his mobility and ability to exercise and left him feeling overwhelmed by his growing medication list. In the renal clinic, he expressed frustration that his renal function had declined further despite all his efforts to adhere to the medical advice of his multiple health care providers.

INTRODUCTION

CKD is a critical global public health problem associated with high morbidity and mortality, poorer quality of life and increased health care expenditures [1]. Comorbid conditions like diabetes, hypertension, hyperlipidemia, hyperuricemia, heart failure and cardiovascular disease are highly prevalent in CKD [2, 3] and associated with increased mortality [4, 5]. This constellation of conditions can be difficult to manage, often leading to polypharmacy in an attempt to manage comorbidities and mitigate the progression of CKD [6–8]. Indeed, as kidney function declines, patients experience additional complications, including anemia, bone mineral disorders, acidosis, hypervolemia and cardiovascular complications, all of which often require medication therapy. Most CKD patients take an average of 8–13 medications [9]. The number of prescribed medications is a recognized predictor of prescribing problems, including inappropriate dosage, drug-drug interactions and drug–disease interactions [10]. The use of multiple complex medication regimens in CKD increases drug-related problems [11] and inappropriate drug use is associated with 40% higher mortality in patients with CKD compared with those with preserved kidney function [12].

Our index case highlights a prescribing cascade, a process whereby the side effects of drugs result in more prescriptions, which causes additional side effects and unanticipated drug interactions [13]. Prescribing cascades similar to the example above are not uncommon in managing diabetic kidney disease.

Balancing the management of CKD, including associated comorbidities and complications, with the minimization of necessary and appropriate medications is challenging. However, the nephrologist now has sodium-glucose cotransporter 2 inhibitors (SGLT2is), a novel class of diabetic medications with many potentially helpful uses. Large clinical trials of SGLT2is have demonstrated remarkable benefit among patients with T2DM in reducing the risk of cardiovascular death, heart failure hospitalization and progression of renal disease [14]. The pleiotropic effects of SGLT2is beyond glycosuria suggest a promising role in managing multiple problems with a single once-daily pill, yet the efficacy and safety profile in moderate CKD is less clear. In this review we present a typical case of a patient with multiple comorbidities seen in CKD clinic, highlighting the complexity in management and resultant polypharmacy. We discuss the current evidence and guidelines for the use of SGLT2is in patients with diabetic CKD. We review the roles that SGLT2is may play in mitigating CKD complications, managing comorbidities and decreasing medication burden in this population, as well as the potential adverse effects of SGLT2is. We conclude with a proposal for safer deprescribing methods when initiating SGLT2is in the renal clinic.

Cardiovascular and renal protective effects of SGLT2is and current guideline recommendations

The US Food and Drug Administration (FDA) approved the use of SGLT2is for T2DM and cardiovascular risk reduction in patients with an estimated glomerular filtration rate (eGFR) >45mL/min/1.73m². The characteristics of the study populations and the cardiovascular and renal outcomes of the pivotal trials of SGLT2is [15–18] are summarized in Table 1. The study population typically represented a group of obese patients with long-standing, poorly controlled T2DM and with various degrees of preexisting cardiovascular and renal disease who were receiving the standard of care for the management of diabetes and cardiovascular disease. Notably, the EMPA-REG Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients–Removing Excess Glucose (EMPA-REG) and Canagliflozin Cardiovascular Assessment Study (CANVAS) study populations had high cardiovascular disease burden, the Evaluation of the Effects of Canagliflozin on Renal and Cardiovascular Outcomes in Participants With Diabetic Nephropathy (CREDENCE) trial population had high renal disease burden and the Multicenter Trial to Evaluate the Effect of Dapagliflozin on the Incidence of Cardiovascular Events (DECLARE-TIMI58) had the lowest cardiovascular and renal disease burdens. The EMPA-REG, CANVAS and CREDENCE trials demonstrated reduced major adverse cardiovascular events (MACEs), whereas the DECLARE-TIMI58 did not, probably reflecting less severe cardiovascular burden in the study population. Uniquely, all four trials showed reduced heart failure hospitalizations irrespective of cardiovascular disease burden. All three SGLT2is reduced the renal composite outcomes compared with placebo. The CREDENCE trial observed the highest renal event rates and absolute risk reduction, followed by the EMPA-REG, CANVAS and DECLARE-TIMI58 trials, which is a downtrend likely corresponding to the degree of renal disease burden. In summary, SGLT2is are effective in the prevention of heart failure hospitalizations and progression of CKD and reducing cardiovascular events in patients with high cardiovascular risk.

The 2019 American Diabetes Association (ADA) guidelines recommend SGLT2is as the preferred class of agents to be added after metformin in patients with T2DM and a history of heart failure or CKD, if eGFR is >30mL/min/1.73m² [19, 20]. SGLT2is are also recommended as one of the two preferred agents (the other is GLP-1 receptor agonists) to be added after metformin in patients with atherosclerotic cardiovascular disease (ASCVD). Furthermore, clinicians should consider switching from other diabetes agents without cardiovascular or renal benefit to SGLT2is, even in patients who are currently at their target hemoglobin A1c level. In addition, the ADA recommends prescribing SGLT2is in patients who would benefit clinically from weight loss and to minimize the risk of hypoglycemia. The ADA also acknowledges that in those without established cardiovascular disease or CKD, SGLT2is are the last recommended class of agents for use because of the high drug price. The cost-effectiveness of SGLT2is compared with other oral hypoglycemic drugs in patients with cardiovascular disease, heart failure or CKD is yet to be determined.

The pleiotropic effects of SGLT2is on polypharmacy in diabetic CKD

The highly prevalent comorbidities and associated polypharmacy highlight the complexity of care for patients with diabetic
The pleiotropic effects of SGLT2is show great promise in addressing these complex polypharmacy issues in diabetic CKD, including the management of proteinuria, hyperkalemia, volume overload, hyperuricemia, hypoglycemia, obesity and anemia (Table 3).

SGLT2is as an add-on or rescue therapy to RAAS blockers for proteinuria. The angiotensin-converting enzyme inhibitors (ACEis) and angiotensin II receptor blockers (ARBs) are the cornerstone classes of medications to reduce proteinuria and slow CKD progression. However, the rate of hyperkalemia from RAAS blockade is 3-fold higher in patients with CKD than in those without CKD [26]. Incident hyperkalemia is associated with a dose reduction or discontinuation of RAAS blockers [27], increased emergency room visits [27] and higher mortality [26]. The trend of ACEi/ARB usage rates in patients with diabetes and CKD has decreased since the early 2000s [28, 29], possibly due to resultant hyperkalemia. Dietary consultation on low potassium diets and coprescribing of kaliuretic diuretics and intestinal potassium binders are the current potassium-lowering strategies to allow reintroduction of ACEis/ARBs.

Table 2. The prescribing cascade in the management of CKD

| Medications Used for            | Unintended consequence                        | Added medication burden            |
|---------------------------------|------------------------------------------------|-----------------------------------|
| ACEI/ARB/spironolactone         | Proteinuria, hypertension, heart failure       | Hyperkalemia                       | Patiromer, diuretics               |
| Loop and thiazide diuretics     | Hypertension, heart failure, hyperkalemia      | Hyperuricemia                      | Urate-lowering agents             |
| Insulin/insulinotropic agents   | Diabetes                                       | Hyperglycemia                      | Diabetic agents                   |
|                                 |                                                | Weight gain                        | Weight reduction medications      |
|                                 |                                                | Sodium retention                   | Diuretics, antihypertensives      |
|                                 |                                                | Hypoglycemia                       | Not applicable                    |

CKD (Table 2) [21]. The pleiotropic effects of SGLT2is show great promise in addressing these complex polypharmacy issues in diabetic CKD, including the management of proteinuria, hyperkalemia, volume overload, hyperuricemia, hypoglycemia, obesity and anemia (Table 3).
bular secretion and compensatory sodium reabsorption from effective drug concentration due to proteinuria and impaired tu-

cance [45]. Many strategies to overcome diuretic resistance have been attempted, but none have demonstrated long-term clinical benefit [46]. Loop diuretics are the most commonly used drugs for decongestion in CKD. Chronic loop diuretic use increases distal nephron sodium retention via the Na-Cl cotransporter. The combination of thiazide diuretics and loop diuretics has been shown to promote natriuresis and decongestion in loop diuretic–resistant patients, but long-term benefit in reducing cardiovascular mortality remains uncertain and metabolic and electrolyte disorders are common [47].

Multiple large clinical trials have demonstrated that SGLT2is significantly reduce heart failure hospitalizations regardless of a history of ASCVD or existing heart failure [14]. A recent study demonstrated a mutually adaptive synergy between SGLT2is and loop diuretics, and combination therapy was superior to either drug alone in promoting natriuresis [39]. Interestingly, despite diminished blood glucose–lowering effects of SGLT2is as renal function worsens, the antihypertensive and cardioprotective effects persisted across all eGFR groups [48, 49], suggesting that SGLT2is maintain natriuresis in patients with reduced eGFR despite lower drug delivery to the proximal tubules. Studies are currently under way examining SGLT2is [50] or thiazide diuretics [51] in combination with loop diuretics on heart failure outcomes and mortality. In euvolemic patients who are on a stable diuretic regimen, the addition of SGLT2i may require down-titration or discontinuation of existing diuretics to avoid overdiuresis.

SGLT2is mitigate hyperuricemia and hyperglycemia from loop and thiazide diuretics. Loop and thiazide diuretics are commonly used for salt-sensitive hypertension, volume management or hyperkalemia. Loop and thiazide diuretics cause increased uric acid net absorption from the proximal tubules by direct effects on urate transporters [52, 53] and by the indirect effect on volume contraction. Compared with nondiuretic anti-

hypertensives, the use of diuretics increases the serum uric acid effect on volume contraction. Compared with nondiuretic anti-

hypertensives, the use of diuretics increases the serum uric acid level by 0.7–0.9 mg/dL [54, 55] and increases the risk of gout attacks [55], which can potentially lead to worse cardiovascular and renal outcomes [56]. Also, loop and thiazide diuretics are associated with insulin resistance [57] and dose-dependent increased risk of incident diabetes [58, 59], probably related to compensatory sodium reabsorption coupled with increased glucose reabsorption via SGLT2 [39]. Since hyperuricemia, metabolic syndrome and diabetes are closely related and coexist in patients with CKD, the frequent use of loop or thiazide diuretics for blood pressure and volume management places CKD patients at risk for developing new comorbidities.

SGLT2i as an add-on to overcome diuretic resistance. Diuretic resistance is commonly seen in CKD patients and leads to poor outcomes. Poor drug absorption due to intestinal edema, reduced effective drug concentration due to proteinuria and impaired tubular secretion and compensatory sodium reabsorption from unblocked sodium transporters (such as Na+/H+ exchanger 3, Na-CI cotransporter and SGLT2) all contribute to diuretic resistance [45]. Many strategies to overcome diuretic resistance have been attempted, but none have demonstrated long-term clinical benefit [46]. Loop diuretics are the most commonly used drugs for decongestion in CKD. Chronic loop diuretic use increases distal nephron sodium retention via the Na-Cl cotransporter. The combination of thiazide diuretics and loop diuretics has been shown to promote natriuresis and decongestion in loop diuretic–resistant patients, but long-term benefit in reducing cardiovascular mortality remains uncertain and metabolic and electrolyte disorders are common [47].

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SGLT2is for diabetic kidney disease

| Clinical indication | Current therapy | Possible benefits when combining or substituting with SGLT2is besides cardiac and renal protection | Optimization Strategy |
|--------------------|----------------|------------------------------------------------------------------------------------------|----------------------|
| Prevent adverse renal and cardiovascular events | ACEI/ARB, spironolactone [22, 23] | Synergy in proteinuria reduction Reduce hyperkalemia from RAAS blockers | Coprescribe |
| Secondary hyperparathyroidism | Active vitamin D analogs [24] | Mitigate the SGLT2-mediated up-regulation of FGF23 and suppression of 1,25-dihydroxyvitamin D [25] | Coprescribe if indicated |
| Volume overload | Loop and thiazide diuretics | Synergy in natriuresis Less metabolic derangement | Coprescribe if indicated with dose adjustment |
| Glucose control | GLP-1 RAs | Less metabolic derangement Additional glycemic control with low risk of hypoglycemia | Coprescribe if indicated |
| | DPP-4 inhibitors | Additional glycemic control with low risk of hypoglycemia | |
| | Thiazolidinediones | Avoid sodium retention and exacerbation of heart failure | Deprescribe |
| | Insulin/insulinotropic agents | Weight loss, less sodium retention and lower hyperglycemic risk | Deprescribe |
| Prevent hyperkalemia | Loop and thiazide diuretics | Less metabolic derangement | Deprescribe |
| Patiromer | Lower medication cost and simpler dosing schedule | |
| Hypertension | CCB, α1-blocker, clonidine | No | Deprescribe |

BP, blood pressure; CCB, calcium channel blocker; ESA, EPO-stimulating agent.
metabolic derangements of loop and thiazide diuretics and allow for deprescribing of uric acid–lowering agents.

**SGLT2is as diabetic agents with low hypoglycemic risk and weight reduction effect.** Insulin and sulfonylureas are well-known to cause hypoglycemia [19, 63–66], especially in patients with CKD [67], whereas the newer classes of glucose-lowering agents, such as SGLT2i, glucagon-like peptide-1 receptor agonists (GLP-1 RA) and dipeptidyl peptidase 4 inhibitors pose a lower risk of hypoglycemia but are underprescribed in CKD patients [68]. Diabetes and CKD together compound the risk for incident hypoglycemia, which is associated with excess mortality [69].

The higher incidence of hypoglycemia in CKD patients is likely related to reduced insulin clearance and renal gluconeogenesis as renal function declines [70]. Moreover, insulin directly suppresses gluconeogenesis in the proximal tubules, while inhibition of SGLT2 enhances gluconeogenesis via activation of sirtuin1/peroxisome proliferator-activated receptor γ coactivator-1α [71], thus providing mechanistic insights into the higher risk of hypoglycemia seen with insulin and sulfonylureas, especially in patients with CKD, and justification for substituting them with SGLT2is. SGLT2is have been used in patients with eGFR >30 mL/min/1.73 m² in clinical trials [15, 17, 18] and have shown a low risk of hypoglycemia [72]. As an addition to insulin-based or sulfonylurea-based glucose-lowering regimens, SGLT2is improved glycemic control with a lower risk of hypoglycemia [73, 74].

Weight reduction improves cardiovascular and renal risk factors [75, 76] and independently improves renal outcomes [77]. Insulin and sulfonylureas cause weight gain, which often leads to serial escalations in the treatment of diabetes, joint pain, hypertension, hyperlipidemia or proteinuria. SGLT2is can reduce weight by 2–4 kg on average [72] due to total body water reduction upon initiation and then by increasing fat metabolism with chronic use [78]. The weight loss effect is maintained in mild to moderate CKD [49] and attenuated in moderate to severe CKD [79].

**The adverse effects of SGLT2is**

While SGLT2is have demonstrated great promise for cardiovascular and renal protection, the potential adverse effects of SGLT2is should not be overlooked. The common adverse effects include osmotic diuresis, volume depletion and genital fungal infections. Less common adverse effects that have been reported in some clinical trials but not seen in meta-analyses [38, 72] include urinary tract infection, diabetic ketoacidosis, lower extremities amputation and bone fracture. Diabetic ketoacidosis was only seen in the CREDEnCE and DECLARE-TIMI58 trials and the lower extremities amputation was only seen in the CANVAS trial, but not in the CREDEnCE, EMPA-REG or DECLARE-TIMI58 trials. Last but not least, 55 cases of necrotizing fasciitis of the perineum were reported in case series [80] but not seen in clinical trials.

Of note, the risk of bone fracture is controversial. In both healthy volunteers [25] and T2DM patients with moderate CKD [81], canagliflozin increased serum phosphate, which stimulated fibroblast growth factor 23 (FGF23) and decreased 1,25-dihydroxyvitamin D [25] and accelerated the loss of hip bone mineral density [82]. A higher risk of bone fracture was seen in the CANVAS trial. However, the risk of bone fracture was neither higher in the SGLT2i arm in the CREDEnCE, EMPA-REG or DECLARE-TIMI58 trials [15, 16, 18] nor in the meta-analysis of the safety profile of SGLT2is in CKD patients [38]. The magnitude and variability of bone mineral adverse effects of SGLT2is are yet to be determined in the postmarket safety surveillance. It is advisable to monitor patient’s parathyroid hormone (PTH) level while on SGLT2is and treat with active vitamin D analogs if the PTH level uptrends above the goal.

In summary, starting SGLT2is in a highly select group of CKD patients after meticulously weighing the risks and benefits and frequent monitoring of volume status, genital and foot hygiene, electrolytes, kidney function and bone mineral biomarkers are the keys to ensuring the safety of patients on SGLT2is.

**The controversy around using SGLT2is for renoprotection in moderate to severe diabetic CKD**

The glucose-lowering effect of SGLT2is when the eGFR is <45 mL/min/1.73 m² is almost negligible. At present, the FDA does not recommend the use of canagliflozin, empagliflozin and dapagliflozin when the eGFR is <45 mL/min/1.73 m². However, diabetic patients with moderate to severe proteinuric CKD have a very high risk of progression to ESRD despite the current standard of care, which is a substantial unmet medical need. The CREDEnCE trial and the subgroup analysis of the EMPA-REG and CANVAS trials showed that the cardiovascular risk reduction, heart failure hospitalization reduction and composite renal outcome reduction were maintained in patients with an eGFR of 30–45 mL/min/1.73 m² and the safety profile was similar to the patients with preserved renal function, which argues for the ‘off-label’ use of SGLT2is in T2DM patients with proteinuria and an eGFR of 30–45 mL/min/1.73 m² [20]. Other clinical trials of SGLT2is that target cardiovascular and renal outcomes in both diabetic and nondiabetic CKD patients are currently under way [EMPA-Kidney (The Study of Heart and Kidney Protection With Empagliflozin; NCT03594110) and DAPA-CKD (A Study to Evaluate the Effect of Dapagliflozin on Renal Outcomes and Cardiovascular Mortality in Patients With Chronic Kidney Disease; NCT03036150)].

**Deprescribing principles when using SGLT2is in patients with diabetic CKD**

The pleiotropic effects of SGLT2is can potentially break the prescribing cascade that contributes to polypharmacy (Figure 1). The following proposed deprescribing principles for SGLT2i use are intended only for diabetic kidney disease.

The first principle is to ‘think SGLT2i first’. Adding an SGLT2i or switching to an SGLT2i is recommended in type 2 diabetic patients with an eGFR >30 mL/min/1.73 m² and with established ASCVD, heart failure or CKD [19, 20]. For CKD patients with adequate glycemic control who are seen in a CKD clinic, initiation of or switching to an SGLT2i by the treating nephrologist may reduce the likelihood of polypharmacy and hypoglycemia, providing more individualized diabetes and renal care.

The second principle is to ‘coprescribe other agents for synergy or mitigation of side effects’ (Table 3). For example, coprescribing RAAS blockers has synergy in proteinuria reduction and renal protection and mitigates the hyperkalemia caused by RAAS blockers; coprescribing active vitamin D analogs mitigates the induction of FGF23 and suppression of 1,25-dihydroxyvitamin D by SGLT2is [25].

The third principle is to ‘deprescribe less desirable agents when possible’. The less desirable agents may have a similar
treatment effect but less desirable features, such as diabetic agents with no cardiovascular or renal protection benefit, dys-synergy with existing treatment, safety concerns or agents that may yield poor adherence due to regimen complexity or side effects (Table 3). From our experience, empagliflozin initiation necessitated adjustments to diabetes, hypertension and diuretic regimens in almost all patients. Whether SGLT2i use reduces the medication burden warrants further investigation. The deprescribing process requires careful planning, active surveillance and interdisciplinary communications [83].

The final principle is that ‘when taking a holistic approach to medication management, safety comes first’. This principle requires the establishment of individualized treatment goals and consideration of the whole patient at the time of prescription or deprescription [67, 84]. Monitor closely for adverse effects when starting or stopping medications. We provide a list of practical considerations (Table 4) in the decision-making process of medication management in patients with CKD, specifically related to the use of SGLT2is.

The outcome of the index clinical case
After the introduction of empagliflozin to the patient’s medication regimen, he experienced significant diuresis in the first 4 weeks and his serum creatinine increased from 1.21 (eGFR = 62 mL/min/1.73 m²) to 1.58 mg/dL (eGFR = 45 mL/min/1.73 m²) and potassium fell < 4 mEq/L. We discontinued his

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**FIGURE 1:** Prescribing cascade in CKD and SGLT2is for deprescribing. A hypothetical prescribing cascade after prescribing ACEi/ARB for proteinuria in a diabetic CKD3a patient. The multifaceted effects of SGLT2is show great promise in the management of diabetic CKD and its comorbidities. ESAs, EPO-stimulating agents.

**Table 4. Practical considerations for when to defer initiation or withhold SGLT2is**

| Clinical conditions                                      | Concerns                                                                 | Recommended actions                                      |
|----------------------------------------------------------|--------------------------------------------------------------------------|----------------------------------------------------------|
| Cognitive impairment                                     | Unable to follow instructions for surveillance and medication titration; at risk for dehydration | Avoid SGLT2is; assess cognitive impairment                |
| Poorly controlled hyperglycemia and a history of diabetic ketoacidosis | Poor adherence; risk of hyperglycemia-induced dehydration; risk of ketoacidosis | Avoid SGLT2is; referral to diabetologist                  |
| Unhealed diabetic foot wound                             | Risk of amputation                                                        | Avoid SGLT2is; referral to podiatry                       |
| History of frequent urinary tract infections, indwelling urinary catheter or self-catheterization | Risk of urinary tract infection                                           | Avoid SGLT2is                                            |
| Frequent vaginal candidal infections or unable to maintain genital hygiene for medical (e.g. phimosis) or social (e.g. insecure housing) reasons | Risk of genital fungal infection                                          | Avoid SGLT2is                                            |
| Peripheral vascular disease                              | Risk of amputation                                                        | Use with caution; frequent foot exam while on SGLT2is; referral to vascular surgery |
| Osteoporosis or renal osteodystrophy                      | Risk of bone fracture                                                     | Use with caution; monitor PTH and total vitamin D levels; referral to osteoporosis specialist for fracture risk assessment |
| Dynamic volume status (poor oral intake, diarrhea) or labile blood pressure | Dehydration and hypotension                                                | Use with caution; deprescribe other diuretics and antihypertensives |
| Frequent nocturia                                          | Patient intolerant of polyuria                                             | Reduce dose or withhold                                   |
appropriate patients even when glycemic control is adequate. Further and careful surveillance for adverse effects are the keys to ensure CKD. Meticulous patient selection, individualized treatment plans

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CONCLUSION

Diabetic CKD is complex to manage because of the high prevalence of comorbidities and resultant polypharmacy. The pleiotropic effects of SGLT2is show remarkable cardiovascular and renal benefits and great promise to address polypharmacy issues in diabetic CKD. Meticulous patient selection, individualized treatment plans and careful surveillance for adverse effects are the keys to ensure safety in patients on SGLT2is. SGLT2is are recommended in appropriate patients even when glycemic control is adequate. Further study on whether SGLT2is decrease medication burden for patients with diabetic kidney disease is warranted.

FUNDING

J.L. is supported by the Ben J. Lipps Research Fellowship from the American Society of Nephrology. J.M.P. is supported by National Institutes of Health NIDDK K23 grant (1K23DK100447).

CONFLICT OF INTEREST STATEMENT

None declared. The results presented in this article have not been published previously in whole or part, except in abstract format.

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