Use of Canagliflozin in Kidney Transplant Recipients for the Treatment of Type 2 Diabetes: A Case Series

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Diabetes is highly prevalent in kidney transplant recipients (KTR). Simultaneous pancreas-kidney transplant recipients (SPKTR) are also at risk for developing type 2 diabetes following transplantation, when insulin secretion may be insufficient to maintain normoglycemia. Transplant-specific risk factors associated with the development of type 2 diabetes include the use of diabetogenic immunosuppressive medications, hypomagnesemia, and posttransplant weight gain (1).

In nontransplant populations with type 2 diabetes and established cardiovascular (CV) disease, the use of sodium–glucose cotransporter 2 inhibitors (SGLT2i) can improve glycemic control, promote weight loss, and reduce the risk of CV events (2). Given the increased incidence of posttransplant diabetes and the high CV burden in transplant recipients, the use of SGLT2i in this population is attractive. Of concern, however, is the lack of safety data regarding SGLT2i in transplant recipients. The purpose of this study is to describe our short-term experience of KTR and SPKTR treated with canagliflozin at our institution.

All adult KTR or SPKTR treated with the SGLT2i canagliflozin from 1 January 2015 to 1 November 2016 were included in this study. Baseline demographic and metabolic variables at the time of canagliflozin initiation were collected. Adverse events, including hypoglycemia, acute kidney injury (AKI), hyperkalemia, yeast and urinary tract infections, ketoacidosis, allergic reactions, and graft rejection, were collected over follow-up.

Baseline characteristics of study patients and mean changes in metabolic and hemodynamic parameters over 80.5 person-months of follow-up after canagliflozin initiation are summarized in Table 1.

There were no urinary or mycotic infections diagnosed during treatment. One patient experienced hypoglycemia that did not require hospitalization and one patient developed cellulitis. No patients experienced acute rejection or AKI.

Although SGLT2i have been widely used in the nontransplant population, to our knowledge this is the first report describing the use of these agents in transplant recipients. Given the susceptibility to infectious complications of patients with diabetes and concomitant immunosuppression, clinicians may avoid SGLT2i because of their side effects. In this small observational cohort, canagliflozin was generally well tolerated.

We did not observe any episodes of AKI. As expected based on data in nontransplant patients, we observed small reductions in estimated glomerular filtration rate (eGFR), an effect that has been associated with renal afferent arteriole vasoconstriction due to increased sodium delivery at the macula densa and tubuloglomerular feedback (3). In experimental models, vasoconstriction at the afferent arteriole reduces hyperfiltration—an effect that mitigates renal disease in patients with diabetes (4). While it is not known if such renoprotective effects extend to transplanted kidneys, effects on eGFR in this study suggest the hemodynamic-based eGFR changes occur even though transplanted kidneys are denervated. The characteristic eGFR "dip" is therefore unlikely to be caused by changes in autonomic function.

We observed overall improvements in glycemic control, weight, and blood pressure, which were similar in magnitude to effects reported in nontransplant cohorts.

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Table 1—Baseline characteristics of study patients at the time of canagliflozin initiation and mean changes in hemodynamic and metabolic parameters over follow-up

Baseline characteristic	SPKTR ($N = 4$)	KTR ($N = 6$)
Age at time of canagliflozin initiation, years	49.4 ± 8.9	61.6 ± 12.6
Female sex	2 (50)	1 (17)
PTDM	4 (100)	4 (67)
Prior DM therapy	3 (75)	5 (83)
Time from transplant to canagliflozin treatment, years	3.5 ± 3.9	4.4 ± 3.3
Time on canagliflozin treatment, months	5.6 ± 3.4	10.1 ± 4.2
Hemoglobin A_{1c}, %	7.4 ± 1.1	8.6 ± 1.4
Hemoglobin A_{1c}, mmol/mol	57 ± 12.0	70 ± 15.3
eGFR, mL/min/1.73m^2	60 ± 14	78 ± 18.2
Serum creatinine, μmol/L	108.3 ± 21.6	90.2 ± 22.9
ACEi therapy	1 (25)	0 (0)
ARB therapy	0 (0)	2 (50)
Diuretic therapy	3 (75)	2 (50)
Calcium channel blocker therapy	4 (100)	3 (75)
α-Adrenergic antagonist therapy	1 (25)	1 (25)
Beta blocker therapy	4 (100)	2 (50)

Parameter over follow-up	Mean (SD) change	*P* value
Hemoglobin A_{1c}, % ($N = 9$)	−0.84 (1.2)	0.07
Hemoglobin A_{1c}, mmol/mol ($N = 9$)	−9.2 (13.1)	0.07
Weight, kg ($N = 8$)	−2.14 (2.8)	0.07
Serum sodium, mmol/L ($N = 10$)	0.6 (2.2)	0.4
Serum potassium, mmol/L ($N = 10$)	0.2 (0.5)	0.2
Systolic blood pressure, mmHg ($N = 8$)	−6.5 (10.8)	0.13
Diastolic blood pressure, mmHg ($N = 8$)	−4.8 (12)	0.3
Hematocrit, % ($N = 10$)	1.6 (2.5)	0.08
Serum creatinine, μmol/L ($N = 10$)	9.7 (14.6)	0.06
eGFR, mL/min/1.73^2 ($N = 10$)	−4.3 (12.2)	0.3

Data are mean ± SD or *N* (%) unless otherwise indicated. ACEi, ACE inhibitor; ARB, angiotensin II receptor blocker; DM, diabetes mellitus; PTDM, posttransplant diabetes mellitus.

In nontransplant populations, SGLT2i reduce diastolic dysfunction, major adverse cardiac events, and diabetic nephropathy risk (2,3,5). In transplant recipients, in whom hypertension and CV disease are common, SGLT2i may therefore be an important therapeutic option.

In conclusion, our data suggest that SGLT2i in KTR and SPKTR are well tolerated and may have similar therapeutic efficacy compared with nontransplant patients. Our experience highlights the importance of studying SGLT2i in a larger cohort of KTR over an extended period of time.

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