Positive Impact of a Pilot Pharmacist-Run Diabetes Pharmacotherapy Clinic in Solid-Organ Transplant Recipients

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ABSTRACT

Purpose. Post-transplant diabetes mellitus (PTDM) can lead to significant morbidity and cardiovascular death with a functioning graft. A paucity of literature exists regarding glycemic control in solid-organ transplant (SOT) recipients, including pharmacist management of PTDM. This study aimed to assess the impact of pharmacist interventions on diabetes management in a pharmacist-run PTDM clinic.

Methods. This was a single-center, prospective, observational study of 24 adult SOT recipients enrolled in a pilot pharmacist-managed PTDM clinic from 1 January to 30 June 2015.

Results. Improvements were realized in markers of glycemic control, including changes in A1C, average daily self-monitoring of blood glucose (SMBG) results, fasting SMBG results, and pre-lunch SMBG results from enrollment through at least 3 months of follow-up. Median A1C decreased significantly from 8.05% (interquartile range [IQR] 6.33–11.75) at baseline to 6.45% (IQR 6.05–7.3) at the last follow-up encounter (P = 0.0010). Average daily SMBG results decreased significantly from a median of 191 mg/dL (IQR 138–232 mg/dL) at baseline to 125 mg/dL (IQR 111–167 mg/dL) at the final encounter (P = 0.0023). Median fasting and pre-lunch SMBG results decreased significantly from 153 mg/dL (IQR 117–208 mg/dL) at baseline to 120 mg/dL (IQR 102–134 mg/dL) (P = 0.0064) and from 212 mg/dL (IQR 159–258 mg/dL) to 122 mg/dL (IQR 110–169 mg/dL) (P = 0.0161), respectively. Changes from baseline in other SMBG values, lipid levels, and BMI were not statistically significant.

Conclusion. The results of our study demonstrate that a pharmacist-managed PTDM clinic can significantly affect glycemic control in SOT recipients.

According to current Scientific Registry of Transplant Recipients data, ~30% of kidney transplant and 25% of liver transplant recipients are diagnosed with type 2 diabetes before transplantation (1,2). Furthermore, in addition to traditional risk factors for type 2 diabetes, specific factors further increasing diabetes risk after receiving a solid-organ transplant (SOT) include chronic administration of calcineurin inhibitors and/or corticosteroids, weight gain, and viral infections such as hepatitis C (3–10). Transient post-transplant hyperglycemia, which by definition occurs during the first 45 days after transplantation, is present in up to 90% of kidney transplant recipients; 10–20% of these patients will have persistent hyperglycemia and will be newly diagnosed with post-transplant diabetes mellitus (PTDM), with the incidence increasing over time post-transplant (2,5,6). Furthermore, up to 25% of liver and 40% of heart

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https://doi.org/10.2337/ds17-0029

Diabetes Spectrum Online Ahead of Print, published online December 27, 2017

and lung transplant recipients will receive a new diagnosis of PTDM (1,6,11–13).

PTDM itself is an independent risk factor for infections, cardiovascular disease, graft failure, and death with a functioning allograft (3,5,6,14,15). Because of the complex nature of post-transplant recipients, who often have numerous comorbidities and a greater risk for drug interactions and changes in organ function, diabetes management in this population can be challenging and time-consuming. Although some transplantation centers may opt to refer their patients to diabetes specialists, many transplant patients rely on transplant physicians as primary care providers to oversee all aspects of their medical care. As the post-transplantation population increases, the demand for more focused, effective management of diabetes in this population will also increase, with the goal of improving long-term allograft and patient survival.

One logical option for providing more SOT recipients with enhanced long-term pharmacological care is to expand the role of the transplant clinical pharmacy specialist (CPS). The benefit of having CPSs independently manage chronic disease states such as diabetes via collaborative practice agreements has been previously demonstrated in the general population and has become common practice within some public health systems and in several states (16–23). Having a CPS closely monitor SOT recipients and independently engage in hyperglycemia/diabetes management and cardiovascular disease risk reduction strategies could potentially improve outcomes in this challenging population. Thus, the hypothesis of this study was that a pilot pharmacist-managed hyperglycemia/diabetes pharmacotherapy clinic providing guideline-driven diabetes care to SOT recipients would positively affect glycemic control post-transplant.

Materials and Methods

This single-center, prospective, observational study was approved by The University of Texas Health Science Center at San Antonio's investigational review board and the University Health System Clinical Research Department. The purpose was to measure the impact of pharmacist interventions on prospectively selected short-term outcomes in the management of post-transplant hyperglycemia/diabetes. All patients provided informed consent. The study was conducted in full accordance with the principles of the Declaration of Helsinki and Good Clinical Practice guidelines and adhered to local and national regulatory requirements and laws.

Inclusion criteria for patient enrollment in the pilot PTDM pharmacotherapy clinic included SOT recipients ≥18 years of age who were diagnosed with post-transplant hyperglycemia or with type 2 diabetes (pre- or post-transplant). Patients diagnosed with post-transplant hyperglycemia had received a transplant within 45 days of clinic enrollment and exhibited blood glucose levels ≥200 mg/dL or had already been receiving at least one antidiabetes medication at the time of clinic enrollment. Patients who were >45 days post-transplant were also included if a diagnosis of PTDM was made by a physician at the time of clinic enrollment using at least one of the following diagnostic criteria from the American Diabetes Association (ADA) *Standards of Medical Care in Diabetes—2015*: A1C ≥6.5%, fasting plasma glucose ≥126 mg/dL, or random plasma glucose ≥200 mg/dL with classic symptoms of hyperglycemia (5,8). Exclusion criteria for clinic enrollment included patients with type 1 diabetes, those whose blood glucose was managed via an insulin pump, and those whose glycemia was being managed by a diabetes specialist or endocrinologist. Referred patients who met the inclusion criteria were enrolled in the pilot clinic and managed by a postgraduate year 2 SOT pharmacist resident, under the direct supervision of a transplant CPS between 1 January and 30 June 2015.

Patients were referred to the pilot clinic either directly by a transplantation provider or after identification by the pharmacist as needing a referral. The pharmacist performed a daily review of all patients attending routine transplant clinic appointments and patients admitted to the inpatient transplantation service to identify those who met inclusion criteria. All referred patients were contacted directly by the pharmacist, who explained the risks of diabetes and benefits of diabetes management and offered enrollment in the pilot clinic. Patients were informed at the time of enrollment that PTDM management would be transferred back to their transplant provider at the conclusion of the pilot clinic.

All possible interventions were performed by the pharmacist as determined by the physician-pharmacist-patient team. The scope of diabetes management in collaboration with the physician and patient included the provision of diabetes self-management education, counseling on lifestyle factors affecting diabetes, and counseling on diabetes medications. The teach-back technique was used at the end of each encounter to assess patient understanding of the information provided by the pharmacist (24).

Interventions involving medication initiation or discontinuation or dosage adjustments received either verbal approval (in person or via telephone) or written approval (via email) of a transplant provider before implementation into each patient care plan. All interventions performed by the pharmacist were documented in patients' electronic medical records within 24 hours of each encounter, with a transplant provider added as a cosigner to each progress note. Treatment regimens were initiated or modified following recommendations

Diabetes Spectrum Online Ahead of Print, published online December 27, 2017

from the 2013 international consensus meeting on PTDM and general recommendations for antidiabetes therapy in type 2 diabetes as outlined in the 2015 ADA Standards of Care (5,8). Using these recommendations as a guide, metformin, dipeptidyl peptidase-4 (DPP-4) inhibitors, glucagon-like peptide-1 (GLP-1) receptor agonists, and basal/bolus insulin therapy were selectively used either as monotherapy or in different variations as combination therapy (Figure 1). Medications being initiated were ordered by the pharmacist on behalf of a transplant provider and provided to the patient the day of the encounter, either in clinic or delivered directly to the patient by a local dispensing specialty pharmacy.

Data were collected during each patient encounter and documented in the electronic medical record. Data collection included patient demographics (age, height, actual body weight, date and type of organ transplant, history of diabetes, calcineurin inhibitor and/or corticosteroid use, and history of hepatitis C virus infection), drug intolerances/allergies, and appropriate use of medications and interventions as recommended in the 2015 ADA Standards of Care (8). Baseline and follow-up data included A1C and fasting lipid panel (all measured at the health system's certified laboratory), SMBG results, diabetes and primary/secondary cardiovascular disease prevention regimens, any missed doses of antidiabetes medications or incidences of hypoglycemia in the past 7 days, and incidence of diabetes-related hospitalizations in the preceding 90 days.

Primary outcomes included changes in A1C (analyzed using a Premier Hb9210 HbA1c Analyzer; Trinity Biotech, Jamestown, N.Y.) and mean SMBG results from baseline to a minimum of 3 months after clinic enrollment. Mean SMBG results were defined as the average of all patient self-reported SMBG values over a 7-day period at clinic enrollment and before clinic discharge.

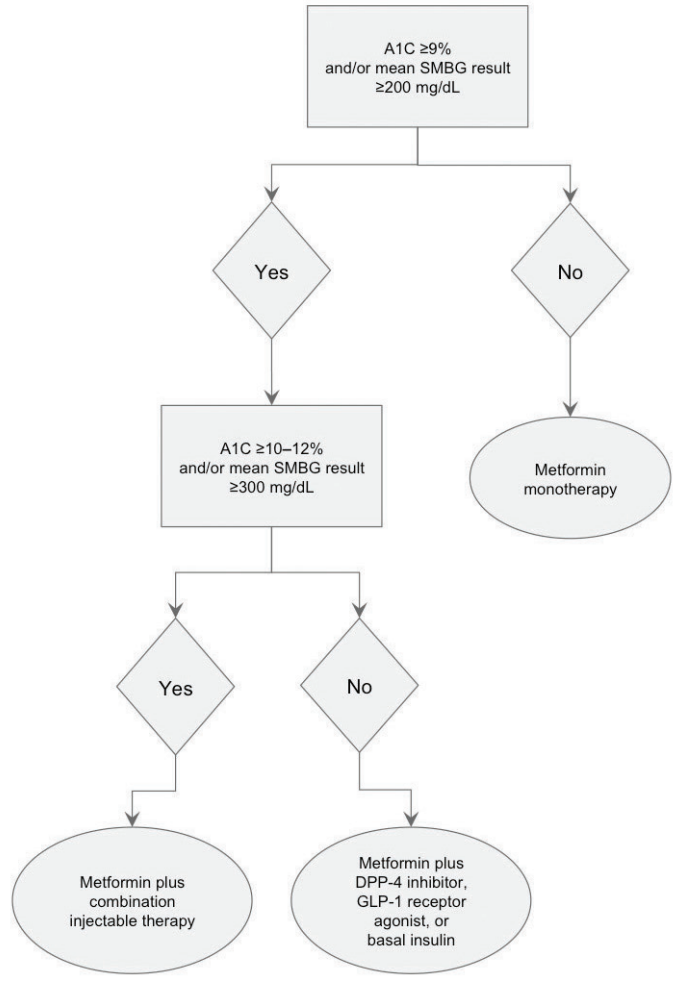

FIGURE 1. Treatment algorithm used for managing patients enrolled in the pilot pharmacist-managed PTDM pharmacotherapy clinic. Metformin, DPP-4 inhibitors, GLP-1 receptor agonists, and basal/bolus insulin therapy were selectively used either as monotherapy or in different variations as combination therapy depending patients' A1C, SMBG results, concomitant medications received (including corticosteroids), and patient-specific comorbidities (including hepatitis C virus infection). Metformin plus combination injectable therapy included basal insulin plus mealtime insulin or a GLP-1 receptor agonist.

Secondary outcomes included pre- to post-intervention analysis of patients followed in the clinic for a minimum of 3 months for the following: average fasting, pre-lunch, pre-dinner, 2-hour post-dinner, and bedtime SMBG results; BMI; incidences of hypoglycemia or missed doses of any antidiabetes medications within the past 7 days; incidence of diabetes-related hospitalizations within the past 90 days; and any medication-related intervention made by the pharmacist during the study period. Hypoglycemia was defined as any symptomatic incidence of blood glucose <70 mg/dL and requiring self-treatment for hypoglycemia in the past 7 days.

Descriptive statistics were used for patient demographics. A paired *t* test or Wilcoxon ranked-sum test was conducted to compare continuous variables before and after intervention where appropriate. An a priori significance level of <0.05 was defined as statistically significant.

Results

Thirty-three SOT recipients with PTDM or post-transplant hypergly-

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cemia were enrolled in the PTDM pharmacotherapy clinic for blood glucose management (Figure 2). Twenty-four patients were included in the final analysis; of the patients excluded, four were lost to follow-up, two were actively being managed by outside providers, one was diagnosed with a terminal illness, one self-withdrew from clinic, and one was hospitalized for >1 month for nondiabetes complications. All patients enrolled in the PTDM pharmacotherapy clinic provided informed consent except for one patient who initially consented but subsequently rescinded enrollment and self-withdrew from the clinic for personal reasons.

The pharmacist conducted face-to-face or telephone visits for initial encounters that were ~60 minutes in length. Follow-up encounters were either face-to-face or via telephone and ranged in length from 15 to 30 minutes depending on individual patient needs.

Baseline characteristics of the study population are reported in Table 1. The mean age was 56 years, and 16 patients (67%) were male. Fourteen patients (58%) were Hispanic, and roughly one-third of the population had a diagnosis of type 2 diabetes before transplant. A total of 10 kidney (42%), 8 liver (33%), 5 lung (21%), and 1 lung/kidney (4%) transplant recipients were included in the final analysis.

The mean time between date of transplant and clinic enrollment was 52 months (6 patients were >5 years post-transplant, 5 were 1–5 years post-transplant, and 13 were <1 year post-transplant). Five patients were enrolled in the clinic within 45 days post-transplant (Figure 2). Of these, one kidney transplant and one liver transplant recipient had type 2 diabetes before their transplant and remained on insulin therapy post-transplant; the remaining three patients were lung transplant recipients, two of whom went on to develop PTDM. For the 19 patients enrolled who were ≥45 days post-transplant, 5 had type 2 diabetes pre-transplant and 14 developed PTDM. All patients were receiving a calcineurin inhibitor at clinic enrollment (23 tacrolimus and 1 cyclosporine), and 17 (71%) were receiving prednisone (4 lung transplant recipients receiving >5 mg/day, and 10 kidney recipients, 1 lung recipient, 1 lung/kidney recipient, and 1 liver recipient each receiving ≤5 mg/day). Active hepatitis C virus infection was present in four liver and two kidney transplant recipients at enrollment; two liver transplant recipients had prior hepatitis C virus infection, although current hepatitis C virus infection status was unknown. The mean time of follow-up was 121 ± 19 days. No patients were treated for any form of allograft rejection during this study.

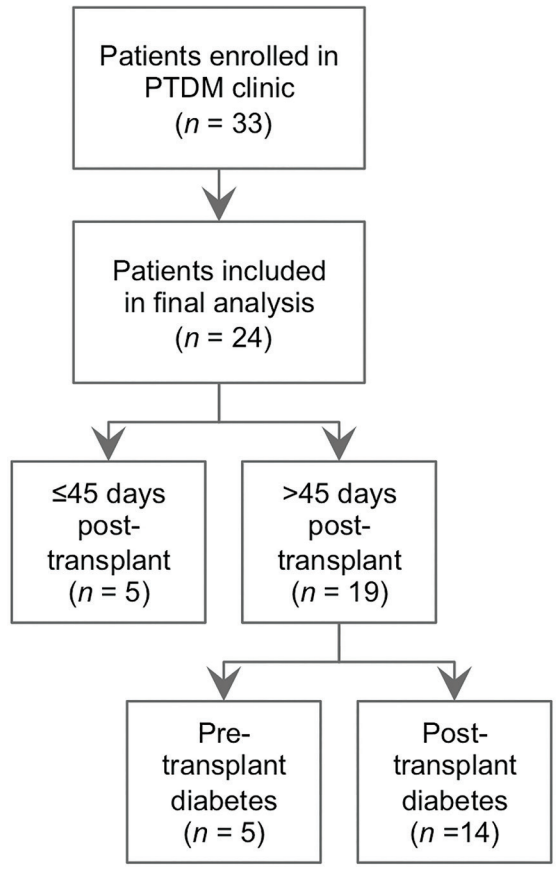

FIGURE 2. Patients enrolled in the pilot pharmacist-managed PTDM pharmacotherapy clinic.

Primary and secondary outcomes are listed in Figure 3 and Table 2. Improvements were realized in markers of glycemic control, including primary outcomes, mean fasting SMBG result, and mean pre-lunch SMBG result (Figure 3). Median A1C decreased significantly from 8.05% at baseline to 6.45% at the last follow-up encounter ($P = 0.0010$). Accordingly, the median 7-day SMBG result (with a median of 4 readings/day at baseline and final encounter) decreased significantly from 191 mg/dL at baseline to 125 mg/dL at the final encounter ($P = 0.0023$). Median fasting and pre-lunch SMBG results decreased significantly from 153 to 120 mg/dL ($P = 0.0064$) and from 212 to 122 mg/dL ($P = 0.0161$), respectively. Changes from baseline in other SMBG values, lipid levels, and BMI were not statistically significant (Table 2).

Interventions performed by the pharmacist are summarized in Table 3. The median number of encounters

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TABLE 1. Patient Demographics (*n* = 24)

Age (years; mean ± SD)	56 ± 8
Male (*n* [%])	16 (67)
Race/ethnicity (*n* [%])	
Hispanic/Latino	14 (58)
White	9 (38)
African American	1 (4)
Transplanted organ (*n* [%])	
Kidney	10 (42)
Liver	8 (33)
Lung	5 (21)
Lung/kidney	1 (4)
Mean time since transplant (months)	52
Transplant immunosuppression (*n* [%])	
Tacrolimus	23 (96)
Cyclosporine	1 (4)
Prednisone	17 (71)
>5 mg daily	4 (17)
5 mg daily	12 (50)
<5 mg daily	1 (4)
Diabetes pharmacotherapy (*n* [%])	
Insulin	19 (79)
Long-acting (basal)	2 (8)
Short-acting (bolus)	3 (13)
Basal plus bolus	14 (58)
Metformin	1 (4)
Thiazolidinedione	1 (4)
None	4 (17)
Nonadherence* (*n* [%])	7 (29)
Diabetes diagnosis pre-transplant (*n* [%])	7 (29)
Hepatitis C virus infection (*n* [%])	
Active infection	6 (25)
History of infection	2 (8)
BMI (*n* = 23) (kg/m^2, mean ± [SD])	27.33 ± 4.28
A1C (*n* = 20) (% [IQR])	8.05 (6.33–11.75)
7-day SMBG result (*n* = 20) (mg/dL, mean [IQR])	191 (138–232)
Fasting SMBG result (*n* = 19) (mg/dL, mean [IQR])	153 (117–208)
Pre-lunch SMBG result (*n* = 12) (mg/dL mean [IQR])	212 (159–258)

**At least one self-reported missed dose of an antidiabetes medication in the past 7 days.*

per patient was 6. For patients receiving insulin, the median number of dosage adjustments per patient was 3. The mean number of dosage adjustments for the two patients receiving a GLP-1 receptor agonist was 3.5. All three patients receiving metformin at the time of enrollment had doses decreased from 1,000 to 500 mg orally twice daily. Metformin and the DPP-4 inhibitor sitagliptin were initiated in 50 and 25% of patients during the intervention period, respectively. Insulin was the most commonly discontinued medication (six patients), and two patients were switched (one from 70/30 NPH/regular and one from 75/25 insulin lispro protamine/insulin lispro) to insulin detemir/insulin aspart. Four patients were initiated on aspirin, and five patients were initiated on a statin for primary or secondary cardiovascular disease prevention. Metformin plus combination injectable therapy was the most common regimen patients were receiving at the conclusion of the pilot study (seven patients). Other combinations of antidiabetes medications patients were receiving at the time of discharge from the pilot clinic are listed in Table 4.

One-half of all patients reported experiencing at least one episode of hypoglycemia requiring self-treatment in the 7 days preceding clinic enrollment; 21% of all patients reported at least one diabetes-related inpatient admission within the preceding 90 days (Table 5). Fewer patients reported episodes of hypoglycemia in the past 7 days at clinic discharge, and no patients reported having any diabetes-related inpatient admissions in the past 90 days at clinic discharge. There were no changes in self-reported medication adherence from baseline to clinic discharge. Nausea was the most common adverse event reported by patients receiving a GLP-1 receptor agonist. No significant drug interactions were identified during the study period.

Discussion

This observational study demonstrated that direct pharmacist management of hyperglycemia/diabetes significantly improved short-term diabetes-related outcomes in SOT recipients at our transplant center. Specifically, improvements in glycemic control were noted for the primary outcomes within the 6-month intervention period, with a median

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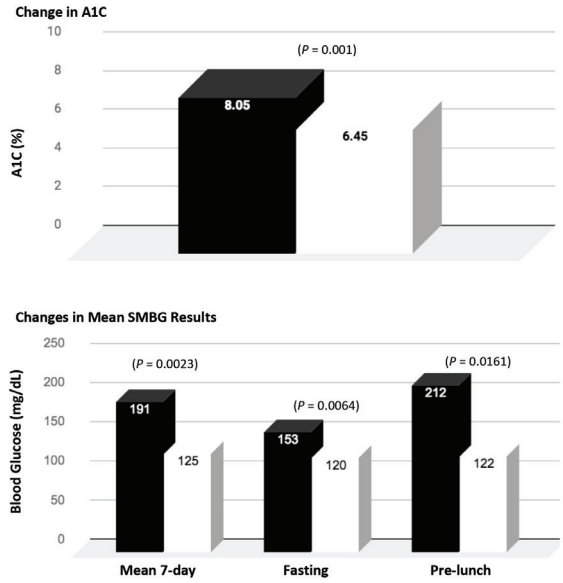

FIGURE 3. Significant changes in A1C and mean 7-day, fasting, and pre-lunch SMBG results. Black bars = baseline, white bars = follow-up. Patients included in final analyses: change in A1C (n = 20), change in mean 7-day SMBG result (n = 20), change in mean fasting SMBG result (n = 19), and change in mean pre-lunch SMBG result (n = 12).

reduction in A1C of 1.6% and a median reduction in mean 7-day SMBG result of 66 mg/dL. Significant reductions were also observed in both fasting and pre-lunch SMBG results. Although not statistically significant, hypoglycemic episodes and inpatient admissions due to diabetes-related complications were also numerically reduced.

These positive outcomes are most likely a direct reflection of the close follow-up by the pharmacist, with a median of six encounters per patient during the intervention period. During each encounter, the pharmacist reinforced the importance of diet and lifestyle modifications and reassessed the safety and efficacy of each diabetes regimen. This cohort of patients was older (age ≥45 years) and overweight (BMI >25 kg/m^2); in addition, two-thirds were of high-risk race/ethnicity (e.g., Hispanic/Latino or African American), and one-third had a history of hepatitis C virus infection. The significance of the pharmacist's impact is further magnified by this relatively high-risk population (5,7,8,15,25).

The pharmacist was inclined to start antidiabetes medications that transplant providers were previously reluctant to use in the post-transplant population, mainly because of the close follow-up required. Sulfonylureas were avoided because of the potential for maladaptation of pancreatic β-cells and evidence suggesting significantly increased all-cause mortality in patients prescribed sulfonylureas compared to metformin (26,27).

One-half of the study population was initiated on metformin, a biguanide insulin sensitizer that may potentially improve basal and postprandial SMBG results, especially in an overweight patient population (28). Metformin may also directly counteract the cumulative diabetogenic effects from chronic administration of calcineurin inhibitors and corticosteroids, as well as hepatitis C virus, by decreasing insulin resistance (3,7,9,28). However, metformin warrants close monitoring of liver and kidney function in this vulnerable population because of the risk of lactic acidosis (28).

Although the maximum recommended daily dose of metformin is 2,550 mg in adults, a maximum daily dose of 1,000 mg was conservatively used because of the potential for changes in liver and/or kidney function, as accumulating observa-

TABLE 2. Other Clinical Outcome

Variable	Baseline	Follow-Up
Pre-dinner SMBG result (n = 11) (mg/dL)	190 (159–244)	142 (113–206)
2-hour post-dinner SMBG result (n = 8) (mg/dL)	139 (114–211)	116 (105–148)
Bedtime SMBG result (n = 4) (mg/dL)	185 (135–243)	122 (103–184)
Total cholesterol (n = 10) (mg/dL)	172 (148–196)	175 (139–207)
LDL cholesterol (n = 9) (mg/dL)	73 (58–104)	81 (36–100)
HDL cholesterol (n = 9) (mg/dL)	55 (39–62)	45 (42–59)
Triglycerides (n = 10) (mg/dL)	214 (116–356)	209 (125–278)
BMI (n = 23) (kg/m^2)	27.33 ± 4.28	27.29 ± 4.16

All values expressed as median (IQR) except BMI, which is expressed as mean ± SD. All P values for outcomes listed in this table were not statistically significant (P >0.05).

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TABLE 3. Pharmacist Interventions

Patient encounters (*n* = 24) (median number per patient [IQR])	6 (4–7.75)
Dosage adjustments (number per patient)	
Insulin (*n* = 20) (median [IQR])	3 (2–4)
GLP-1 receptor agonist (*n* = 2) (mean ± SD)	3.5 ± 0.7
Metformin (*n* = 3) (mean ± SD)	1 ± 0
Medication initiations (*n* [%])	
DPP-4 inhibitor	6 (25)
GLP-1 receptor agonist	2 (8)
Metformin	12 (50)
Basal/bolus insulin	2 (8)
Long-acting insulin only	1 (4)
Omega-3 fatty acids	2 (8)
Fenofibrate	1 (4)
Statin	5 (21)
Aspirin	4 (17)
Medication discontinuations (*n* [%])	
Insulin	6 (25)
Thiazolidinedione	1 (4)
Metformin	1 (4)
Statin	1 (4)
Ezetimibe	1 (4)

TABLE 4. Antidiabetes Pharmacotherapy Regimens Patients Were Receiving at the Time of Discharge From the Pilot Clinic

Antidiabetes Regimen	Patients (*n* [%])
Metformin only	1 (4)
Metformin plus DPP-4 inhibitor	1 (4)
Metformin plus GLP-1 receptor agonist	1 (4)
Metformin plus basal insulin	1 (4)
Metformin plus basal/bolus insulin	7 (29)
Metformin plus basal insulin plus GLP-1 receptor agonist	1 (4)
Basal insulin only	1 (4)
Basal/bolus insulin	4 (17)
Basal insulin plus DPP-4 inhibitor	2 (8)
DPP-4 inhibitor only	2 (8)
No pharmacotherapy	3 (12)

tional data suggest that metformin may be safely continued down to a glomerular filtration rate as low as 30 mL/min/1.73 m^2 at reduced dosages (28–31). In addition, the U.S. Food and Drug Administration recently required labeling changes to expand metformin's use in certain patients with reduced kidney function, further supporting the safety of metformin use in patients with mild-to-moderate renal impairment (31).

One-third of patients were started on a GLP-1 receptor agonist (liraglutide or exenatide) or a DPP-4 inhibitor (sitagliptin). These agents may also directly counteract the pancreatic β-cell toxicity associated with chronic administration of calcineurin inhibitors and corticosteroids, thus leading to improvements in glycemic control by conferring potential β-cell protection (32–36). However, these agents are often challenging to initiate because of dose-limiting side effects, unfamiliarity due to lack of evidence in the SOT population, and lack of data to date demonstrating a reduction in cardiovascular morbidity and mortality in the general population. GLP-1 receptor agonists, for example, require subcutaneous injections and can cause nausea, vomiting, and/or diarrhea, sometimes necessitating discontinuation of the drug (33–35). For these reasons, patients receiving a GLP-1 receptor agonist had more frequent follow-up contacts. Moreover, many insurance plans require prior authorization for agents in these drug classes because they tend to be expensive.

The majority of patients were already on an insulin regimen at clinic enrollment. Patients on insulin therapy also had more frequent follow-up contacts because of the potential for hypoglycemia, especially if they were on a corticosteroid taper and there was a need for more frequent dose titration to maintain euglycemia. The pharmacist made frequent adjustments to these regimens (a median of three adjustments per patient during the follow-up period) and switched insulin formulations in two patients. In addition, the pharmacist discontinued insulin in six patients, all of whom remained off insulin and on either oral antidiabetes therapy or on no pharmacotherapy for diabetes. Of these six patients, only one (a de novo lung transplant recipient) was receiving >5 mg/day of prednisone, and one (a lung transplant recipient) was receiving 5 mg/day of prednisone at the time of clinic enrollment. The remaining four patients (two kidney and two liver transplant recipients) were not receiving any corticosteroids at the time of clinic enrollment.

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TABLE 5. Incidences of Hypoglycemia, Nonadherence, and Diabetes-Related Hospitalizations

Outcome	Pre-Clinic Enrollment (n [%])	At Clinic Discharge (n [%])
Hypoglycemia*	12 (50)	2 (8)
Nonadherence†	7 (29)	7 (29)
Inpatient hospitalization‡	5 (21)	0 (0)
Hyperglycemia§	3 (13)	
Hypoglycemia‖	2 (8)	

**Blood glucose <70 mg/dL, symptomatic, and requiring self-treatment for hypoglycemia in past 7 days.*
†At least one self-reported missed dose of an antidiabetes medication in the past 7 days.
‡Inpatient hospitalization with primary diagnosis related to diabetes in the past 90 days.
§Hyperglycemia secondary to diabetic ketoacidosis or hyperosmolar hyperglycemic state.
‖Hypoglycemia leading to loss of consciousness and subsequent inpatient admission.

That most of these patients were not receiving corticosteroids at all or as part of a taper schedule suggests that the improvements in blood glucose were not because of a lack of effects of corticosteroids, but rather from the close follow-up and intervention of the pharmacist.

Pharmacist-run clinics have demonstrated positive outcomes in chronic disease state management, including diabetes, hypertension, and hyperlipidemia management in the general, nontransplant population (16–20,22). In the transplant population, much of the literature accentuating the impact of transplant pharmacists centers on adherence and the impact of clinical pharmacy services in the ambulatory care setting (21,23,37–39). Wang et al. (38) reported improved blood glucose in renal transplant recipients after clinical pharmacist intervention in a renal transplant clinic. Chisolm-Burns et al. (39) reported a significantly higher overall adherence rate and improvement in fasting blood glucose in renal transplant recipients after implementation of clinical pharmacy services in a renal transplant clinic. With regard to direct pharmacist management of diabetes, Pinelli et al. (21) successfully implemented a pharmacist-managed diabetes and cardiovascular risk reduction clinic in kidney transplant recipients and demonstrated improved patient outcomes and reduced health care resource utilization after implementation. However, no other studies regarding pharmacist management of diabetes in the transplant population have been reported to date.

Inherent limitations of this single-center, observational study design restrict the external validity of the findings. The pilot clinic was established as a residency project and managed primarily by a postgraduate trainee and thus had to be completed in a 1-year timeframe. The enrollment period was limited to 3 months with a follow-up period of 3–6 months and no historical or contemporary control group was used; thus, a small heterogeneous sample size was included in the final analysis without a control group for comparison, and only short-term outcomes in glycemic control were measured to serve as surrogate markers for long-term allograft and patient survival and comorbidities associated with post-transplant diabetes.

A1C and SMBG results were selected as markers of blood glucose control in this study because they are the two primary techniques available for health care providers and patients to assess the effectiveness of management plans on glycemic control in the general, nontransplant population (8). The shortcomings of using the A1C as an indicator of glycemic control in the SOT population include the possible effect of pre- or post-transplant anemia or receipt of blood transfusions on the A1C, especially within the first year post-transplant (5,8). Furthermore, a limitation of using patient self-reported SMBG results includes adherence to monitoring schedules as instructed and potential for recall bias as data from glucose meters were not transmitted in real time, and the SMBG values recorded by patients were not routinely verified by the pharmacist against patients' glucose meter data. Although the oral glucose tolerance test is considered the gold standard for diagnosing PTDM, it was not used in this study because it is too time consuming and impractical for use in large transplant programs (5).

At our transplant center, no physician-pharmacist collaborative practice agreements currently exist; hence, pharmacists do not have the ability to order laboratory tests or medications independently without physician authorization. As a result, not all patients enrolled in the pilot clinic had baseline and follow-up laboratory tests such as an A1C and a fasting lipid panel. Data on pharmacist interventions accepted or rejected by a transplant provider were not specifically documented; thus, we cannot report the percentage of pharmacist interventions accepted during this study.

The means by which patients were selected for enrollment could have introduced selection bias for more difficult-to-control patients, including those with recent diabetes-related hospitalizations or potentially those being seen in the clinic more often.

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Although selection of these more difficult-to-manage patients could have made the impact of the pharmacist appear greater, these may actually be an ideal sample of patients who could benefit most from pharmacist intervention.

Finally, 17% of patients (n = 4) were receiving >5 mg/day of prednisone at the time of clinic enrollment. Improvements in glycemic control observed in these patients may have been partly due to decreased steroid-induced hyperglycemia as prednisone doses were being tapered down to maintenance doses, thus making it less clear if these improvements were exclusively from pharmacist interventions or from fewer effects of these drugs.

In patients with PTDM, there is a paucity of data linking SMBG results and A1C levels with endpoints such as patient/graft survival and rates of microvascular and macrovascular complications and cardiovascular events (5). Thus, collaboration between multiple transplant centers in large, adequately powered clinical trials is vastly needed, and transplant pharmacists can serve as vital practitioners in meeting this important need.

Conclusion

A pharmacist-managed post-transplant diabetes clinic can significantly affect glycemic control in SOT recipients. We plan to use the positive outcomes from our study to justify a full-time transplant CPS in our outpatient transplant clinic to assist with managing hyperglycemia and diabetes in the post-transplant population.

Acknowledgments

The authors thank all of the patients who participated in this study. They also thank Curtis Triplitt, PharmD, for reviewing the manuscript, and Heather Dobie, PharmD, Elvia Shope, RN, and Michelle Templeton, RN, for their support during the study.

Duality of Interest

No potential conflicts of interest relevant to this article were reported.

Author Contributions

D.M.N. participated in research design, the performance of the research, data analysis, and the writing of the paper. A.R.E. participated in research design, the performance of the research, and the writing of the paper. R.C.H. participated in research design, data analysis, and the writing of the paper and contributed analytical tools. P.R.M. participated in research design, the performance of the research, data analysis, and the writing of the paper. D.M.N. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Prior Publication

An abstract of this study was previously published in an online supplement to the *American Journal of Transplantation* after the presentation of a poster on this study at the 2016 American Transplant Congress in Boston, Mass.

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