Ochsner Journal 17:218–219, 2017

Mobile Technology Can Improve Adherence and Lessen Tacrolimus Variability in Patients Receiving Kidney Transplants

Julia Torabi, BS,[1,2] Krystina Choinski, BA,[1,2] Alesa Courson, PharmD,[2] Alana Zanetti-Yabur, MD,[1] Juan P. Rocca, MD,[1,2] Jay A. Graham, MD[1,2]

[1]Albert Einstein College of Medicine, Bronx, NY [2]Montefiore-Einstein Center for Transplantation, Montefiore Medical Center, Bronx, NY

TO THE EDITOR

Medication adherence is of paramount importance in transplant recipients. Studies have demonstrated that variability in tacrolimus blood concentrations is associated with de novo formation of donor-specific antibodies and an increased incidence of rejection following renal transplantation.[1-3] These findings are sobering, considering that up to 30% of transplant recipients have self-reported that they miss doses of immunosuppression during the course of a year.[4] We investigated whether the use of mobile technology influenced variability in tacrolimus blood concentrations.

The mobile application (app) Transplant Hero is free to download at the Apple App Store and provides a medication schedule and dose reminder alarm. Offering positive reinforcement for medication adherence, the app also rewards patients with virtual awards for taking their medication on time. While other apps with similar functionality are available, Transplant Hero is the only app designed solely for transplant patients. We tested the impact of Transplant Hero on medication compliance in a small study.

STUDY DESIGN AND RESULTS

Sixty-seven renal transplant recipients were prospectively enrolled and randomized into 2 groups: 18 app users and 49 nonusers. App users were defined as patients who downloaded Transplant Hero onto an Apple iPhone or iPad, and nonusers were patients without an iPhone or iPad. Demographic group differences were understandably nondiscernable because this study was performed in the Bronx, one of the poorest boroughs of New York City, where approximately 30% of the population lives below the poverty line and blacks and nonwhite Hispanics account for more than 80% of the population.[5] At the time of our study, Transplant Hero was only available on the Apple iOS platform; however, it can now be used on any Android device.

App users had a mean age of 53.7 $\pm$ 14.3 years; 13 (72%) received deceased donor renal transplants (DDRTs), 4 (22%) received living donor renal transplants (LDRTs), and one (6%) received a simultaneous pancreas-kidney transplant (SPK). App nonusers had a mean age of 51.6 $\pm$ 13.5 years, and the cohort included recipients of 43 (88%) DDRTs, 3 (6%) LDRTs, 2 (4%) SPKs, and 1 (2%) pancreas-after-kidney transplant.

Tacrolimus whole blood concentrations and serum creatinine were measured during the course of 3 months. Inpatient tacrolimus levels were excluded to account for increased medication adherence during hospital admissions. The variability in tacrolimus levels was calculated using the coefficient of variability (CV): CV = (standard deviation/mean tacrolimus) $\times$ 100. CV has been shown to be a critical indicator of chronic rejection determined during protocol biopsies of renal allografts.[6]

In our patient cohort, CV was significantly lower in app users compared to nonusers at 1 month (27.7 vs 37.0, respectively, P=0.014) but not different at 3 months (33.6 vs 35.4, respectively, P=0.63). Furthermore, no difference was found in serum creatinine in app users and nonusers at 1 and 3 months (P=0.65 and P=0.83, respectively). Using a logistic regression model, we analyzed which variable had the most significant impact on app usage vs nonusage to confirm our initial findings. CV at 1 month was a significant predictor of app utilization (odds ratio 0.916; 95% confidence interval 0.858-0.977; P=0.007). CV at 3 months remained insignificant (P=0.145), as did age (P=0.95).

DISCUSSION

While this study is limited in scope, the significant CV reduction in app users at 1 month is encouraging. As such, mobile technology represents a powerful tool to intervene in the early postoperative period when patients may be at highest risk for medication nonadherence. Studies have demonstrated that a higher CV corresponds with worse clinical outcomes as defined by graft loss, biopsy-proven chronic allograft nephropathy, and declining renal function.[2,6] Given that CV has been proposed as a surrogate marker for nonadherence,[3] our data suggest that mobile technology may promote adherence to posttransplant immunosuppression while lowering tacrolimus blood concentration variability. In this study, comparative CV improvement early (at 1 month) but not later (at 3 months) may represent a positive reinforcement effect during the initial medication regimen learning period following transplantation.

Mobile health platforms are the future and will define how we interact and communicate with our patients. This brief observational study should encourage other institutions to embrace innovation and define the benefits of eHealth. Here, we demonstrate an association between app usage and decreased tacrolimus variability. Further efforts can be correlated with patient behavior (no-show rates), readmission rates, and rejection episodes so as to more fully

understand the advantages provided by this app and other technology.

ACKNOWLEDGMENT

Dr Jay Graham is the chief executive officer/founder of Transplant Hero.

REFERENCES

1. Borra LC, Roodnat JI, Kal JA, Mathot RA, Weimar W, van Gelder T. High within-patient variability in the clearance of tacrolimus is a risk factor for poor long-term outcome after kidney transplantation. *Nephrol Dial Transplant*. 2010 Aug;25(8): 2757-2763. doi: 10.1093/ndt/gfq096.
2. Prytula AA, Bouts AH, Mathot RA, et al. Intra-patient variability in tacrolimus trough concentrations and renal function decline in pediatric renal transplant recipients. *Pediatr Transplant*. 2012 Sep;16(6):613-618. doi: 10.1111/j.1399-3046.2012.01727.x.
3. Hsiau M, Fernandez HE, Gjertson D, Ettenger RB, Tsai EW. Monitoring nonadherence and acute rejection with variation in blood immunosuppressant levels in pediatric renal transplantation. *Transplantation*. 2011 Oct 27;92(8):918-922. doi: 10.1097/TP.0b013e31822dc34f.
4. Dew MA, DiMartini AF, De Vito Dabbs A, et al. Rates and risk factors for nonadherence to the medical regimen after adult solid organ transplantation. *Transplantation*. 2007 Apr 15;83(7): 858-873.
5. Bronx, New York (NY) Poverty Rate Data: Information About Poor and Low-Income Residents. http://www.city-data.com/poverty/poverty-Bronx-New-York.html. Accessed June 7, 2017.
6. Vanhove T, Vermeulen T, Annaert P, Lerut E, Kuypers DRJ. High intrapatient variability of tacrolimus concentrations predicts accelerated progression of chronic histologic lesions in renal recipients. *Am J Transplant*. 2016 Oct;16(10):2954-2963. doi: 10.1111/ajt.13803.