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Transplant surgery enters a new era: Increasing immunosuppressive medication adherence through mobile apps and smart watches

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ABSTRACT

The high rate of immunosuppressive medication non-adherence in transplant recipients demands the search for a solution that targets modifiable risk factors and incorporates mobile health technology to better engage and educate patients. Kidney transplant recipients (kidneys alone or multi-organ) were randomized to receive a mobile app known as Transplant Hero, both the app and a smart watch, or neither. The coefficient of variability (CV) of tacrolimus levels was measured at one and three months. No statistically significant differences in CV levels were observed between the three groups at either one or three months. Although mobile health apps are a promising strategy for increasing medication adherence, further research is required to determine how to best use this technology.

Introduction

Medication non-adherence may be defined as "deviation from the prescribed medication regimen sufficient to influence adversely the regimen's intended effect."[1] This pitfall to successful care is particularly critical for immunosuppressive medication in solid organ transplant recipients. In this population, rates of non-adherence are reported as high as 65%.[2] Studies differ regarding the rates for specific organs, with kidney recipients either having the highest or lowest rates of non-adherence.[3,4]

Intense efforts to increase rates of adherence in transplant management have long been underway due to the proven complications resulting from missing medication doses. Non-adherence to immunosuppressive regimens increases the odds of graft failure sevenfold compared with adherent individuals, and 36% of graft failures have been associated with medication non-adherence.[5] Other complications include increased rates of acute rejection, reduced renal function, and increased healthcare costs.[5]

A comprehensive strategy to combat this problem must first identify why patients are non-adherent. Risk factors for non-adherence may be divided into five classes, namely (1) socioeconomic; (2) patient-related; (3) disease-related; (4) treatment-related; and (5) health provider and system.[1] Specific modifiable risk factors include lack of a reminder system, low conscientiousness, lack of medical knowledge, and an inability to educate patients.[1,2] With this in mind, successful strategies have incorporated targeting more than one risk factor in a multilevel approach, including both patient-related factors and health-systems based ones. Methods that combine educational, affective, and behavioral interventions have further improved adherence rates.[1] Affective interventions include targeting feelings, emotions, and social relationships, whereas behavioral interventions include reminders, rewards, skill building activities, packaging medications, and dosage modification.[6]

The past two decades have further seen a change in how these interventions have been implemented. In 2016, the World Health Assembly recognized mobile heath (mHealth) as possessing "the potential to revolutionize how populations interact with national health services."[7] More individuals are using smartphones and possess a positive attitude toward using mobile health apps.[8] Previous studies in pediatric liver transplant recipients have shown that text reminders increase medication adherence rates.[9]

We sought to test whether a mobile app (Transplant Hero) targeting multiple levels of risk factors for non-adherence can increase immunosuppressive medication adherence in adult kidney, pancreas, and/or liver transplant recipients. We have previously shown the app increases patient education, with patients using the app more likely to remember their medication regimen than those

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not using it.[10] Further, the app is designed to increase adherence through social influences, allowing users to invite family and friends to join in their care; as well as through positive reinforcement, providing virtual rewards for completed tasks; and alarm reminders.[10,11] These thus comprise the three realms of interventions mentioned previously to coalesce into increased medication adherence: educational, affective, and behavioral.

Materials and methods

This is a single center prospective cohort of patients >18 years who received deceased donor renal transplant (DDRT), living donor renal transplant (LDRT), simultaneous pancreas – kidney transplant (SPK), or liver-kidney transplant at Montefiore Medical Center between January 2015–December 2016. Mobile application (App) Transplant Hero® was utilized in this study to function as an interactive alarm and to remind patients to take their medications as well as provide educational content. Users were randomly offered either the mobile app or the mobile app in addition to a wearable smart watch that connected through Bluetooth ®. A Pebble Smart watch Technology® was used for this study to display the reminder notifications.

Maintenance immunosuppression included a tacrolimus, a mycophenolic acid derivative, and a prednisone taper starting at the time of transplantation that was reduced to and then maintained a level of 5 mg/day by 3 months after transplantation.

Adherence was compared using the coefficient of variability (CV) = (standard deviation/mean tacrolimus)*100 which has previously been used as a marker for chronic rejection.[12] Groups were compared using a two-tailed *t*-test or chi-squared test to determine p-values, with a p-value of less than 0.05 considered significant. SPSS version 24.0 was used for analysis.

Results

A total of 108 patients were enrolled in our study. 19% of patients received both the smart watch and mobile app (watch/mobile app user; WMAU), 35% received the mobile app alone (mobile app user; MAU), and 46% received neither the mobile app nor the smart watch (no app user; NAU) (Table 1). Demographics were collected and displayed in Table 1. There were no significant difference between groups.

In both the WMAU group and the MAU group, the most common transplant was a DDRT (70% and 62%, respectively). In the NAU group, the most common transplant was an LDRT (58%) (Table 2).

The coefficient of variability (CV) of tacrolimus levels was calculated at both one month and three month post-transplant for all three groups. The CV for the NAU group was 31.7% at one month and 32.8% at three months; for the MAU group it was 30.4% at one month and 33.0% at three months; and for the WMAU group it was 35.5% at one month and 33.8% at three months. No significant difference was observed when comparing the WMAU group to the NAU group ($p = .96$ at 1 month; $p = .81$ at 3 months); nor when comparing the MAU group to the NAU group ($p = .68$ at 1 month; $p = .45$ at 3 months). (Table 3).

Discussion

The integration of mobile apps into healthcare delivery provides a key complement to the electronic medical record (EMR): it allows patients to take their own “EMR” home from the hospital and to sustain the health improvements from their admission. Previous studies have described how mobile health can better enable patients to monitor their diabetes, hypertension, fitness, and other health concerns.[13] This is particularly important for transplant

Table 1
Patient demographics.

	No App User (NAU)	Mobile App User (MAU)	Watch/Mobile App User (WMAU)	p - value
N	50	38	20	
Mean Age	53	52	50	NS
% Female	28	35.9	25	NS
BMI	29.7	29.0	28.2	NS
DM (%)	36	50	37	NS
HTN (%)	100	100	100	NS
Employment (%)	40.4	23.5	57.9	NS
Employment Under 65 (%)	47.5	27.3	61.1	NS
Requiring Interpreter	17	26.5	15.8	NS
Married (%)	48.9	58.8	36.8	NS
Race (%)				
Black or African American	36.2	41.2	47.4	NS
Spanish/Hispanic/Latino	31.9	20.6	15.8	NS
White	10.6	8.8	21.1	NS
Unknown/Other	21.3	29.3	15.8	NS

Table 2
Transplant type.

	No App User (NAU)	Mobile App User (MAU)	Watch/Mobile App User (WMAU)
% Living donor renal transplant (LDRT)	58	23	25
% Deceased donor renal transplant (DDRT)	36	62	70
% Multi-organ transplant	6	15	5

Table 3
Coefficient of variability (CV) of Tacrolimus levels.

	No App User (NAU)	Mobile App User (MAU)	p-value	Watch/Mobile App User (WMAU)	p-value
1 Month CV Tacro	31.7	30.4	.68	35.5	.96
3 Month CV Tacro	32.8	33.0	.45	33.8	.81

surgeons, for whom a long-term successful transplant requires strict outpatient immunosuppressive medication adherence.[14]

Moreover, as patients become more engaged in their health management through mobile apps, these apps further serve as a vehicle for increased patient education.[15] As mentioned above, educating patients about their diseases has been associated with improved medication adherence.[1] Thus, this study represents one of the first to test whether this mobile health technology, by engaging and educating, can increase specifically immunosuppressant medication adherence.

The coefficients of variability in this study ranged from 30.4 to 35.5. Previous studies measuring coefficients of variability have created tertiles, with the highest tertile of patients containing mean CV values of 31.1±7.8.[12] All of the groups in our study would thus fit into the highest tertile. Patients in this tertile were believed to be less adherent to their medications and at greater risk of rejection than patients in the lower two tertiles.[12]

Ultimately, our study did not show an increase in medication adherence through the use of mobile health apps. However, our study contained certain limitations. Adherence rates of the technology were not measured, thus preventing us from determining patient utilization of the mobile app or smart watch. The limited sample size may have led to a type II error, and a true difference between the two groups may not have been observed. Despite these results, this study shows that although mobile apps and smart watches may provide a promising target for increasing adherence, more work and research is required to establish how to best use this technology.

What is clear is that “taking immunosuppression must become as second nature to patients as checking email or texts on their smartphones or the time on their smart watches”. However, it is yet unclear what technological approach would be of most benefit to patient and offer ease of adaptability. As such, future studies are needed to address mHealth influence on adherence in this vulnerable population.

Disclosures

Jay A. Graham is owner and CEO of Transplant Hero LLC. No other authors have conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amjsurg.2019.02.018.

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