Exploring the usage of a mobile phone application in transplanted patients to encourage medication compliance and education

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ABSTRACT

Background: Medication non-adherence in transplant patients is a grave problem that results in increased rejection episodes, graft loss and significant morbidity.
Methods: The efficacy of users and non-users of a mobile phone application (mobile app) in promoting medication adherence was investigated. The Beliefs about Medicine Questionnaire (BMQ) and Morisky Medication Adherence Scale (MMAS-8) were used in these cohorts to assess the predilection for poor adherence. Serum tacrolimus, creatinine levels, and rejection episodes were also recorded. Lastly, the patients were tested on their recall of their immunosuppression.
Results: Overall, patients had extremely negative beliefs about medication reflected in their tendency toward higher predicted rates of non-adherence. Interestingly, though not significant, app users had higher rates of medication recollection.
Conclusions: The high-risk nature of this population demands efforts to abrogate non-adherence. Caregivers are charged with the responsibility to offer patients a feasible option to safeguard treatment compliance. Mobile apps are a potentially powerful tool, which can be used to decrease non-adherence.

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1. Introduction

Medical non-adherence in transplant patients represents a serious problem and results in poorer outcomes due to increased rates of rejection and graft loss. Conservative estimates purport that one half of rejection episodes and 15% of graft losses are due to immunosuppression non-adherence.[1,2] A meta-analysis by Butler et al. validated these findings and purported a sevenfold increased risk of graft failure in patients that were non-adherent.[3] A prospective study by Vlaminck et al. would further corroborate the aforementioned results and demonstrate in kidney transplant patients a 23% incidence of non-adherence.[4] More importantly, 21% of those patients that were non-adherent were beset by rejection as compared to 8% in the adherent recipient group.

Notably, efforts to curb non-adherence have proved challenging, as up to 30% of patients may "miss doses" of their immunosuppression during the course of one year.[5] Given that even slight variations from an immunosuppression regimen may correlate with poorer patient and graft outcomes, it is important to identify those at-risk.

A tacit realization of the major problem of non-compliance in transplant patients has led to the adoption of many tools that may aid in prediction of adherence. Self-assessment scoring systems, like the Beliefs about Medicines Questionnaire (BMQ) and 8-item Morisky Medication Adherence Scale (MMAS-8) have been used with some success in other disease models to predict the likelihood of compliance.[6–9] As such, these instruments have been adopted as with other self-appraisal tools to gain a foothold on foreseeing compliance issues.[10]

However, identification of the problem is not enough and clinicians have looked to solutions to abrogate non-adherence. Endeavors like the electronic pill dispenser have attempted to address

medication adherence in "real-time". While this market is occupied by different products, the logic usually dictates that a "smart" pillbox alerts and allots medication according to preset times. However, the promise of this technology has not always lived up to its touted benefits given that medication dispensing does not always correlate with patient adherence.[11]

Here we describe another adjunct to aid in immunosuppression adherence that approaches this difficult issue by serving to educate the patient. In keeping with the rapid advances of technology, a mobile phone application (mobile app) was adopted to assist transplant recipients with taking their medication. Importantly, this group was studied and compared to another group that did not utilize the mobile app. The two groups were surveyed during the peri-operative period with a seemingly beneficial effect for the transplant recipients using the mobile app. Interestingly, while rejection rates were exceedingly low in both groups, patients using the mobile app seem to remember more of their immunosuppressive regimen, which may ultimately prove valuable down the road.[12]

2. Methods

2.1. Study cohort

Patients over 18 years old who underwent kidney or liver transplant at Montefiore Medical Center over a 6-month period beginning June 2015 were asked to participate in this study with informed consent. Patient unwilling to participate were excluded from the study. The patients self-selected themselves into two arms of the cohort with the possession or lack of possession of an Apple® iPhone or iPad. Users were defined as those who downloaded the mobile app onto an iPhone or iPad and non-users as those without an iPhone or iPad (the iPhone application only functioned on iOS (Apple's operating system). The mobile app entitled Transplant Hero™ can be downloaded for free for on the Apple® App Store.

2.2. Mobile phone application

A mobile phone application named Transplant Hero™ was used to help transplant patients deal with the seemingly impossible task of taking their immunosuppression medications in a timely fashion. Recognizing that no person is an island, this medication reminder also helps improve the communication between Transplant Heroes and their family and friends, allowing them to participate in their care as a tool to maximize better health post-operatively through medication adherence.

At the core, Transplant Hero™ is an alarm system that alerts the user when it is time to take their medication. The software is an interactive, educational and simple to use tool that offers users positive reinforcement for medication adherence.

2.3. Questionnaire appraisal

Three surveys were used to question patients about their personal beliefs about medication and their immunosuppressive treatment recall. The BMQ was used to assess specific and general medication beliefs. Administered to patients during their initial hospital stay, this 17-question survey provided an assessment of their general perception of medication while also measuring their concerns directed at their specific condition. It is validated as a tool to predict medication non-adherence, the BMQ is devised to shed light of the causative factors by prompting the patient to answer questions centered on generalized fear of the *harmful* effects of medication or their *overuse*. More specifically, the subjects were also queried as to their opinion about the *necessity* about their

medication and their *concern* about adverse effects. A Likert-scoring system was used for questions and summation of increasing value coincided with negative views toward medication.[13,14]

The MMAS-8 was administered at approximately 3 months post-transplant. Another tool of self-assessment, this 8-question survey has also been validated as an important tool in gauging adherence patterns.[10] This questionnaire is comprised of 8 questions that indirectly evaluate medication habits by querying issues that may upset these efforts, such as problems with recall, substantial drug side effects and increasing demands of the medication regimen. Patients answer in a binary "Yes or No" fashion for the first 7 items, the last item is comprised of a Likert-scale question. Each positive response accounts for one point on the final score resulting in a total scale that has a range from 0 to 8 with an alpha reliability of 0.83 in previous publications.[7] We have used a 100% completion criterion for establishing eligibility and achieving a compliance scale based on score: low adherence (<6), medium adherence ($6 \leq 8$) and high adherence ($=8$). Notably, item number 5 requires a reversion of the code response in a positive direction.

The *Immunosuppression Assessment Test* (IAT) is an ad hoc test devised by our study group and used to gauge the capability of patients to properly remember their immunosuppressive treatment. While not validated, the IAT provides a simple, tangible and basal approach to measure patient immunosuppression recall. The IAT was administered concomitantly with the MMAS-8 and consisted of the patient prompt to document their immunosuppressive regimen. The IAT assigns 1-point for each correct medication with a maximum of 3-points. Correct answers are denoted by the correct name of the immunosuppressive drug and not the dose or schedule.

2.4. Serum tacrolimus, creatinine and rejection assessment in the patient cohort

In addition to these 3 surveys, the patient's serum tacrolimus and creatinine levels were documented at every interval over the 3-month period. Biopsy proven acute rejection (BPAR) was also documented in this patient cohort over the duration of this study.

2.5. Statistical analysis

The actuarial method of Kaplan and Meier was used to measure the compliance and educational gain of post-transplanted patients using a mobile phone application with 95% confidence intervals. Adherence was assessed during the peri-operative period up to 3 months post-transplant, and results from mobile phone application users and non-users were compared using a two-tailed *t*-test. A p-value < 0.05 was considered significant.

3. Results

3.1. Patient characteristics

The Albert Einstein College of Medicine Internal Review Board approved this study. 74 subjects who met the aforementioned criteria were captured in this study. Patients were self-selected into 2 groups as described above. There were 21 mobile app users and 53 non-app users. The average age was 52.6 and 54.1 years old for users and non-users respectively. Of all the subjects who underwent transplantation, 67 received a kidney transplant (n = 43 males and n = 24 females); and 7 received a liver transplant (n = 4 males and n = 3 females).