Parent and patient perspectives on barriers to medication adherence in adolescent transplant recipients

Simons LE, McCormick ML, Mee LL, Blount RL. Parent and patient perspectives on barriers to medication adherence in adolescent transplant recipients.


Abstract: The aim of this study was to identify barriers to medication adherence in adolescent transplant recipients. Eighty adolescent transplant recipient families reported in an open-ended manner about barriers to medication adherence. These responses were then coded to reflect potentially important themes associated with medication adherence. The themes derived included: forgot/distracted, poor planning/scheduling issues, physical barriers/medication issues, and voluntary resistance/attempts to be normal. Inter-rater reliability for barrier coding was very high (k = 0.91). Patients who were classified as non-adherent reported significantly more overall barriers, more forgot/distracted barriers, and more voluntary resistance/attempts to be normal barriers than those classified as adherent. Non-adherence was also found to be more likely when adolescents, as opposed to parents, were responsible for administering the medication. Further, non-adherence was more likely when taking morning rather than evening doses. These findings are explained with an emphasis on potential remedies that directly address the stated barriers.

Adherence to a medical regimen is commonly defined as “the extent to which patients take medications as prescribed by their healthcare providers” (1). For patients with chronic medical conditions, including organ transplantation, medical advances have resulted in improved survival rates and a longer lifespan, making the necessity of patients’ adherence to complex medication regimens paramount for managing the illness and improving quality of life. Thus, adherence has become a prominent focus for healthcare providers.

Non-adherence can result in serious negative consequences, from slowing the healing process to death among patients with certain disorders. This impacts not only the patient, but also the healthcare system resulting in increased health-care costs. The rate of adherence for chronically ill adolescents is about 50% (2). For pediatric solid organ transplant recipients, non-adherence can result in extended hospitalizations, late rejection, and mortality (3). Transplantation requires life-long adherence to medical prescriptions to care for the transplanted organ. Therefore, conducting research that informs professionals about potential barriers to adherence is critical for this population. Barriers to medication taking may include a variety of factors, from simply forgetting to disliking the side effects of the medication.

Barriers to adherence can be identified through use of either close-ended or open-ended measures. Close-ended barrier measures employ a series of specific barrier statements wherein the patient provides a yes, no, or how often response (e.g., Do you have trouble swallowing your medication?) to generate a total barrier score (4, 5). With open-ended barriers, patients respond to questions in an unrestricted manner.

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Abbreviations: MACS, multidimensional adherence classification system; MAM, medication module of the medication adherence measure; MEMS, medication event monitoring system.
Medication barriers and adherence

(6–8). Means of collecting open-ended barriers range from simply asking for any barriers experienced in the past two wk (6) to more detailed approaches of asking why taking medications and doing treatments are difficult for each component of the treatment regimen (8). Although this method provides a rich source of information that may direct future interventions, few studies have employed this methodology.

Studies examining barriers to medication/regimen adherence in an open-ended manner in children with HIV (6), children with asthma (7), and children with cystic fibrosis and asthma (8) have resulted in a list of common obstacles for the pediatric population. Most common is simply forgetting to take medication. Other common themes contributing to non-adherence include undesirable properties of the medication (e.g., side effects, too many pills to take) and familial interpersonal dynamics (e.g., oppositionality, lack of social support). Less common themes included time management problems, limited access to medication at dosing time, decreased motivation to take medication over time, and poor understanding of the prescribed regimen. In addition to identifying these obstacles, a greater number of barriers were associated with non-adherence (6, 8). Although these studies supported the importance of examining barriers in this manner, these results did not indicate what barriers are most influential on non-adherence and did not provide tangible suggestions for aiding patients to overcome these obstacles.

The current study sought to augment the limited amount of research examining barriers to medication adherence in the adolescent solid organ transplant population through the use of open-ended questions. This paper will (i) assess, categorize, and determine frequencies for open-ended barriers responses, (ii) examine the relationship between types and number of open-ended barriers and patients’ adherence classification, (iii) examine the relationship between adherence and organizational strategies used by the patients, the patients’ and parents’ role in medication responsibility, and the time of day that doses are most often missed and (iv) provide potential strategies for addressing barriers to medication adherence.

Although the previous barrier themes found in other areas of the literature provided a framework for our conceptualization, we allowed the data provided by the patients and families to guide the process of categorization. We hypothesized that those classified as non-adherent would report significantly more barriers than those classified as adherent. We also hypothesized that adolescents who did not employ an organizational strategy would be more likely to be classified as non-adherent. For regimen responsibility, we hypothesized that teens who were primarily responsible would be more likely to be non-adherent, as parent involvement has been shown to be a protective factor in relation to barriers to adherence (4) and initial evidence in a group of renal patients demonstrated a relationship between adolescent responsibility and non-adherence (9). Lastly, we hypothesized that the morning dose would most likely be missed, given the often hectic nature of mornings for adolescents.

Method

Of the 87 families recruited for this study, 80 pediatric solid organ transplant families consented to participate. Reasons for non-participation included no time (n = 3), not comfortable with release of medical records (n = 1), and no reason cited (n = 3). Inclusion criteria for this study required participants to be English speaking, at least 11 yr old, living at home with parents, and transplanted at least four months prior to involvement in the study.

The 80 participating families included 80 parents and 82 adolescents (two families had adolescent siblings with transplanted organs). Ages ranged from 11 to 21 yr of age (M = 15.8; s.d. = 2.4). Forty-seven kidney recipients, 20 liver recipients, and 14 heart recipients comprised the sample, 23 of whom received their transplants from living donors. Mean age at transplant was 11 yr, and mean years since transplant at the time of participation was 4.8. The number of medications adolescents were taking ranged from 1 to 18 (M = 6.4; s.d. = 3.3). The adolescent sample included 54% males. Additionally, 61% were Caucasian, 32% were African American, 1% were Asian-East Indian, and 6% identified as other. Parents were composed of 61% married, 36% non-married (single, divorced, separated, widowed, and life partner), with 3% providing no information. Mothers made up 87% of the parents interviewed. Eleven adolescents did not participate in the interview after assent, seven due to significant developmental delay and four due to unavailability. Two parents were unable to be reached after consent and thus were not involved in the interview. The resultant sample of interviewees consisted of 78 parents and 71 adolescents, including 68 parent/adolescent dyads from the same family.

Measures

A medical record review was conducted to obtain data regarding date and type of transplant, donor type for kidney and liver patients, current prescribed medication regimen, drug assay levels, and rejection episodes six months prior to the interview.

Parent and self-reported medication adherence, regimen responsibility, organizational strategy

The MAM (10, 11) was used in order to assess adherence to medical regimens. Parents and adolescents individually reported how many doses of each medication the adolescent missed or took late in the previous seven days. The number of prescribed minus number of missed doses, divided by
number prescribed, times 100 yielded a percentage of missed and late doses. Preliminary data on the MAM suggest adequate convergent validity with established measures of adherence. In a sample of patients with renal disease (N = 25), the percent of missed doses identified on the MAM was significantly correlated with the missed doses tracked by the MEMS electronic technology (r = 0.40, p = 0.04). In another study of outcomes among renal transplant recipients (N = 29), percent of missed doses identified on the MAM was associated with the number of documented acute rejection episodes by year 2 post-transplant (r = 0.62, p < 0.001), suggesting good predictive validity of clinical outcomes in this population (10).

Additional questions from the MAM assessed parent perceptions regarding who has primary responsibility for administering medications and how the adolescents’ medications were organized. For primary responsibility, parents were asked one question, “who takes primary responsibility for making sure your child takes his/her medication?” Initial examination of adherence, as measured by the MAM, indicates that parent responsibility is associated with better adherence as compared to children who were primarily responsible in adolescent renal patients prior to transplantation (10). For organizational system, response choices included “no system,” “pill box,” “special shelf/cabinet,” “refrigerator,” “plastic bag,” or “in my room” (10, 11).

Immunosuppressant drug assay levels
Levels of immunosuppressant blood levels were collected for the year preceding the patient’s interview or since transplantation, if that occurred less than one yr earlier. Standard deviations for tacrolimus levels were calculated, with higher s.d. indicating medication level instability and suggestive of more irregular medication taking. Only blood levels taken in the outpatient clinic during routine visits were included in the analyses, given that levels may fluctuate as a result of illness or aggressive treatments during inpatient stays. Literature has shown that higher s.d. of tacrolimus were predictive of negative clinical outcomes, such as rejection, and were indicative of poor adherence (12, 13). Blood levels of cyclosporine (outside of 150–400 ng/mL) or tacrolimus (outside of 5–17 ng/mL) that were out of the therapeutic range were also examined as potentially suggestive of poor adherence (12), although this determination was made in consultation with the transplant coordinator responsible for each patient who took into account factors such as time since transplantation, recent medication changes, or recent aggressive medical treatments.

Qualitative barriers to medication adherence
Participants were asked to respond to an open-ended question regarding medication taking behavior, “What has made it difficult for you (your child) to take your (his/her) anti-rejection medication on schedule every day?” All participants responded to this question regardless of whether they reported any non-adherent behavior; as individuals may be adherent yet still have challenges that make it difficult to take the medication on schedule every day. Verbatim answers were recorded by the interviewer. Responses were grouped into themes, detailed in the results section.

Procedure

Recruitment
Following Human Subjects approval at Emory University and Children’s Healthcare of Atlanta, potential participants were contacted during their clinic appointments or via telephone by the transplant coordinator. They were given a brief description of the study, and, if interested, either contacted the principle researcher, completed an interest form, or gave verbal consent. The researchers then gave interested participants a detailed description of the study. Written consent and assent were obtained via mail or while attending a clinic appointment.

Interview
Over a five-month period interviews were conducted. Each scale was administered verbally by trained research assistants. Interviewers were encouraged to build rapport with interviewees, be sensitive to participants’ responses, and present questions in an unbiased manner. The parent and adolescent interviews were conducted separately, with each instructed to leave the room during the other individual’s interview. The vast majority of interviews (98%) were conducted over the phone. Each interviewee was compensated with a 20 dollar gift card to a local discount department store.

Adherence classification
The MACS (4) was utilized to provide a four group categorization based on parent and adolescent reports of adherence on the MAM and immunosuppressant serum drug levels. The four categories are: (i) those who report high adherence and have acceptable drug levels (adherent/stable, “Genuinely Adherent”), (ii) those who report high adherence and have serum drug levels outside of the acceptable range or with a s.d. of 3 or more of tacrolimus drug levels (adherent/unstable, “Deniers/Medically Complicated”), (iii) those who report non-adherence, yet have acceptable drug levels (non-adherent/stable, “At-risk”) and (iv) those who reported non-adherence and have concerning drug levels (non-adherent/Unstable, “Genuinely Non-adherent”). Initial validity data for the MACS are promising with 57.1% of non-adherent/unstable individuals having experienced a rejection episode in the previous six months, in comparison to 19.0% of non-adherent/stable individuals, 19% of adherent/unstable individuals, and 4.8% of adherent/stable individuals (Simons LE, Gilleland J, Blount RL, Amaral S, Berg A, Mee LL, in preparation) experiencing rejections. See Table 1 for detailed category descriptions and criteria.

Participants classified into each of the four adherence groups included: “Genuinely Adherent” (n = 21), “Deniers/Medically Complicated” (n = 10), “At-risk” (n = 28), and “Genuinely Non-adherent” (n = 21), resulting in a non-adherence rate of 59.8%.

Data analyses
Data were analyzed with parametric and non-parametric tests using spss 14.0 for Windows. Descriptive statistics were obtained on all variables. For barrier coding, we calculated inter-rater agreement and Kappa coefficients between raters. One-way ANOVA and Pearson Product Moment Correlation analyses were used to examine differences based on demographic and medical factors. Paired sample t-tests were used to assess differences in barrier reporting between parents and adolescents. One-way ANOVAs were conducted to examine the effect of adherence category on number of barriers. Lastly, chi-squared analyses were used to examine the relationship between regimen responsibility and organizational strategy with adherence category.
Barrier category development

After reviewing all barrier responses for themes, the initial categories consisted of: (i) forgot/distracted, (ii) competing activities, (iii) scheduling issues, (iv) no plan, (v) peer influence/adolescent issues and (vi) physical barriers/medication issues. Definitions were generated for each category. These initial categories were refined through a multi-step process.

The principle investigator (L.S.) and the second author (M.M.) coded each barrier using the initial six categories. Initial agreement between L.S. and M.M. was 79.6%. In instances of disagreements, the categorization was discussed and a consensus was reached. Then, an independent researcher (B.R.), not involved with the initial development of the coding scheme coded each of the barriers. Inter-rater agreement between the two coders was 64.3%. The categories of competing activities, scheduling issues, and no plan had much lower category agreement.

After some revision, we collapsed competing activities/scheduling issues and no plan into one category, given their similar content, resulting in four mutually exclusive categories: (i) forgot/distracted, (ii) poor planning/scheduling issues, (iii) physical barriers/medication issues, and (iv) voluntary resistance/attempts to be normal (see Table 2 for category definitions). Inter-rater agreement between L.S. and M.M. was 97%, \( \kappa = 0.96 \). There was a consensus reached between these two coders. Codes were then compared to a new independent coder (G.A.), with an agreement of 92.9%, \( \kappa = 0.91 \). These Kappa values indicate ‘almost perfect agreement’, according to established guidelines (14, 15).

Results

Preliminary analyses

Potentially influential demographic and medical variables were examined with regard to barriers. Child age, gender, type of transplanted organ, time since transplant, and number of medications the child is taking were all examined. Only gender emerged with significant differences. Adolescent females reported forgetting (\( M = 0.44, \) s.d. = .50) as a barrier significantly more frequently than males (\( M = 0.18, \) s.d. = .39), \( F(1,69) = 5.93, p = 0.02 \).

Number of barriers reported

For the 78 parents who participated in this study, 38% (\( n = 30 \)) did not indicate any barriers, 31% (\( n = 25 \)) described one barrier, 28% (\( n = 22 \)) described two barriers, and 4% (\( n = 3 \)) described three barriers. For the 71 adolescents who participated in this study, 34% (\( n = 24 \)) did not indicate any barriers, 32% (\( n = 23 \)) described one barrier, 28% (\( n = 20 \)) described two barriers, and 6% (\( n = 4 \)) described three barriers to medication adherence. The mean number of barriers for both parents and adolescents was approximately 1 (parent: \( M = 0.98, \) s.d. = 0.90; adolescent: \( M = 1.06, \) s.d. = 0.92). The Pearson correlation between parent and adolescent report
was $r = 0.58$, $p < 0.00$. There was no significant difference between parent and adolescent reports in the number of total barriers or across types of barriers. The frequency of barriers by type is described in Table 3.

Barriers and adherence categories

We examined differences between adherence groups in the number of barriers reported. For optimal power, we first examined differences between the two higher-order groups, adherent and non-adherent. These results are detailed in Table 4. Overall barriers for parents and teens were significantly greater for those classified as non-adherent. For specific barrier types, non-adherent adolescents reported a greater number of forgot/distracted barriers and parents of non-adherent adolescents reported significantly greater number of voluntary resistance/attempts to be normal barriers.

To examine barriers more closely across the four adherence categories, we calculated the percentage of patients in each of the four adherence categories who reported barriers. As detailed in Table 3.

### Table 3. Descriptive information for barriers

<table>
<thead>
<tr>
<th>Barrier type</th>
<th>Examples</th>
<th>Parent reported barriers</th>
<th>Adolescent reported barriers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of barriers</td>
<td></td>
<td>76</td>
<td>73</td>
</tr>
<tr>
<td>Forgot/distracted</td>
<td>“Not paying attention to how much is left; ran out”; “Completely forgot. Doing something else”</td>
<td>13 (17.1)</td>
<td>21 (28.8)</td>
</tr>
<tr>
<td>Poor planning/scheduling problems</td>
<td>“Keeping 12-h pill rotation is difficult”; “On weekends, sleeping in”</td>
<td>52 (68.4)</td>
<td>42 (57.5)</td>
</tr>
<tr>
<td>Physical barriers/medication issues</td>
<td>“Too tired”; “Nauseous in the morning”; “If she’s sick”</td>
<td>4 (5.3)</td>
<td>7 (9.6)</td>
</tr>
<tr>
<td>Voluntary resistance/attempts to be normal</td>
<td>“When I see that my friends don’t have to take it, I don’t want to take it”; “Teenage lifestyle”; “Just not doing it”</td>
<td>7 (9.2)</td>
<td>3 (4.1)</td>
</tr>
</tbody>
</table>

### Table 4. Overall barriers for parents and teens

<table>
<thead>
<tr>
<th>Barriers</th>
<th>Reporter</th>
<th>Adherent†</th>
<th>Non-adherent†</th>
<th>d.f.</th>
<th>$F$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any barriers</td>
<td>Parent</td>
<td>0.71</td>
<td>1.14</td>
<td>0.84</td>
<td>1.78</td>
</tr>
<tr>
<td></td>
<td>Adolescent</td>
<td>0.66</td>
<td>1.25</td>
<td>0.86</td>
<td>1.69</td>
</tr>
<tr>
<td>Forgot/distracted</td>
<td>Parent</td>
<td>0.16</td>
<td>0.16</td>
<td>0.37</td>
<td>1.78</td>
</tr>
<tr>
<td></td>
<td>Adolescent</td>
<td>0.13</td>
<td>0.38</td>
<td>0.49</td>
<td>1.69</td>
</tr>
<tr>
<td>Poor planning/scheduling problems</td>
<td>Parent</td>
<td>0.52</td>
<td>0.76</td>
<td>0.72</td>
<td>1.78</td>
</tr>
<tr>
<td></td>
<td>Adolescent</td>
<td>0.43</td>
<td>0.69</td>
<td>0.75</td>
<td>1.69</td>
</tr>
<tr>
<td>Physical barriers/medication issues</td>
<td>Parent</td>
<td>0.03</td>
<td>0.06</td>
<td>0.24</td>
<td>1.78</td>
</tr>
<tr>
<td></td>
<td>Adolescent</td>
<td>0.04</td>
<td>0.13</td>
<td>0.33</td>
<td>1.69</td>
</tr>
<tr>
<td>Voluntary resistance/attempts to be normal</td>
<td>Parent</td>
<td>0.00</td>
<td>0.14</td>
<td>0.35</td>
<td>1.78</td>
</tr>
<tr>
<td></td>
<td>Adolescent</td>
<td>0.00</td>
<td>0.06</td>
<td>0.24</td>
<td>1.69</td>
</tr>
</tbody>
</table>

*p < 0.05; **p < 0.01.
†Parent report (n = 80); adolescent report (n = 71).
Table 5, the “At-Risk” and “Genuinely Non-adherent” groups had the highest percentage of individuals reporting any barriers. These two categories were followed by the deniers/medically complicated patients. The “Genuinely Adherent” group had the lowest percentage of individuals reporting barriers across all categories, except for parents’ reports of physical barriers/medication issues. Using one-way ANOVA, we examined the number of open-ended barriers endorsed by the parents and adolescents in each of the four adherence categories. For overall number of barriers, the effect of adherence category was significant, $F(3,67) = 2.99$, $p = 0.04$, for number of adolescent reported barriers. Post hoc analyses using the Tukey HSD test indicated that the mean number of adolescent barriers was significantly higher for the “At-Risk” group ($M = 1.26$, s.d. = 0.86) and the “Genuinely Non-adherent” group ($M = 1.24$, s.d. = 0.89) compared to the “Genuinely Adherent” group ($M = 0.47$, s.d. = 0.83), $p < 0.05$. No other differences were statistically significant.

Lastly, we examined differences between adolescents who had experienced a rejection episode in the past six months and those who did not in relation to reported number of barriers (see Table 6). Of the 82 adolescent transplant recipients, 21 (25.6%) experienced a rejection episode in the past six months. Those who experienced a rejection episode reported significantly greater overall barriers, physical barriers/medication issues, and voluntary resistance/attempts to be normal barriers as compared to adolescents who had not experienced a rejection episode in the past six months.

Other barriers to adherence: organizational strategy, regimen responsibility, and time of day

We examined whether organizational strategies and who is responsible for the regimen was

Table 5. Percentage and frequency of parents and teens reporting barriers by adherence group

<table>
<thead>
<tr>
<th>Barriers</th>
<th>Adherent</th>
<th>Non-adherent</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Genuinely adherent % (n)</td>
<td>Deniers/MC % (n)</td>
</tr>
<tr>
<td>Any barriers</td>
<td>Parent 38.1 (8)</td>
<td>50 (5)</td>
</tr>
<tr>
<td></td>
<td>Adolescent 26.7 (4)</td>
<td>62.5 (5)</td>
</tr>
<tr>
<td>Forgot/distracted</td>
<td>Parent 9.5 (2)</td>
<td>20.0 (2)</td>
</tr>
<tr>
<td></td>
<td>Adolescent 6.7 (1)</td>
<td>25.0 (2)</td>
</tr>
<tr>
<td>Poor planning/scheduling problems</td>
<td>Parent 28.6 (6)</td>
<td>40.0 (4)</td>
</tr>
<tr>
<td></td>
<td>Adolescent 26.6 (4)</td>
<td>37.5 (3)</td>
</tr>
<tr>
<td>Physical barriers/medication issues</td>
<td>Parent 4.8 (1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td></td>
<td>Adolescent 0 (0)</td>
<td>12.5 (1)</td>
</tr>
<tr>
<td>Voluntary resistance/attempts to be normal</td>
<td>Parent 0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td></td>
<td>Adolescent 0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

For parents: genuinely adherent (n = 21); deniers/medically complicated (n = 10); at risk (n = 28); genuinely non-adherent (n = 21). For adolescents: genuinely adherent (n = 15); deniers/medically complicated (n = 8); at risk (n = 27); genuinely non-adherent (n = 21).

Table 6. Comparison between adolescents who experienced a rejection episode on number of barriers reported

<table>
<thead>
<tr>
<th>Barriers</th>
<th>No rejection†</th>
<th>Rejection†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>s.d.</td>
</tr>
<tr>
<td>Any barriers</td>
<td>Parent 0.93</td>
<td>0.90</td>
</tr>
<tr>
<td></td>
<td>Adolescent 0.90</td>
<td>0.89</td>
</tr>
<tr>
<td>Forgot/distracted</td>
<td>Parent 0.13</td>
<td>0.34</td>
</tr>
<tr>
<td></td>
<td>Adolescent 0.25</td>
<td>0.44</td>
</tr>
<tr>
<td>Poor planning/scheduling problems</td>
<td>Parent 0.63</td>
<td>0.80</td>
</tr>
<tr>
<td></td>
<td>Adolescent 0.60</td>
<td>0.77</td>
</tr>
<tr>
<td>Physical barriers/medication issues</td>
<td>Parent 0.00</td>
<td>0.00</td>
</tr>
<tr>
<td></td>
<td>Adolescent 0.06</td>
<td>0.24</td>
</tr>
<tr>
<td>Voluntary resistance/attempts to be normal</td>
<td>Parent 0.10</td>
<td>0.30</td>
</tr>
<tr>
<td></td>
<td>Adolescent 0.00</td>
<td>0.00</td>
</tr>
</tbody>
</table>

*p < 0.05; **p < 0.01.
†Parent report (n = 80); adolescent report (n = 71).
related to adherence using chi-squared analyses. All families reported using at least one organizational strategy for their medication. The strategies and the frequency of use are as follows: shelf/cabinet 41% (n = 33), pill box 38% (n = 30), plastic bag 19% (n = 15), and the teen’s bedroom 3% (n = 2). There was no relationship between adherence group and type of organizational strategy. For regimen responsibility, only 29% (n = 23) of adolescents had primary responsibility for their medication taking. As expected, the group of adolescents with primary responsibility (M = 17.3, s.d. = 2.14) was significantly older than the group of adolescents who did not have primary responsibility (M = 15.1, s.d. = 2.23), F(1,78) = 15.48, p < 0.00. Time since transplant and the occurrence of a rejection episode in the past six months did not differ between the two groups. However, there was a higher proportion of adolescents who were responsible for their medication taking to be classified as non-adherent (74%) when compared to adolescents whose parents were primarily responsible (56%), χ²(1, N = 80) = 2.18, p = 0.05, one-tailed.

Finally, we examined the time of day adolescents were most likely to miss their medication. Of the 39 adolescents who reported missing one or more doses in the past week, 85% (n = 33) missed their morning dose, as compared to 15% (n = 9) who missed their bed-time dose. From the parent perspective, of the 29 parents of adolescents who reported their child missed one or more doses in the past week, 65% (n = 19) missed their morning dose, as compared to 35% (n = 10) who missed their bed-time dose.

Strategies for overcoming barriers to adherence

Based on the four types of barriers provided by the patients and their parents, as well as specific examples families provided, we constructed a list of strategies to improve medication adherence. These recommendations are provided in Table 7.

Discussion

Adolescent transplant recipients and their parents described perceived barriers to medication adherence in an open-ended response format for this investigation. Four barrier categories were developed from their responses: poor planning/scheduling issues, forgot/distracted, physical barriers/medication issues, and voluntary resistance/attempts to be normal. These categories are generally consistent with the previous adherence literature in other areas of pediatrics, supporting the role of cognitive barriers (5–7), the aversive properties of the medication (6, 16), and voluntary resistance to medication taking (7). The use of open-ended responses in this study, however, further dismantles “cognitive barriers,” distinguishing barriers related to forgetting or being distracted from those of not planning or scheduling properly. In addition to categorizing these barriers, the relative frequency of specific barriers was calculated. Although forgetting to take the prescribed dose is often reported in the literature as the most common barrier to adherence (7, 8), in this investigation poor planning/scheduling issues were substantially more frequently reported (63%) as compared to forgot/distracted (23%). Thus, allowing patients to generate individualized responses may more clearly illuminate the specific types and frequency of barriers they face.

As hypothesized, adolescents classified as non-adherent and their parents reported significantly more perceived barriers to medication. With regard to specific barriers types, non-adherent adolescents generally reported more barriers across all domains. As shown in Table 5, statistically significant differences emerged with non-adherent individuals reporting more forgot/distracted barriers and voluntary resistance/attempts to be normal barriers. It may be that these less frequently stated barriers are more powerful and salient obstacles to medication taking behavior when they are present, as opposed to the more commonly occurring class of poor planning/scheduling barriers.

Number of rejection episodes was also examined with regard to reported barriers. Results from these analyses suggest that adolescents’ reports of the total number of barriers, as well as the specific categories of voluntary resistance/attempts to be normal and physical barriers/medication issues differentiated those who had experienced rejections in the past six months. Parental reports of barriers were not different for the patients with or without rejections. These findings suggest at least two potentially very important findings. First, adolescent reports of barriers may be more important than parents’ reports in regards to rejections. Secondly, although lower frequency than the other two categories, adolescents’ reports of voluntary resistance/attempts to be normal and physical barriers/medication issues may be particularly important when they are reported. These findings should be further investigated in future research.

An interesting descriptive finding emerged in this investigation is that the deniers/medically complicated group had the third highest number of reported barriers, as shown in Table 5. This
group was classified as adherent, based on the adolescents’ and parents’ self-report, yet had troubling serum immunosuppressant levels. Finding a greater number of reported barriers supports the notion that at least some members of the group may indeed be non-adherent, though perhaps not to the extent of those in the two non-adherent groups. It is possible that using open-ended questions may be a more sensitive index of non-adherence than asking the patients directly about the number of missed or late doses. Further research should consider this issue.

Organizational strategies, responsibility of regimen, and the time of day that doses are most frequently missed are also potentially important factors that influence medication adherence. All parents and adolescents in this study reported using at least one organizational strategy. However, there were no differences in adherence across the specific strategies.

With regard to regimen responsibility, data indicated that adolescents who were primarily responsible for their medication regimen were more likely to be classified as non-adherent. Although adolescents normally assume more responsibility as they mature into adulthood, they may not yet possess certain cognitive capabilities for decision making and may not recognize the potential consequences of occasionally skipping doses of immunosuppressant medication. Thus, transitioning adolescents to full responsibility of medication taking may necessitate intermittent adult monitoring and supervision, and a slow progression based on their demonstrated competence and follow-through, rather than based on their age per se (17).

Lastly, as hypothesized, morning doses were overwhelmingly missed more frequently than bed-time doses (85% vs. 15%). This finding supports the importance of generating preventive and responsive measures to missed doses that are tailored to this high-risk time. Some of the recommendations in Table 7 directly address this issue.

With the unique strengths we noted for asking patients and parents open-ended questions about their barriers to medication

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**Table 7. Strategies to improve medication adherence**

<table>
<thead>
<tr>
<th>Specific barriers</th>
<th>Potential intervention strategies</th>
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<tr>
<td><strong>Forgot/distracted:</strong> Incorporate salient cues to take medication into the daily routine.</td>
<td>Morning/evening dose: Reminder placed at the front door; medication next to breakfast, toothbrush, or nightstand (19). School time dose: Reminder from teacher or nurse; schedule doses at a specific event during the day (mealtime) (19). General forgetfulness: Digital watch with alarm set for dosing time; automatic reminders on computer, phone, etc. (16). Schedule doses at specific event times, if possible; schedule dose during an activity where mom or dad are present to provide an additional prompt (e.g., dinner, breakfast); organizational system for medications (e.g., pill box) (1).</td>
</tr>
<tr>
<td><strong>Forgot to refill prescription:</strong> Automatic refill system established with pharmacy; put reminder to order medications on electronic (e.g., cell phone, computer), or wall calendar (19).</td>
<td><strong>Poor planning/scheduling problems:</strong> Plan ahead for expected or potential schedule changes by having extra doses of medication available in accessible locations (e.g., school, car). Have cues in place when the routine is disrupted. Rushed in the morning/sleep late: Extra medication dose in the car; set alarm when sleeping late on weekends to wake up and take medication at prescribed time (20). At a friend’s house: Extra dose at friend/family’s house where likely to spend the night; have a medication travel bag prepared at all times as regular item to pack. Out to dinner: Parents carry an extra medication dose (e.g., purse, briefcase, backpack) (20); schedule dinner around dosing schedule. Changes in schedule: Change times of doses to fit schedule; check expected vs. actual medication intake at end of day; have an ‘away from home’ storage container medications (e.g., small bag, hip pack).</td>
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<td><strong>Physical barriers/medication issues:</strong> Increased medical team-patient communication and potentially employ circumscribed treatments to overcome aversions to medication.</td>
<td>Hard to swallow: Seek out alternative medications (e.g., liquid form, smaller pills) (16); behavioral treatment for pill swallowing fear (21). Doesn’t like the taste: Use a favorite beverage or strongly flavored food to disguise the taste; use rewards or incentives for quickly taking medication (7). Side-effects; not feeling well: Physician and patient discuss ways to alleviate/ameliorate side-effects that are impacting quality of life (12); increase communication about the influence of current state of health on medication taking behavior (e.g., nausea, current illness) (1).</td>
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<td><strong>Attempts to be normal:</strong> Identify what is important to a teenage patient (e.g., hanging out with friends) and link appropriate medication taking to being able to enjoy those valued activities (e.g., staying out of the hospital).</td>
<td>Don’t want friends to see: Encourage child to share with and enlist support of close friends (22). Defiance: Offer positive reinforcement and incentives (8); individual or family counseling to address issues surrounding resistance to medication taking; use motivational interviewing techniques (23).</td>
</tr>
</tbody>
</table>
adherence is that it provides a vehicle for designing interventions to overcome those obstacles. If successful, these interventions may result in improved health outcomes for the patients, lower healthcare utilization and costs, and improved quality of life for each family member. To help realize this potential, we provided multiple recommendations in Table 7 to specifically address the barriers patients and their parents described. We hope that these strategies will prove a heuristic for clinicians who are involved in direct patient care, as well as for the design of intervention research targeting adherence.

This study must be viewed in light of its limitations. The responses provided by the parents and adolescents in this study represent individuals from one institution at a regional hospital. It is possible that responses may differ at different medical centers, emphasizing the importance of multi-site studies to examine complex variables such as adherence. Also, it is possible that additional barriers may be more important for members of other ethnic groups (e.g., Hispanic, Asian-American) that did not constitute the majority of this sample. Although we made efforts to ask about barriers in a non-judgmental manner, individuals may have been reluctant to admit to barriers as they may think this suggests non-adherence. Our data do not necessarily suggest this as the number of barriers across adherence groups was consistent with expectations. In addition, we must acknowledge that the magnitude of differences in number of barriers between adherent and non-adherent teens was quite small. This is likely due to a restricted range of frequency (0–3) and one third of individuals not endorsing any barriers. Given the constraints of the data, finding significance was actually more difficult; perhaps emphasizing the importance of any barriers patients and parents endorse. Lastly, drug assay levels are an imperfect measure of medication adherence. Although considered a more objective means of collecting adherence data, several values in this study were discarded at the transplant coordinators’ discretion. Only under carefully controlled conditions can drug assays be considered a completely reliable measure of adherence.

This investigation provides support for the importance of simply asking adolescents and their parents, “What makes it difficult to take your medication on time?” This open and straightforward question offers patients and their families a forum for expressing barriers otherwise not noted when using checklists that list specific barriers and provides clinicians with insight into the patient’s unique struggles, facilitating greater communication about these issues. Future studies using the barrier categories developed in this study are needed to validate these codes. Another potential implication is to assess barriers in an open-ended manner at the pretransplantation phase; this may serve to anticipate and prevent the manifestation of maladaptive medication taking patterns. Lastly, adding an open-ended component to existing closed-ended barrier measures, such as the Illness Management Survey (5) or the Parent and Adolescent Mediation Barriers Scales (4, 18) would likely enhance the information collected. We hope that this approach will reduce the stigma associated with life challenges that impede medication adherence and enhance the clinician’s ability to help patient families overcome these obstacles.

References

Medication barriers and adherence