Brief Report: Barriers to Treatment Adherence in Pediatric Inflammatory Bowel Disease

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Objective To examine perceived barriers to medication adherence in inflammatory bowel disease (IBD) treatment and their relationship with adherence using a combined forced choice and semi-structured interview assessment approach. Methods Sixteen adolescents with IBD and their parents participated in an open-ended interview regarding adherence barriers and completed quantitative measures of adherence, barriers to treatment, and disease severity. Results The most commonly identified barriers to adherence were forgetting, interference with other activities, difficulty swallowing pills, and not being at home. Number of reported barriers was positively correlated with objective nonadherence for 6-MP/azathioprine. Nonadherence frequency was 42% for 6-MP/azathioprine and 50% for 5-ASA medications. Conclusions Using a combined assessment approach, patients and parents reported several barriers to treatment adherence that are appropriate for clinical intervention. This is critical given the significant medication nonadherence observed in this sample and the relationship between total number of barriers and disease management problems.

Key words adherence; barriers; compliance; inflammatory bowel disease; medication.

Inflammatory bowel disease (IBD), comprised of Crohn’s disease and ulcerative colitis, is diagnosed in approximately 71 of 100,000 individuals in the United States (Kappelman et al., 2007) and approximately one-quarter of patients are diagnosed during childhood or adolescence. Disease features of IBD include chronic, intermittent inflammation of the gut; diarrhea; abdominal pain; and growth failure. Treatment of IBD primarily involves the use of oral medications, which may vary in dosing frequency and number of pills to be taken by patients per dose. This, combined with negative side effects (e.g., weight gain) of adjunctive medications such as prednisone and an unpredictable disease course, presents significant self-management challenges to children and their families.

Treatment adherence is a significant health concern in pediatric chronic illness management, with 50–75% of children and adolescents not adhering adequately to their prescribed regimens (Logan, Zelikovsky, Labay, & Spergel, 2003; Rapoff, 1999). Data on adherence in the pediatric IBD population is limited but consistent with other pediatric populations, with nonadherence prevalence ranging from 50% to 88% depending on the medication and method of assessment (Hommel, Davis, & Baldassano, 2008, 2009; Mackner & Crandall, 2005b; Oliva-Hemker, Abadom, Cuffari, & Thompson, 2007; Riekert & Drotar, 2002). While these data clearly demonstrate that adherence is a significant challenge for children and adolescents with IBD, it does not provide insight into the particular barriers that might prevent patients and families from taking their medication as prescribed.

Barriers to treatment adherence have been examined in several pediatric populations. Much of this research has identified similar barriers including forgetting, taste/palatability issues, oppositional behavior, side effects, time constraints, failure to refill prescriptions, organizational difficulties, and interference with other activities in populations such as cystic fibrosis and asthma.
(Modi & Quittner, 2006), sickle cell disease (Witherspoon & Drotar, 2006), and transplant recipients (Simons & Blount, 2007). Moreover, there is evidence that increased number of barriers is related to poorer adherence (Logan et al., 2003; Riekert & Drotar, 2002). A recent study in IBD reported that forgetting, being away from home, and interference with activities were the most common barriers to adherence, and that greater number of barriers were correlated with poorer self-reported adherence (Ingerski, Baldassano, Denson, & Hommel, 2009). However, this study relied exclusively on forced-choice quantitative data, and the self-reported adherence estimates were likely overestimated by participants (Ingerski et al., 2009). Reliance on forced choice measures alone, which is common in adherence research, may result in some barriers being missed if they were not included in the questionnaire. Moreover, the use of both deductive and inductive methodologies provides a complementary focus on a specific behavioral process such as treatment adherence, and may enhance data accuracy as a result.

At this early stage of adherence research in IBD, it is important to get both quantitative and qualitative data regarding barriers to treatment adherence so that the development of interventions can consider all possible factors and target the most salient barriers contributing to poor adherence. Thus, the primary objective of this study was to examine patient- and parent-reported barriers to treatment adherence in IBD using a quantitative forced-choice questionnaire as well as a qualitative open-ended interview assessment in order to obtain comprehensive data on barriers in this population. A secondary objective was to examine the relationship between the number of perceived barriers and nonadherence. Consistent with prior research, it was anticipated that greater number of perceived barriers would be positively correlated with nonadherence.

Methods
Participants and Procedure
Inclusion criteria for this study were: (a) diagnosis of Crohn’s disease or ulcerative colitis, (b) 13–17 years of age, (c) current prescription of 6-mercaptopurine (6-MP)/azathioprine and 5-aminosalicylic acid (5-ASA), which are the two most commonly prescribed types of medication for IBD, and (d) English fluency for patients and parents. Exclusion criteria were: (a) diagnosis of pervasive developmental disorder and (b) comorbid chronic illness. Eighteen consecutive patients who met eligibility criteria were recruited; two declined participation (one was not interested and one did not have enough time). Thus, the final sample was comprised of 16 adolescents and their parents.

Participants were recruited from a pediatric IBD treatment center in the northeastern United States. Patients were identified via medical chart review and approached during clinic appointments. After informed consent and assent was obtained, participants completed quantitative measures of adherence and treatment barriers, followed by an open-ended interview designed to elicit discussion by parents and adolescents regarding treatment adherence. Study personnel completed disease severity assessments using patient chart note data and laboratory values from the clinic appointment corresponding to the study visit. Total time for participation was approximately 30–60 min. Participants were compensated $50. This study was approved by the Institutional Review Board.

Measures
Treatment Adherence Interview
An interview designed for this study utilizing open-ended questions was used to elicit patient- and parent-generated responses regarding treatment adherence barriers across educational (e.g., knowledge of regimen), organizational (e.g., placement of medication in house), and behavioral (e.g., refusal to take medication) domains. Individual (i.e., patient-parent dyads) interviews were chosen rather than focus groups in order to avoid consensus effects on qualitative data integrity. Interviews were administered jointly to patients and parents. Example discussion questions include: “Tell me about your medication regimen and how each medication is supposed to work,” “How is your medication organized and who is in charge of making sure medication is taken?” and “What kinds of things get in the way or prevent you from taking your medication.”

Medical Adherence Measure
The Medical Adherence Measure (MAM) (Zelikovsky & Schast, 2008) is a structured interview-based assessment of patient knowledge, adherence behaviors, organizational systems, and barriers to disease management over the past week. Participants indicate whether they perceive each of 12 common barriers to impact their adherence. The measure also asks respondents to report the number of doses of particular medications they have missed in the past seven days. Study personnel administered the measure jointly to patients and caregivers. The MAM has demonstrated adequate reliability and validity (Zelikovsky & Schast, 2008; Zelikovsky, Schast, Palmer, & Meyers, 2008).
**Pill Counts**

Study personnel conducted pill counts of medications prescribed to the patient during the clinic visit (or via telephone within 48 hr of the clinic visit if the patient did not bring his/her medications to clinic). Prior research has demonstrated no significant differences between pill counts conducted in person compared to telephone assessment (Pieper, Rapoff, Purviance, & Lindsley, 1989). Consistent with prior research, adherence was restricted to 0–100% (Modi & Quittner, 2006) to minimize error resulting from dumping and/or combining of pills for each medication.

**Pediatric Crohn’s Disease Activity Index**

The Pediatric Crohn’s Disease Activity Index (PCDAI) (Hyams et al., 1991) is a well-established and validated disease severity assessment for pediatric Crohn’s disease. Scores range 0 to 100, with higher scores representing more severe disease, and the measure includes subjective criteria (e.g., pain), objective criteria (e.g., physical exam), laboratory findings, and growth parameters. Scores <15 = inactive disease; 15–30 = mild to moderate disease, and >30 = severe disease activity (Otley et al., 1999).

**Lichtiger Colitis Activity Index**

The Lichtiger Colitis Activity Index (LCAI; Lichtiger et al., 1994) is a validated disease severity measure for ulcerative colitis. It is scored 0–21, with higher scores representing more severe disease, and eight ulcerative colitis related variables including number of daily stools, nocturnal diarrhea, visible blood in stool, fecal incontinence, abdominal pain or cramping, general well-being, abdominal tenderness, and need for anti-diarrheal medication are assessed.

**Data Management and Analyses**

Interviews were conducted by a doctoral level licensed clinical psychologist. These interviews were 20–45 min in duration; audio recordings were transcribed by a professional transcriptionist and checked for accuracy by the interviewer. NVivo 7 software was used for qualitative data coding and analyses. Two trained master’s level psychology graduate students coded transcripts under the supervision of the principal investigator. Quantitative data were analyzed using SPSS 17.0 software. Descriptive statistics were performed for demographic data, disease severity, adherence, and adherence barriers data. PCDAI and LCAI disease severity scores were treated as continuous variables for analyses. Nonadherence frequency was calculated as: 100 – (number of pills taken/number of pills prescribed × 100). Nonadherence prevalence was defined as the percent of the sample taking <80% of a medication. Bivariate correlations were conducted to determine the relationship between perceived barriers and adherence frequency.

### Results

**Preliminary Analyses**

Adolescents (11 male, 5 female) had a mean age of 15.75 years (SD = 1.08 years); 94% were diagnosed with Crohn’s disease and 6% with ulcerative colitis. Ninety-four percent of participants were Caucasian and 6% African American. The modal annual household income category was $75,001–$100,000 and the majority of parents had at least a bachelor’s degree (62.5% of mothers; 56.3% of fathers). Mean parental age was 46.44 years for mothers and 48.81 years for fathers, and 81.3% of mothers and 75% of fathers were married. Inter-rater reliability for qualitative data, calculated as percent agreement between coders, was 90%. Mean disease severity was in the mild to inactive range for the PCDAI (10.67) and LCAI (7.00).

**Primary Analyses**

Mean pill count nonadherence frequency for 6-MP/azathioprine was 42% (SD = 26.34); nonadherence prevalence was 81.3% for 6-MP/azathioprine. Pill count nonadherence frequency for 5-ASA was 50% (SD = 23.61); nonadherence prevalence was 93.3% for 5-ASA. On the MAM, mean nonadherence frequencies for 6-MP/azathioprine and 5-ASA were 8% (SD = 7.49) and 5% (SD = 7.01), respectively. Nonadherence prevalence for both 6-MP/azathioprine and 5-ASA was 13% on the MAM.

Ten of the 12 barriers to treatment adherence on the MAM were reported by participants (“hate the taste” and “other” were not). The most commonly reported barriers reported on the MAM were “just forget,” “wasn’t home,” and “interferes with activity.” Number of barriers reported ranged from 2 to 5 with a mean of 3.44. There was a moderate positive correlation between number of reported barriers on the MAM and objective pill count nonadherence frequency for 6-MP/azathioprine (Table I).

**Table I. Correlations Between Reported Barriers and Nonadherence Frequency**

<table>
<thead>
<tr>
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<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Number of reported barriers</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. 5-ASA MAM Nonadherence</td>
<td>.19</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. 6-MP/azathioprine MAM Nonadherence</td>
<td>.30</td>
<td>.92**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. 5-ASA Pill Count Nonadherence</td>
<td>-.14</td>
<td>.34</td>
<td>.33</td>
<td></td>
</tr>
<tr>
<td>5. 6-MP/azathioprine Pill Count Nonadherence</td>
<td>.54*</td>
<td>.34</td>
<td>.29</td>
<td>.45</td>
</tr>
</tbody>
</table>

*p < .05; **p < .01.
Qualitative analyses of interview data revealed that the most commonly reported barriers were “forgetting,” “other activities,” and “difficulty swallowing pills.” Additional barriers (Table II) emerged from qualitative data that could not have been reported and analyzed quantitatively. Patients and parents reported that the regimen complexity (e.g., number of medications and pills per dose) acted as a barrier to adherence and occasionally resulted in arbitrary changes to regimens by parents or patients as noted here.

Mother of 14 y/o male: . . . the calcium is just a supplement that we’re giving him and he can have it three times a day to get the maximum amount and not too long ago, I just took away the morning one. . . .that’s a pretty big pill and so I said to him, let’s just back off on that one.

16 y/o female: Um, well, at first it was difficult cause I had to take, like, over twenty pills a day, and I just didn’t want to. So, I skipped it a lot.

Another issue that emerged as a barrier to adherence was patient perceptions of how effective the medication is at relieving symptoms immediately.

17 y/o female: . . . it’s hard I think with this stuff cause, if I don’t take it, I don’t see an immediate, like, effect from not taking it. Like, it doesn’t feel like it’s a problem missing it.

16 y/o female: . . . I guess I think I don’t need to take my medicine because, you know, I’ve felt fine for over a year. So, if I miss a few days, it won’t hurt me at all, but I guess in the long run it could cause a flare-up.

Finally, embarrassment from taking medication in front of peers was reported as a barrier to adherence.

Mother of 14 y/o male: . . . I just think it’s one of those things where his friends aren’t on medication. And I’ll have to bring it to a sleep-over, and it’s embarrassing sometimes.

Discussion

This is the first study to incorporate both quantitative and qualitative assessments of barriers to medication adherence in pediatric IBD. Objective findings suggest that patients miss ~42% of 6-MP/azathioprine and 50% of 5-ASA doses, and that 81% and 93% of patients do not take at least 80% of 6-MP/azathioprine and 5-ASA doses, respectively. The most commonly reported barriers to treatment adherence were forgetting, interference by other activities, not being at home, and difficulty swallowing pills. In contrast to a recent study demonstrating the relationship between barriers and subjective nonadherence (Ingerski et al., 2009), results of this study revealed a significant correlation between number of reported barriers and objective nonadherence to 6-MP/azathioprine was observed, indicating that as the number of barriers to adherence increases, so does nonadherence to 6-MP/azathioprine. This discrepancy might suggest a unique difference in the barriers-adherence relationship between the two study samples or it might underscore the disparate sample sizes resulting in contrasting findings. Nevertheless, this issue warrants further empirical investigation. Overall, the results of this study highlight the value added benefit of obtaining both quantitative and qualitative data for assessment of treatment adherence barriers as additional barriers might

### Table II. Patient- and Parent-Reported Barriers on MAM Interview and Qualitative Interview

<table>
<thead>
<tr>
<th>Barriers identified on MAM</th>
<th>No. of times identified</th>
<th>Barriers identified in qualitative interview</th>
<th>No. of times identified</th>
</tr>
</thead>
<tbody>
<tr>
<td>Just forget</td>
<td>14</td>
<td>Forgetting</td>
<td>15</td>
</tr>
<tr>
<td>Interferes with activity</td>
<td>11</td>
<td>Other activities</td>
<td>15</td>
</tr>
<tr>
<td>Hard to swallow pills</td>
<td>1</td>
<td>Difficulty swallowing pills</td>
<td>9</td>
</tr>
<tr>
<td>Don’t like the side effects</td>
<td>2</td>
<td>Side effects</td>
<td>7</td>
</tr>
<tr>
<td>Can’t afford</td>
<td>2</td>
<td>Financial issues</td>
<td>2</td>
</tr>
<tr>
<td>Refuse to/Defiant</td>
<td>4</td>
<td>Oppositional behavior in patient</td>
<td>7</td>
</tr>
<tr>
<td>Don’t think it’s necessary</td>
<td>2</td>
<td>Family or parent–child conflict about taking medications</td>
<td>5</td>
</tr>
<tr>
<td>Wasn’t home</td>
<td>12</td>
<td>Not allowing sufficient time for treatment</td>
<td>6</td>
</tr>
<tr>
<td>Not feeling well</td>
<td>4</td>
<td>Do not plan ahead for treatment</td>
<td>6</td>
</tr>
<tr>
<td>Ran out/Didn’t fill (prescription)</td>
<td>3</td>
<td>Delayed medication effect</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Regimen Complexity</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Psychological comorbidity</td>
<td>1</td>
</tr>
</tbody>
</table>
not have been identified without the open-ended qualitative interview used in this study.

From a clinical perspective, these data underscore the importance of using patient history and clinical interview data in a complementary manner with quantitative measures when assessing barriers to adherence. With respect to intervention planning, there are several barrier targets that would be appropriate for problem solving interventions (e.g., interferes with activity, not being at home, not planning ahead for treatment), behavioral treatment (e.g., pill swallowing, oppositional behavior, parent–child conflict), and medical team intervention (e.g., regimen complexity, side effects). Further, although forgetting was the most commonly reported barrier across quantitative and qualitative assessments, clinical intervention needs to address the underlying cause of forgetting, such as managing unexpected events, change in routines, etc. Moreover, it is likely critical to the success of any intervention that the underlying cause of nonadherence, whether accidental or volitional, be appropriately addressed.

The findings of this study should be considered within the context of a few limitations. First, a modest sample size was used. However, prior qualitative research has demonstrated that data saturation can occur within 12 interviews (Guest, Bunce, & Johnson, 2006). Indeed, data saturation occurred within the first 10 interviews for this study. Second, the sample was primary Caucasian and had fairly high annual incomes. Although this is representative of other studies in IBD (Hommel et al., 2008; Mackner & Crandall, 2005a) and the IBD population overall, generalization of these findings to ethnic minorities or individuals with lower annual incomes is not suggested. Third, this represents a small scale mixed method study of adherence barriers in pediatric IBD using a novel, combined quantitative and qualitative methodology for assessment; thus, findings should be viewed as preliminary and requiring further investigation.

Future research should focus on replication of these findings and further evaluation of the utility of this combined quantitative and qualitative assessment approach. Further, the results of this and future studies using this methodology might inform continued refinement of assessment measures to accurately identify additional barriers to treatment adherence that patients and families are experiencing. Moreover, inclusion of patients who represent lower socioeconomic status in future studies will likely shed light on unique barriers experienced by this subgroup of patients with IBD. Finally, this study identified potential targets for intervention that could be included in testing of behavioral treatment protocols. It will be important to examine the influence of particular barriers on nonadherence and to determine the relative impact on treatment outcome that results from targeting various adherence barriers in this population.

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