

Anxiety and Depression Symptoms Moderate the Role of Barriers to Treatment Adherence in Adolescents with Inflammatory Bowel Disease

Gray WN, Denson LA, Baldassano RN, Hommel KA. Treatment adherence in adolescents with inflammatory bowel disease: the collective impact of barriers to adherence and anxiety/depressive symptoms. J Pediatr Psychol 2011;37:282–91.

Study Overview

Objective. To determine the effect of barriers to adherence and emotional functioning on adherence to treatments for inflammatory bowel disease (IBD) in an adolescent population. More specifically, this study sought to determine if anxiety and depression moderate the relationship between barriers to adherence and adherence to IBD treatment regimens.

Design. Cross-sectional study utilizing data from a larger study investigating the relationship between treatment adherence and health outcomes in adolescents with IBD.

Setting and participants. The study took place at 2 specialty clinics in the United States—one in the Midwest ($n = 34$) and the other in the Northeast ($n = 45$). Participants were 79 adolescents ages 13 to 17 years currently receiving treatment for either Crohn’s disease or ulcerative colitis and their parents. Adolescents were eligible if they had a current prescription for oral 5-aminosalicylic

acid (5-ASA) and/or 6-mercaptopurine (6MP)/azathioprine. Participants were excluded if they had a neurocognitive disorder, other chronic illness, limited English literacy, or were currently on a corticosteroid treatment that exceeded 1 mg/kg per day. To assess behavioral and emotional functioning in the last 6 months, adolescents completed the Youth Self Report (YSR) version of the Child Behavior Checklist [1]; the anxiety/depression subscale was used in these analyses. The Medication Adherence Measure (MAM) [2] was used to assess barriers to adherence. Adolescents indicated reasons they miss taking their medication, and the number of barriers was summed with higher scores indicating more barriers to adherence. Disease activity was collected using the Pediatric Crohn’s Disease Activity Index for those with Crohn’s disease or the Lightiger Colitis Activity Index for youth with ulcerative colitis [3,4].

Main outcome measure. Self-reported adherence to treatment regimens. Using the MAM, adolescents rated

Outcomes Research in Review SECTION EDITORS

JASON P. BLOCK, MD, MPH
Brigham and Women’s Hospital
Boston, MA

ASAF BITTON, MD, MPH
Brigham and Women’s Hospital
Boston, MA

ULA HWANG, MD, MPH
Mount Sinai School of Medicine
New York, NY

MAYA VIJAYARAGHAVAN, MD
University of California, San Diego
San Diego, CA

MELANIE JAY, MD, MS
NYU School of Medicine
New York, NY

WILLIAM HUNG, MD, MPH
Mount Sinai School of Medicine
New York, NY

KRISTINA LEWIS, MD, MPH
Harvard Medical School
Boston, MA

how well on average they take their medications using an 11-point scale where 0 = hardly ever and 10 = always. Such global ratings of self-management have been shown to predict adherence more accurately than specific ratings of adherence, such as number of missed pills in a given time period [5].

Main results. The sample was predominantly Caucasian (91.1%) and 55.6% were female. Almost all patients (96.2%) reported at least 1 barrier to adherence, with forgetting to take medication the most common barrier. The adolescents reported a relatively high level of adherence to medication, with a mean of 8.63. The majority of adolescents in the sample (87.3%) had normal levels of anxiety/depressive symptoms. Fewer patients reported anxiety/depression at borderline (6.3%) or clinical levels (6.3%).

Regression analysis revealed that when controlling for disease severity, anxiety/depressive symptoms moderated the relationship between barriers and medication adherence. For those with higher levels of anxiety/depressive symptoms, adherence declined by 12.6% as barriers increased; this relationship was not significant among those with lower levels of anxiety/depression, who only experienced a 2% decline in adherence.

Conclusion. The majority of adolescents with IBD report barriers to adherence to treatment regimens. This study found that higher levels of anxiety/depression in adolescents with IBD moderate the relationship between barriers and poor adherence. In other words, when faced with barriers, adolescents with higher levels of anxiety/depression are less adherent to their medication than those with lower levels of anxiety/depression. In order to optimize health outcomes, interventions designed to improve adherence in adolescents with IBD should focus on reducing barriers as well as levels of anxiety/depression.

Commentary

IBD is a chronic disease involving severe abdominal pain, weight loss, fatigue, and growth problems. Approximately 25% of patients with IBD are diagnosed during childhood or adolescence [6]. During adolescence there is a decline in adherence to treatment for chronic diseases; 50% to 66% of adolescents with IBD are nonadherent to treatment [7]. This high rate of nonadherence may be attributed in part to developmental changes that occur during adolescence, complicated treatment regimens, and unpleasant side ef-

fects associated with the treatments. During adolescence, teenagers seek independence from their parents, and the responsibility of monitoring and treating IBD symptoms often shifts from parent to child. This push for autonomy has been shown to interfere with the parental support that adolescents with chronic illnesses need to help maintain adherence to treatment [8,9]. Adolescents may also have trouble with the complexity of IBD treatment regimens which frequently include multiple medications with varying doses, strict dietary restrictions, frequent hospital visits, and sometimes even surgery [10,11]. Furthermore, these treatments are frequently accompanied by negative side effects, such as weight gain, facial swelling, and emotional fluctuations [10,11].

Another factor that may impact adherence to IBD treatment regimens is anxiety or depression. A study by Burke and colleagues [12] found that in adolescents recently diagnosed with IBD, 14% fit the criteria for major depression disorder and 28% for an anxiety disorder. This high prevalence of depression is particularly concerning given that depression has been negatively correlated with adherence in patients with chronic diseases like asthma, HIV, and diabetes [13,14]. The research on anxiety and adherence in adolescents with chronic disease is less well defined. Some studies show that high levels of anxiety are associated with inadequate adherence to medication in older adolescents with asthma [15]. Others found that adolescents with cystic fibrosis and anxiety disorders were more adherent to treatment than those without an anxiety disorder [16].

Despite the high prevalence of anxiety or depression in adolescents with IBD, very few studies have investigated the relationship between anxiety/depression and adherence in this population. The current study is the first to explore the additive effect of anxiety/depression on the relationship between barriers to adherence and adherence to IBD medication. The researchers used well-validated measures and a strong analytical plan to assess the moderating effect of anxiety/depression on the relationship between barriers and medication adherence. The study findings contribute to the literature by identifying factors that may contribute to the high rates of nonadherence in adolescents with IBD.

Results should be interpreted in light of the study's limitations. One methodologic concern is that the authors use the Child Behavior Checklist Youth Self-Report to measure "anxiety/depression" as one construct. However, anxiety and depression likely differentially

impact the relationship between barriers and adherence to medication. Based on previous studies in youth with chronic illnesses, depression is consistently associated with nonadherence, whereas anxiety is sometimes correlated with increased adherence [13–15]. Another limitation is the heavy reliance of self-report measures, which frequently overestimate adherence [17,18]. In addition, the power of this study is questionable given that with a sample size of 79, less than 10 participants actually presented with clinical levels of anxiety/depression. Lastly, the study may not be generalizable to other adolescent populations with IBD given that over 90% of the sample was Caucasian. Future research should attempt to replicate these findings in a prospective study with a larger, more diverse sample using separate measures for anxiety and depression.

Applications for Clinical Practice

Given that adolescents with IBD and higher levels of anxiety/depression were significantly less adherent to their medications than those with lower levels of anxiety/depression, it is important for clinicians to screen youth with IBD for anxiety and depression. Teenagers with IBD and higher levels of anxiety/depression may require referral to a mental health specialist for further treatment. Results also suggest interventions intended to reduce barriers to adherence should aim to lower levels of anxiety/depression in patients who exhibit these psychiatric symptoms. Currently, interventions for youth with IBD focus on overcoming barriers in order to increase adherence to medication. Educational interventions, organizational interventions, and interventions that combine education, parental involvement, self-monitoring, and reinforcement strategies have been found to increase adherence. Despite the high rates of comorbidity between chronic illnesses like IBD and anxiety or depression, almost no interventions target anxiety or depression in order to improve adherence. The current finding that anxiety/depression moderates the relationship between barriers and treatment adherence supports the need for new interventions focused on decreasing these psychiatric symptoms in nonadherent adolescents with IBD.

—*Alexandra E. Lamm, BA, Melanie Jay, MD, MS, and Jean-Marie Bruzzese, PhD*

References

1. Achenbach T. Manual For The Child Behavior Checklist. Burlington: University of Vermont Research Center for

- Children, Youth and Families; 1988.
2. Zelikovsky N, Schast, AP. Eliciting accurate reports of adherence in a clinical interview: development of the medical adherence measure. *J Pediatr Nurs* 2008;34:141–6.
3. Hyams J, Ferry G, Mandel F, et al. Development and validation of a pediatric Crohn’s disease activity index. *J Pediatr Gastroenterol Nutr* 1991;12:439–47.
4. Lichtiger S, Present D, Kornbluth A, et al. Cyclosporine in severe ulcerative colitis refractory to steroid therapy. *N Engl J Med* 1994;330:1841–5.
5. Greenley R, Kunz J, Biank V, et al. Identifying youth non-adherence in clinical settings: data-based recommendations for children and adolescents with inflammatory bowel disease. *Inflamm Bowel Dis* 2012;18:1254–9.
6. Kappelman M, Rifas-Shiman S, Kleinman K, et al. The prevalence and geographic distribution of Crohn’s disease and ulcerative colitis in the United States. *Clin Gastroenterol Hepatol* 2007;5:1424–9.
7. Mackner LM, Crandall WV. Oral medication adherence in pediatric inflammatory bowel disease. *Inflamm Bowel Dis* 2005;11:1006–12.
8. Quittner AL, Espelage DL, Ievers-Landis C, et al. Measuring adherence to medical treatments in childhood chronic illness: considering multiple methods and sources of information. *J Clin Psychol Med Settings* 2000;7:41–54.
9. Rhee H, Belyea MJ, Basch J. Family support and asthma outcomes in adolescents: barriers to adherence as a mediator. *J Adolesc Health* 2010;47:472–8.
10. Greenley R, Stephens M, Doughty A, et al. Barriers to adherence among adolescents with inflammatory bowel disease. *Inflamm Bowel Dis* 2010;16:36–41.
11. Ingerski L, Baldassano R, Denson L, et al. Barriers to oral medication adherence for adolescents with inflammatory bowel disease. *J Pediatr Psychol* 2010;35:683–91.
12. Burke P, Neigut D, Kocoshis S, et al. Correlates of depression in new onset pediatric inflammatory bowel disease. *Child Psychiatry Hum Dev* 1994;24:275–83.
13. Bender B. Risk taking, depression, adherence, and symptom control in adolescents and young adults with asthma. *Am J Resp Crit Care* 2006;173:953–7.
14. Gonzalez J, Peyrot M, McCarl L, et al. Depression and diabetes treatment nonadherence: a meta-analysis. *Diabetes Care* 2008;31:2398–403.
15. Mawhinney H, Spector S, Heitjan D, et al. As-needed medication use in asthma usage patterns and patient characteristics. *J Asthma* 1993;30:61–71.
16. White T, Miller J, Smith G, et al. Adherence and psychopathology in children and adolescents with cystic fibrosis. *Eur Child Adolesc Psychiatry* 2009;18:96–104.
17. Hommel K, Mackner L, Denson L, et al. Treatment regimen adherence in pediatric gastroenterology. *J Pediatr Gastroenterol Nutr* 2008;47:526–43.
18. La Greca A, Schuman W. Adherence to prescribed medical regimens. New York: Guilford Press; 1995: 55–83.