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Research paper

Enhancing quality of life among adolescents with bipolar disorder: A randomized trial of two psychosocial interventions☆

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ABSTRACT

Background: Adolescents with bipolar disorder (BD) report lower quality of life (QoL) than adolescents with other psychiatric disorders. This study compared the efficacy of family-focused therapy for adolescents (FFT-A) plus pharmacotherapy to brief psychoeducation (enhanced care, or EC) plus pharmacotherapy on self-rated QoL in adolescents with BD over 2 years.

Methods: Participants were 141 adolescents (mean age: 15.6 ± 1.4yr) with BD I or II who had a mood episode in the previous 3 months. Adolescents and parents were randomly assigned to (1) FFT-A, given in 21 sessions in 9 months of psychoeducation, communication enhancement training, and problem-solving skills training, or (2) EC, given in 3 family psychoeducation sessions. Study psychiatrists provided patient participants with protocol-based pharmacotherapy for the duration of the study. QoL was assessed with *The KINDL^R Questionnaire* (Ravens-Sieberer and Bullinger, 1998) during active treatment (baseline to 9 months) and during a post-treatment follow-up (9–24 months).

Results: The two treatment groups did not differ in overall QoL scores over 24 months. However, adolescents in FFT-A had greater improvements in quality of family relationships and physical well-being than participants in EC. For quality of friendships, the trajectory during active treatment favored EC, whereas the trajectory during post-treatment favored FFT-A.

Limitations: We were unable to standardize medication use or adherence over time. Quality of life was based on self-report rather than on observable functioning.

Conclusions: A short course of family psychoeducation and skills training may enhance relational functioning and health in adolescents with BD. The effects of different psychosocial interventions on peer relationships deserves further study.

1. Introduction

Bipolar Disorder (BD) is a chronic illness characterized by severe mood fluctuations and profound functional deficits. Up to 65% of individuals with BD have illness onset before age 18, and 28% before age 13 (Perlis et al., 2004) Childhood-onset BD is associated with a more severe course of illness than adult-onset BD, including more polarity switches, longer periods with subthreshold symptoms, and increased suicidal behaviors (Birmaher et al., 2009; Geller et al., 2008; Goldstein et al., 2012; Perlis et al., 2004; Propper et al., 2015). Although a number of studies have examined the impact of early-onset BD on psychosocial functioning (Huxley and Baldessarini, 2007; Kessler et al., 2006; Merikangas et al., 2007; Perlis et al., 2004), fewer studies have considered its influence on quality of life (QoL).

QoL is a subjective sense of well-being in various life domains including school or work, family relationships, peer/romantic relationships, physical health, and self-esteem. Adult patients with BD report lower QoL than patients with various medical conditions or other psychiatric disorders (Dean et al., 2004; Michalak et al., 2005a; Revicki et al., 2005). Lower QoL is associated with a greater risk for suicidal behavior in adults with BD (de Abreu et al., 2012). A study examining health values (i.e., subjective satisfaction, distress, and undesirability of having a health condition) among adult outpatients with BD found that, on average, patients were willing to give up 39% of their life

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expectancy for a healthier mental state than their current one (Tsevat et al., 2000) Relatedly, childhood-onset patients with BD have lower QoL in the areas of psychosocial, physical, and emotional well-being compared to children with major depression, anxiety disorders, disruptive behavior disorders, or no psychiatric history (Freeman et al., 2009; Gomes et al., 2016; Rademacher et al., 2007; Stewart et al., 2009).

High levels of depression, which are persistent throughout the course of BD (Altshuler et al., 2006), are strongly associated with low self-reported QoL in adults and youth with BD (Dean et al., 2004; Freeman et al., 2009; Michalak et al., 2005a, 2005b, 2008). However, adult and adolescent patients who are in continuous remission from depressive symptoms report lower QoL than their unaffected siblings or age-matched healthy controls (Coryell et al., 1993; Olsen et al., 2012).

Two clinical trials have examined whether medical treatment for manic symptoms improves QoL in BD (Revicki et al., 2005). Olanzapine, divalproex, and quetiapine were each associated with increases in QoL in adolescents after an episode of mania or mixed disorder, in the domains of school behavior, family functioning, and mental health (Olsen et al., 2012; Rademacher et al., 2007). In the STEP-BD randomized trial of adults with BD, each of three psychosocial treatments (family-focused therapy (FFT), interpersonal and social rhythm therapy, and cognitive-behavioral therapy) in combination with pharmacotherapy had a greater impact on life satisfaction and relational functioning than brief psychoeducation with pharmacotherapy over 1 year, even when levels of depression were covaried (Miklowitz et al., 2007). There are currently no treatment studies examining the impact of psychosocial treatments on QoL in childhood-onset BD.

This study examined the efficacy of FFT for adolescents (FFT-A), a 9-month, 21-session psychoeducational treatment, compared to enhanced care (EC), given in 3 sessions of family psychoeducation, on self- and parent-reported QoL among adolescents with BD. Four randomized trials have found that FFT and pharmacotherapy are more effective than brief psychoeducation or individual supportive therapy and pharmacotherapy in reducing symptom severity and delaying recurrences among bipolar adults (Miklowitz and Chung, 2016). The empirical record of FFT-A is less certain in adolescents with BD, with one study showing significant reductions in depressive symptoms among adolescents who received FFT-A compared to EC (Miklowitz et al., 2008). Another study, reporting results from this current trial, showed no differences between FFT-A and EC on time to recovery or recurrence, but found secondary effects of FFT-A on mania symptoms (Miklowitz et al., 2014b). The effects of psychosocial treatment on patients' quality of life ratings have not been examined among adolescents with BD in this or any other study.

In the trial comparing FFT-A to EC described by Miklowitz et al. (2014b), we obtained regular quality of life assessments from adolescents (N = 141) with BD I or BD II disorder and their parents. Adolescents had experienced an episode of depression, mania/mixed disorder, or hypomania in the 3 months before enrollment. We hypothesized that 1) adolescents in FFT-A would report better QoL over time than those in EC in the areas of family relationships and emotional well-being (both of which are targets of the FFT model); and 2) these group differences would be independent of baseline differences among adolescents in depressive or manic symptoms.

2. Methods

2.1. Participants

This study ran from August 2006 to July 2010 at three U.S. sites: University of Colorado, Boulder, CO; University of Pittsburgh School of Medicine, Pittsburgh, PA, and the University of Cincinnati/ Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio. Participants were recruited from referrals from community practitioners, inpatient and outpatient units, print and online advertisements, and public presentations.

Participants were between the ages of 12 years, 0 months to 18 years, 1 month and met criteria for a DSM-IV-TR (American Psychiatric Association, 2000) diagnosis of bipolar I or II disorder. The key diagnostic assessment instrument was the "Kiddie" Schedule for Affective Disorders and Schizophrenia for School-Age Children, Present and Lifetime Version (KSADS-PL; Chambers et al., 1985; Kaufman et al., 1997) administered to the adolescent and at least one parent at study entry, with ratings based on a consensus between the two reports. Participants had to have at least one week of manic, hypomanic, or mixed symptoms or at least 2 weeks of depressive symptoms in the past 3 months, with symptoms of at least moderate severity for mania ($\geq$17 on the K-SADS Mania Rating Scale; Axelson et al., 2003) or depression ($\geq$16 on the K-SADS Depression Rating Scale; Chambers et al., 1985)). Reliabilities (intraclass rs), calculated across the three sites (12 K-SADS tapes rated by an average of 12 raters) were .89 for KSADS Depression Rating Scale Scores and .81 for Mania Rating Scale scores. Participants were ineligible if they met DSM-IV-TR criteria for a current substance abuse/dependence disorder or pervasive developmental disorder. At least one parent or stepparent agreed to attend all family sessions with the adolescent.

Participants agreed to receive pharmacotherapy from board-certified psychiatrists using the algorithms of the Child Psychiatric Workgroup on Bipolar Disorder (Kowatch et al., 2005) as supervised by expert child psychopharmacologists. These algorithms recommend treatment with mood stabilizers and second-generation antipsychotics, with adjunctive antidepressants, psychostimulants, or anxiolytics as needed.

This study was approved by the institutional review boards of all three universities. Parents, adolescent patients, and all other family members (e.g. siblings) gave written consent or assent to participate after receiving full explanations of the trial procedures. Further study design details are given in a previous manuscript reporting results from this trial (Miklowitz et al., 2014b).

2.2. Study procedures: psychosocial treatments

After the initial KSADS-PL evaluation and a separate medical evaluation by a child psychiatrist, participants were randomly assigned in a 1:1 proportion to either pharmacotherapy plus FFT-A or pharmacotherapy plus EC, using a modified version of Efron's biased coin toss (Begg and Iglewicz, 1980). The groups were balanced at each study site by bipolar subtype (I and II) and mood state at study entry (depressed, manic/hypomanic, mixed).

2.2.1. Family-focused treatment for adolescents

Adolescents in FFT-A received 21 one-hr sessions over 9 months (12 weekly, 6 biweekly, and 3 monthly) with their parent(s) and available siblings. The first module focused on psychoeducation related to having BD, medication adherence, and developing a relapse prevention plan. The next phase, communication training, consisted of role-play exercises to rehearse active listening, make requests for changes in one another's behavior, offer positive feedback, or offer constructive criticism about specific behaviors. In the third phase, participants learned to define specific problems, generate and evaluate solutions to these problems, select solutions, and develop solution-implementation plans. Much of the content of FFT-A emphasized the adolescents' adaptation to the school and social environment, greater awareness of triggers for mood instability, maintaining stability in sleep/wake rhythms, keeping a balance between under- and over-activity in social engagements, and negotiating conflicts within the family.

2.2.2. Enhanced care

Participants, parents, and siblings who received EC attended three weekly 1 h. sessions in the first month after randomization. These sessions focused on mood monitoring, identifying early warning signs