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Brief Report

ARIPIPRAZOLE AUGMENTATION OF INCOMPLETE TREATMENT RESPONSE IN AN ADOLESCENT MALE WITH OBSESSIVE-COMPULSIVE DISORDER

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We report the case of adolescent male with obsessive-compulsive disorder (OCD) who had an incomplete response to combined cognitive-behavioral therapy (CBT) and sertraline before successful augmentation of CBT with aripiprazole. Standardized assessments indicated significant reductions in OCD symptomatology associated with both initial treatment and aripiprazole augmentation. This case suggests that aripiprazole may have utility as an augmenting agent of CBT in adolescents with OCD and underscores the need for conducting controlled studies to test this hypothesis. Depression and Anxiety 25:172–174, 2008. *© 2008 Wiley-Liss, Inc.*

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INTRODUCTION

Obsessive-compulsive disorder (OCD) is a common, chronic, and oftentimes disabling disorder with a childhood onset in approximately 50–80% of cases [Pauls et al., 1995]. The only established first-line treatments for OCD are Cognitive Behavioral Therapy (CBT) and the Serotonin Reuptake Inhibitors [SRIs; see Storch and Merlo, 2006 for a review]. Many pediatric patients do not experience complete symptom resolution with either modality. Pharmacological options for these cases include switching to a different medication, increasing the SRI dose, or augmentation with another agent [Thomsen, 2000]. Among the pharmacological augmentation strategies, adjunctive antipsychotic medications have the most empirical support among adults as well as frequent use in clinical practice among pediatric OCD patients.

Research examining antipsychotic augmentation in treatment-resistant pediatric OCD patients is scant. Studies investigating atypical antipsychotic augmentation among adults have shown a modest response rate ranging from 33 to 50% [Bloch et al., 2006]. Only two studies have examined antipsychotic augmentation in children who have not responded to previous SRI therapy. Thomsen [2004] reported a non-blinded open 12-week trial of low dose (≤ 2 mg daily) adjunctive risperidone in 17 adolescents with severe OCD who remained symptomatic following two SRI monotherapy trials. Mean scores on the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) showed a significant reduction from baseline (24.2 ± 2.6 to 19.9 ± 2.9). Fitzgerald et al. [1999] reported on successful risperidone augmentation of four child SRI non-responders in a non-blinded open trial that did not use quantitative measures. Side effects of risperidone and other atypical antipsychotic medications include somnolence and weight gain, both of which were reported in the previous studies.

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Aripiprazole is an atypical antipsychotic medication that works via partial dopaminergic and serotonin 1A receptor agonist activity, and has fewer side effects when compared to other atypicals [Rugino and Janvier, 2005]. To date, there is no research on using aripiprazole to augment treatment for pediatric OCD patients who continue to experience residual symptoms following treatment. Observations of improved comorbid OC symptoms in adults and youth with Tourette's Syndrome treated with aripiprazole [Bubl et al., 2006; Murphy et al., 2005], and a case series of adults with OCD [Connor et al., 2005] have been reported suggesting the potential merit of this agent. Therefore, this report presents a case example of a child who benefited from an initial trial of aripiprazole and then aripiprazole augmentation for residual symptoms after CBT and SRI treatment.

PRESENTATION

Sam was a 13-year-old Caucasian male referred by his previous psychologist to our pediatric OCD clinic. Sam reported that his primary symptom of counting "everything" (e.g., square shapes, cars, people, and breathing) started approximately 2 years before treatment without any identifiable antecedent. Throughout that time, Sam described himself as counting objects "all the time" and feeling extreme anxiety regarding the need to count with associated relief after performing the ritual. Sam noted that his symptoms had become extremely distressing and impairing immediately preceding his referral. For example, he noted being unable to concentrate during school (he was an honors student) due to the uncontrollable urge to count stimuli. Not surprisingly, Sam also met criteria for depression that we conceptualized as linked to his impairing symptom presentation. No current or past history of psychosis was reported and Sam exhibited excellent insight into the nature of his symptoms. Notably, his constant obsessions about counting and his counting rituals severely incapacitated Sam's ability to engage in age-appropriate self-care, social, and academic behaviors.

TREATMENT

Sam initially participated in 14, 90-min individual CBT sessions over 20 weeks. Treatment followed the manual used by the Pediatric OCD Treatment Study team [2004], focusing on exposure and response prevention to rituals, as well as developing cognitive restructuring skills. Initially, Sam and his mother were educated about the nature of CBT, namely that his anxiety would habituate following repeated exposure to compulsion eliciting events without ritual engagement. A hierarchy of distressing situations was established thereafter, and Sam was progressively exposed to situations or objects that he rated as moderately anxiety provoking (e.g., counting square objects) while refraining from counting. As his anxiety habituated within these early exposures, Sam was further exposed to situations that he rated as highly anxiety provoking (e.g., counting headlights or people). In each instance, Sam was coached to continue with the exposure exercise until his anxiety decreased significantly without the use of rituals.

Sam's baseline score on the Children's Yale-Brown Obsessive-Compulsive Scale [CY-BOCS; Scahill et al., 1997] was 30 (15 each on the Obsessions and Compulsions Severity Scales) corresponding with severe OCD. After three CBT sessions, Sam was initiated on aripiprazole at 1.25 mg/day given the minimal improvement that he had experienced in CBT at this point (CY-BOCS Total Score = 27) together with his elevated distress and OCD-related impairment. Regarding the latter, Sam was quite fearful that his symptoms would impact his academic performance and social relationships. Although recommended strategies suggest that SRIs are added in the case of a non- or partial-responder [e.g., March et al., 1997], aripiprazole was added before providing an SRI given: (1) the long latency for improvement in OCD with SSRIs and the need for a relatively fast-acting intervention to reduce Sam's distress, (2) the positive clinical experiences of the last author, (3) preliminary evidence supporting its use in OCD patients [Connor et al., 2005; Murphy et al., 2005], (4) evidence suggesting its antidepressant role [Möller, 2005; Sachs et al., 2006], and (5) Sam's heightened anxiety level made it extremely difficult for him to engage in exposure and response prevention exercises. Sam exhibited a rapid and significant improvement per his report after aripiprazole was initiated; given that he was more stable, the decision was made to initiate standard SSRI therapy with the goal to eventually taper and discontinue the aripiprazole. Therefore, he began taking sertraline approximately 3 weeks later and was gradually titrated to 100 mg where he remained on this dose for approximately 10 weeks. After approximately 16 weeks since presentation, aripiprazole was discontinued due to improved symptoms and mild side effects while on combination therapy (e.g., headache, nausea). Thereafter, he continued on combined CBT and sertraline treatment until session 14 (at approximately week 20 of treatment). At session 14, Sam's CY-BOCS score was 12 corresponding with the presence of mild but still problematic symptoms. Sam believed that aripiprazole had superior efficacy to sertraline for OCD related distress and impairment. Given this, Sam was weaned off sertraline after session 14, and aripiprazole was reinitiated and titrated up to 5 mg/day while continuing bi-weekly CBT. Following continued aripiprazole and six additional CBT sessions spanning 3-months, Sam's CY-BOCS score decreased to 3. At this point, aripiprazole was decreased to 2.5 mg without a return of symptoms. This symptom level remained stable over a 5-month follow-up period. No significant adverse effects were reported at the higher

dose. No clinically significant changes in weight or laboratory values were found between when aripiprazole was started the initial time and the final treatment session.

DISCUSSION

This case report is noteworthy for several reasons. First, the latter trial of aripiprazole represents the first known report of aripiprazole augmentation of CBT in a pediatric OCD patient who experienced problematic OCD symptoms following "gold standard" psychiatric and psychological treatment. To date, there is little efficacy or safety/tolerability data regarding pharmacological augmentation strategies for pediatric OCD, particularly atypical antipsychotics, despite some evidence that this takes place relatively frequently. This is an important extension of existing clinical knowledge, as it shows that aripiprazole may have merit as an augmenting agent in pediatric OCD patients who have an incomplete response to adequate CBT and SRI trials. Second, the initial trail of aripiprazole provides preliminary evidence for its use in pediatric OCD patients who are experiencing considerable distress that may negatively impact their overall functioning and ability to participate in CBT. The length until improvement in OCD symptoms with SSRIs may not be tolerable for some youth requiring safe and fast-acting intervention to reduce distress. Finally, covert symptoms like counting may be more likely to be refractory to traditional approaches [Ball et al., 1996]. Aripiprazole may have particular merit in such difficult-to-treat anxiety and OCD cases by virtue of its dual impact on serotonergic and dopaminergic mechanisms [Gao et al., 2006]. Further study in larger samples is warranted to examine this.

Overall, the present results provide preliminary support that aripiprazole may be one augmentation approach with reasonable safety and tolerability. As Sam was receiving CBT and aripiprazole simultaneously, it is not possible to conclusively determine which may have been accountable for improvement in the final phase of treatment. The continued implementation of CBT or the intervening course of an SRI may have contributed to further improvement as well. However, when aripiprazole was reinitiated, it was believed that CBT associated gains had been maximized. Additionally, although Sam did not gain significant weight, he was also extremely physically active. Other studies of aripiprazole in youth have found modest increases in weight [Murphy et al., 2005; Rugino and Janvier, 2005] so conclusions that can be made about safety and tolerability are limited. Further controlled research is needed to clarify the efficacy of atypical antipsychotic augmentation in treatment resistant OCD patients, and if this approach has superior efficacy and tolerability to cognitive-behavioral and other pharmacologic approaches.

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