Summary of the Recent Literature on the Treatment of Obsessive Compulsive Disorder in Children and Adolescents 6-17 Years

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The proposed lifetime prevalence of obsessive compulsive disorder (OCD) is 2 - 3% in adolescents and adults. Approximately half of all OCD patients first present in childhood, before age 15 (Busatto et al., 2001). Childhood onset OCD is associated with a poorer treatment response, higher familial risk and a high rate of comorbid tic, disruptive and developmental disorders (Mancuso, Faro, Joshi, & Geller, 2010). Many children have a chronic course and continue to meet diagnostic criteria at follow-up years later.

Cognitive-Behavioral Therapy (CBT). In addition to being recommended as the first line approach to treatment, CBT should be considered for all youth who have an incomplete response to initial medication monotherapy. The efficacy rates of CBT trials is quite high, ranging from 57-88% and has shown excellent maintenance of symptom reduction at follow-up in pediatric populations (Abramowitz, Taylor, & McKay, 2005; Shalev et al., 2009). CBT for OCD is a structured approach to teaching both the child and family skills for responding to symptoms. The premise that compulsions are performed to reduce or avoid anxiety that is associated with obsessions underlies the approach of CBT for pediatric OCD. CBT is composed of three core components: exposure, response prevention, and cognitive restructuring. CBT with Exposure/Response Prevention (E/RP) for OCD is distinguished from other “talk-therapies” (e.g., Play-based, supportive, insight-oriented, relaxation, psychoanalytic, and psychodynamic therapies) that have no supported efficacy in the literature. Children with oppositional defiant disorder have low response rates in trials with paroxetine (Geller et al., 2003a), and are likely not to be as successful in CBT trials unless pretreatment with parent training occurs.

Pharmacotherapy: The efficacy of pharmacotherapy for OCD in pediatric populations has been demonstrated in several controlled trials with SRIs and SSRIs. The earliest researched SRI in the treatment of pediatric OCD is the tricyclic antidepressant (TCA) clomipramine (Grados & Riddle, 2001). Overall, a meta-analysis of pharmacotherapy trials in children identified clomipramine to be significantly superior over SSRIs in reducing OCD symptoms (Geller et al., 2003a). Nevertheless, the risk profile, adverse effects, and required EKG and blood-level monitoring associated with TCAs (e.g., anti-adrenergic, anticholinergic, and anti-histaminergic adverse effects), are of concern with clomipramine.

Several placebo-controlled trials have demonstrated the efficacy of SSRIs. In a 20-week double-blind placebo-controlled trial of the SSRI fluoxetine in children and adolescents with OCD, significant reductions in OCD symptoms were reported (Riddle et al., 1992). A 13-week controlled trial conducted by Geller et al (2001) also demonstrated the efficacy of fluoxetine with 55% of patients treated with fluoxetine rated as much or very-much improved (Geller et al., 2001). Another 16-week placebo-controlled trial of fluoxetine in children reported that 57% of patients demonstrated significant improved ratings on the CGI (Liebowitz et al., 2002). Many
open trials also present favorable findings for the use of fluoxetine for pediatric OCD (Mancuso et al., 2010).

Controlled trials have found fluvoxamine and paroxetine to be efficacious for treatment of children and adolescents with OCD. Riddle et al. (2001) found that 42% of patients responded to fluvoxamine (based on a 25% reduction on the CYBOCS) while participating in a 10-week multicenter placebo controlled trial (Riddle et al., 2001). In a response rate analysis from a large pediatric paroxetine trial, the response rate for patients with a diagnosis of OCD only (75%) was significantly greater than patients with comorbid psychopathology, e.g., ADHD (56%), tic disorder (53%), and ODD (39%) (Geller et al., 2003b).

Data also support the use of the SSRI sertraline for the treatment of pediatric OCD. March et al. (1998) conducted a 12-week multicenter, randomized placebo-controlled trial in children and adolescents with OCD (March et al., 1998). Forty-two percent of patients receiving sertraline were rated as much or very much improved. Further, in a 52-week open-label extension of the previous study, 71% of children (ages 6-12) and 61% of adolescents (ages 13-18) demonstrated 25% decreases on the Children’s Yale-Brown Obsessive Compulsive Scale (CYBOCS) and were rated as much/very much improved (Cook et al., 2001).

Combination of CBT and medication should be considered in most with moderate to severe OCD. The Pediatric Obsessive Compulsive Treatment Study (POTS), a large-scale, multisite randomized placebo-controlled trial of CBT/sertraline in children with OCD, found that clinical remission was attained at a higher rate for those randomized to a combination of CBT and sertraline (53.6%) compared to CBT alone (39.3%), sertraline alone (21.4%) and placebo (3.6%) (POTS, 2004).

Overall, clinically significant reductions in OCD symptomology have been documented in children and adolescents using SSRIs including fluoxetine, sertraline, fluvoxamine, and paroxetine with a relatively minimal side effect profile (as compared to clomipramine). Based on these findings, SSRIs are the consensus first-line medication for pediatric OCD. Although there are no controlled comparisons between these medications in children, research suggests that the SSRIs are equally efficacious in children and the specific choice should be based on the patient's medical history, concomitant medications, and the adverse events profile*. Additionally, clinical response is unlikely within the first several weeks of an SSRI - generally, 10-12 weeks at adequate dosage is necessary to evaluate the efficacy of the medication. Children with mild to moderate OCD should be given a trial of CBT whenever possible before trying medications.

Pharmacotherapy Adverse Effects: SSRIs are generally well tolerated in the pediatric population when it comes to the somatic side effects, however, the most troublesome side effects are the neuropsychiatric side effects with the most common of these including behavioral activation, and occasionally enuresis, tremor, tics, apathy and sedation (Murphy, Segarra, Storch, & Goodman, 2008) Behavioral activation may present at any time during treatment but is most common in the initial two weeks and often is dose-dependent, warranting use of the lowest possible starting dose. Behaviorally activated youth are described as having a worsening of their clinical presentation, and/or being more hyperactive, impulsive, silly, talkative, or “mean”. This (at least transient) behavioral toxicity...
may be due to variable effects from neurotrophic responses of increased serotonin concentrations on the developing brain (Olivier, Blom, Arentsen, & Homberg, 2010). Concerns regarding increased suicidality in children and adolescents taking SSRIs (4% versus 2% in placebo controls) prompted the FDA to require “black box” warning labels on all SSRIs. In a review article, Bridge and colleagues (2007) identified 27 randomized placebo-controlled trials comparing second generation antidepressants versus placebo in children and adolescents meeting DSM IV criteria for either MDD (n=3430), OCD (n=718) or non-OCD anxiety disorders (n=1162) (Bridge et al., 2007). They concluded that efficacy appears greater for non-OCD anxiety disorders (Number Needed to Treat (NNT)=10) and for OCD (NNT=6) and more modest for MDD (NNT=3), whereas the NNH (number needed to harm based on suicidal risk) was 143, 200, and 112 respectively. They concluded that the balance is in favor of benefit over harm with no statistically significant increase for suicidality in the OCD trials (Bridge et al., 2007). A conservative approach is useful in minimizing any potential agitation from the medication, beginning with doses as low as available for several days or a week before titrating upward. Close monitoring for these symptoms is especially important during the first weeks after initiation of medication treatment or subsequent dosage increases. Fortunately, upon detection, activation symptoms usually abate after decreasing or discontinuing the medication.

**Augmentation Strategies:** Although SSRIs have demonstrated efficacy relative to placebo for pediatric OCD, it is well recognized that many patients (~40%) do not respond to treatment, complete remission is uncommon (e.g., (POTS, 2004)), and undesirable side effects may be present (SSRI AE Paper). Poor clinical response to one SSRI is not necessarily predictive of failure with other SSRIs, suggesting adequate trials of multiple SSRIs may be indicated before augmentation. In pediatric cases that are unresponsive to CBT and trials with multiple SSRIs, second-line pharmacological treatments include augmentation (Dougherty et al., 2002). Data on evidence-based augmentation for youth who are partial or non-responders to SSRI therapy is scant. Although antipsychotic augmentation has empirical support in adults with OCD, this approach has not been well-studied in youth. Augmentation approaches for refractory pediatric OCD may include atypical neuroleptics (e.g., aripiprazole, risperidone) and clomipramine. Although two pediatric case-series suggest that SSRI augmentation with clomipramine resulted in marked improvement; it is notable that this combination requires diligent blood, EKG, and side effect monitoring (Figueroa, Rosenberg, Birmaher, & Keshavan, 1998; Simeon, Thatte, & Wiggins, 1990).

New pharmacotherapy approaches: Clinical observations, genetic studies, and neuroimaging studies have converged to support the importance of the glutamatergic system in OCD (Rosenberg et al., 2000; Rotge et al., 2010; Ting & Feng, 2008). A number of studies have demonstrated the benefit of this approach in treating patients who do not respond to SSRIs alone (Greenberg et al. 2010). Augmentation trials of glutamate-modulating agents have been recently completed in adult OCD using riluzole (Coric et al., 2005) and memantine (Stewart et al., 2010). Promising results have also been reported in open-label studies for riluzole in adolescents and children with OCD (Grant et al. 2007) and with memantine in children with treatment-resistant OCD (Hezel, Beattie, & Stewart, 2009).
Pearls

- Mild to moderate OCD, try CBT first.
- In addition to repetitive behaviors, children with OCD may present with melt-downs, oppositional behavior, school decline, and sensory defensiveness.
- Typically, children are not non-responders but typically partial responders to treatment.
- Medication dosing is highly variable with some children responding to lower doses (especially those with comorbid conditions) and some require higher doses (typically those with long standing pure OCD).
- Treatment of comorbid condition such as tics or ADHD (if impairing enough) first, may improve treatment outcomes for OCD.
- In sudden and dramatic onset OCD, consider infectious trigger such as a streptococcal pharyngitis or mycoplasma upper respiratory infection.

References


1. USF adolescent guidelines 2010 smaller format.qxp  01/19/2011  8:36 AM  Page 34


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