Obsessive-compulsive disorder in children and adolescents: Treatment overview

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INTRODUCTION

Obsessive-compulsive disorder (OCD) is characterized by recurrent intrusive thoughts, images, or urges that cause anxiety or distress (obsessions), and by repetitive mental or behavioral acts (compulsions) that the individual feels driven to perform. Compulsions are done in response to the obsession (ie, to decrease distress or prevent a feared consequence from occurring). Almost all individuals with OCD have both obsessions and compulsions.

OCD typically starts in childhood or adolescence. If not successfully treated, it often persists throughout life and produces substantial impairment in functioning.

Treatments with the most empirical support for OCD in children and adolescents include serotonergic antidepressants (eg, selective serotonin reuptake inhibitors [SSRIs] or clomipramine), cognitive-behavioral therapy with exposure and response prevention (CBT-ERP), or a combination of the two. (See 'Initial treatment' below.)

This topic reviews our preferred choices for treatment of OCD in children and adolescents. The epidemiology, pathogenesis, clinical manifestations, course, assessment, and diagnosis of OCD in children and adolescents and discussion of pediatric acute-onset neuropsychiatric syndrome (PANS) and pediatric autoimmune neuropsychiatric disorder associated with group A streptococci (PANDAS) are discussed separately. Topics related to OCD in adults are also found separately.

- (See "Obsessive-compulsive disorder in children and adolescents: Epidemiology, pathogenesis, clinical manifestations, course, assessment, and diagnosis".)
- (See "Management of obsessive-compulsive disorder in adults".)
- (See "Obsessive-compulsive disorder in adults: Epidemiology, clinical features, and diagnosis".)
- (See "Obsessive-compulsive disorder in adults: Psychotherapy".)
- (See "PANDAS: Pediatric autoimmune neuropsychiatric disorder associated with group A streptococci".)

INITIAL TREATMENT

Our preference for initial treatment modality is based on severity of symptoms, presence of active comorbid disorder, and past treatment history. We prioritize patient/caregiver preference and typically initiate treatment with the patient preferred option. For example, if an individual expresses an interest in combined treatment, we would begin with this, if available. If the individual refuses to begin psychotherapy (despite our recommendation) or if psychotherapy has been ineffective, we would treat with pharmacologic management as monotherapy. (See 'Mild or moderate symptoms' below and 'Severe symptoms or active comorbid disorder' below.)

Mild or moderate symptoms — For youth with obsessive-compulsive disorder (OCD), whose symptoms are mild or moderate (eg, Children's Yale-Brown Obsessive Compulsive Scale [CY-BOCS] <24), who do not have an active co-occurring disorder, and who are willing to participate in psychotherapy, cognitive-behavioral therapy with exposure and response prevention (CBT-ERP) is our preferred choice (see 'Administration of CBT-ERP' below and 'Efficacy of CBT-ERP' below). No other psychotherapies for OCD in youth have received comparable study nor have they demonstrated consistent efficacy in clinical trials.

Administration of CBT-ERP — CBT-ERP may be administered in person or via internet.

- **In-person cognitive-behavioral therapy (CBT)** – The basic approach and components of effective CBT programs for children with OCD are similar [1]. The program consists of 14 hour-long sessions over a 12-week period in sessions with the child and one or more family members [2]. These are supplemented by 10-minute phone sessions most weeks. The therapy is typically provided individually, but evidence supports its use in groups and with/without participating family members [3,4]. The framework and administration described here are from a widely used and well-studied program [2]. (See 'Components' below.)

- **Internet-delivered** – Internet-delivered CBT may be as effective as face-to-face CBT for pediatric OCD. In most countries, children and adolescents with OCD have limited access to CBT provided by a specialist; internet-delivered treatment may help CBT to reach more individuals by breaking down the barriers to accessibility [5].

  In one trial, 152 youth with OCD were assigned to receive 16 weeks of internet-delivered stepped-care CBT versus face-to-face CBT [5]. At six-month follow-up, improvements in children and adolescents using internet-delivered CBT were not statistically different from those using face-to-face CBT (mean difference 0.91 points on the 40-point CY-BOCS).

Components — We involve parents/caregivers in all aspects of treatment with CBT when it is used to treat pediatric OCD. In treating children with CBT, we customize the treatment to the developmental limitation of the child. CBT has been used with good results in children as young as five years.

The program is delivered in five phases of treatment [2]:

- Psychoeducation
- Cognitive training
- Mapping OCD and case formulation [6] – "Mapping OCD" is a process of identifying and describing hypothesized causes/origins of symptoms, and addressing triggers of symptoms and problematic behaviors
- Graded exposure and response prevention
- Relapse prevention and generalization training

Further discussion of psychotherapy for anxiety disorders in children, administration and components of CBT in treatment of adults with OCD, and overview of psychotherapies is found elsewhere. (See "Overview of psychotherapies" and "Obsessive-compulsive disorder in adults: Psychotherapy" and "Psychotherapy for anxiety disorders in children and adolescents".)

Efficacy of CBT-ERP — Clinical trials indicate that treatment with CBT-ERP, as compared with control, waitlist, or placebo condition, leads to a greater reduction in symptom severity [7-11]. For example, in a meta-analysis including nine trials and 645 youth with OCD, treatment with CBT-ERP was compared with control condition [9]. Subjects in the CBT group had a greater reduction OCD symptom severity as compared with the control group (mean difference 6.81 points on the CY-BOCS, 95% CI 8.45-5.18). However, the findings are of low certainty due to heterogeneity of methods and risk of bias.

Severe symptoms or active comorbid disorder — In individuals with severe symptoms (eg, CY-BOCS score ≥24) and in those with active comorbid disorders (eg, depression, anxiety disorder) we prefer treatment with combined modality including pharmacotherapy and CBT-ERP. However, in some cases the severity of the comorbid disorders may preclude participation in CBT-ERP, or CBT-ERP may be unavailable. In these cases, we typically begin with pharmacologic management until the individual can effectively work in CBT to address the symptoms of OCD.

SSRI as first pharmacologic choice — For individuals who will be starting on pharmacotherapy alone (eg, prior unresponsiveness to psychotherapy, refusal to engage in psychotherapy) or as part of combination treatment (ie, severe symptoms, co-occurring disorder, patient preference), our preference is treatment with a selective serotonin reuptake inhibitor (SSRI) rather than other antidepressants (eg, clomipramine, serotonin-norepinephrine reuptake inhibitors). Our preference for SSRIs is based on their efficacy combined with their superior side effect profile (as compared with clomipramine), and their ease of use. (See 'Choosing among SSRIs' below.)

Choosing among SSRIs — We choose from among SSRI medications based on the side effect profile, drug-drug interactions, prior treatment response, and family history. In cases where the individual has successfully responded to an agent in the past, we often choose that agent again. Additionally, if there is a family history of response to specific medication, we would typically choose this as the first pharmacologic choice.

Several SSRI medications including fluoxetine, fluvoxamine, sertraline, paroxetine, and the non-SSRI, clomipramine have shown favorable comparison to placebo in the treatment of pediatric OCD (see 'Efficacy of SSRIs' below) [12-27]. However, few comparative treatment studies have been performed and there is minimal guidance on preferred choice of SSRIs in the treatment of pediatric OCD. Medications used in the treatment of pediatric OCD are shown on the associated table (table 1).

Starting and titrating SSRI — We start at a low initial starting dose and increase slowly and in small increments in all youth being treated with SSRIs for pediatric OCD. We do this to avoid side effects and increase tolerability. As an example, when using sertraline, we typically begin at 12.5 (for a child) to 25 mg per day (for an adolescent) and monitor for one week. We then titrate, as tolerated, by 25 mg (for a child) to 50 mg (for an adolescent) no faster than every two weeks (depending on patient response and tolerance) to a dose at the lower end of the maintenance daily dose range (eg, 25 to 75 mg) (table 1).

Dose and length of trial — We monitor for 12 weeks at the lower end of the maintenance daily dose range (eg, 25 to 75 mg). If adequate response is not achieved, we make subsequent gradual increases in weekly increments to maximize efficacy and minimize toxicity. We increase the dose until clinical response is seen or the maximum tolerated dose within the maintenance dose range is reached. We monitor at this dose for 6 to 12 weeks. For example, in the above trial using sertraline in the treatment of an adolescent with OCD, after 12 weeks at the lower end of maintenance dose range (eg, 25 to 50 mg) we would increase by 25 mg per day increments once weekly until clinical response is achieved or the maximum dose of 200 mg is reached.

We consider a full therapeutic trial to be at least 12 weeks with at least six at the maximum tolerated dose within the daily dose range. However, improvement of OCD symptoms may occur more slowly with fluoxetine than with other SSRIs (eg, more than eight weeks on a therapeutic dose to manifest significant benefit). We explain this to the patient and their family so that they do not prematurely stop the medication before a full therapeutic trial has been completed.

We use a dosing strategy to maximize tolerability of SSRIs. Pediatric patients are reported to have an increased risk of side effects associated with SSRIs including treatment emergent suicidal ideation, behavioral activation, and mania. Titrating the dose upward toward maximum tolerated ranges in children who do not or only partially respond to minimum-dose SSRI therapy is acceptable, particularly given the more benign side effect profile of SSRIs compared with other pharmacologic options in pediatric OCD.

However, the safety profile of supratherapeutic-dose SSRI treatment has not been sufficiently studied and, contrary to adult OCD, we do not recommend exceeding the US Food and Drug Administration (FDA)-recommended dose ranges in children and adolescents with OCD [28].

Our clinical experience and available research suggests that pediatric patients with OCD who demonstrate a clinical response, but not full or partial remission, to 12 weeks of SSRI treatment (with at least six weeks at maximum tolerated dose) continue to experience further improvement (average approximately 30 percent) beyond the 12-week duration of clinical trials [29,30]. An uncontrolled trial tested the continuation of sertraline (50 to 200 mg/day) for 52 weeks in 72 6- to 12-year-olds and 65 13- to 18-year-olds with OCD who already completed a 12-week clinical trial of sertraline [29]. At the end of the study period, 55 percent of patients met criteria for full remission (CY-BOCS ≤8) and 31 percent met criteria for partial remission (CY-BOCS ≤15).

Monitoring and defining response — In outpatient practice, we typically monitor individuals who have started on antidepressants weekly for the first month, twice monthly for one month, and then at least monthly thereafter [31]. The frequency of the visits depends on the severity of symptoms, whether suicidal ideation or mania is emergent, the complexity of comorbid disorders and the presence of side effects. Individuals with any of these are seen more frequently.

At each visit, we evaluate for symptomatic improvement using the CY-BOCS, a self-report or family report scale. Response is defined as a reduction in CY-BOCS score of 35 percent. Partial treatment response is defined as a reduction in CY-BOCS score between 25 to 35 percent. Remission is defined as a total score of ≤12. (See "Obsessive-compulsive disorder in children and adolescents: Epidemiology, pathogenesis, clinical manifestations, course, assessment, and diagnosis", section on 'Rating scales'.)

Additionally, we review for the presence of mania or suicidal thoughts and for the presence of medication side effects (see 'Side effects' below). We get caregiver perspective on the patient progress and reiterate to the patient and family the need for a full therapeutic trial. (See 'Dose and length of trial' above.)

Side effects — We review side effects and adverse effects of medication at each visit. Additionally, as treatment emergent suicidal ideation or medication-induced mania are a consideration in youth treated with SSRI medication, therefore we assess for these symptoms at each visit.

Side effects of SSRI medications are typically dose dependent and often dissipate over time [32-35]. The most common side effects include headache, abdominal pain, nausea, diarrhea, sleep changes, weight gain, and jitteriness or agitation.

Suicidality — Despite controversy about the relationship between SSRI use and suicidality in children, we monitor for suicidality at each visit. All antidepressants used in the United States have a boxed warning by the FDA about suicidality. There appears to be a slightly increased risk of suicidal thoughts and behaviors (but not completed suicide) among a small group of children and adolescents who are treated with antidepressant medications compared with placebo; however, the evidence is inadequate to conclusively establish this association, which is described in more detail separately. (See "Effect of antidepressants on suicide risk in children and adolescents".)

In a meta-analysis that included six clinical trials of antidepressants for pediatric OCD, the baseline risk of suicidal ideation/suicide attempts in youth with OCD was low, and not statistically different than the rate found in those treated with placebo (0.5 percent, 95% CI -1.2

to 2.2) [35,36]. Review of evidence on the association between SSRIs and suicidality has not found any one SSRI to have a stronger or weaker relationship to suicide than the others. (See "Effect of antidepressants on suicide risk in children and adolescents".)

Antidepressant-induced mania — Although the risk of induction of mania in pediatric patients with depression or anxiety is relatively rare (<2 percent), we are careful to monitor for antidepressant-induced mania in children and adolescents being treated with antidepressants, particularly in those with a history of bipolar disorder.

The role of antidepressants in inducing a patient's switch in mood to mania is controversial. In a sample of 4786 patients age 5 to 29, younger children (age 10 to 14) had a higher risk of mania when treated with antidepressants compared with adolescents and young adults [37]. However, increases in behavioral disinhibition or "behavioral activation" (eg, impulsivity, silliness, irritability, inability to control activity level, attention, and emotions) occur in approximately three to eight percent of youth taking antidepressants [38]. Many patients may also be especially inhibited prior to treatment initiation [39], and differentiation between healthy childhood behavior, "disinhibition," and mania is important. (See "Bipolar major depression in adults: Efficacy and adverse effects of antidepressants", section on 'Risk of switching to mania'.)

Efficacy of SSRIs — Clinical trials support the efficacy of serotonergic medications as compared with placebo, in the treatment of pediatric OCD [7,12-18,40-42]. However, there are few trials directly comparing efficacy of SSRIs in its treatment.

In a meta-analysis including 12 trials and 1044 youth with OCD the effects of serotonergic medications (SSRIs and clomipramine) as compared with placebo was investigated [14]. The overall effect size for medication versus placebo was 0.46 (standardized mean difference, 95% CI 0.37-0.55), equivalent to approximately four points on the CY-BOCS.

In clinical trials, sertraline [7,12], fluoxetine [15,16], fluvoxamine [17], and paroxetine [13] each provided greater improvement in symptoms of pediatric OCD than placebo. As an example, in a trial, 187 youth with OCD were randomly assigned to 12 weeks treatment with sertraline (up to 200 mg/day) or placebo [12]. Subjects treated with sertraline, as compared with those treated with placebo, had a higher rate of response (42 versus 26 percent) and greater improvement on measures of OCD symptoms (CY-BOCS adjusted mean difference -6.8 versus -3.4). Of note, a greater percentage of subjects treated with sertraline, as compared with placebo, terminated treatment early (12 versus 3 percent).

- **Comparing and combining modality** – Treatment with CBT or pharmacologic management with an SSRI appear to have similar efficacy to each other, each with superior efficacy as compared with wait list or control [7-9]. As examples:

- In a multisite trial 112 youth with a diagnosis of OCD and a CY-BOCS score indicating moderate severity OCD (ie, score of ≥16) were randomly assigned to 12 weeks of treatment with CBT alone, sertraline alone, combined CBT plus sertraline, or pill placebo alone [7]. Sertraline was dosed using a flexible strategy with an average dose of 170 mg/day (range 25 mg to 200 mg/day). Both sertraline alone and CBT alone reduced OCD symptoms to a similar degree and each greater than placebo. The rate of clinical remission (as defined by CY-BOCS ≤10) was similar between the CBT group (39 percent; 95% CI 24-58) and medication group (21 percent; 95% CI 10-40). Each was greater than the remission rate in the placebo/control group (4 percent; 95% CI 0-19 percent). There were significant site differences in outcomes, suggesting that patient adherence and quality of CBT may have an important effect on efficacy.

- In a meta-analysis of treatments for pediatric OCD including 3 trials and 146 subjects, treatment with either CBT or SSRIs led to similar decreases in OCD severity (mean difference -0.75, 95% CI -3.8 to 2.3) [9].

Combined treatment with CBT and a serotonin reuptake inhibitor appears to be more effective than either treatment alone [7,43]. For example, in the trial above [7], a greater proportion of youth treated with combined treatment experienced remission of symptoms as compared with patients receiving sertraline alone or placebo alone (56 versus 21 versus 4 percent). Additionally, there was a trend towards greater rate of remission with combined treatment than with CBT alone (56 versus 39 percent). Similar findings have been reported in other studies [43].

However, despite the potential superiority of combined treatment over monotherapy with either treatment, our preference is to provide individuals with treatment that is both effective and with the least potential for side effects. While SSRIs have a relatively benign side effect profile, younger patients may be particularly prone to side effects. In contrast, CBT has no physical side effects while offering comparable symptomatic improvement to treatment with serotonergic medications. However, practical limitations (eg, greater cost, higher frequency of appointments, availability of trained CBT-ERP therapists) may limit the availability of and willingness to participate in psychotherapy.

RESPONSE TO INITIAL TREATMENT

Adequate response

Response to CBT-ERP — As the clinical effects of cognitive-behavioral therapy with exposure-response prevention (CBT-ERP) can decline over time [44], we often offer booster sessions at progressively longer intervals (eg, 1, 3, 6, and 12 months) for the first year after successful treatment. It is estimated that approximately 20 percent of individuals with adequate response to cognitive-behavioral therapy (CBT) may experience recurrent symptoms that require further treatment. The 12 months after CBT completion appear to be a critical period and patients are less likely to experience a relapse in obsessive-compulsive disorder (OCD) if they maintain therapeutic gains throughout this period [45]. Booster sessions oriented toward reminding the child of previously learned exposure-response prevention techniques, supplementing patient knowledge, and checking-in with patients and their family members on treatment progress, may prevent or reverse clinical decline.

Response to SSRI — We continue medications for at least one year in individuals who have adequately responded to initial selective serotonin reuptake inhibitor (SSRI) treatment. However, our treatment plan is individualized to address other factors such as difficulty in reaching stabilization, level of psychosocial impairment, history of prior exacerbation after medication discontinuation, symptom severity, or the presence of clinically active comorbidity. For example, in a youth with OCD who has had recurrence of symptoms in the past upon medication tapering we would likely continue the medication for a longer period of time (eg, two or more years). For an individual with severe symptoms that caused significant psychosocial disruption and in whom stabilization was difficult (eg, several medication trials) we would likely continue treatment for longer than one year.

If the decision is made to taper medications, we attempt a gradual taper. Typically, we taper medications by up to 25 percent each month; however, as the dose gets lower, we taper more slowly (eg, 25 percent every two months).

When tapering medication, we monitor the child closely and educate the patient and their caregivers about warning signs that symptoms of OCD may emerge. For individuals who have responded to CBT previously, booster CBT sessions may be helpful to prevent symptom relapse during medication tapering.

Inadequate response — For individuals with a partial or inadequate response to initial treatment to any modality (monotherapy, combined therapy), we take the following steps prior to making treatment changes:

- Confirm adherence to medication treatment. Ask about adverse side effects that may be limiting adherence.

- Assess for factors limiting effect of CBT-ERP (ie, motivation for treatment, frequency of sessions, capacity for introspection, adequate exposure rituals being practiced).

- Review history of illness to reconfirm the diagnosis and assess for the presence of an undiagnosed comorbid disorder.

SUBSEQUENT TREATMENT

After addressing the factors that might be affecting response to initial treatment (see 'Inadequate response' above), our subsequent management of obsessive-compulsive disorder (OCD) in youth is as follows:

Longer term cognitive-behavioral therapy with exposure-response prevention — For patients with pediatric OCD who initially have a partial response, or fail to respond to cognitive-behavioral therapy (CBT) treatment, our preference is additional CBT treatment to reduce symptoms [46].

Our preference is based on the findings of a clinical trial in which 54 youth (age 7 to 17 years) who failed to respond (posttreatment Children's Yale-Brown Obsessive Compulsive Scale [CY-BOCS] ≥16) to an initial course of CBT (14 sessions of weekly individual exposure-based CBT) were randomly assigned to receive either 10 additional CBT treatment sessions, or treatment with sertraline, over 16 weeks [41]. No significant differences were seen in outcomes between treatment groups. However, nearly half of patients in each treatment group (50 percent for CBT, 45.4 percent for sertraline) experienced reduced OCD symptoms.

However, patient preference is strongly considered in all treatment options. For example, in a patient that is unwilling to engage in further psychotherapy, despite our recommendation as the next step, we would agree to continue treating with medication only.

Pharmacologic management — Subsequent pharmacologic management of youth with inadequate response to management to this point is discussed below. Our preference is to try the following sequentially.

SSRI trials — Our preference is to try two selective serotonin reuptake inhibitor (SSRI) trials, if response is not achieved, prior to other medication trials (eg, clomipramine, antipsychotic) in youth with refractory OCD:

- For those individuals who have not had a medication trial to this point, we add an SSRI to the current psychotherapy (see 'Choosing among SSRIs' above and 'Starting and titrating

SSRI' above and 'Dose and length of trial' above). If this is ineffective, we discontinue the medication and try a second SSRI.

- For those individuals who are already on an SSRI treatment our preference is to stop the first medication and immediately start a second medication at an equivalent dose. Overlap in mechanisms of action between SSRIs typically prevents discontinuation symptoms that might otherwise occur when an SSRI is suddenly stopped. However, some clinicians prefer cross-titration (ie, lowering the ineffective medication while simultaneously introducing the new medication) (table 1).

Change to clomipramine — Clomipramine, a tricyclic antidepressant (TCA) that inhibits reuptake of serotonin and norepinephrine, is the only TCA with demonstrated effectiveness in pediatric OCD [47].

- **Prior to starting clomipramine** – We review the youths past medical history with attention to prior heart disease including conduction system disease (eg, congenital QT syndrome). We obtain clearance from a cardiologist or primary care provider prior to beginning medication if there is a history of cardiac illness, blood pressure or pulse abnormalities, or adverse electrocardiogram (ECG) findings.

- **Dose titration and monitoring** – We typically begin clomipramine for pediatric OCD starting at 25 mg/day (table 1). We monitor for tolerability for one to two weeks following each dose adjustment. If the medication is tolerated, we increase the dose by 25 mg each week to a total dose of 100 mg/day is reached. At this dose, we monitor for four to six weeks. If therapeutic effect is not seen we increase further in 25 mg intervals until therapeutic effect is seen, side effects limit further increases, or maximum dose of 200 mg per day is reached. Problematic side effects often limit dose escalation.

  Clomipramine levels do not correlate with clomipramine dose. However, we occasionally use clomipramine levels to assess for compliance and toxicity.

  Anticholinergic side effects of clomipramine include sedation, dry mouth, constipation, urinary delay, and orthostatic hypotension [47]. Clomipramine can delay cardiac conduction and like other TCAs may be associated with the rare occurrence of sudden cardiac death in youth. When prescribing clomipramine, we recommend that the patient avoid grapefruit and grapefruit juice, as these can raise the mean plasma concentration of clomipramine [48]. (See "Tricyclic and tetracyclic drugs: Pharmacology, administration, and side effects", section on 'Clomipramine'.)

- **Efficacy** – Clomipramine has been established as an effective treatment for pediatric OCD for over three decades [14].

  In a meta-analysis including five trials and 182 youth with OCD, clomipramine was found to be superior to placebo or desipramine (a TCA) in the treatment of pediatric OCD [14]. For example, in one trial, 60 youth with OCD were randomly assigned to receive eight weeks of treatment with clomipramine or placebo [19]. At treatment end, subjects in the active treatment group had a greater reduction in OCD symptoms as compared with placebo (37 versus 8 percent). However, a greater percentage of patients in the treatment group (35 to 68 percent) as compared with the placebo group (9 to 16 percent) experienced dry mouth, somnolence, dizziness, or fatigue.

  Although available research in children suggests that clomipramine may be more efficacious than SSRIs in pediatric OCD, SSRIs are the preferred treatment because they are better tolerated and safer than clomipramine [14,49].

  Head-to-head trials comparing clomipramine with SSRI have not shown either to be superior for treatment of youth with OCD [20-26]. However, a meta-analysis of trials that did not directly compare SSRIs with clomipramine suggested that clomipramine has a greater effect size than SSRIs in adult OCD [49].

Augment with a second-generation antipsychotic — We typically use second-generation antipsychotics agents to augment SSRIs in pediatric patients with OCD who have responded insufficiently to treatment to this point.

We typically use lower doses of antipsychotics when augmenting serotonin reuptake inhibitor (SRI) medications as compared with those used for treatment of psychotic disorders. For example, we start risperidone at 0.25 mg/day and increased weekly in 0.25 mg increments to a maximum of 1.5 to 2 mg/day. A one-month trial is often sufficient to determine effectiveness. In some cases, a longer time period may be necessary particularly if higher doses (eg, 1 to 2 mg/day are needed).

Youth treated with atypical antipsychotics are vulnerable to serious metabolic side effects. Children, especially preadolescents, are more sensitive to side effects than other patients, particularly to weight gain, diabetes, carbohydrate abnormalities [50].

A table provides a recommended schedule for monitoring metabolic effects of first and second-generation antipsychotics (table 2). We assess more frequently in patients at higher risk (eg, baseline elevated lipids, glucose, weight) or for patients on specific antipsychotics (eg,

olanzapine, quetiapine, and clozapine) where there is clear evidence of an increased risk of insulin resistance [51].

First-generation antipsychotic agents are typically not considered as first-line augmenting agents in youth with OCD because of their side effect profile and limited study in this population.

Augmentation with second generation antipsychotic medications is supported by naturalistic open trials of youth with OCD who did not respond sufficiently to monotherapy. Both risperidone and aripiprazole were associated with symptom improvement during a comparative study of 69 children with tic-related OCD that did not respond to SSRI monotherapy [52]. Two open trials of 43 and 39 treatment refractory youth found that aripiprazole augmentation of an SRI was associated with symptom improvement in 58 and 59 percent of these patients [53,54]. Risperidone augmentation of an SRI was also associated with OCD symptom improvement in a case series including four youth with OCD who had not responded sufficiently to monotherapy [55].

However, risperidone was associated with serious metabolic adverse events, such as weight gain, and sedation, while aripiprazole was associated with mild to moderate agitation.

Clomipramine plus SSRI — In individuals who have inadequate response to treatment to this point, our next trial is a combination of clomipramine plus an SSRI.

We are cautious in adding an SSRI to clomipramine as there is the possibility that clomipramine can raise the blood levels and adverse effects of most SSRIs. These adverse effects include serotonin syndrome, characterized by mental status changes (eg, agitation, hallucinations, delirium, and coma), autonomic instability (eg, tachycardia, labile blood pressure, dizziness, diaphoresis, flushing, hyperthermia), neuromuscular changes (eg, tremor, rigidity, myoclonus, hyperreflexia, incoordination), seizures, and/or gastrointestinal symptoms (eg, nausea, vomiting, diarrhea). This is particularly true with the combination of clomipramine and the SSRIs, fluoxetine, fluvoxamine, or paroxetine. (See "Serotonin syndrome (serotonin toxicity)" and "Selective serotonin reuptake inhibitors: Pharmacology, administration, and side effects", section on 'Drug-drug interactions' and "Selective serotonin reuptake inhibitors: Pharmacology, administration, and side effects", section on 'Serotonin syndrome'.)

SSRIs can also raise the blood levels and hence the adverse effects of clomipramine (eg, QTc prolongation and seizures).

Uncontrolled studies of 13 youth with OCD have suggested that therapeutic effects of clomipramine may be improved and adverse effects reduced by using low doses of each drug

[56,57]. In particular, doses of clomipramine should not exceed 75 mg/d unless the blood clomipramine level is monitored. ECG monitoring of the QTc interval is also recommended [58].

TREATMENTS WITH LIMITED SUPPORT

Glutamate modulators — Converging lines of evidence suggest that glutamate has an important role in the neurobiology of obsessive-compulsive disorder (OCD) [59]. Several glutamate-modulating agents have been used and/or tested in the treatment of OCD; however, limited data support their use. We do not use these medications as treatment for pediatric OCD unless symptoms persist despite the above measures. Their use is in adult OCD is reviewed elsewhere. (See "Management of obsessive-compulsive disorder in adults".)

- **Riluzole** – Despite promising preliminary results [60], in a randomized trial, 51 subjects were assigned to 12 weeks of treatment with riluzole versus placebo. At treatment end, similar improvements were reported between treatment and placebo groups [61].

- **N-acetylcysteine (NAC)** – Initial reports from a 12-week, double-blind, placebo-controlled randomized trial [62] and from several case studies [63-65] have noted that augmentation of serotonin reuptake inhibitor (SRI) treatment with NAC, an antioxidant molecule that modulates glutamate transmission in the brain, successfully decreased OCD symptom severity in participants with treatment refractory OCD. However, the results from a 16-week, double-blind, placebo-controlled randomized trial [66] and an additional case study [67] were mixed. Evidence to support the use of NAC to augment more traditional OCD therapies remains limited at this time. Further studies are warranted.

- **D-cycloserine** – In a trial, 27 youth with OCD compared were randomly assigned to 50 mg of d-cycloserine or placebo given immediately after each of 10 cognitive-behavioral therapy sessions. Both groups improved and maintained their gains at one-year follow-up, but no significant advantage was seen between groups at any time point [68].

- **Memantine** – A single case report describing OCD symptom remission supports use of memantine [69].

Neuromodulation therapies/surgical lesioning — Use of neurostimulation with transcranial magnetic stimulation (TMS) or deep brain stimulation (DBS), or other surgical lesioning is not recommended for pediatric OCD cases.

- **TMS** – TMS has been found to be well-tolerated as a treatment for a number of other pediatric disorders [70,71]. However, there are currently no studies which have examined

the use of repetitive TMS in pediatric OCD and its use is currently not recommended for pediatric OCD cases.

- **Neurosurgery** – Neurosurgical techniques for OCD, such as DBS or surgical lesioning, are not indicated for children and adolescents. A substantial proportion of pediatric OCD cases remit over the long-term and using invasive neurosurgical techniques of unknown efficacy are not appropriate for pediatric OCD.

Others — The following agents have minimal support as monotherapy or augmenting agents in the treatment of pediatric OCD. We do not typically use these agents for treatment of pediatric OCD.

- Lithium augmentation of selective serotonin reuptake inhibitors (SSRIs) and clomipramine [72,73]
- Buspirone augmentation of SSRIs [74]
- Thyroid-hormone augmentation of clomipramine [73]

TREATMENT OF ASSOCIATED SYNDROMES

- **Tic-related obsessive-compulsive disorder (OCD)** – For individuals with a comorbid tic disorder or tic-related OCD, we prefer initial treatment with cognitive-behavioral therapy (CBT) with or without pharmacotherapy with a selective serotonin reuptake inhibitor (SSRI) [40]. The presence of a comorbid tic disorder does not appear to impact response to CBT, but may predict a poorer response to pharmacotherapy in the acute treatment of pediatric OCD [75,76].

  Individuals who do not respond to CBT may benefit from supplementing CBT with pharmacotherapy with an SSRI [40,77]. Individuals who do not respond to an SSRI, or have severe tics, may require additional supplementation with an antipsychotic medication (eg, risperidone or aripiprazole) [52]. However, due to serious metabolic side effects, symptoms and side effects should be monitored carefully, and all indicated laboratory tests should be completed at baseline, three-month, and one-year follow-up.

- **Pediatric autoimmune neuropsychiatric disorders (PANDAS/PANS)** – Our treatment of OCD symptoms and behaviors in children with a possible diagnosis of pediatric autoimmune neuropsychiatric disorder associated with group A streptococci [PANDAS]) or pediatric acute-onset neuropsychiatric syndrome (PANS) is based on the recommendations described here for OCD, whether the patient has evidence of recent group A streptococci infection [12,40,78,79].

We do not delay treatment of psychiatric symptoms pending confirmation or treatment of PANDAS. Treatment of PANDAS is described in greater detail separately. (See "PANDAS: Pediatric autoimmune neuropsychiatric disorder associated with group A streptococci", section on 'Management'.)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Obsessive-compulsive disorder and related disorders".)

SUMMARY AND RECOMMENDATIONS

- **Obsessive-compulsive disorder (OCD)** – OCD typically starts in childhood or adolescence. It is characterized by recurrent intrusive thoughts, images, or urges that cause anxiety or distress (obsessions), and by repetitive mental or behavioral acts (compulsions) that the individual feels driven to perform (often in response to obsessions). (See 'Introduction' above.)

- **Initial treatment** – Our preference for initial treatment is based on results of clinical trials. We consider symptom severity, past history, and the presence of active comorbid disorders. We prioritize patient/caregiver preference and typically initiate treatment with the patient-preferred option. (See 'Initial treatment' above.)

  - **Mild to moderate symptoms** – For youth with mild to moderate symptoms, who do not have an active co-occurring disorder we suggest cognitive-behavioral therapy with exposure and response prevention (CBT-ERP), rather than medication management, as the first treatment choice (**Grade 2C**). (See 'Mild or moderate symptoms' above.)

  - **Severe symptoms or active comorbid disorder** – For youth with severe symptoms, or in those with an active comorbid disorder (eg, depression, anxiety) we suggest treatment with combined modality, including cognitive-behavioral therapy (CBT) and pharmacotherapy, rather than either alone (**Grade 2C**).

- **Initial pharmacologic management** – For youth with OCD who will be treated with pharmacologic management (either with or without psychotherapy) we suggest treatment with a selective serotonin reuptake inhibitor (SSRI) rather than other categories of antidepressants or clomipramine (**Grade 2C**).

- **Suicidality** – While there is controversy about the relationship between SSRI use and suicidality in children, we monitor children or adolescents who are treated with SSRIs weekly during the first month, and at least monthly thereafter. (See 'Suicidality' above.)

- **Subsequent treatment** – For individuals with inadequate response to initial treatment we confirm adherence to treatment recommendations (ie, taking medication as recommended, engaged in CBT), reconfirm the diagnosis, and assess for the presence of an undiagnosed comorbid disorder. (See 'Inadequate response' above.)

  - **Longer term CBT** - For patients with pediatric OCD who initially have a partial response, or fail to respond to CBT treatment, our preference is additional CBT treatment to reduce symptoms. (See 'Longer term cognitive-behavioral therapy with exposure-response prevention' above.)

  - **Subsequent pharmacologic options** – Subsequent pharmacologic management of youth with inadequate response to management to this point includes the following in sequential order:

    - Treatment with SSRI – Our preference is to give two SSRI trials prior to other pharmacologic options. For those that have not been on an SSRI, we begin one. For those already on an SSRI, we change to another SSRI. (See 'SSRI trials' above.)

    - Change to clomipramine. (See 'Change to clomipramine' above.)

    - Augment with a second-generation antipsychotic. (See 'Augment with a second-generation antipsychotic' above.)

    - Clomipramine plus SSRI. (See 'Clomipramine plus SSRI' above.)

- **Treatment of associated syndromes** (see 'Treatment of associated syndromes' above)

  - **Tic-related OCD** – For individuals with a comorbid tic disorder or tic-related OCD, we prefer initial treatment with CBT with or without pharmacotherapy with an SSRI. The presence of a comorbid tic disorder may predict a poorer response to pharmacotherapy in the acute treatment of pediatric OCD.

  - **Pediatric autoimmune neuropsychiatric disorder (PANDAS)** – Our preference is to treat youth with OCD symptoms and behaviors possibly due to a diagnosis of pediatric autoimmune neuropsychiatric disorder associated with group A streptococci (PANDAS) based on the recommendations above. We do not delay treatment of psychiatric symptoms pending confirmation of PANDAS.

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