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Management of Obsessive-Compulsive Disorder

Phillip J. Seibell[1]* and Eric Hollander[2,3]

Addresses: [1]Department of Psychiatry, Weill-Cornell Medical College/New York Presbyterian Hospital, 21 Bloomingdale Road, White Plains, NY, 10605, USA; [2]Albert Einstein College of Medicine/Montefiore Medical Center, Child Psychiatry Annex, 3340 Bainbridge Avenue, Bronx, NY 10467, USA; [3]Spectrum Neuroscience and Treatment Institute, 901 Fifth Avenue, New York, NY 10021, USA

* Corresponding author: Phillip J. Seibell (phs2007@med.cornell.edu)

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Abstract

Obsessive-compulsive disorder (OCD) is a common, often debilitating disorder characterized by the presence of obsessions and compulsions. Obsessions are repetitive thoughts or images which are experienced as intrusive and unwanted; they cause marked anxiety and distress. Compulsions (also known as rituals) are repetitive behaviors or mental acts that individuals with OCD perform in an attempt to decrease their anxiety. Patients tend to hide their symptoms due to shame; the amount of time between onset of symptoms and appropriate treatment is often many years. The disorder likely results from several etiological variables; functional imaging studies have consistently shown hyperactivity in the orbitofrontal cortex, anterior cingulate, thalamus, and striatum. The mainstays of treatment include cognitive-behavioral therapy in the form of exposure and response prevention (ERP) and serotonin reuptake inhibiting medications. Several pharmacological augmentation strategies exist for treatment-resistant OCD, with addition of antipsychotics being most commonly employed. Radio and neurosurgical procedures, including gamma knife radiation and deep brain stimulation, are reserved for severe, treatment-refractory disease that has not responded to multiple treatments, and some patients may benefit from transcranial magnetic stimulation.

Introduction

OCD is an often debilitating disorder characterized by the presence of obsessions and compulsions. Obsessions are repetitive thoughts or images which are experienced as intrusive and unwanted; they cause marked anxiety and distress. Compulsions (also known as rituals) are repetitive behaviors or mental acts that individuals with OCD perform in an attempt to decrease their anxiety [1]. For example, an individual with contamination obsessions may experience great anxiety after touching a public toilet seat. In response to this anxiety, the individual may wash his or her hands repetitively in an attempt to get rid of the "contamination". A vicious cycle develops in OCD whereby every time a compulsive behavior or mental act (for example, neutralizing a "bad" thought with a "good" thought) is performed, OCD worsens, leading to an intensification of obsessions and compulsions [1]. Certain symptom categories are common in OCD. These include contamination, symmetry, ordering/counting, forbidden thoughts/images/scrupulosity, and harm. Those with contamination symptoms will experience contamination obsessions and cleaning/washing compulsions. Symptoms in the symmetry category include a need for alignment of objects. Some patients engage in ordering or counting to prevent a dreaded outcome. Patients may experience forbidden/horrific thoughts or images and attempt to neutralize them with compulsions. Scrupulosity obsessions and compulsions that are outside the typical boundaries of a particular religion are also common. Those with harm OCD experience symptoms related to harm coming to self or others; checking compulsions are common in this category (for example, in order to prevent a fire, an individual may repetitively check to see whether or not the stove has been turned off). The recently published

Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition (DSM-V) has moved OCD out of the "Anxiety Disorders" category and placed it within a new category: Obsessive-Compulsive and Related Disorders [1]. In creating this new category of disorders, hoarding, previously categorized as a subtype of OCD, is now its own disorder (hoarding disorder). We will focus here on OCD, but the reader may consult a review on the treatment of hoarding [2].

Epidemiology

OCD occurs in 1.2% of the population [3,4] in the United States and similar rates are seen across cultures [5]. In childhood, males are more commonly affected; the reverse is true in adulthood [4,5]. The mean age of onset is 19.5 years; males tend to have an earlier age of onset than females [4]. Onset after age 35 is rare but can occur. The onset of symptoms is generally gradual. If OCD goes untreated, the course is typically chronic with waxing and waning symptoms, and remission rates are low [6,7].

Etiology/Pathophysiology

OCD likely results from multiple variables. Genetic factors are implicated: Monozygotic twins are much more likely to exhibit OCD symptoms than dizygotic twins [8]. Studies of first-degree relatives have indicated that family members are at greater risk [9]. It has been argued that there is an autosomal dominant mode of transmission [9–12]. There is an association between pregnancy and the development of obsessive-compulsive symptoms: Among 59 female OCD patients, 39% of women described onset of OCD symptoms during pregnancy [13]. Onset of symptoms after striatal lesions or head trauma has also been described [14]. As the mainstay of pharmacological treatment for OCD includes serotonin reuptake inhibiting medications, it appears clear that dysfunction within the serotonin system plays a role in pathophysiology [15]. Functional neuroimaging studies have illustrated that a hyperactive brain circuit exists in OCD; areas involved include the orbitofrontal cortex, anterior cingulate, thalamus, and striatum [16]. Evidence for dysfunction in these areas also appears to exist in children [17]. A decrease in metabolic activity in the hyperactive brain circuit has been shown to occur after administration of selective serotonin reuptake inhibitors (SSRIs) or cognitive-behavioral therapy [18,19]. In addition, some patients appear to develop or experience an exacerbation of OCD symptoms following beta-hemolytic streptococcal infection. It is thought that antibodies that are produced cross-react with basal ganglia proteins; this phenomenon has been named "PANDAS" (pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection) [20].

Diagnosis/Rating Scales

The diagnosis of OCD is typically made using DSM-V criteria as a guide [1]. The Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) is the most widely used measure of OCD symptoms. It has been demonstrated to be valid and can be used as a self-report or clinician-administered scale; both adult and child versions exist [21]. Both versions have a symptom checklist and a severity rating scale. The symptom checklist provides clinicians with data on specific symptom types/domains that require further attention. The severity scale has 10 questions — 5 about obsessions and 5 about compulsions — and the overall score is used to rate symptom severity.

Treatment

The mainstay of treatment for OCD includes cognitive-behavioral therapy in the form of ERP and medication management (most commonly with serotonin reuptake inhibitors, or SRIs). The initial treatment choice depends on illness severity. A mild to moderate severity of illness, which is indicated by a Y-BOCS score of 8 to 23, can be treated with either ERP or administration of an SRI alone [22]. However, most medication trials in OCD used only a 25% to 35% reduction in Y-BOCS scores as a benchmark of efficacy in order to gain US Food and Drug Administration (FDA) approval. In addition, in a study that examined ERP versus drug treatment alone, ERP was found to be more effective [23]. Therefore, if it is available, ERP is generally recommended as the first-line treatment for mild to moderate symptoms. For more severe symptoms, medication management in combination with ERP is recommended. In fact, some patients with severe OCD will have difficulty engaging in ERP if they are not exhibiting a medication response beforehand.

Exposure and Response Prevention

An individual with OCD who engages in treatment with a skilled cognitive-behavioral/ERP therapist can make significant gains overall in level of functioning and quality of life. The effectiveness of ERP has been clearly demonstrated in OCD [23,24]. The first step in any OCD treatment includes providing psychoeducation about the illness and the ERP process. Patients are encouraged to complete a 24-hour obsession and compulsion symptom log after the Y-BOCS is administered, and these data are used in the construction of a hierarchy of symptom triggers. Symptom triggers are rated on a scale from 0 to 100, often using 10-point intervals. For example, a patient with contamination symptoms might consider touching a public doorknob less anxiety-provoking (rated a lower number) than touching a public toilet seat. Patients are then encouraged to work on doing "exposures" by moving up their hierarchies. An example of an exposure exercise

would be holding on to a "contaminated" doorknob. The individual is encouraged to continue holding onto the doorknob until his or her anxiety decreases substantially. It is important that patients are encouraged to expose themselves to triggers during therapy sessions and that they leave sessions with well-defined ERP homework assignments. We recommend that patients engage in at least one hour of ERP each day in order to increase the odds of a successful outcome. It is important to emphasize that provoking OCD on purpose (planned exposures) is just as important as resisting the urge to engage in compulsions following an unplanned (naturalistic) exposure.

Medication Management

Five compounds have FDA approval for the treatment of OCD: clomipramine (a tricyclic antidepressant) and four SSRIs (fluoxetine, fluvoxamine, paroxetine, and sertraline). Numerous studies have assessed the efficacy of SSRIs for OCD and they are generally considered to be similar in efficacy [25]. Clomipramine generally has a higher side-effect burden than SSRIs. Therefore, an SSRI is recommended as first-line pharmacological treatment [26]. When choosing an SSRI, consider potential drug-drug interactions, comorbid medical conditions, individual side-effect profiles, patient age, prior treatment response, and family history of treatment response [26]. A true trial of an SSRI in OCD includes at least a moderate dose for at least 12 weeks. Please see Table 1, adapted from [26], for details. We have eliminated citalopram from the table because of increasing concern about corrected QT (QTc) prolongation with this agent, especially at higher doses (see [27] for details). Although escitalopram is not FDA-approved for the treatment of OCD in the US, it has an indication for the treatment of OCD in Europe and has been shown to improve levels of disability and work-related functioning [28]. Please be mindful that children who have been prescribed SSRIs should be monitored closely for possible changes in suicidal ideation [29].

Clomipramine

Clomipramine is a tricyclic antidepressant with the active metabolite desmethylclomipramine. It is more anticholinergic and sedating than SSRIs. It also tends to cause more weight gain. The potential for cardiac toxicity exists and regular electrocardiograms (EKGs) are useful in monitoring heart rate, rhythm, and QTc interval. Blood levels of clomipramine and desmethylclomipramine must also be monitored. However, for those who do not respond to one or more SSRI trials (defined by a less than 25% reduction in overall Y-BOCS score [22]), clomipramine is a good option, as a meta-analysis has suggested that it is more effective than the SSRIs [30]. Clomipramine is serotonin-specific and desmethylclomipramine is norepinephrine-specific; the drug is converted to desmethylclomipramine by CYP1A2. Fluvoxamine inhibits CYP1A2. Therefore, some clinicians attempt to raise the clomipramine/desmethylclomipramine ratio by adding 25 mg of fluvoxamine to existing clomipramine treatment. This strategy is employed in order to increase the serotonin reuptake inhibition of clomipramine. When clomipramine is combined with any SSRI, regular monitoring of blood levels and EKGs is recommended in order to avoid cardiac and central nervous system toxicity [31]. Levels that have been recommended for effective treatment [31] include 225 to 350 ng/mL for clomipramine and combined clomipramine and desmethylclomipramine levels of less than or equal to 500 ng/mL. Please note that individuals with low CYP1A2 metabolic activity require lower doses of clomipramine.

Augmentation of Serotonin Reuptake Inhibitors with Antipsychotics

If an individual does not respond to initial SSRI treatment (<25% reduction in Y-BOCS score) or exhibits a partial response, he or she may benefit from augmentation of the SSRI with an antipsychotic medication [32]. The antipsychotic drugs that have evidence for their use include

Table 1. Adult selective serotonin reuptake inhibitor dosing guidelines for obsessive-compulsive disorder

Serotonin reuptake inhibitor	Starting[a]	Usual target	Usual maximum	Occasional[b]
Clomipramine	25	100-250	250	_[c]
Escitalopram	10	20	40	60
Fluoxetine	20	40-60	80	120
Fluvoxamine	50	200	300	450
Paroxetine	20	40-60	60	100
Sertraline[d]	50	200	200	400

Doses are presented as number of milligrams per day. [a]Some patients may need to start at half this dose or less to minimize undesired side effects such as nausea or to accommodate anxiety about taking medications. [b]These doses are sometimes used for rapid metabolizers or for patients with no or mild side effects and inadequate therapeutic response after 8 weeks or more at the usual maximum dose. [c]Combined plasma levels of clomipramine plus desmethylclomipramine 12 hours after the dose should be kept below 500 ng/mL to minimize risk of seizures and cardiac conduction delay. [d]Sertraline, alone among the selective serotonin reuptake inhibitors, is better absorbed with food.

haloperidol, risperidone, and aripiprazole; less evidence exists for the use of quetiapine or olanzapine [33–41]. Please consult our more detailed treatment manual [25] for details on dosing strategies for antipsychotic augmentation. Determining the best time during course of treatment to begin antipsychotic augmentation has often been questioned, given that a true SRI trial in OCD is at least a moderate dose for a full 12 weeks. A meta-analysis [40] suggests that when compared to initiating antipsychotic augmentation before 12 weeks of SRI treatment, over 25% more patients will respond with a longer duration of the initial SRI treatment. In addition, this meta-analysis provided evidence that OCD with comorbid tics responds particularly well to antipsychotic augmentation of SRIs. Moreover, a recent study [42] compared the effects of augmenting SRIs with ERP (17 sessions twice weekly) versus risperidone (up to 4 mg/day) or placebo. Patients receiving ERP had significantly greater reductions in week-8 Y-BOCS scores compared to those receiving either risperidone or placebo, and more patients receiving ERP responded as defined by a mean Y-BOCS score decrease of greater than or equal to 25% (80% responded in the ERP group, 23% in the risperidone group, and 15% in the placebo group). Interestingly, reductions in Y-BOCS scores for those receiving risperidone augmentation did not differ significantly from reductions exhibited by those receiving placebo.

Augmentation of Serotonin Reuptake Inhibitors with Other Agents

A different augmentation strategy that targets the serotonin system includes augmenting SRIs with 5-HT_3 antagonists. Preliminary evidence exists for ondansetron and granisetron [43–45]. In fact, an additional recent study of ondansetron augmentation of SRIs found that 12/21 (57%) of patients responded to ondansetron augmentation initiated at 0.25 mg twice a day for 2 weeks, titrated to 0.5 mg twice a day for an additional 10 weeks [46]. After discontinuation of ondansetron, Y-BOCS scores increased (worsened) by an average of 15.5% in the whole sample of participants and by 38.3% in the sample of participants who responded to the initial augmentation. In addition, there has been interest in augmenting SRIs with memantine [47], lamotrigine [48], opiramate [49,50], d-amphetamine, and caffeine [51].

Radio/Neurosurgical Procedures

For cases that are documented to be extremely severe, not responding to multiple therapeutic interventions, gamma knife radiosurgery and deep brain stimulation have been used. Gamma knife radiosurgery was used in OCD prior to deep brain stimulation. It is not FDA-approved and consists of anterior capsulotomy, limbic leucotomy, and cingulotomy [26]. Deep brain stimulation is now also an option as it has received a "Humanitarian Device Exemption" from the FDA for severe, intractable OCD. To date, a relatively small number of patients have had the procedure, and the targets and programming paradigms are not standardized. Some targets include the nucleus accumbens, ventral internal capsule, and ventral striatum [52].

Transcranial Magnetic Stimulation

The data on transcranial magnetic stimulation (TMS) for OCD are mixed. In addition to questions about efficacy, there are questions about what sites should be targeted. Some studies suggest that targeting the pre-supplementary motor area with low-frequency (1 Hz) TMS can be useful [53,54]. In addition, targeting the anterior cingulate cortex with high-frequency (20 Hz) stimulation with deep TMS [55] may be effective in resistant OCD, but further controlled studies are required to establish the efficacy of this approach.

Conclusions

OCD is an often debilitating condition that is treatable. Unfortunately, many patients hide their symptoms due to shame, and much misdiagnosis and provision of ineffective treatment exists. Patients often suffer either in silence or in ineffective treatment for many years. Even with appropriate treatment, symptoms can wax and wane. Initiation and continuation of appropriate treatment, the mainstays of which are ERP and SRIs, is crucial. ERP is recommended as first-line treatment for mild to moderate symptoms as measured by the Y-BOCS. For more severe symptoms or when ERP is not available, an SRI is recommended as first-line treatment as SRIs are better tolerated than clomipramine, although clomipramine appears to be more effective than the SRIs. Several pharmacological augmentation strategies exist, and radio/neurosurgical procedures are reserved for documented severe, treatment-refractory cases. We highly recommend that clinicians and patients visit the International OCD Foundation's website when searching for treatment providers or support groups (www.ocfoundation.org).

Abbreviations

EKG, electrocardiogram; ERP, exposure and response prevention; DSM-V, *Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition*; FDA, US Food and Drug Administration; OCD, obsessive-compulsive disorder; SRI, serotonin reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TMS, transcranial magnetic stimulation; Y-BOCS, Yale-Brown Obsessive-Compulsive Scale.

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