Strategies for Treatment-Resistant OCD

By Stefano Pallanti, MD, PhD

The clinician's role is to “translate” symptoms of OCD and understand the dysfunctional circuits at play to decide on the most appropriate treatment for each patient.

Obsessive-compulsive disorder (OCD) is characterized by the presence of disabling obsessions and/or compulsions, with a lifetime prevalence of 1% to 3% in the general population. It is associated with significant burden on quality of life, interpersonal relationships, and work and academic activities.

First-line treatments for OCD are SSRIs and the exposure and response prevention model of cognitive-behavioral therapy (CBT). However, effect sizes are not remarkable: pharmacotherapy rates range from 0.37 to 1.09; CBT rates range from 0.99 to 1.13. Many OCD patients do not respond adequately to an initial SSRI. As a general rule, treatment response is defined as much or very much improved on the Clinical Global Impressions scale and/or a greater than 35% reduction from baseline on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS). Partial response is defined as a reduction between 20% and 35% on the Y-BOCS; treatment resistance is defined as no response to an SSRI trial; and treatment refractory is defined as minimal or no response to at least 2 SSRI trials.

The use of the Y-BOCS is strongly recommended in clinical practice: the Y-BOCS can define the percentage of symptom response, making it a good indicator for continuing treatment. Although no response might indicate a switch to a different first-line treatment, partial response involves a qualitative analysis of nonresponse, stage, and level (Figure, Table), including comorbidities that are often present in treatment-refractory OCD.

Pharmacological treatment and combination therapy

The most common pharmacological next step once treatment resistance is established is augmentation with a neuroleptic agent. Unfortunately, however, even augmentation with an antipsychotic produced a significant response in only one-third of patients. Efficacy was more evident for comorbid tics and in patients with a history of more than 12 weeks of maximal SSRI monotherapy.

In a recent meta-analysis of second-generation antipsychotic augmentation in OCD, risperidone was found to be better than placebo on the primary outcome measure (odds ratio = 0.17; 95% confidence interval [CI], 0.04 - 0.66) and in the reduction of anxiety and depression (standardized mean difference, 7.60; 95% CI, 12.37 - 2.83). In a meta-analysis of quetiapine (n = 5), risperidone (n = 3), olanzapine (n = 2), aripiprazole (n = 1), and haloperidol (n = 1), only risperidone was found to have superior efficacy over placebo.

Other strategies include continuing with the chosen SSRI for an extended period (3 to 6 months), titrating the dose to the highest tolerated level, switching to another first-line agent, or augmenting the SSRI with an agent from a different drug class.

Contrary to the depression literature, a meta-analysis of SSRIs for OCD found that high doses (high end of recommended dosage) were more effective than medium or low doses as first-line treatment of OCD. However, tolerability was a significant issue compared with lower doses, so this strategy requires caution. The FDA raised a safety warning in 2011 against high-dose citalopram because of the increased risk of arrhythmias.

CASE VIGNETTE

Steve, aged 32 years, presents at an outpatient clinic after 7 years of unsuccessful treatment of an OCD washing subtype. He has been treated with all FDA-approved SSRIs at the higher tolerable doses augmented with risperidone 1 mg, but only a minimal reduction of symptoms has been achieved. His Y-BOCS score is 34, and he spends a total of 6 hours a day showering. He explains, “I can't resist when I start washing, everything has to be done according to my 'special need' for symmetry: I have to proceed symmetrically, from my feet and onto the rest of my body.” When asked if he has cravings to wash his body, he answers, “Yes, I would say so; also during the...
In this case, the ethanol-like experience suggests that μ-agonists and glutamate antagonists might be an option during the exacerbation of symptoms. However, these treatments warrant further validation.¹⁰

**Further options**

Intravenous administration of drugs may have a better effect than oral administration in OCD patients. Results from a study of intravenous citalopram for OCD patients who had not responded to at least 2 adequate oral SSRI trials showed a response rate of 59%. The efficacy of intravenous clomipramine was tested in a double-blind controlled trial of pulse-loaded intravenous versus oral clomipramine, followed by open-label oral clomipramine for 12 weeks. Intravenous pulse loading did not induce a more rapid or greater Y-BOCS score decrease than oral pulse loading; however, intravenous pulse loading seemed to induce more rapid and greater improvement than expected in treatment-resistant OCD.¹¹

**The role of CBT**

Generally preferred by patients, combination treatment with CBT and pharmacotherapy has shown good efficacy.¹² Findings indicate that CBT can lead to a significant reduction in OCD symptoms in patients who remain symptomatic despite an adequate trial of an SSRI.¹³ However, additional studies are needed.

The patient’s family is an integral part of the exposure and response prevention model of CBT. Often family members inadvertently help the patient maintain his or her OCD. Examine the interaction between family members and the patient to gauge whether there is overt or covert maintenance of the illness and to what extent. Then give specific instructions to family members about the way they should behave. Along with the patient, family members require close follow-up to make sure they are adhering to CBT instructions.

**Emerging treatments**

The American Psychiatric Association treatment guidelines for OCD recommend a switch to another second-generation antipsychotic or to a different SSRI; augmentation with clomipramine; or augmentation with a drug from another class, such as inositol, pindolol, morphine sulfate, or d-amphetamine.¹⁴ Findings from an international cross-sectional study indicate that current OCD treatments in the clinical setting are in line with evidence-based treatment guidelines.¹⁵ Beyond the guidelines and beyond FDA-approved treatment of OCD, there are a myriad of case reports that show about a 50% treatment response in patients with treatment-resistant OCD. Of course, the 50% response to augmentation with d-amphetamine is not in the same patients who respond to augmentation with ondansetron. Thus, the clinician must “translate” symptoms and understand the dysfunctional circuits at play to decide on the most appropriate treatment for each patient.

When step-up treatments fail, augmentation with newer agents other than second-generation antipsychotics might be tried. Recent research has found glutamatergic abnormalities to be involved in OCD pathophysiology.¹⁶ Compounds that interact with the glutamate system have been tested in a few open-label studies and randomized controlled trials (RCTs). In open-label studies, riluzole has been found to be effective.¹⁷ RCTs have also shown efficacy for memantine and N-acetylcysteine.¹⁸,¹⁹ The use of topiramate was supported in open-label trials, but evidence from RCTs is inconclusive.¹⁵,²⁰⁰⁻²²

Transcranial magnetic stimulation is another emerging treatment that targets specific circuits that may be involved in the pathophysiology of OCD. Currently, there is enough evidence of its efficacy and safety, and it may be an option as augmentation with an SSRI or the exposure and response prevention model of CBT.

**Comorbidities**

Assessment of comorbidity in OCD is the rule rather than the exception in treatment resistance; comorbidity may be the reason for any negative outcomes. In fact, comorbid psychiatric disorders are predictive of worse treatment outcomes as well as a worse quality of life. Lifetime comorbidity rates in patients with OCD range from 78% to 91% and current comorbidity rates range from 42% to 55%, with anxiety disorders and mood disorders occurring most frequently.²³,²⁴ Other comorbidities include tic disorder (12.5%), body dysmorphic disorder (8.71%), self-injurious behavior (7.43%), MDD (15%), social anxiety disorder (14%), generalized anxiety disorder (13%), and dysthymic disorder (13%). With psychiatric comorbidities, treatment is first focused on the comorbid condition rather than on the OCD. Treatment is started with a drug of choice for the
comorbid condition and then an anti-OCD medication is added.

Conclusions
While the clinical description of OCD does not differ that much from the previous DSM, the organization of the chapter in DSM-5 implies a new vision of the disorder. The emphasis is now on dysfunction of the reward system as well as dysfunction of the orbitofrontal cortex-dorsal striatum. This suggests a distinctive trait closely aligned with substance use disorders, which are related to ventral striatum dysfunction. This new approach might improve both researcher and clinician capacity to design new treatment and to establish new targets for both pharmacological and nonpharmacological interventions for treatment-resistant OCD.

Figure. Treatment algorithm for treatment-resistant OCD: levels of non...

Table: Obsessive-compulsive disorder stages of response

Disclosures:
Dr Pallanti is Professor of Psychiatry and Behavioral Sciences at UC Davis Health System in Sacramento, Calif, and Professor of Psychiatry at the University of Florence, Italy. He reports no conflicts of interest concerning the subject matter of this article.

References:


Links:
[5] [http://www.psychiatrictimes.com/authors/stefano-pallanti-md-phd](http://www.psychiatrictimes.com/authors/stefano-pallanti-md-phd)