Pharmacological Treatment of Obsessive-Compulsive Disorder

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KEYWORDS

• Obsessive-compulsive disorder • OCD • Pharmacotherapy • SSRI • Antidepressant • Augmentation

KEY POINTS

- About two thirds cases of obsessive-compulsive disorder will improve with appropriate pharmacotherapy.
- The mainstay of pharmacotherapy is the use of selective serotonin reuptake inhibitors.
- Second-line options include clomipramine and augmentation with neuroleptics.
- A substantial minority of patients remain refractory to aggressive pharmacotherapy.

Abbreviations

CBT	Cognitive behavioral therapy
MDD	Major depressive disorder
NMDA	N-methyl-d-aspartate
OCD	Obsessive compulsive disorder
SRI	Serotonin reuptake inhibitor
SSRI	Selective serotonin reuptake inhibitor

INTRODUCTION

Obsessive-compulsive disorder (OCD) can present a significant management challenge to the clinical psychiatrist. OCD affects approximately 1.3% of the population in any given year and up to 2.7% over the course of a lifetime.[1] Symptoms consist of obsessions and compulsions; although either alone suffices for a diagnosis, it is typical for a patient to have both.[2] Obsessions are repetitive, stereotyped thoughts

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that cause anxiety or distress. These obsessions are generally experienced as intrusive or egodystonic, and they are typically recognized as unrealistic or excessive; this distinguishes them from delusions, although the distinction can become unclear in some severe cases. Compulsions are ritualized actions that are undertaken to mitigate distress, often in response to obsessions. Typical obsessions and compulsions include preoccupations with contamination accompanied by repeated or ritualized washing; fear of harm to self or others accompanied by checking rituals; and a need for symmetry or order, accompanied by ordering or arranging compulsions.

OCD can be treated using pharmacotherapy, specialized psychotherapy, anatomically targeted treatments, or their combination.[3] First-line treatments include cognitive behavioral therapy (CBT) and pharmacotherapy with the selective serotonin reuptake inhibitors (SSRIs). In this article, the authors review evidence-based pharmacotherapies for OCD, as well as alternatives that may be considered in refractory patients. Other treatment modalities are reviewed in other articles in this issue.

Unfortunately, even with optimal treatment, many patients continue to experience significant symptoms. Remission of moderate or severe OCD is uncommon, and long-term management is often necessary. The development of new, more effective treatment interventions represents an urgent clinical need.

SEROTONIN REUPTAKE INHIBITORS

The SSRIs are the mainstay of the pharmacologic treatment of OCD. The tricyclic antidepressant clomipramine was shown to be of benefit in the early 1980s,[4] but side effects limit its use as a first-line agent. Fluvoxamine was first shown to be beneficial in individuals with OCD by Goodman and colleagues[5] in 1989. Since then, more than 20 blinded, placebo-controlled studies have firmly established the efficacy of SSRI monotherapy in OCD.[6,7] Because of the combination of proven efficacy and a typically benign side-effect profile, SSRIs are the first-line pharmacological option for the treatment of OCD.[3]

Closer examination of these studies permits several generalizations with respect to the clinical use of SSRIs for OCD.

Although fluvoxamine was the first SSRI shown to be efficacious and is still often thought of (and marketed) as a preferred OCD drug, there is no evidence of differential benefit among the SSRIs[7]; the choice of agent is therefore best made from of side effects, drug interactions, patient preference, and similar considerations.

SSRIs are more efficacious in OCD when used at high doses, in excess of the typical dose range established by their suppliers (which are generally derived from studies of major depressive disorder [MDD]). For example, doses of up to 80 mg of fluoxetine, 40 mg of escitalopram, 300 mg of fluvoxamine, and 100 mg of paroxetine are often needed; sometimes even higher doses are used.[3] The benefit of these higher doses has been clearly shown by a meta-analysis of multiple studies.[8] Interestingly, this contrasts with the use of the same agents in the treatment of MDD, in which higher doses have been shown to carry a higher side-effect burden without increased benefit.[9] OCD symptoms typically also take longer to respond to SSRI monotherapy than do those of MDD; an adequate trial is 8 to 12 weeks.[3] The reasons for these differences between OCD and MDD response to SSRIs remain unclear.

Although these adages—higher dose and longer treatment—are widely accepted by OCD specialists, their relevance to clinical treatment of individual patients should not be overstated. The number needed to treat (NNT) for OCD patients treated with SSRI monotherapy at standard (antidepressant) doses is approximately 5, meaning