

Clinical practice guidelines for Obsessive-Compulsive Disorder

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INTRODUCTION

Obsessive-compulsive disorder (OCD) is a common psychiatric illness with lifetime prevalence of 1-3% [1]. It is the fourth-most common psychiatric illness and a leading cause of disability. OCD is associated with significant impairment in functioning, quality of life and disability. If untreated, OCD is a chronic illness with a waxing and waning of symptoms. A recent meta-analysis of long-term naturalistic prospective studies demonstrated that nearly a half of patients experience remission with much higher rates of remission in Indian patients compared to those in the west [2]. Early diagnosis and appropriate treatment may improve outcomes. Despite OCD being a common mental illness, most seek treatment after several years of suffering. Those who suffer from OCD tend to be secretive about their symptoms and suffer from shame and embarrassment. Less than a third of OCD sufferers receive appropriate pharmacotherapy and even less receive evidence-based psychotherapy.

Symptoms

The hallmarks of OCD are presence of obsessions and compulsions. Obsessions are repetitive, unwanted,

intrusive thoughts, images or urges that are mostly ego-dystonic and cause severe distress or anxiety. Compulsions (or rituals) are repetitive behaviours or mental acts that are performed in response to an obsession to reduce anxiety/distress or prevent a dreaded consequence. Obsessions and compulsions are time consuming, distressing and are often resisted unsuccessfully. Clinical manifestations of OCD are remarkably similar across cultures and geographic locations. Common obsessions and compulsions and symptom dimensions identified through factor-analytical studies are shown in Table 1.

Diagnosis

Many people experience intrusive thoughts and exhibit repetitive behaviours. A diagnosis of OCD is made only if symptoms are time consuming (e.g., more than an hour per day), distressing or cause significant interference in functioning. This is reflected in DSM-5 diagnosis of OCD and in the upcoming ICD-11 [3]. The ICD-11 criteria for OCD are likely to be very similar to the DSM-5 criteria [3, 4]. The ICD-11 may include an insight specifier along the same lines as DSM-5. There are sweeping changes to the description of OCD in the proposed ICD-11. Duration criteria and subtyping of OCD may be removed in the revision for lack of evidence and clinical relevance. In ICD-10, a diagnosis of OCD was discouraged in the presence of schizophrenia, tic disorder or depression. This criterion too may be removed paving the way to make a diagnosis of OCD even in the presence of these comorbid disorders.

Another major change to the diagnosis of OCD is creation of OCD and related disorders in DSM-5 (and in the ICD-11) and exit from the group of anxiety disorders. Many disorders are included in this group: body dysmorphic

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Table 1: Common symptoms of OCD**Obsessions****Contamination related obsessions**

- Concern/disgust with bodily secretions and waste such as stools and urine
- Fear of dirt or germs/infections, concern with sticky substances
- Fear of getting ill because of contaminants (e.g., AIDS)

Sexual obsessions

- Unwanted, forbidden sexual thoughts, images or urges about strangers, family friends, etc
- Sexual thoughts of molesting children, thoughts of sexual identity (am I a gay?)

Harm/aggression related obsessions

- Fear might harm self or others (fear of jumping off the building, fear of harming babies, stabbing a friend, running over pedestrians while driving etc)
- Violent/horrific images (murders, mutilated bodies, accidents)
- Fear of uttering obscenities

Religious/blasphemy

- Sacrilege and blasphemy (blasphemous thoughts, fear of uttering insults to God)
- Excessive concern about right/wrong, morality

Pathological doubts about daily activities (doubts of having not locked doors, turned off gas knobs)**Need for symmetry and exactness**

- Concern about things being not properly aligned, symmetrical, perfect or exact
- With magical thinking (child may have an accident if things are not properly arranged in kitchen)

Miscellaneous

- Need to know/remember (number plates, advertisements etc.)
- Intrusive non-violent images, thoughts
- Superstitious fears (passing a cat, cemetery)
- Lucky/unlucky numbers, colors

Compulsions

Washing/Cleaning (excessive or ritualized hand washing, showering, bathing, brushing/excessive cleaning of household items, floors, kitchen vessels etc) in response to contamination obsessions

Checking

- In response to pathological doubts (appliances, locks, stove, doors)
- To prevent harm to self or others (check to make sure that you have not caused accident, examining for injuries etc.)

Repeating

- Re-reading or rewriting because you didn't understand or write properly
- Repeating routine activities (going in and out of doorway, sit and stand up repeatedly, repeating till you feel just right)

Counting (money, floor tiles)**Ordering and arranging (often till you feel just right)****Miscellaneous**

- Mental rituals (praying, replacing bad thought with good thought)
- Superstitious behaviours
- Need to tell/ask/confess

Symptom dimensions[41]

- Contamination fears and cleaning/washing
- Forbidden thoughts (aggression, sexual, religious, and somatic obsessions and checking compulsions)
- Symmetry (symmetry obsessions and repeating, ordering, and counting compulsions)
- Hoarding (hoarding obsessions and compulsions)

disorder (BDD), trichotillomania (TTM), skin picking disorder, hoarding disorder, substance/medication-Induced obsessive-compulsive and related disorder and obsessive-compulsive and related disorder due to another medical condition. In the upcoming ICD-11, few

other conditions find a place in this group that include tic disorders, hypochondriasis and olfactory reference syndrome. All these disorders are grouped together based on shared clinical features (e.g., repetitive behaviours), comorbidity patterns, familiarity, neuropsychological deficits, treatment response and importantly shared brain circuitry abnormalities. Hoarding disorder which may not share many features with OCD is grouped along with OCD because of historical association with OCD and obsessive-compulsive personality disorder.

Comorbidity

OCD is often comorbid with other psychiatric disorders. It is important to assess all patients with OCD for associated psychiatric comorbidity since they may have an effect on treatment outcome if left untreated. Depression and anxiety disorders are present in over a half of patients seeking treatment for OCD. Common comorbid disorders are listed in Table 2. Those with early onset OCD, in particular those with onset in childhood have high rates of attention deficit hyperactivity disorder (ADHD), oppositional defiant disorder (ODD) and tic disorders.

Bipolar disorder, in particular type 2, is reported to be not uncommon in OCD [5]. Similarly, OCD is not uncommon in those with primary diagnosis of bipolar disorder [6, 7]. OCD when comorbid with bipolar disorder tends to run an episodic course [8] with worsening of symptoms in depressive phases and improvement in hypomania/mania phases. It is important to recognise OCD-bipolar comorbidity because of treatment implications. The specific serotonin-reuptake inhibitors (SSRIs) traditionally used to treat OCD may induce switch to mania or rapid cycling course.

Obsessive-compulsive symptoms and OCD are not uncommon in schizophrenia. Nearly a third of schizophrenia patients report OC symptoms or OCD. Presence of OCD may have a negative effect on the long-term course of schizophrenia. Therefore treatment of OCD with SSRIs and cognitive-behavior therapy (CBT)/behavior therapy (BT) may have to be considered although there is not much of systematic evidence supporting their efficacy in treatment of OCD in schizophrenia.

COMMON INGREDIENTS OF MANAGEMENT PLAN

Common ingredients of managing OCD include the following:

1. Detailed assessment of symptoms and comorbid patterns including suicidal behaviours either by unstructured clinical interview alone or supplementation with structured assessments.
2. Decision on setting for treatment (outpatient vs. inpatient)

Table 2: Comorbid disorders in OCD**Mood disorders**

- Major depression
- Dysthymia
- Bipolar disorder

Anxiety disorders

- Panic disorder
- Generalized anxiety disorder
- Social Phobia

OCD related disorders

- Body dysmorphic disorder
- Hypochondriasis
- Trichotillomania
- Skin picking disorder
- Tic disorders

Attention deficit hyperactivity disorder**Oppositional defiant disorder****Personality disorders**

- Obsessive-compulsive personality disorder
- Anxious-avoidant personality disorder
- Borderline personality disorder
- Schizotypal personality

Differential diagnoses to consider

- Depression (depressive ruminations are usually ego-syntonic, reflective of depressive cognitions such as self-criticism, failure, regret, guilt, pessimism without any compulsions)
- Generalized anxiety disorder (anxious ruminations are about real-life concerns and not associated with compulsions)
- Body dysmorphic disorder (concerns limited to physical appearance)
- Trichotillomania (limited to hair pulling)
- Skin picking disorder (confined to excessive skin picking)
- Hoarding disorder (difficulty in discarding or parting with possessions, accumulation of possessions; not secondary to obsessions)
- Eating disorders (confined to weight and food)
- Tics (often preceded by premonitory sensations and not aimed at neutralizing obsessions)
- Psychotic disorders (Even poor insight/delusional OCD is associated with typical obsessional content and compulsions whereas delusions have persecutory, grandiose themes with other symptoms such as hallucinations or formal thought disorder)
- Obsessive-compulsive personality disorder (enduring and pervasive pattern of excessive preoccupation with perfectionism, orderliness and rigid control; rigidity, stubbornness, scrupulosity and over conscientiousness. Typically ego-syntonic. No obsessions and compulsions)

care depending upon the severity, treatment resistance etc.)

3. Detailed psychoeducation of the patient and family member (s) about OCD, its course and treatment options including duration of treatment.
4. Choice of treatment: drugs vs. CBT vs. combination
5. In the Indian context, SSRIs are first-line treatments preferred over CBT because of feasibility, affordability and limited number of trained therapists. CBT may be considered if SSRIs alone are not beneficial.
6. Discussion on side-effects of drugs; in women risks vs. benefits of drugs during pregnancy and in the post-partum period
7. Follow-up plan after initiating treatment

ASSESSMENT AND EVALUATION

In routine clinical practice, use of structured / semistructured interviews and rating scales may not be necessary. They are optional. However, they may be used when the clinician needs supplementary information. A list of useful instruments in the assessment of OCD is provided in Table 3.

The Yale-Brown Obsessive-Compulsive Scale (YBOCS) is the most widely used severity rating scale for OCD in both adults [9] and children [10] and is considered a gold standard instrument to measure severity of OCD. It is a 10-item observer-rating scale, also available as self-rated instrument. It measures the overall severity of obsessive-compulsive symptoms for the preceding week. The YBOCS is a global measure of symptoms and does not provide severity of individual symptom dimensions. A total score of ≥ 16 is considered to be indicative of clinically significant OCD. The YBOCS severity scale also has an associated symptom check list of 15 categories of obsessions and compulsions including miscellaneous symptoms. The checklist elicits both current (1 month) and past symptoms.

On the YBOCS item-11 insight scale, the insight is graded as follows: 0 = excellent (fully rational thinking), 1 = good insight (readily acknowledges absurdity or excessiveness but has some lingering doubts), 2 = fair insight (reluctantly admits absurdity, but waivers; has some unrealistic fear but no fixed conviction), 3 = poor insight (overvalued ideas; maintains they are not unreasonable or excessive, but acknowledges validity of contrary evidence), and 4 = lack of insight (delusional). A higher score on the Y-BOCS item-11 indicates poorer insight.

FORMULATING A TREATMENT PLAN

Formulating a treatment begins with correct diagnosis of OCD as per the DSM or ICD classificatory systems. When feasible a structured clinical interview is recommended to obtain a comprehensive account of patient's problems. Once a diagnosis is established, a detailed assessment of symptom profile is mandatory. Family members often accommodate patient's rituals and contribute to poor outcome. In most severely ill patients, an elaborate family assessment may be needed. Once assessment is complete, short-term and long-term goals of treatment have to be established. Enhancing treatment adherence is a vital aspect of formulating a treatment plan. It is important to educate patients about lag in the onset of action of drugs and that improvement may occur over several months of continuous treatment. Brief education about basic principles of psychotherapy should be explained if psychotherapy is being planned. Essentials of formulating a treatment plan are summarized in Table 4. All patients and their immediate family members should be provided psychoeducation about OCD (Table 5).

Table 3: Commonly used instruments to assess OCD (optional)**Diagnostics interview schedules**

- The Mini International Neuropsychiatric Interview (MINI)[42]
- Structured Clinical Interview for DSM-5 (SCID-5)[43]

Severity rating scales

- Yale-Brown Obsessive-Compulsive Scale (YBOCS): symptom checklist and severity rating scale (adult and child versions)[9,10]
- Dimensional YBOCS (DYBOCS)[44]

Scales to assess insight in OCD

- Yale-Brown Obsessive-Compulsive Scale (YBOCS), Item 11[9]
- Brown-Assessment of Beliefs Scale (BABS)[45]
- Overvalued Ideas scale (OVIS)[46]

Obsessive-beliefs questionnaire (OBQ) to measure beliefs underlying obsessions [47]

The **Family Accommodation Scale (FAS)** assesses the degree to which family members of those with OCD accommodate patient's compulsions/rituals[48]

CHOICE OF TREATMENT SETTINGS

In the Indian scenario, treatment is either on an outpatient or an inpatient basis. Outpatient treatment is usually sufficient for most OCD patients who are mild to moderately ill and for those who are likely to be adherent to treatment. Patients may be followed-up at periodic intervals, initially once in a month or two and subsequently at longer intervals depending upon the response to treatment and tolerability and side-effects. Hospital treatment may be considered for those who are at high suicide risk, dangerous to self or others, and intolerant to side-effects. Many severely ill and treatment-resistant patients may require prolonged (2-3 months) hospitalization for intensive treatment with CBT and for rationalization of pharmacotherapy. Inpatient care may also be required for severe depression, mania or psychosis that may be comorbid with OCD. Admission in rehabilitation services may be necessary for some patients who may not have benefited from standard treatments including inpatient care.

PHARMACOLOGICAL TREATMENT

The clinical practice guideline is framed based on a review of relevant scientific literature. As a first step, we framed relevant questions which arise in the minds of the practitioner while treating a patient suffering from OCD. A literature search was conducted in PubMed to answer these questions. We also reviewed the existing guidelines on treatment of OCD [11-14]. After a thorough literature review, the treatment strategies were rated based on the Strength of Recommendation Taxonomy (SORT) [15].

Consistent evidence from multiple randomized controlled trials (RCT) constitutes the highest level of evidence for a recommendation. However, the external validity of RCTs has been questioned due to the rigid protocols in undertaking the studies. A practitioner may make a clinical decision based on the available evidence considering other relevant factors that influence the decision making process. A non-exhaustive list of these factors might include psychiatric and other medical

Table 4: Essentials of formulating a treatment plan

Establishing a diagnosis of OCD

Diagnosis of comorbid disorders (optional structured clinical interview)

Detailed evaluation for a range of OCD symptoms (clinical interview/YBOCS or similar check list)

Detailed symptom evaluation

- Identify principal symptoms that are the target of treatment (especially useful to identify principal symptoms if CBT is planned)
- Identify proxy compulsions, avoidance and safety behaviours
- Determine level of insight
- Assess family accommodation of patient's rituals

Short-term goals

- To achieve clinical response and if possible remission
- Remission of depression, if comorbid
- Help deal with suicidal thoughts, behaviour if any
- To determine tolerability to medicines
- Identify and manage side-effects

Long-term goals

- Achieve recovery
- Restore psychosocial functioning and enhance quality of life
- Long-term treatment to prevent relapses

Enhancing treatment adherence

- Psychoeducation to the patient and family members
- Provide education materials to patient and family members
- Deal with unrealistic expectations of quick recovery; educate patients and family about lag in the onset of action of drugs and that improvement may occur over several months
- Sensitize patient about potential side-effects and help to deal with them
- Use medicines that are effective, easily available and affordable
- Treat comorbid disorders and personality disorders if any; if left untreated may contribute to poor treatment adherence

Enhancing adherence to psychotherapy (CBT)

- Detailed education about principles behind exposure and response prevention
- Reassure that exposure and response prevention will be graded and tasks will be determined based on collaborative approach
- Emphasize the role of motivation, home-work compliance and need to tolerate some anxiety
- Reduce unrealistic expectations of quick recovery

comorbidities, previous treatment trials, affordability, accessibility, hypersensitivity, side-effect profile, patients' values etc.

RELEVANT CLINICAL ISSUES**1. First-line pharmacological treatment for OCD**

Meta-analyses of RCTs show that selective-serotonin reuptake inhibitors (SSRIs) are significantly more effective than placebo in the treatment of OCD [16]. SSRIs are associated with many adverse effects but are usually well tolerated. The only other medication which has shown to be consistently effective in OCD is the serotonergic tricyclic antidepressant clomipramine. Clomipramine has been found to be significantly more effective than placebo in multiple RCTs and meta-analysis of RCTs [16]. Network meta-analysis comparing the efficacy of clomipramine vs. SSRIs failed to find any efficacy advantage over SSRIs [16]. Most head-to-head comparison trials have not found any significant difference between the efficacy of clomipramine and SSRIs [17]. Further, meta-analyses and individual RCTs have found that the tolerability of clomipramine is worse than that of SSRIs

Table 5: Components of psychoeducation

- Obsessions and compulsions are symptoms of OCD and that they are similar in most people who suffer from OCD; OCD is a brain disorder
- Obsessions are not a reflection of one's character or unresolved mental conflicts
- Explain the link between the components—Obsessions, compulsions and distress
- Clarify myths and misconceptions about the illness
- Explain the biological and psychological basis of OCD : OCD is a problem of aberrant functioning of certain brain circuits involved in disregarding unwanted thoughts, dysfunction of certain neurotransmitter systems such as serotonin and glutamate, faulty interpretation and excessive importance given to certain intrusions resulting in manifestation of obsessions
- Discuss the course and outcome of OCD—regarding the waxing and waning course with optimism that outcome is good in a majority of the people if adequately treated
- Provide information regarding the available treatment strategies : pharmacotherapy and cognitive behavior therapy
- Sensitize with the idea that treatment is a continued process and often long-term
- Educate that medications take time to work, sometimes as long as few months before appreciable improvement is seen
- Psychological treatment too needs sustained efforts and sometimes booster sessions
- Prevention of relapse addressed within the general context of OCD as a chronic disorder
- Educate the family regarding the need to reduce expressed emotions such as criticality, accommodative behaviors and proxy compulsions; thus being supportive in the treatment process

[13, 17]. The anticholinergic, cardiac and neurological side effects of clomipramine may be problematic in this regard.

CONSIDERING THE CONSISTENT EFFICACY AND BETTER TOLERABILITY, GUIDELINES RECOMMEND SSRIs AS FIRST LINE TREATMENT FOR OCD (TABLE 6).

Choice of SSRI

Meta-analyses comparing the different SSRIs [16] and direct head-to-head comparisons [17,18] have not shown superiority of any one SSRI over the other. SSRIs differ to some extent in their propensity to cause certain adverse effects and drug interactions. However, there is no unequivocal evidence to suggest that these differences may be clinically meaningful. Recently, concerns have been raised regarding cardiac adverse effects with high dose of citalopram, which is commonly used in OCD. Hence, high-dose citalopram may be used with caution in those with risk for arrhythmias.

THE PRACTITIONER IS RECOMMENDED TO CHOOSE AN SSRI FOR AN INDIVIDUAL PATIENT BASED ON FACTORS SUCH AS PREVIOUS RESPONSE, COMORBIDITY, TOLERABILITY, ACCEPTABILITY, ADVERSE EFFECTS, COST AND DRUG INTERACTIONS.

Dose of SSRI

It is generally recommended that OCD be treated with a

Table 6: Medications recommended as monotherapy in OCD

Drug	Suggested dosage	Strength of recommendation*
Escitalopram	20-30 mg	A
Fluoxetine	60-80 mg	A
Fluvoxamine	200-300 mg	A
Paroxetine	40-60 mg	A
Sertraline	150-200 mg	A
Citalopram	40-60 mg	A
Clomipramine	150-225 mg	A
Venlafaxine	225-300 mg	B

*Based on modified Strength of Recommendation Taxonomy (SORT)[15]

A – Consistent, good-quality patient-oriented evidence i.e., Meta-analysis of Randomized controlled trials (RCT) with consistent findings or high quality individual RCT

B – Inconsistent or limited-quality patient-oriented evidence i.e., systematic review/meta-analysis of lower quality clinical trials or studies with inconsistent findings/lower quality clinical trial/cohort study/case-control study

C – Consensus based clinical guidelines extrapolations from bench research, disease-oriented evidence, usual practice, opinion, case-series

Table 7: Predictors of response to SSRIs

Clinical predictors of poor response

- Early age of onset
- Longer duration of illness
- Poor insight
- Presence of hoarding, sexual/religious obsessions, cleaning/washing, repeating/counting compulsions
- Comorbidities in the form of tics and depressive disorder
- Comorbid schizotypal, borderline and anxious avoidant personality disorders

Neuroimaging predictors

- Lower baseline orbitofrontal cortex (OFC) and anterior cingulate cortex (ACC) metabolism and greater pretreatment caudate metabolism predicted better response (PET studies)
- Reduction in thalamic volume and increase in OFC volume is associated with SSRI response (structural MRI)
- Increased dorso-lateral prefrontal cortex (DLPFC) activation with Stroop task and decreased activation of frontal regions with symptom provocation task predicted good response

Genetic predictors

- Specific polymorphisms in the promoter region of serotonin transporter (5-HTTLPR) associated with treatment response
- CYP2D6 polymorphisms associated with SSRI response

Ref:[49]

higher dose of SSRI than that used in depression (Table 5). A meta-analysis of fixed-dose comparison studies have found a greater efficacy with higher doses of SSRI (60-80 mg fluoxetine equivalent) compared to medium (40-50 mg fluoxetine equivalent) and low doses (20-30 mg fluoxetine equivalent) [19]. However, all three dose ranges were significantly more effective than placebo. The increased efficacy comes at the cost of poor tolerability as evidenced by increased dropouts due to adverse effects [19]. A review of individual fixed-dose comparison studies found that the dose-response relationship is more evident for escitalopram, fluoxetine and paroxetine, while it is less clear-cut for citalopram and sertraline [17]. Clomipramine has not been tested in such fixed dose comparison studies. However, most studies have employed a flexible dosing at 150-250 mg [17]. It should be remembered that there is likely to be inter-individual differences in

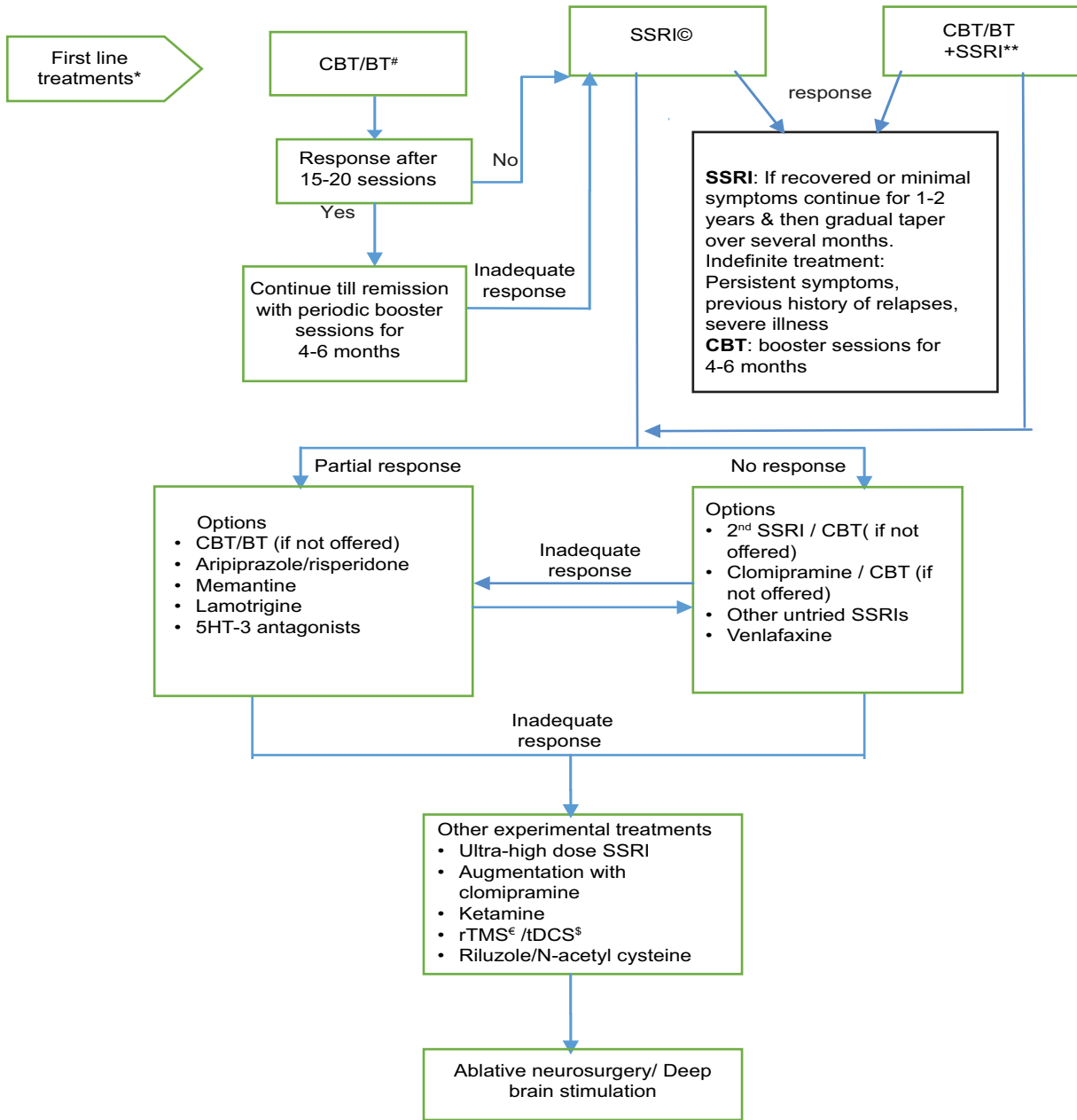


Figure 1: Treatment algorithm for treating a patient with OCD. *First line treatment chosen based on feasibility and severity of illness, #CBT/BT- Cognitive behavior therapy/Behavior therapy, @SSRI – Selective serotonin reuptake inhibitor, %rTMS- repetitive transcranial magnetic stimulation, \$ - tDCS- transcranial direct current stimulation. ** Preferred for severe OCD

pharmacokinetic profile of drugs due to intrinsic variations in drug metabolism and drug interactions.

GUIDELINES RECOMMEND TREATMENT OF OCD WITH HIGHER DOSE OF SSRIs. HOWEVER, IF AN INDIVIDUAL PATIENT IS NOT ABLE TO TOLERATE HIGHER DOSE, LOW TO MEDIUM DOSE TREATMENT CAN BE CONSIDERED.

Duration of trial and dose titration

A recent meta-analysis of 17 RCTs found that SSRIs separate from placebo as early as 2 weeks and that

majority of improvement occurs early on in the course of treatment [20]. However, improvements seen early in the course of treatment may not be always clinically meaningful. In many patients, clinically meaningful improvements may be seen only after weeks or months of treatment. It is recommended that an adequate trial of a SSRI (or clomipramine) should be at least for 12 weeks to account for the lag in the onset of action. The APA guidelines recommend upward titration to the maximum FDA-approved doses by 4-6 weeks and continuation in that dose for another 6-8 weeks or so to determine efficacy [11]. Certain clinical and biological predictors of treatment

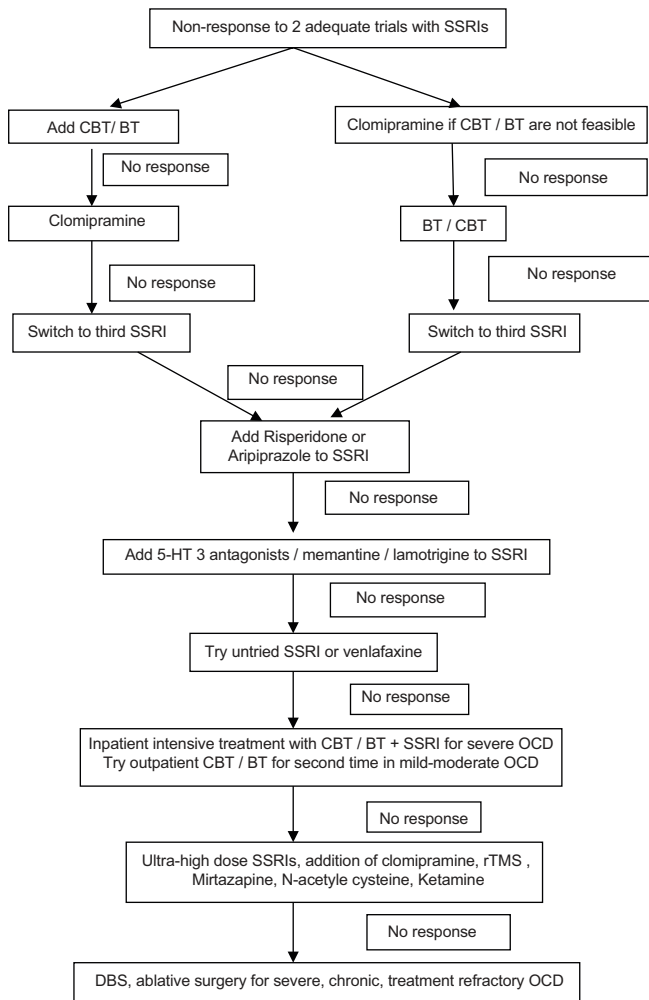


Figure 2: Strategies for non-responders to SSRIs. SSRI- Selective serotonin reuptake inhibitors, CBT/BT-Cognitive behavior therapy/behavior therapy, rTMS- repetitive transcranial magnetic stimulation

response to SSRIs have been identified but they are not robust predictors (Table 7).

GUIDELINES RECOMMEND CONTINUING MAXIMALLY TOLERATED EFFECTIVE DOSE OF A SSRI FOR AT LEAST 12 WEEKS FOR JUDGING ITS EFFICACY. GUIDELINES ALSO RECOMMEND DOSE ESCALATION TO EFFECTIVE DOSE RANGES WITHIN 4-6 WEEKS AND CONTINUATION IN THE SAME DOSE FOR ANOTHER 6-8 WEEKS.

2. Other medications that can be tried as monotherapy in OCD

Venlafaxine, a serotonin-norepinephrine reuptake inhibitor with preferential serotonergic action, has been studied in comparison to paroxetine in a double blinded study and clomipramine in a single blinded study. The studies found no difference in the efficacy between venlafaxine and the comparator agents in acute control of OCD.

Given the absence of evidence from placebo-controlled trials, venlafaxine is not the first-line treatment for OCD. Hence, the guidelines consider venlafaxine as a second-line monotherapy agent in the treatment of OCD.

Mirtazapine has been studied as a monotherapy in two small open-label trials with inconsistent findings. Therefore, mirtazapine cannot be recommended as monotherapy in treatment of OCD.

3. Treatment strategy for non-responders to first-line treatment

Definitions of treatment outcome [21] are given in Table 8. Estimates suggest that around 40-70% patients show an adequate response to a trial of SSRI with a remission rate of 10-40% [16]. Clinicians often face the subsequent challenge of partial and non-response to SSRIs. Continuing improvement has been noticed with prolonged trial of SSRIs as discussed above. Hence, the initial trial may be continued further if there is evidence of ongoing improvement. A general treatment algorithm for OCD and for non-responders to SSRIs is shown in Figures 1 and 2 respectively.

a. Switching to another medication

Switching to another first-line medication has been found to be effective; experts provide a rough estimate of 40-50% response rate for the second SSRI and decreasing response rates with further trials. Switching to a second SSRI is suggested for non-responders to a first SSRI. In partial responders, changing medication may entail loss of the response to the earlier medication. Hence, switching is recommended in partial responders only if there are severe persisting symptoms or upon failure of other augmenting strategies such as CBT and atypical antipsychotics.

b. Switching / Augmenting with CBT/BT

It is uncertain whether initiating a combination of BT/CBT simultaneously with SSRI is advantageous compared to either treatment alone. However, CBT/BT has been proven to be effective as an augmenter in partial/non-responders to SSRIs [18, 22, 23]. Where feasible, CBT/BT is a potential first-line augmenting option for partial/non-responders to SSRI treatment.

c. Augmenting with another medication (Table 9)

The following medications have been commonly tried as augmenters to SSRIs. Atypical antipsychotics, risperidone and aripiprazole have the best evidence.

i Antipsychotics

Antipsychotics are the most widely studied augmenting agents of SSRIs [23]. The literature on antipsychotic augmentation is fraught with methodological limitations

Table 8: Definitions of treatment outcome in OCD

Consensus definitions and operationalization of treatment response, partial response, remission, recovery, and relapse for Obsessive-Compulsive Disorder (OCD)		
	Conceptual Definition	Operationalization
TREATMENT RESPONSE PARTIAL RESPONSE	A clinically meaningful reduction in symptoms (time, distress, and interference associated with obsessions, compulsions, and avoidance) relative to baseline severity in an individual who meets diagnostic criteria for OCD	A $\geq 35\%$ reduction in (C) Y-BOCS scores plus CGI-I rating of 1 ('very much improved') or 2 ('much improved'), lasting for at least one week A $\geq 25\%$ but $< 35\%$ reduction in (C) Y-BOCS scores plus CGI-I rating of at least 3 ('minimally improved'), lasting for at least one week
REMISSION	The patient no longer meets syndromal criteria for the disorder and has no more than minimal symptoms. Residual obsessions, compulsions, and avoidance may be present but are not time consuming and do not interfere with the person's everyday life	<i>If a structured diagnostic interview is feasible</i> , the person no longer meets diagnostic criteria for OCD for at least one week <i>If a structured diagnostic interview is not feasible</i> , a score of ≤ 12 on the (C) Y-BOCS plus CGI-S rating of 1 ('normal, not at all ill') or 2 ('borderline mentally ill'), lasting for at least one week
RECOVERY	The patient no longer meets syndromal criteria for the disorder and has had no more than minimal symptoms. Residual obsessions, compulsions, and avoidance may be present and slightly fluctuate in severity over time but, overall, they are not time consuming and do not interfere with the person's everyday life and therefore require no further treatment. The clinician may begin to consider discontinuation of treatment or, if the treatment continues, the aim is to prevent relapse	<i>If a structured diagnostic interview is feasible</i> , the person no longer meets diagnostic criteria for OCD for at least one year <i>If a structured diagnostic interview is not feasible</i> , a score of ≤ 12 on the (C) Y-BOCS plus CGI-S rating of 1 ('normal, not at all ill') or 2 ('borderline mentally ill'), lasting for at least one year
RELAPSE	After response or remission or recovery was achieved, the patient experiences a return of symptoms. For patients who were in remission or recovered, obsessions, compulsions, and avoidance are again sufficiently time consuming, distressing, and impairing for the individual to meet diagnostic criteria for OCD	<i>For responders who did not necessarily remit/recover</i> : The person no longer meets the definition of $\geq 35\%$ reduction on (C) Y-BOCS scores (relative to pre-treatment) plus CGI-I rating of 6 ('much worse') or higher for at least one month <i>For remitters/recovered</i> : OCD criteria are met again, according to a structured interview (if feasible). Alternatively, the person no longer meets the definition of remission/recovery (i.e., the person again scores 13 or above on the (C) Y-BOCS) plus CGI-I rating of 6 ('much worse') or higher for at least one month or needs to be withdrawn prematurely from the trial before one month has elapsed due to a severe worsening of OCD symptoms. Discontinuation of the trial due to reasons other than a worsening in OCD symptoms (e.g., suicide risk) is not considered a relapse

Abbreviations: CGI-I – Clinical Global Impression Improvement; CGI-S – Clinical Global Impression Severity; (C) Y-BOCS – (Children's) Yale-Brown Obsessive Compulsive Scale; OCD – Obsessive-Compulsive Disorder. Ref: [21]. This table is reprinted with permission from the lead author of the Delphi survey. The table is not part of the publication

including small sample sizes, varying doses and duration of treatment with both antipsychotics and concomitant SSRIs, varying degree of treatment resistance etc. Two recent meta-analyses of 14 RCTs on antipsychotic augmentation found that antipsychotic as a group was significantly more effective than placebo in decreasing YBOCS scores [24, 25]. About a third of patients responded to antipsychotic augmentation. Aripiprazole and risperidone are consistently found to be effective as augmenting agents. The evidence for haloperidol should be interpreted with caution as it was based on a single study. A fairly large RCT comparing CBT, risperidone and pill placebo augmentation of SSRI found that risperidone did not separate from placebo in augmenting efficacy [26]. This study has raised questions on the efficacy of risperidone as an augmenter. Quetiapine and olanzapine have not been consistently found to be effective, while other antipsychotics have not been studied

adequately. Meta-analyses do not throw any light on adequate dose and duration of antipsychotic treatment [24]. Antipsychotics should be used in low doses (e.g., 1-3 mg of risperidone, 5-10 mg aripiprazole) for a period of at least 8 weeks for an adequate trial. Use of antipsychotics in the long-run should be considered after weighing the benefits and risks of long-term use.

BASED ON THE AVAILABLE EVIDENCE, ARIPIPRAZOLE AND RISPERIDONE MAY BE CONSIDERED THE FIRST CHOICE FOR PHARMACOLOGICAL AUGMENTATION

ii. Glutamatergic agents

There is a strong theoretical rationale supporting the use of glutamatergic drugs in OCD. The following glutamatergic agents have been studied in OCD [23]:

Table 9: Pharmacological augmenting agents in OCD

Drug	Suggested dosage ^s	Strength of recommendation*
Aripiprazole	5-10 mg	A
Risperidone	1-3 mg	A
Haloperidol	2.5-10 mg	B
Memantine	10-20 mg	B
Lamotrigine	100mg	B
Ondansetron	2-4 mg twice a day	B
Granisetron	1 mg twice a day	B

§ - Rough estimate based on available evidence

*Based on modified Strength of Recommendation Taxonomy (SORT)[15]

A – Consistent, good-quality patient-oriented evidence i.e., Meta-analysis of Randomized controlled trials (RCT) with consistent findings or high quality individual RCT
 B – Inconsistent or limited-quality patient-oriented evidence i.e., systematic review/meta-analysis of lower quality clinical trials or studies with inconsistent findings/lower quality clinical trial/cohort study/case-control study
 C – Consensus based clinical guidelines extrapolations from bench research, disease-oriented evidence, usual practice, opinion, case-series

- Memantine: found effective in 2 double blinded and one single blinded RCT.
- Lamotrigine: found effective in 2 double blinded RCTs
- Topiramate: effective in 2 small double-blind RCTs, but poorly tolerated
- Riluzole: inconsistent results in two RCTs
- N-acetylcysteine: conflicting results from three RCTs, has to be studied further.

BASED ON THE EVIDENCE AND ITS RELATIVELY BETTER TOLERABILITY, MEMANTINE IS PREFERRED OVER LAMOTRIGINE AS THE FIRST CHOICE GLUTAMATERGIC AUGMENTING AGENT.

iii. Serotonergic agents

5HT-3 antagonists including ondansetron and granisetron are reported to be effective and well tolerated in small RCTs [27]. However, due to the methodological limitations of the individual studies, 5HT-3 antagonists are recommended as second line augmenting agents along with glutamatergic agents.

Preliminary evidence suggests that clomipramine can be an effective augmenting agent. Clomipramine and SSRI combination should be used cautiously, especially with fluoxetine and fluvoxamine, as they may increase clomipramine related adverse effects (including serious events like seizures, cardiac effects, serotonin syndrome) due to pharmacokinetic interactions. Clomipramine augmentation of SSRI may be tried but adequate precautions need to be taken keeping in mind the potential adverse effects of the combination.

Mirtazapine augmentation has been found to hasten the response with no significant long term benefits [23] and hence may be considered as an augmenting agent in partial responders and non-responders.

iv. Other augmenting agents

Buspirone, lithium and clonazepam have not been found effective and hence are not recommended as augmenting agents. The safety and efficacy of psychostimulants and opioid drugs have to be systematically studied before they are recommended for routine clinical use. Intravenous ketamine has been found to have acute anti-obsessive effects in a “proof-of-concept” study, which needs replication and long term evaluation before the strategy can be recommended for routine clinical use.

d. Other experimental strategies

While there appears to be some short-term benefits for intravenous clomipramine in treatment resistant patients, the long term benefits are uncertain. This formulation is not available in India and is not recommended at present for clinical use. There are a few uncontrolled trials demonstrating the utility of higher than recommended doses of SSRIs (up to 400 mg of sertraline, 40-50 mg of escitalopram) in resistant patients. This strategy should be considered experimental and may be used only in resistant patients after exhausting other regular safer options.

ROLE OF OTHER NON-SOMATIC TREATMENTS

Around 20% of patients do not respond to available pharmacological and psychological treatments. Neuromodulatory and neurosurgical treatments targeting the cortico-striato- thalamo-cortical (CSTC) circuits have been tried in resistant patients.

NON-INVASIVE BRAIN STIMULATION TECHNIQUES

1. Electroconvulsive therapy(ECT)

ECT has not been systematically evaluated for the treatment of OCD. Available evidence, in the form of case reports and case series, do not provide evidence for the efficacy of ECT [28]. Hence, ECT is not recommended as a treatment for OCD and may be considered for the treatment of comorbid conditions like severe mood and psychotic disorders, if indicated.

2. Repetitive transcranial magnetic stimulation (rTMS)

rTMS entails the possibility of non-invasive and focal stimulation of superficial cortical regions, thereby increasing or decreasing their excitability based on the frequency of stimulation. The regions implicated in OCD are usually not accessible with available technology of rTMS. Hence rTMS has been tried in superficial cortical regions which have connections with other deeper structures implicated in OCD. Controlled trials of low frequency or high frequency rTMS over either dorsolateral prefrontal cortex (DLPFC) have yielded conflicting results

but low frequency rTMS over supplementary motor area (SMA) and orbitofrontal cortex (OFC) appear promising [29]. However, the evidence has not been very consistent. Overall, the findings have to be replicated in larger samples with long term follow-up. There is no convincing evidence that beneficial effects persist for longer than the trial period. The guideline recommends rTMS as an intervention for further research and not for routine clinical use.

3. Transcranial direct current stimulation (tDCS)

tDCS is another focal and superficial cortical modulatory intervention, which either increases or decreases the excitability of the underlying cortex depending on the polarity of the stimulating electrode. There are only a few case reports and an open-label trial on tDCS in OCD. It has to be evaluated more systematically before it can be recommended for clinical use in OCD.

NEUROSURGICAL PROCEDURES

1. Ablative neurosurgery

Ablative neurosurgical procedures involve producing lesions in specific regions of the CSTC circuit, which is hypothesized to be dysfunctional in OCD. Reliable lesions can be produced with the help of “invasive” stereotactic surgery or “non-invasively” with the help of image guided gamma radiation. Anterior cingulotomy and a refined version of capsulotomy known as ‘gamma ventral capsulotomy’ are practiced in treatment refractory OCD in a few centers. Due to the irreversible nature, these procedures are generally employed in treatment refractory patients (Table 10). Evidence primarily in the form of uncontrolled studies suggests that around 40-

60% of patients improve over 6-24 months following surgery. There is some suggestion that capsulotomy may be more effective procedure in OCD [30] and that its efficacy may be similar to that of deep brain stimulation (DBS)[31]. Surgery may be associated with short-term and persistent adverse effects including personality changes, seizures and cognitive adverse effects although rates are not high.

2. Deep brain stimulation

Deep brain stimulation (DBS) is a potentially reversible procedure involving high frequency stimulation of implanted electrodes in the brain. Although the mechanism of action is poorly understood, it is hypothesized to modify dysfunctional circuits. DBS for OCD has been evaluated in sham controlled studies targeting nucleus accumbens, ventral capsule/ventral striatum, anterior limb of internal capsule, ventral caudate and subthalamic nucleus. A recent meta-analysis found a responder rate of 60% with a mean YBOCS reduction of around 45% [32]. DBS is an invasive procedure and is associated with short term and long term adverse effects. Further, the battery needs to be replaced periodically which may be quite expensive. DBS can be recommended in carefully selected refractory OCD patients (Table 10) after discussion regarding the pros and cons of the procedure.

The neurosurgical procedures are not curative in nature and the procedures are only one aspect of a comprehensive treatment program which should continue following surgery.

Surgical procedures may be considered only in selective patients after careful evaluation of patients for treatment refractoriness, severity of illness and comorbidities. Patients should be explained about the realistic possibility of benefits and risks. They should be evaluated by an independent team consisting of a psychiatrist, a neurologist and a neurosurgeon for suitability for surgery. The treatment should be conducted under close collaboration of a team of psychiatrist, neurosurgeon, radiotherapist, imaging specialist and psychologist with close monitoring of adverse effects. Suggested criteria for suitability to undergo surgery are shown in Table 10.

Table 10: Selection criteria for surgery

1. Severe (YBOCS >28) and chronic unremitting OCD
 2. The disorder is causing substantial distress and impairment in functioning (GAF \leq 45)
 3. The following treatment options tried systematically without appreciable effect on the symptoms
 - Adequate trial with at least 2 of the SSRI antidepressants for at least 3 months each
 - Treatment with clomipramine at optimum dosage for at least 3 months unless poorly tolerated
 - Augmentation with at least 2 agents, one of them being an atypical antipsychotic: atypical antipsychotic (ripseridone, aripiprazole), clomipramine, memantine, ondansetron/granisetrone
 - At least one adequate trial of cognitive behavior therapy (at least 20 sessions of exposure and response prevention) or demonstrated inability to tolerate the anxiety due to therapy
 - Previous treatment trials have not been abandoned prematurely due to solely mild side effects
 4. Patient gives informed consent
 5. Willing to participate in the pre-operative evaluation and post-operative periodic follow-up
- Relative contraindications:
1. Comorbid intellectual disability, psychosis, bipolar disorder and severe personality disorders
 2. Clinically significant and unstable neurologic illnesses

PSYCHOLOGICAL TREATMENTS FOR OCD (TABLE 11)

A. Cognitive Behavioral Therapy (CBT) / Exposure and Response Prevention (ERP)

Consistently, CBT/ERP has been shown to be efficacious in the treatment of OCD [33]. All treatment guidelines have suggested the use of CBT as a first-line treatment option. CBT for OCD includes ERP.

CBT/ERP is a first-line treatment option for OCD. ERP is the most important component of CBT along with belief

Table 11: Psychotherapy in OCD

Psychotherapy	Strength of recommendation
Cognitive behaviour therapy (including exposure and response prevention)	A
Behaviour therapy (exposure and response prevention)	A
Mindfulness based cognitive behaviour therapy	C
Acceptance and commitment therapy	C
Stress management and relaxation training	C
Thought stopping	C
Dynamic psychotherapy	C

*Based on modified Strength of Recommendation Taxonomy (SORT)[15]

modification. When facilities are available, CBT/ERP monotherapy may be recommended in mild to moderately ill patients. In severely ill patients a combination of CBT and SSRI is recommended.

CBT as an augmentation strategy

It is uncertain whether initiating a combination of CBT/ERP and SSRI is advantageous compared to either treatment alone. However, CBT/BT is found to be effective in augmenting SSRIs in partial/non-responders to SSRIs [34]. A recent study found CBT to be superior to risperidone and placebo in augmenting SSRIs in OCD [35]. Patients in the CBT group had significantly greater reductions in OCD symptom severity compared with participants taking risperidone or placebo. Risperidone was not superior to placebo on any outcome measures.

When facilities for CBT are available, CBT / BT is recommended as the first line augmenting strategy in partial/non-responders to SSRI treatment.

Mode of CBT/ERP delivery and adaptations

Although various models are available for CBT in OCD, the major components are psychoeducation, development of symptom hierarchy, cognitive restructuring and ERP (Table 12). The method of conducting ERP has been found to be important with 'therapist-assisted' ERP producing a greater change in symptom severity. Therapist-guided exposure is better than self-guided exposure. The numbers of CBT sessions have varied between 12 and 20 sessions across various studies. It has ranged from intensive daily 2 hour sessions for 5 days a week for 3 weeks to less intensive twice weekly sessions in other studies.

Even though group CBT has been compared with individual CBT, the results have been mixed. While a couple of studies have reported comparable efficacy for group and individual forms of CBT, some other studies demonstrated the superiority of individual mode of CBT compared to the group CBT. Another adaptation of CBT which has been examined in the recent years is the internet based CBT (ICBT) and computerized CBT. They are found to be

effective compared to supportive therapy / relaxation methods [36, 37].

Where resources are available, 15-20 hours of therapist assisted CBT / BT may be considered. The evidence for ICBT and computerized CBT is very preliminary and it may be recommended in certain circumstances where regular face-to-face CBT is not feasible.

B. Other Psychological therapies

1. Acceptance and Commitment Therapy

This therapy aims to improve psychological flexibility through the practice of *acceptance* and mindfulness in addition to *commitment* and behavior modification exercises. Preliminary evidence suggests its benefits but it needs to be tested and compared with CBT in larger samples.

2. Stress management and relaxation training

These have been conventionally used in many studies as control arm in studies CBT. Stress management and relaxation training may have non-specific effects but there is no evidence suggesting their efficacy in treatment of OCD.

3. Mindfulness based cognitive therapy

Mindfulness based therapy is thought to be useful in OCD. Preliminary data suggests its utility in treating OCD. Protocols for RCT are published but there is no published evidence in the literature in clinical population.

4. Family inclusive treatments

Family-inclusive treatment (FIT) approaches aim to include the family members in the treatment so as to improve the family functioning, facilitate behavioral therapy etc. Studies targeting family accommodation of obsessive-compulsive symptoms report greater improvements in patient functioning. Family members may be encouraged to participate in CBT since family accommodation of symptoms is associated with poorer treatment outcomes.

5. Others

The other forms of psychological therapies with isolated studies include adjunct motivational interviewing to ERP and Eye Movement Desensitization and Reprocessing (EMDR). There is one study examining the role of brief dynamic therapy in OCD with negative result. In addition, the potential benefits of adding D-cycloserine prior to ERP sessions has been examined in few studies.

MANAGEMENT AS PER THE DIFFERENT PHASES OF ILLNESS

Acute phase

This includes decision on choice of treatment modality (SSRI vs. CBT), implementation of treatment, monitoring for the response and side-effects, and planning for sequential

Table 12: Components of CBT for OCD

Step	Components
Assessment	<ul style="list-style-type: none"> • Assess nature and severity of OCD symptoms (YBOCS symptom checklist and severity rating) • Examine insight in to the OCD symptoms • Assessment of safety behaviors and avoidance strategies employed by the patient • Look for current comorbid conditions such as depression that may interfere with CBT • Assess the motivation levels and personality attributes of the patient • Family's involvement (accommodating the symptoms, proxy compulsions, expressed emotions) needs to be explored
Psychoeducation	<ul style="list-style-type: none"> • Educate regarding the nature of obsessions and compulsions • Explain the cycle of propagation of obsessions through performing compulsions and by avoiding the stimuli • Discuss in detail the rationale behind CBT (concepts of habituation, fear extinction and the role of dysfunctional beliefs) • Educate the family members about principles in CBT
Formulate the therapy	<ul style="list-style-type: none"> • Formulation needs to be personalized • Identify the specific cognitive distortions (maladaptive thinking patterns) such as exaggerated threat perception, inflated responsibility, perfectionism, need to control thoughts etc. • Develop a collaborative understanding of the formulation with the patient (e.g., the goal is to eliminate fear of HIV infection and not reduce/prevent the chances of contracting HIV) • Explain the "neutral spectatorship" principle towards obsessions (don't interpret them, observe) • Demonstrate how offering active resistance to obsessions is counterproductive and increases their salience
Handling the thoughts	<ul style="list-style-type: none"> • Foster the practice of gathering evidence for the thoughts (how likely would it happen/what is the worst consequence/less threatening alternative explanations etc.) • Socratic questioning initiated • Examining the faulty appraisals with examples • Preparing for behavioral experiments (exposure and response prevention)
Challenging the dysfunctional beliefs	<ul style="list-style-type: none"> • ERP forms the core of CBT. Exposure to anxiety provoking situations in a graded manner with negotiations and contracts at every step • Rationale of ERP with examples-explain the habituation and extinction principle with the aim of anxiety reduction as well as disconfirmation of the fears • Make a list of anxiety provoking situations/triggers in a hierarchical manner using subjective units of distress (0 to 10 subjective rating by the patient) • Expose the patient starting from the lowest anxiety provoking situation and gradually escalate the level. Each session lasting for 1-1 ½ hours , till the patient experiences reduction in distress/anxiety • Homework assignments, consistent performance of ERP tasks insisted upon
Behavioral Experiments-Exposure and Response prevention	<ul style="list-style-type: none"> • Explain that treatment is a continuous process • Periodic booster sessions to review the situation and to troubleshoot emerging issues • Anticipation of future concerns such as change in the form of symptoms, relapse under stress, emergence of subtle avoidance behaviors etc • Encourage regular work and other normal behaviors
Relapse prevention	

treatment trials if initial treatments failed to produce satisfactory improvement.

Maintenance treatment (How long the treatment should be continued?)

There is evidence for ongoing improvement with continued use of SSRIs and clomipramine in long term continuation studies for a period of up to 1 year[18]. Guidelines recommend continuation of SSRIs / clomipramine for at least 1-2 years after achieving remission. Clinical experience dictates that discontinuation of medication beyond that period may be associated with increased chance of relapse. Hence discontinuation of medications should be carefully considered based on individual patient factors including severity and duration of illness, past history of relapse on discontinuation, residual symptoms, comorbidities etc. Most patients may require continued pharmacotherapy to prevent relapses. Medications are generally recommended to be continued at the same dose that resulted in improvement, unless the dosage is not tolerated.

MANAGEMENT OF COMORBID CONDITIONS

Depression and Anxiety disorders

Most common co-occurring illness is major depression. The Pharmacological treatment strategy does not change much, however in severe depression CBT/ERP for OCD needs to be kept on hold until the patient recovers from depression. Severe depression with prominent suicidal ideas needs to be evaluated thoroughly and ECT may be considered if indicated. Comorbid dysthymia is common and may require individual therapy.

Comorbid anxiety disorder needs to be treated aggressively since untreated anxiety disorder may contribute to poor treatment outcome. Comorbid anxiety disorders may require CBT in addition to SSRIs.

Tic disorders

Tic disorders show best response to antipsychotics (haloperidol, pimozide, risperidone and aripiprazole).

Although antipsychotics may be more effective, adrenergic α_2 agonists (clonidine and guanfacine) may be tried first to treat tics in view of adverse effects associated with antipsychotics. Habit-reversal therapy (HRT) is a potential first-line treatment option instead of or in combination with pharmacotherapy.

OCD patients with tic disorders may require a combination of an SSRI and an antipsychotic. There is evidence that OCD comorbid with tic disorders may not respond satisfactorily to SSRI alone.

Bipolar Disorder

Comorbid bipolar disorder calls for a different treatment strategy because SSRIs are well known to cause/exacerbate hypomania or mania. Mood stabilization should be the primary goal in treating OCD-bipolar patients [38]. In many patients with comorbid bipolar disorder, OCD often manifests / increases in severity in depressive episodes but improves in mania / hypomania episodes. In such patients, treatment with mood stabilizer alone may be considered. If OCD persists outside of the mood episodes, CBT may be preferred over SSRIs. However, if patient requires an SSRI, it has to be prescribed under the cover of mood stabilizers or an atypical antipsychotic.

Psychosis

OC symptoms and OCD are not uncommon in those with schizophrenia; up to 25% of the schizophrenia patients report clinically significant OCD symptoms. SSRIs may be used in treating OCD comorbid with schizophrenia, but there is limited published evidence. Some atypical antipsychotics such as clozapine, risperidone and olanzapine may induce or even worsen OCD symptoms. In case of drug-induced OC symptoms, if feasible, one may consider reducing dose or changing to another antipsychotic.

Personality disorders

20% of the participants suffer from at least one comorbid personality disorder (PD). The most common are obsessive-compulsive, narcissistic and anxious avoidant personality disorders. Presence of PD can complicate the course and outcome. OCD patients with different comorbid PDs differ in their therapeutic response to treatment. Borderline, obsessive-compulsive and schizotypal personality disorders can contribute to poor outcome. There are no systematic studies comparing the effects of treatment in OCD coexisting with PD. Generally it is agreed upon that a combination of medications, CBT-ERP and individual therapy are advocated.

OCD during pregnancy and lactation

Medication should be guided primarily by its safety data, severity of the illness, and benefit vs. risk to the developing fetus. For newly diagnosed OCD during pregnancy and in the post-partum period, CBT/ERP is the preferred option [39]. Pre-pregnancy counseling for all women should include planning pregnancy, folate supplementation,

discussion with patient and spouse regarding options, and active liaison with obstetricians, ultrasonologists and pediatricians.

Following is the summary of SSRIs in pregnancy and lactation:

1. If the patient is symptom-free for a long period, an attempt may be made to withdraw the SSRI gradually. However, a risk of relapse following discontinuation should be discussed.
2. Benefits vs. risks of continuing SSRIs during pregnancy should be discussed keeping in mind the fact that OCD can relapse following discontinuation.
3. SSRIs as a group do not appear to be major teratogens.
4. SSRIs, paroxetine in particular have been associated with increased risk for cardiac malformations (septal defects) (1.5-2%), as compared to the general population (1%) but the evidence is inconsistent. Paroxetine may be avoided; it is less safe than the other SSRIs.
5. Some studies have reported an association between SSRI use in first trimester and anencephaly, craniosynostosis, and omphalocele. However, it must be emphasized that the risks are rare and absolute risks are small.
6. When taken in late pregnancy, SSRIs may increase the risk of persistent pulmonary hypertension by more than twofold in the newborn (absolute risk, 3 infants per 1000 exposed vs. 1.2 infants per 1000 unexposed).
7. SSRIs have also been associated with decreased gestational age, low birth weight and spontaneous abortion
8. Following birth, serotonergic toxicity and antidepressant discontinuation symptoms may manifest, therefore it is important to liaise with pediatricians.
9. Sertraline, fluvoxamine and paroxetine are present in very low concentrations in plasma of breast-fed infants (<3% of maternal dose). It is surmised that they are relatively safe during breast feeding. With fluoxetine and citalopram, infants can receive up to 15% of the maternal dose.

OCD in child and adolescent population

SSRIs and clomipramine are efficacious in treating OCD and are superior to placebo with modest effect size [40]. CBT has superior efficacy compared to SSRIs in children [40]. A combination of CBT and SSRI seems to have no additional advantage over CBT alone indicating that SRI treatment adds little to concomitant CBT. However, combined treatment is better than SSRI alone. In partial responders to SSRIs, adding CBT is superior and efficacious as compared to continuing a SSRI. In view of superior efficacy of CBT, many guidelines advocate CBT as the first line treatment in children. In children, where facilities are available, CBT may be preferred over SSRIs as the first-line treatment. In children with severe OCD, a combination of CBT and SSRI is recommended over SSRI alone. SRIs are the alternative first-line treatment for OCD in children in situations where

Table 13: Side-effects of SSRIs

Somnolence	Comment	Management
Drowsiness, insomnia	All SSRIs can cause somnolence Insomnia more common with fluoxetine	Drowsiness: Prescribe bulk of dose at bedtime Insomnia: Fluoxetine may be prescribed in the morning. Benzodiazepines, Trazadone or zolpidem may be used for insomnia
Hypotension Conduction disturbances	Not a usual side-effect SSRIs have no effect on QTc and are not associated with arrhythmias and conduction disturbances Exception: Citalopram (? escitalopram) is associated with dose related increase in QTc and Torsades de pointes in overdose	SSRIs are generally safe in patients with cardiovascular diseases including the post myocardial infarction period Sertraline appears to be the safest. Citalopram and escitalopram should be used with caution in those at risk for arrhythmia Most get over the side-effects. If they are troublesome, reduce the dose or change the SSRI
Anticholinergic	Not prominent with SSRIs except with paroxetine	
Gastrointestinal	Nausea, vomiting, diarrhea, dyspepsia and anorexia are common. Nausea more common with Fluvoxamine. Paroxetine can cause constipation SSRIs may increase the risk of gastrointestinal bleeding	Common GI side-effects usually settle down with continued use. If they persist, reduce dose or change the SSRI. Proton pump inhibitors may be useful Use SSRIs with caution when co-administered with aspirin, NSAIDs or oral anticoagulants
Neurological	Headache (and worsening of migraine), tremors and rarely akathisia, extrapyramidal symptoms, seizures and dyskinesias	Fine tremors, akathisia may respond to propranolol. Extrapyramidal symptoms respond to trihexiphenidyl. Headache responds to acetaminophen prn Increase the dose gradually; benzodiazepines may help
Activation/ agitation	Usually seen with fluoxetine	
Switch to mania/ hypomania	Risk of switch to mania/hypomania is known in those with bipolar disorder	Always use under the cover of mood stabilizers or atypical antipsychotics
Sexual dysfunction	All SSRIs are associated with sexual dysfunction; prevalence may be as high as 60% All phases of sexual response are affected including decreased libido, erectile dysfunction, decreased vaginal lubrication, delayed orgasm, and ejaculatory delay. Erectile dysfunction and ejaculatory delay are worse with paroxetine compared to other SSRIs	Identify if other causes such as depression and medical causes are contributing to sexual dysfunction If possible, reduce dose or employ drug holidays but this approach has the risk of relapse Change to other SSRI may be considered Sildenafil or tadalafil, cyproheptadine, and bupropion may improve sexual dysfunction
Hyponatremia	SSRIs are associated with hyponatremia because of syndrome of inappropriate secretion of antidiuretic hormone (SIADH). Risk factors include old age, female gender, co-administration of drugs known to cause hyponatremia (diuretics, NSAIDs, ACE inhibitors etc), reduced glomerular filtration rate, and medical comorbidity	Hyponatremia is common in elderly. Monitoring is essential. Referral to specialists if serum level is <125 mmol/L
Serotonin syndrome	Nausea, vomiting, diarrhea, tremor, sweating, disorientation, restlessness, agitation, headache, increased heart rate, changes in blood pressure & temperature, twitching, tremors, myoclonic jerks, hyperreflexia, high fever, seizures, arrhythmias, agitation, confusion, delirium and even coma Can occur with very high doses of SSRIs or a combination of SSRIs in high doses	Stop the offending drugs immediately. Symptomatic management: benzodiazepines to treat agitation and/or seizures, intravenous fluids to maintain hydration, anti-emetic and anti-pyretic medications. In severe cases, cyproheptadine (8-12mg/day) is given orally
Weight gain	Known with all SSRIs although there may be initial weight loss. Paroxetine is associated with weight gain more than other SSRIs	If weight gain is significant, an attempt may be made to shift to another SSRI Lifestyle modification may be discussed Drugs such as topiramate may be tried
Suicidal behavior Discontinuation syndrome	SSRIs are associated with increased suicidal ideation and attempts in children Abrupt discontinuation may cause discontinuation syndrome, particularly with short-acting drugs (dizziness, nausea, vomiting, diarrhea, headache, fever, sweating, chills, insomnia, paresthesias, electric-shock-like sensations, anxiety, agitation, irritability, disorientation). Reported mostly with paroxetine. Typically occur within a week of discontinuation	Children on SSRIs should be monitored closely for emergence of suicidal thoughts Withdraw gradually. Taper SSRI by no more than 25% per week
Drug interactions	Fluoxetine, paroxetine and fluvoxamine inhibit cytochrome P-450. Inhibit the metabolism and elevate levels of drugs metabolized by this system	Caution should be exercised in combining certain SSRIs with drugs that are essentially metabolized by cytochrome P-450 system. SSRIs can elevate clomipramine level resulting in more side effects, particularly seizures and serotonin syndrome; this combination should be used judiciously and patients have to be monitored closely

CBT is either not available or the child cannot comply with CBT.

SSRIs in medically ill

SSRIs are generally safe in patients with cardiovascular

Table 14: Summary of treatment recommendations

- Establish a diagnosis of OCD. Assess for comorbid conditions such as depression and anxiety disorders and certain personality disorders. It is important to treat comorbid conditions since untreated comorbidity may contribute to poor outcome
- Where feasible, employ instruments such as the YBOCS to assess symptoms and their severity
- Psychoeducation of the patient and family about OCD, its course and treatment options is essential
- SSRIs and CBT are the first-line evidence based treatment options for OCD. In the Indian context, SSRIs are often the preferred first-line treatment options
- All SSRIs are equally effective but they differ in their side-effect profile. Choice of an SSRI for an individual patient is based on factors such as previous response, tolerability, acceptability, adverse effects, cost and drug interactions
- Most patients require higher than the usual antidepressant dose of an SSRI
- There is no convincing evidence that clomipramine is superior to SSRIs. Since clomipramine has many side-effects, it is not recommended as the first-line treatment option. It may be considered if patient fails to respond to 2 or more SSRIs
- An adequate trial of an SSRI (or clomipramine) should be for at least 12 weeks in optimum doses. Premature discontinuation is not recommended since most patients show improvement gradually over several weeks
- SSRI has to be continued at least for 1-2 years after remission. However, most patients may require indefinite continued treatment with a SSRI to prevent relapses particularly those with severe and chronic illness, past history of relapse on discontinuation and clinically significant residual symptoms. SSRIs are generally recommended to be continued at the same dose that resulted in improvement, unless the dose is not tolerated
- CBT alone may be recommended in mild to moderately ill patients if facilities for CBT exist. However, most severely ill patients benefit from a combination of an SSRI and CBT
- In partial responders and non-responders to SSRIs, addition of CBT is recommended as the first option. If CBT is not feasible, an atypical antipsychotic in low dose (risperidone and aripiprazole) may be added as an augmenting agent
- Inpatient treatment is recommended for severely ill, treatment resistant patients and for comorbid conditions such as severe depression
- ECT has no proven value in the treatment of OCD. There is inconsistent evidence regarding the efficacy of rTMS; hence it is not recommended for routine use
- DBS and ablative surgery may be considered in chronic, severely ill treatment refractory OCD patients

problems. Citalopram (? Escitalopram) is associated with arrhythmias but the risk is low and may not be clinically significant, but may be used with caution or avoided in those at risk for arrhythmias. SSRIs are widely used to treat depression in diabetes. They may improve diabetic parameters: improvement in HbA1c levels, reduced insulin requirement, enhanced insulin sensitivity and improved glycemic control. SSRIs are not hepatotoxic, but they need to be used in lower doses and with caution in the presence of significant hepatic impairment since all SSRIs are biotransformed in liver. All SSRIs are metabolized by the Cytochrome P450 system and fluoxetine, fluvoxamine, and paroxetine also significantly inhibit P450 enzymes. Therefore, these agents may potentially interfere with wide variety of other medications. Interactions with other drugs

need to be considered, particularly in elderly who are likely to be on many medications for other medical conditions. Citalopram / escitalopram and sertraline do not substantially inhibit P450 enzymes and therefore are associated with less drug interactions. All SSRIs are renally excreted. Depression is common in those with chronic kidney disease (CKD) and end stage renal disease (ESRD). If indicated SSRIs are the preferred antidepressants. SSRIs such as paroxetine, citalopram and escitalopram may have to be administered in lower doses in CKD and ESRD in the background of compromised renal functions. Since many patients with CKD and ESRD also suffer from cardiovascular disorders, citalopram (and perhaps escitalopram) may be used with caution since high doses of citalopram is associated with QTc prolongation and torsades de pointes.

Side Effects of SSRIs

The dosage of anti-obsessive drugs is usually higher than the usual anti-depressant dose; hence it is important for the clinician to discuss regarding the common side-effects. This issue is important because patients need to be on medications for a long duration. Sometimes an adjustment in dose or a switch in the time of the day the dose is taken is all that is needed. Rarely, stopping a particular medication and switching to another medication may be required. Side-effects of SSRIs and possible remedies are given in Table 13.

Summary

Recommendations are summarized in Table 14. The SSRIs and CBT are the first-line treatment options for OCD. CBT alone may be tried in mild to moderately ill patients if facilities for CBT are available. In severe OCD, a combination of SSRI and CBT is recommended. In the Indian context, SSRIs are the preferred first-line treatment for OCD because of limited resources for delivering CBT. SSRIs are effective, well tolerated and safe. For partial responders and non-responders to SSRIs, CBT is an effective augmenting agent followed by atypical antipsychotics. Although an attempt may be made to taper and stop SSRI after 1-2 years of sustained remission, most patients may require indefinite continued treatment with a SSRI. DBS and ablative surgery may be considered in chronic, severe OCD if other established treatment options have failed to produce any clinically significant improvement.

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