Human Journals **Review Article** 

September 2020 Vol.:19, Issue:2

© All rights are reserved by Sarita Jangra Bhyan et al.

# Synchronization between Pharmacotherapy and Psychotherapy: Frontier for OCD



Sarita Jangra Bhyan<sup>1\*</sup>, Seema Singh<sup>2</sup>, Prakhar Jain<sup>3</sup>, Kartikey Pathak<sup>3</sup>, Shubham Sarkar<sup>3</sup>, Saqib Rehan<sup>3</sup>

<sup>1</sup> Internship Coordinator, Assistant Professor, epartment of Pharmacy Practice, Teerthanker Mahaveer College of Pharmacy, Teerthanker Mahaveer University, Delhi Road, Moradabad, NH24, Uttar Pradesh, India. <sup>2</sup>
Associate Professor, Department of Psychiatry, Teerthanker Mahaveer Medical College & Research Centre, Teerthanker Mahaveer University, Delhi Road, Moradabad, NH24, Uttar Pradesh, India. <sup>3</sup> Pharm D Student, Department of Pharmacy Practice, Teerthanker Mahaveer College of Pharmacy, Teerthanker Mahaveer University, Delhi Road, Moradabad, NH24, Uttar Pradesh, India.

Submission: 20 August 2020
Accepted: 26 August 2020
Published: 30 September 2020

**Keywords:** Obsessive-compulsive disorder, Pharmacotherapy, Psychotherapy, Y-BOCS, EXRP

#### **ABSTRACT**

Objective: The OCD affects nearly 2-3% of the general population which results in suffering, functional impairment and economic burden to both patient and health-care system and is a cause of long term disability. OCD is a psychological disorder which is usually taken for granted by the patients as well as by their families until it gets serious. So, correct line of treatment and synchronization between pharmacotherapy and psychotherapy is being discussed. Method: A scientific and selective search is conducted on articles relevant to OCD and treatment related to OCD and various review articles been studied. Results: Combination of both psychotherapy and pharmacotherapy shown promising results among patients in comparison to individual therapy. SSRIs remain the drug of choice among majority of individuals and EXRP among psychotherapy shown better results in comparison to other therapies. Conclusion: OCD is a chronic disorder which needs to be treated as the symptom arises or before the worsening of condition and SSRIs shown good results among individuals suffering from OCD and augmentation therapy works as a support in patient with comorbidities and time to time session of psychotherapy mainly EXRP plays a vital role in betterment of the patient and performing both in a synchronized manner will help in reduction of symptom within lesser span.





www.ijppr.humanjournals.com

#### **Abbreviation:**

SSRIs- Selective Serotonin Reuptake Inhibitors

Y-BOCS- Yale Brown Obsessive Compulsive Score

OCD- Obsessive Compulsive Disorder

EXRP/ERP- Exposure and Response Prevention

**CBT-** Cognitive Behavioral Therapy

#### INTRODUCTION

Not all Microbial or Infectious diseases are chronic or the reason to worry, there are some psychological problems or diseases which causes lifetime disability and can become chronic if overlooked or taken for granted and OCD is one of those disorders.

Obsessions and Compulsions are the characteristics of Obsessive-compulsive disorder (OCD). Obsessions can be defined as unwanted and distressing thoughts, images, or urge whereas, on the other side, compulsions are repetitive behaviors or mental acts that a person feels compelled to perform, typically with a wish to resist. The lifetime prevalence of OCD is found to be 2 to 3% in the population and it is linked with significant suffering, economic burden and functional impairment to both health care systems as well as to the individual [1].

Initially, OCD was considered as an element of depression, that's why it was called "anankastic depression." In 1980s this concept was questioned, it was found that only antidepressants with serotonin-reuptake inhibition activity were effectual in curing obsessions and compulsions. There has been an important fundamental shift in last few years, including other neurotransmittorial systems in the presumed pathophysiological mechanisms implicating in OCD, such as dopamine, glutamate, noradrenaline and GABA. This prompts a theory that OCD might be an etiologically heterogeneous condition, in this way being influenced by a wide range of comorbidities, people with OCD as often as possible have extra psychiatric disorders associatively or eventually during their lifetime [2].

OCD is typically connected with dramatic disabilities in interpersonal and occupational functioning and is one of the most impairing medical conditions with considerable direct and indirect economic and societal costs [3]. Despite the fact that the etiology and pathophysiology of OCD remain indistinct, developing evidence proposes that this illness is associated with

dysfunctions in the orbitofronto-striato-pallido-thalamic circuitry including the dorsolateral prefrontal cortex (DLPFC), orbitofrontal cortex (OFC), medial prefrontal cortices, anterior cingulated gyrus, supplementary motor area (SMA), and basal ganglia [4,5,6].

OCD symptoms are usually same in children as well as in adults. In contrast to many adults, the younger ones mostly do not find anything unusual with them, as they think it's a better way to be away from any kind of infection, so they wash their hand much more than normal and do not able to distinguish between obsessional thought and normal thought, sometimes upon exaggeration of thoughts, these thoughts start causing more trouble and frighten them and their family members.

Practically, these obsessional thoughts are against the will of an individual and are like the parasite which feed upon their ability to think up properly. Quality of Life generally decreases due to this among OCD sufferers. Youth show risky peer relations, academic challenges, sleep problems and take an interest in less recreational exercises than coordinated friends <sup>[7]</sup>.

OCD has grown out to be a big topic as it become more prevalent over time or people usually suffer more from psychological disorders. OCD may have relapsing symptoms, highly probable that these thoughts intervene with daily deeds, treatment has been given since its start in various form whether pharmacological or non-pharmacological and also with various research in its field, treatment approaches has changed a bit over time from monotherapy to educating patient to Cognitive Behavioral Therapy, to augmentation with other agents [8].

Cognitive behavioral therapy and pharmacotherapy with selective serotonin reuptake inhibitors (SSRIs) are the choice of treatment for OCD. SSRIs have been shown to have better efficacy to placebo. Many OCD specialists support the utilization of higher and rapidly heightening dosages of SSRI for the treatment of OCD, when compared with different situations where antidepressants are efficacious, for example, other anxiety disorder and major depressive disorder. The American Psychiatric Association Practice Guidelines suggest higher target doses of SSRIs required in the treatment of OCD than required for depression. The clinical meanings of treatment resistance and refractory OCD require patients to fail to experience enhancement on multiple SSRI at the highest tolerated dose for a sufficient span (at least 2 months). OCD patients are treated with higher doses of SSRI contrasted with many different conditions before progressing to unconventional or enhancement treatment. However, controlled studies have not normally demonstrated benefit from higher doses of

SSRIs, which may have a higher side effect concern <sup>[9]</sup>. Current first-line treatment techniques for OCD incorporate high doses of selective serotonin reuptake inhibitors (SSRIs; e.g., citalopram, paroxetine) or clomipramine, a tricyclic antidepressant given for long duration of time and additionally combined with cognitive behavioral therapy <sup>[10]</sup>.

In OCD resistant patients, pharmacological therapy has been extended to incorporate serotonin-norepinephrine reuptake inhibitors, intravenous clomipramine or citalopram, or atypical antipsychotics <sup>[11]</sup>. In any case, even with such diverse therapeutic alternatives, up to 60% of patients with OCD are either unable to endure drug reactions or just partly improve following treatment, and are left with determined symptoms with enduring repercussions on their worldwide working and prosperity<sup>[6]</sup>.

Cognitive Behavioral Therapy lays foundation for the betterment of OCD patient. Observational assessment of the impacts of thought conquerment on thought recurrence and different factors have in this way become to the purpose for comprehending and treating OCD <sup>[12]</sup>. Psychological mediations have become undeniably an important slice of the treatment for this condition <sup>[13]</sup>. On quality of evidence, cognitive behavioral therapy (CBT) has been suggested by the AMERICAN PSYCHIATRIC ASSOCIATION <sup>[14]</sup> and the National Institute for Health and Care Excellence <sup>[15]</sup> as the treatment decision for OCD.

HUMAN

# MATERIALS AND METHODS

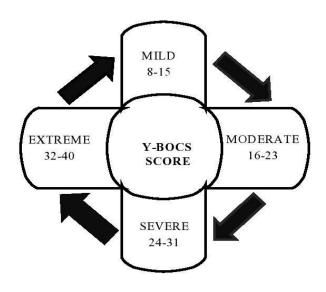
This review is focused on OCD treatment literature and efficacy of Pharmacotherapy and Psychotherapy when performed simultaneously. Therefore PubMed (Medline), Elsevier, Cochrane and Google Scholar databases were searched using the terms 'Obsessive-Compulsive Disorder' or 'Psychotherapy' or 'Pharmacotherapy' or 'Combination of Pharmacotherapy and Psychotherapy' or 'Current Treatment Trends in OCD'. Furthermore, we searched the currently available scientific literature.

#### RESULTS AND DISCUSSION

With all new research, studies, interventions, most effective and promising results are shown by patients after the use of SSRIs in any age group, which is liable to restore or balance the level of serotonin in the brain cells  $^{[16,17]}$ , treatment and dosing of drugs usually depends upon the severity of OCD, which is evaluated by either Y-BOCS Scale as shown in  $fig.1^{[18]}$  or partly by WHO-5 Well Being Scale which evaluate the grade of depression due to OCD  $^{[19]}$ , still lead to treatment failure if not used adequately.

#### ASSESSMENT SCALE

Yale brown Obsessive Compulsive Score (Y-BOCS) is used to assess the severity of disease, most commonly and widely used scale for OCD patients, severity is examined on the basis of score calculation as per their complaints.



**#Y-BOCS** severity checker for OCD Patients

# FIGURE NO. 1: SEVERITY IS CALCULATED ON THE BASIS OF SCORE AS SHOWN IN FIGURE

Various research findings suggest that synchronized treatment with both drug therapy and psychotherapy mainly ERP, plays a defining role in treating patient effectively within short span in comparison to one drug alone, [20,21] This be like treating patient with both hands from both side.

Use of mainly fluvoxamine or sertraline is suggested among SSRIs, fluoxetine, paroxetine is also used partly mentioned in *table 1 and 2*, and symptoms might be relapsing in many patients when SSRIs used alone, augmentation with neuroleptics showed promising results among OCD with comorbid disorders like tics rather than OCD alone, as suggested by various studies [22,23].

Most prominent psychological treatment came out among OCD sufferers is mainly, Exposure with response prevention (EX/RP), most of the researchers have placed it above medications alone as it involves dealing with patients psychology, involves interaction with patient, there is also lower relapse rate in comparison to medications, therapy generally includes 12-16 sessions, beginning with in-depth evaluation about patient triggers for obsessive thoughts, its compulsion in return to these thoughts and the amount of anxiety it causes while such thoughts pops out. Accordingly, exposure for patient has been planned and afterwards therapy started [24,25].

Several herbal and nutritional supplements emerges out as augmentation therapy for patient by various studies, like Vit. B12 and folate, zinc and selenium can be effective because of its antioxidant effects [26].

Effects of N-acetyl cysteine, Glycine, Myoinositol, St. John's wort, Milk thistle is also being studied and reviewed and found to be effective if used in a correct manner [27].

In case of treatment resistant OCD, studies suggest the increase in dose of SSRIs or improvement in psychotherapy suggested and augmentation with Anti Psychotics being prescribed, in case of its failure, use of SNRIs been suggested such as duloxetine and venlafaxine [28,29].

Use of clomipramine for OCD was being suggested before the use of SSRIs being introduced, still came in use in some cases, SSRIs are better choice of drug as it has better tolerability than clomipramine, as shown by various findings<sup>[30]</sup>.

Glutamate modulating drugs are nowadays being used in treatment of OCD and the prime topic of research in the field of OCD. Many Researches or studies are evaluating or examining the role of NMDA Receptor Antagonist (Memantine, ketamine) in OCD patients, some put forward with good results among OCD patients [31,32].

Invasive techniques like Neurosurgery, DBS (Deep Brain Stimulation), rTMS (Repetitive Transcranial Magnetic Stimulation) are required in very severe cases of anxiety caused by OCD [33,34].

#### **PHARMACOTHERAPY**

This is clearly a drug therapy in which drugs are prescribed to the patient following their diagnosis of OCD.

It involves:-

#### **MONOTHERAPY**

This therapy includes prescribing of a drug alone or therapy by just one drug for betterment of patient or for their improval of condition and reduction of symptoms.

TABLE NO. 1: DESCRIBE THE DOSE AND DRUG USED IN MONOTHERAPY FOR OCD

Drug (class)	Dose (depends upon severity)	Route	Side Effects	Grade (Risk: Benefit Ratio)
Fluvoxamine (SSRIs)	50-300 mg	Oral	Anxiety, Nervousness, Sweating, nausea, Decreased appetite, Somnolence	1
Sertraline (SSRIs)	50-100 mg	Oral	Sleepiness, tremor, Nervousness, nausea, Dizziness, insomnia	1
Clomipramine (TCAs)	25-150 mg	Oral	Dry mouth, insomnia, Memory problem, Vision changes	2
Fluoxetine (SSRIs)	20-40 mg	Oral	Nausea, headache, Anxiety, insomnia, Skin rashes, vasculitis	1
Paroxetine (SSRIs)	20-40 mg	Oral	Headache, anxiety, Insomnia, constipation, weakness	1

**SSRIs- Selective Serotonin Reuptake Inhibitors** 

**TCAs- Tricyclic Antidepressants** 

#### Note:-

#### **AUGMENTATION THERAPY**

#### (ANTIPSYCHOTICS AND VITAMINS)

This includes the use of combination of drugs rather than one drug alone to achieve the desired maximal effect.

TABLE NO. 2: DESCRIBE THE AUGMENTED DRUG TO BE USED WITH SSRIS

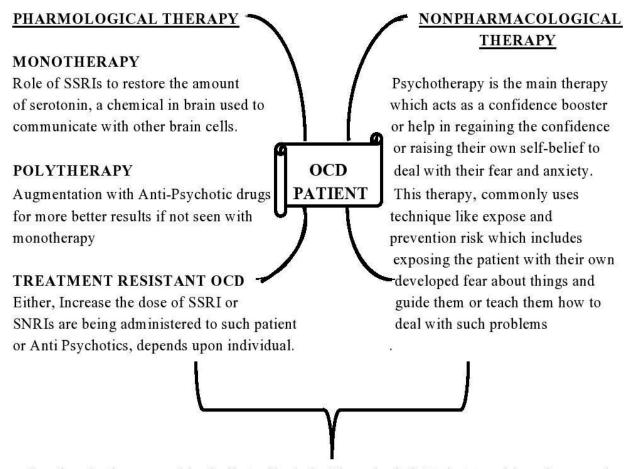
Drugs (class)	Dose (patient specific)	Route
Risperidone	0.5- 6 mg	Oral
(Anti- Psychotics)	0.5 0 mg	Office
Olanzapine	5-10 mg	Oral
( Anti- Psychotics)		
Vit. B12 and Folic Acid	HUMAN	Oral
( Vitamins )		O'ALL
Zinc and Selenium		Oral
( Essential Nutrients)		- Crui

Treating patient with OCD is like breaking or disturbing their own pool of thoughts or making them aware about their own thought process or helping them to manage their own self developed fear about certain things that is responsible for making them suffer or their suffering. The ultimate aim of treatment is to fill an individual with confidence to deal with such problem as lack of confidence, self-faith, and self-belief serve as a factor for OCD.

Pharmacotherapy helps in restoring chemicals in the brain and psychotherapy plays role in boosting confidence as shown in  $fig. 2^{[35]}$ .

<sup>\*</sup> Occurrence of side effect is not necessary among every individual, it varies differently among different individuals.

<sup>\*1-</sup> good (risk: benefit ratio), recommended



Synchronization or combined effect of both the Therapies help Patient to achieve the normal thought process soon and start showing its effect in a better way as both practically and pharmacologically, patient is being treated, and once the patient start regaining concept and start to control their own obsessional thoughts his symptom will reduce automatically.

# FIGURE NO. 2: DEPICTING THE ROLE OF BOTH PHARMACOLOGICAL AND NON PHARMACOLOGICAL THERAPY AND ABOUT ITS SYNCHRONIZATION

Contradictory results came from different studies performed among patients with OCD when both pharmacotherapy and psychotherapy performed together or in a coordinated manner in individual with OCD, some came out with result showing better results in patient when both are applied together, on the other hand few are against the result of adding both therapies together as alone CBT or monotherapy have shown equivalent results [36,37].

The better result can be shown if performed in a better effective manner, results have shown that individuals with comorbid condition like depression, have shown good results when both therapies are combined together [38,39].

Both therapies have their own distinctive role on an individual, ERP should be performed calmly as exposure triggers the patient that might scare them or make them anxious, so its needs to be done by an expert otherwise it will act like an exaggeratory factor for them [40].

Augmentation Therapy also plays a handy role on behalf as it will act as an extra agent in reduction of anxiety and symptom reduction.

#### **CONCLUSION**

This study concluded that various research has been done in this field, various new treatment approaches introduced with time, but SSRIs remains the treatment of choice or first line treatment among individual diagnosed with OCD due to better tolerability and better effectiveness, if that doesn't work then the dose of SSRIs are increased and CBT technique should be introduced for patient, in case of that failure, augmentation with several Anti-Psychotics prescribed and if symptom doesn't improve SNRIs shall be introduced and recent techniques include use of D-cycloserine, NMDA receptor antagonist.

Better effective results shown by various studies is by synchronization of both drug therapy ie pharmacotherapy with psychotherapy that helped patients a lot in improving their symptoms. If both therapy applied carefully under expert supervision and patient cooperation, then it'll come out to deliver the best result but every parameter should fulfill its requirement.

#### **ACKNOWLEDGEMENTS**

We would like to express our heartiest gratitude towards Teerthanker Mahaveer College of Pharmacy for giving us a golden opportunity to work on this article. Special thanks to the Principal of Teerthanker Mahaveer College of Pharmacy, for his support and vision.

Eventually, we would like to thank all who directly or indirectly helped us out in preparing this article.

#### REFERENCES

- 1. Taylor S (2011). Etiology of obsessions and compulsions: a meta-analysis and narrative review of twin studies. Clin Psychol Rev.;31:1361-1372.
- 2. Pallanti S, Grassi G, Sarrecchia ED, Cantisani A, Pellegrini M (2011). Obsessive-compulsive disorder comorbidity: clinical assessment and therapeutic implications. Front Psychiatry.;2:70.
- 3. Markarian Y, Larson MJ, Aldea MA, Baldwin SA, Good D, Berkeljon A, Murphy TK, Storch EA, McKay D (2010). Multiple pathways to functional impairment in obsessive-compulsive disorder. Clin Psychol Rev.:30:78-88.

- 4. Fineberg NA, Chamberlain SR, Hollander E, Boulougouris V, Robbins TW (2011). Translational approaches to obsessive-compulsive disorder: from animal models to clinical treatment. Br J Pharmacol.;164:1044-1061.
- 5. Milad MR, Rauch SL (2012). Obsessive-compulsive disorder: beyond segregated cortico-striatal pathways. Trends Cogn Sci.;16:43-51.
- 6. Berlim MT, Neufeld NH, Van den Eynde F (2013). Repetitive transcranial magnetic stimulation (rTMS) for obsessive-compulsive disorder (OCD): an exploratory meta-analysis of randomized and sham-controlled trials. J Psychiatr Res.;47:999-1006.
- 7. Lack CW (2012). Obsessive-compulsive disorder: Evidence-based treatments and future directions for research. World J Psychiatry.;2:86-90.
- 8. Fineberg NA, Gale TM (2005). Evidence-based pharmacotherapy of obsessive-compulsive disorder. Int J Neuropsychopharmacol.;8:107-129.
- 9. Bloch MH, McGuire J, Landeros-Weisenberger A, Leckman JF, Pittenger C (2010). Meta-analysis of the dose-response relationship of SSRI in obsessive-compulsive disorder. Mol Psychiatry.;15:850-855.
- 10. Stein DJ, Koen N, Fineberg N, Fontenelle LF, Matsunaga H, Osser D, Simpson BH (2012). A 2012 evidence-based algorithm for the pharmacotherapy for obsessive-compulsive disorder. Curr Psychiatry Rep.;14:211-219.
- 11. Abudy A, Juven-Wetzler A, Zohar J (2011). Pharmacological management of treatment-resistant obsessive-compulsive disorder. CNS Drugs.;25:585-596.
- 12. Purdon C (2004). Empirical investigations of thought suppression in OCD. J Behav Ther Exp Psychiatry.;35:121-136.
- 13. Knopp J, Knowles S, Bee P, Lovell K, Bower P (2013). A systematic review of predictors and moderators of response to psychological therapies in OCD: do we have enough empirical evidence to target treatment?. Clin Psychol Rev.;33:1067-1081.
- 14. American Psychiatric Association (2007). Practice guideline for the treatment of patients with obsessive—compulsive disorder. Arlington, VA: American Psychiatric Association.
- 15. National Institute for Health and Clinical Excellence (2006). Obsessive-compulsive disorder: Core interventions in the treatment of obsessive-compulsive disorder and body dysmorphic disorder. Leicester, London, UK: The British Psychological Society and the Royal College of Psychiatrists.
- 16. Soomro GM, Altman D, Rajagopal S, Oakley-Browne M (2008). Selective serotonin reuptake inhibitors (SSRIs) versus placebo for obsessive compulsive disorder (OCD). Cochrane Database Syst Rev.;1:CD001765.
- 17. Kotapati VP, Khan AM, Dar S, Begum G, Bachu R, Adnan M, Zubair A, Ahmed RA. (2019). The Effectiveness of Selective Serotonin Reuptake Inhibitors for Treatment of Obsessive Compulsive Disorder in Adolescents and Children: A Systematic Review and Meta-Analysis. Front Psychiatry.;10:523.
- 18. Castro-Rodrigues P, Camacho M, Almeida S, Marinho M, Soares C, Barahona-Corrêa JB, Oliveira-Maia AJ. (2018). Criterion Validity of the Yale-Brown Obsessive-Compulsive Scale Second Edition for Diagnosis of Obsessive-Compulsive Disorder in Adults. Front Psychiatry.;9:431.
- 19. Topp CW, Østergaard SD, Søndergaard S, Bech P (2015). The WHO-5 Well-Being Index: a systematic review of the literature. Psychother Psychosom.;84(3):167-176.
- 20. Foa EB (2010). Cognitive behavioral therapy of obsessive-compulsive disorder. Dialogues Clin Neurosci.;12(2):199-207.
- 21. Simpson HB, Foa EB, Liebowitz MR, Ledley DR, Huppert JD, Cahill S, Vermes D, Schmidt AB, Hembree E, Franklin M, Campeas R, Hahn CG, Petkova E. (2008). A randomized, controlled trial of cognitive-behavioral therapy for augmenting pharmacotherapy in obsessive-compulsive disorder. Am J Psychiatry.;165(5):621-630.
- 22. Thamby A, Jaisoorya TS (2019). Antipsychotic augmentation in the treatment of obsessive-compulsive disorder. Indian J Psychiatry.;61(Suppl 1): S51-S57.
- 23. Kim D, Ryba NL, Kalabalik J, Westrich L (2018). Critical Review of the Use of Second-Generation Antipsychotics in Obsessive-Compulsive and Related Disorders. Drugs R D.;18(3):167-189.
- 24. Hezel DM, Simpson HB (2019). Exposure and response prevention for obsessive-compulsive disorder: A review and new directions. Indian J Psychiatry.;61(Suppl 1): S85-S92.
- 25. Gillihan SJ, Williams MT, Malcoun E, Yadin E, Foa EB (2012). Common Pitfalls in Exposure and Response Prevention (EX/RP) for OCD. J Obsessive Compuls Relat Disord.;1(4):251-257.

- 26. Kuygun Karcı C, GülCelik G (2020). Nutritional and herbal supplements in the treatment of obsessive compulsive disorder. Gen Psychiatr.;33(2):e100159.
- 27. Oliver G, Dean O, Camfield D, Blair-West S, Ng C, Berk M, Sarris J. (2015). N-acetyl cysteine in the treatment of obsessive compulsive and related disorders: a systematic review. Clin Psychopharmacol Neurosci.;13(1):12-24.
- 28. Skapinakis P, Papatheodorou T, Mavreas V (2007). Antipsychotic augmentation of serotonergic antidepressants in treatment-resistant obsessive-compulsive disorder: a meta-analysis of the randomized controlled trials. Eur Neuropsychopharmacol.;17(2):79-93.
- 29. Mishra B, Sahoo S, Mishra B (2007). Management of treatment-resistant obsessive-compulsive disorder: An update on therapeutic strategies. Ann Indian Acad Neurol;10:145-53
- 30. Kellner M (2010). Drug treatment of obsessive-compulsive disorder. Dialogues Clin Neurosci.;12(2):187-197.
- 31. Marinova Z, Chuang DM, Fineberg N (2017). Glutamate-Modulating Drugs as a Potential Therapeutic Strategy in Obsessive-Compulsive Disorder. Curr Neuropharmacol.;15(7):977-995.
- 32. Pittenger C (2015). Glutamatergic agents for OCD and related disorders. Curr Treat Options Psychiatry.;2(3):271-283.
- 33. Janardhan Reddy YC, Sundar AS, Narayanaswamy JC, Math SB (2017). Clinical practice guidelines for Obsessive-Compulsive Disorder. Indian J Psychiatry.;59(Suppl 1): S74-S90.
- 34. Greenberg BD, Rauch SL, Haber SN (2010). Invasive circuitry-based neurotherapeutics: stereotactic ablation and deep brain stimulation for OCD. Neuropsychopharmacology.;35(1):317-336.
- 35. Foa EB, Franklin ME, Moser J (2002). Context in the clinic: how well do cognitive-behavioral therapies and medications work in combination?. Biol Psychiatry.;52(10):987-997.
- 36. Albert U, Di Salvo G, Solia F, Rosso G, Maina G (2018). Combining Drug and Psychological Treatments for Obsessive-Compulsive Disorder: What is the Evidence, When and for Whom. Curr Med Chem.;25(41):5632-5646.
- 37. Saxena S (2011). Pharmacotherapy of compulsive hoarding. J Clin Psychol.;67(5):477-484.
- 38. Cuijpers P, Sijbrandij M, Koole SL, Andersson G, Beekman AT, Reynolds CF 3rd (2014). Adding psychotherapy to antidepressant medication in depression and anxiety disorders: a meta-analysis. World Psychiatry.;13(1):56-67.
- 39. Skapinakis P, Caldwell D, Hollingworth W, Bryden P, Fineberg N, Salkovskis P, Welton N, Baxter H, Kessler D, Churchill R, Lewis G (2016). A systematic review of the clinical effectiveness and cost-effectiveness of pharmacological and psychological interventions for the management of obsessive compulsive disorder in children/adolescents and adults. Health Technol Assess;20(43)1-392.
- 40. Storch EA, Mariaskin A, Murphy TK (2009). Psychotherapy for obsessive-compulsive disorder. Curr Psychiatry Rep.;11(4):296-301.