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REVIEW

EFFECTIVENESS OF PSYCHOLOGICAL AND PHARMACOLOGICAL TREATMENTS FOR OBSESSIVE-COMPULSIVE DISORDER: A QUALITATIVE REVIEW

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ABSTRACT:

Obsessive-compulsive disorder (OCD) is a relatively common disorder, most of the time under diagnosed and under treated despite the existence of effective treatments. OCD can be discriminated from other disorders, having obsessive or compulsive features on the basis of obsession content or the characteristics of the compulsions. Selective serotonin reuptake inhibitors (SSRIs) and cognitive-behavioral therapy (CBT) seem to be proven treatments for OCD. They cause a significant reduction in symptoms, although complete remission in clinical cases is not seen commonly. Long-term drug treatment with cognitive behavioral therapy has shown better results than drug alone.

Keywords: Obsessive-Compulsive Disorder, Selective serotonin reuptake inhibitors, Cognitive behavioral therapy, Obsessions, Compulsions.

INTRODUCTION

Obsessive-compulsive disorder (OCD) is the most common mental disorder in all over the world. The disorder is often chronic and disabling, with an estimated lifetime prevalence of 2.3% (Attiullah *et al*., 2000). According to American Psychiatric Association, 2000 presence of thoughts, impulses and disturbing images that cause suffering, annoyance or discomfort, associated with repetitive compulsions (behaviors or thoughts) to which the patient is impelled in response to an obsession, with the aim of reducing the discomfort caused, are all regarded as OCD. Other psychological disorders like depression, phobias, panic attacks, generalized anxiety, etc. are often present along with it. Their presence makes treatment more complicated (Keeley *et al*., 2008).

Onset of OCD can be variable often in late adolescence or young adulthood, even in childhood. The course is chronic, waxes and wanes in severity, often in response to stress (Freeman *et al*., 1994). The mean age for the onset of OCD ranges from 22 to 36 years. Only 15 percent of patients older than 35 years develop this condition (Maj M *et al.,* 2002). Males seem to be effected at earlier age. With effective treatment, the severity of symptoms can be reduced, but typically some symptoms remain (Maj M *et al* 2002). On average, OCD patient waste 9 years in visiting three to four doctors before they are properly diagnosed & 17 years from the onset of OCD symptoms to receive proper treatment. Although adequate treatments exist, OCD is under diagnosed and under-treated. More than half of OCD patients (59.5%) in the worldwide receive no treatment at all. Due to improved advance approaches in pharmacologic treatment, many patients with OCD can be treated in primary care settings (Baer *et al*., 1990).

OCD is characterized by obsessions and compulsions but these symptoms are present in

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other disorders too. Obsessions are characterized by recurring thoughts, urges or images. In OCD these are experienced as unknown, disturbing and distressing. Compulsions characterized by repetitive behaviors (rituals) that patients feel compelled to perform (American Psychiatric Association, 2000).

Typical obsessions include preoccupation with contamination, unacceptable violent or sexual thoughts, doubting, concern about asymmetry or imperfections, and thoughts that something will go wrong.

Typical rituals include washing, cleaning, checking, counting, repeating, and arranging. Some patients may have obsessions without any compulsions. Often the compulsive behaviors are simply not recognized, as they can be mental acts or very subtle behaviors. Sometimes an OCD patient might need to have specific thoughts or mental images in order to counter an obsession e.g. the representation of a relative being harmed can be countered by picturing something good happening to that person. OCD Patients generally perform rituals to reduce anxiety created by thoughts of fearful consequences. Furthermore, some patients perform rituals simply because of a general sense of foreboding or because it feels wrong if they do not perform it (American Psychiatric Association, 2000).

OCD patients generally have good insight. They recognize that their fears are unrealistic, yet, their distress compels them to perform rituals. In their awful moments, insight may waver and fears may seem not only realistic but inevitable unless the ritual is performed. However in severe cases of OCD insight may be lost but it must have been present at some time to meet diagnostic criteria. Occasionally it is normal to have unwanted thoughts or perform repetitive or superstitious behaviors accompanied by transient anxiety, but an OCD diagnosis requires that symptoms cause marked distress, be time consuming (≥1 hour/day), or significantly interfere with functioning (Foa *et al*., 2005).

Approximately 6% of OCD patients have obsessive-compulsive personality disorder (OCPD). Although they have some similarities, most of the cases can be distinguished. OCPD Patients may be preoccupied with details and orderliness, perfectionist, overly devoted to work and productivity, overly conscientious, inflexible about moral and ethical issues , incapable of discarding insignificant objects, or may need to have things done their own way. Patients of OCD may have some of these characteristics, but usually in a less global manner. Contrary in OCPD, patients with OCD have intrusive obsessive thoughts and ritualized compulsive behaviors (Katz and DeVeaugh ,1990).

Pharmacological Treatments

First-line treatments

In this group, drugs are selected on the basis of having minor invasiveness with widespread availability and easy dosing schedule. Selective serotonin reuptake inhibitors (SSRIs) fulfill all of these criteria and studies have shown good results. SSRIs are most effective pharmacological treatments for OCD. Their effectiveness in OCD is unique. Other antidepressants are usually not effective in OCD, and there are no other effective pharmacological monotherapy. Furthermore, compared to SSRI treatment of other disorders, SSRI treatment of OCD usually takes longer for response to begin. Higher doses are also required (Mundo *et al*., 2000). Most of studies with SSRIs show that patients should be treated with the maximum tolerated doses for a minimum of 12 weeks although some evidences show that additional improvements may occur later. For this reason many guidelines recommend prolonged treatment at least for 1 to 2 years (Schruers *et al*., 2005, Greist *et al*., 2003, The Expert Consensus Panel For Obsessive-Compulsive Disorder 1997).

Several double-blind studies including placebo-controlled have shown positive results with fluvoxamine (Perse *et al*., 1987; Goodman *et al*., 1989; Jenike *et al*., 1990; Hollander *et al*., 2003), fluoxetine

(Montgomery *et al*., 1993; Tollefson *et al*., 1994) sertraline (Chouinard *et al*., 1990; Greist *et al*., 1995; Jenike *et al*., 1990), paroxetine (Zohar and Judge, 1996, Hollander *et al*., 2003; Kamijima *et al*., 2004), citalopram (Montgomery *et al*., 2001) and more recently included escitalopram (Stein *et al*., 2006). Four of these, clomipramine, fluoxetine, fluvoxamine, and sertraline, have also been approved for treatment of pediatric OCD (Pallanti *et al*., 2002). The Food and Drug Association (FDA), with the exception of the newer citalopram and escitalopram, has approved all SSRIs for use in adults with OCD. Although some of the mentioned drugs were not tested in a controlled, fixed-dose method to evaluate optimal doses (e.g. fluvoxamine).

One of the first SSRIs to be tested in the treatment of OCD was Fluvoxamine. Most studies of fluvoxamine in OCD showed a response at ≥6 weeks, and as with other SSRIs, showed improvement and more patients responding to it over time.

Fluoxetine has been extensively studied in OCD at three fixed doses (20 mg/day, 40 mg/day, and 60 mg/day) and is clearly effective at 40 and 60 mg/day. Efficacy at 20 mg/day is also shown in some studies. Higher doses, especially 80 mg/day, are used frequently in clinical practice, and there are a few studies at 80 mg/day which were also successful in terms of efficacy and tolerability. Obsessions and compulsions were found to respond to fluoxetine treatment independently of any antidepressant effect (Mundo *et al*., 2000).

Various large, randomized placebo-controlled trials have demonstrated the effectiveness of paroxetine in OCD. In one study of paroxetine in three fixed doses, found that 40 and 60 mg/day were more effective than placebo, but 20 mg/day was not effective. The effectiveness of sertraline in OCD has been demonstrated in large, randomized, placebo-controlled trials.

Citalopram appears to be effective in OCD based on the research available to date, which includes one large, randomized, placebo-controlled trial. This trial found that citalopram was more effective than placebo at all doses tested (20, 40, and 60 mg/day) (Montgomery *et al*., 2001). The efficacy of citalopram has been supported by open-label trials.

Evidence supporting the efficacy of SSRIs in OCD is substantial. A single SSRI trial will provide clinically meaningful relief for 40% to 60% of OCD patients. However, drugs rarely bring about remission. Response in OCD treatment is generally defined as a reduction of 25% to 35% in OCD symptoms, and average reduction found is usually in this range. No SSRI has been proven to be more effective than others in OCD. However, individual patients may respond more satisfactorily to one particular drug than to another.

Second-line treatments

Second line drugs are used for drug-resistant patients with OCD (Pallanti and Quercioli, 2006) , otherwise they are similar to first-line ones in terms of the strength of evidence, availability, invasiveness, and complexity of administration. These treatment stages include clomipramine, anti-psychotics, pindolol and megadoses of one of SSRI. Still number of researchers favors clomipramine and antipsychotics.

Clomipramine is a tricyclic anti-depressant (TCA) and serotonin norepinephrine reuptake inhibitors (SNRI). It was the first drug that was found to be effective in OCD. Its effectiveness has been firmly established in adults since the first finding was more than 35 years ago (Fernandez *et al.,* 1967, Dell'osso *et al.,* 2006). In 1989 the first drug which was approved by the FDA for OCD was clomipramine. Randomized, controlled trials have shown clomipramine to be superior when compared with placebo. Although SSRIs have greater tolerability but clomipramine is more effective in OCD.

Several meta-analyses have shown that clomipramine has greater effect size when compared with SSRI's (Cox, 1993; Piccinelli *et al*., 1995; Stein *et al*., 1995; Abramowitz, 1997; Ackerman and Greenland, 2002). However, a few head-to-head studies show two drugs to be equal in efficacy. Several theories explain this noticeable dominance. In particular pharmacodynamic properties of clomipramine are the main reason. This includes desmethylclomipramine (its main metabolite) having noradrenaline re-uptake inhibition effect (Maj *et al*., 1982), and the parent drug having dopamine-blocking activity (Austin *et al*., 1991).

Side-effects of clomipramine includes anticholinergic (constipation, blurred vision, dry mouth and drowsiness), antihistaminergic (weight gain & drowsiness) and anti-α-adrenergic (dizziness and reduced blood pressure). These side effects make it a second-line treatment choice (Canadian Psychiatric Association 2006).

Double-blind, placebo-controlled studies of treatment-resistant OCD patients with antipsychotics haloperidol, risperidone, olanzapine and quetiapine have proved their effectiveness (Kaplan *et al*., 2003). Meta-analyses by Skapinakis *et al*. in 2007 and Fineberg *et al*. in 2006 have established the efficacy of risperidone and haloperidol.

Third-line treatments

Although third-line treatments comprised of same strategies as in 1st and 2nd line treatment with exception of being more invasive (I/V infusion of clomipramine) or other considerable risks like drug abuse, tolerance or development of withdrawal reactions as with oral morphine. These reasons make this treatment option to be used infrequently in the daily clinical practice. The effects of intravenous clomipramine were investigated by (Fallon *et al*., 1998 and Koran *et al*., 1998). Their studies showed significant improvement.

Fourth-line treatments

Treatment at this stage included those therapeutic approaches, which are tested only in treatment resistant OCD patients. These are either the less-invasive and non-complex methods widely available but are not supported by controlled trials. They are so-called 'heroic drug strategies. Or less-invasive and moderately complex methods which are supported by controlled trials but not widely available. Thirdly more-invasive with moderately complex methods that are widely available but not supported by controlled trials (Leonardo *et al*., 2007).

These drug combinations consisted of an SSRI, clomipramine or venlafaxine. Another drug is added which action on another neurotransmitter system. These include dopaminergic "amilsulpiride" (Metin *et al*., 2003), serotonergic "clomipramine" (Browne *et al*., 1993), triptophan (Rasmussen *et al*., 1984), triptans (Stern *et al*., 1998), fenfluramine (Judd *et al*., 1991) and perospirone (Matsunaga *et al*., 2006), noradrenergic (Fontenelle *et al*., 2005), glutamatergic (Coric *et al*., 2003 and Coric *et al*., 2005), memantine (Pasquini *et al*., 2006 and Poyurovsky *et al*., 2005), lamotrigine (Kumar and khanna, 2000) and topiramate (Hollander and Dell'osso, 2006 and Rubio *et al*., 2006). GABAergic (Deltito, 1994) and nicotinic receptors (Lundberg *et al*., 2004 and Pasquini *et al*., 2005) or ion channels (Iwata *et al*., 2006) and oxcarbazepine (Baird *et al*., 2003 and Mcmeekin *et al*., 2002). Monotherapy with high-dose venlafaxine, a similar strategy based on tapping an additional non-serotonergic neurotransmitter system (i.e., the noradrenergic system) was also employed successfully in open-label trials (Hollander *et al*., 2003 and Marazziti *et al*., 2003).

Cognitive–Behavioral Therapy

In Cognitive behavioral therapy (CBT), patients have to face his fear without performing their compulsive practice. For example, a patient having a fear for microbes will contact a contaminated object but not going to wash hands. The explanation for this

therapy is to expose and prevent the reaction or practice. The exposure can be either to actual objects or situations to which patient has false believes, or imaginary pictures of those. If a patient has obsessions but no typical compulsions, exposure is still a successful and important component. Cognitive aspect of the treatment focus on correcting errors of assessing danger and their feelings of responsibility. Cognitive components can be important and are frequently used to encourage patients to attempt exposures or to make them to tolerate it without performing their usual rituals. There is not much sufficient evidence for cognitive therapy to be effective if it does not include the exposure of fear. Therapy that emphasizes the cognitive component seems to be successful if it includes behavioral experiments.

CBT is as effective as SSRIs in the management of patients with OCD (Bloch *et al*., 2006). These views are shared by various experts who agreed for labeling CBT as one of the first therapeutic approach for OCD (The Expert Consensus Panel For Obsessive-Compulsive Disorder, 1997). On the other hand few studies have evaluated the effectiveness of CBT as an amplification strategy for drug resistant OCD patients (Simpson *et al*., 1999;Kampman *et al*., 2002 and Tolin *et al*., 2004). Tolin *et al*., in 2004 found that CBT incorporating exposure and response prevention is helpful for drug resistant OCD patients. Anderson and Booker (2006) have described the effectiveness of psychotherapy when combined with pharmacotherapy, psychoeducation or social skills training. Clomipramine when combined with CBT has proved its efficacy in OCD (Edna *et al*., 2005). Barbara and Martine (2009) have mentioned that CBT alone or when combined with pharmacotherapy like SSRI proves to be more effective in improving the condition of OCD patient when SSRI are used alone. Katharina *et al* (2010) favours psychotherapy to be the first treatment option for OCD.

CBT is believed to be an established treatment for OCD. It appears to be equal to or perhaps superior to pharmacotherapy (Ana *et al*., 2008). CBT is a suitable first-line treatment for OCD. It can be used in both ways i.e. either instead of or in addition to a SSRI. This is based on the motivation of the patient to involve himself in therapy or to take medication. One more important point in managing OCD is to diagnose other mental disorders, if present. For instance in depression as a co morbidity, a SSRI would be a good first-choice treatment, also because patient might not participate in behavioral therapy. On other hand if a patient starts pharmacological treatment but has an inadequate response, CBT should be attempted. Likewise, if CBT is tried out in patient but he is not capable to complete assignments, SSRI trial is indicated. CBT is also valuable for those patients who do not wish to continue pharmacological treatment, as there are evidences that it helps to prevent relapses. Additional studies are needed for CBT to be an augmented approach in patients who are SSRI resistant.

Although individual CBT is quite common, there are evidences that group therapy is more effective. CBT sessions should be weekly or preferably more frequently until significant clinical improvement is achieved. Once a significant improvement is seen clinically, sessions can be reduced in frequency. For relapse prevention it is important for patient to be the part of CBT. When a course of CBT is completed, successful patients can be placed on booster sessions if symptoms reoccur.

CONCLUSION

Since OCD is often runs a chronic course hence a long-term treatment is required. Those SSRIs that have been studied in long-term trials have been shown to be effective beyond the acute treatment time period. Published Expert Consensus Guidelines highly recommend that OCD treatment should be continued for 1-2 years to prevent relapse, and usually longer treatment is needed. When this

prolonged treatment is completed, dose can be slowly taper down to see if symptoms are under good control. In many cases, discontinuation of the medication is not possible. In addition, if a patient has two or more serious relapses, lifelong medication treatment is required.

Studies show lower relapse rates for CBT when compared with medications, if treatments are discontinued. This is especially true when the CBT includes consideration of relapse prevention. There are some evidences that CBT when combined with SSRIs may help in preventing relapses. Definitive research is still required yet, it seems practical to recommend CBT for patients in need of long-term pharmacological treatment.

Treatment for patients with OCD has improved noticeably in recent years. Primary health care physicians may be the first professionals consulted by OCD patients. They can be a source of appropriate pharmacologic treatment as well as therapeutic guidance along with CBT. Psychotherapy remains the first line treatment for mild to moderate symptoms, whereas pharmacotherapy is used for severe or those case who proved to be drug resistant disorders.

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