Editorial

Obsessive-Compulsive Disorder: Towards Better Diagnosis and Outcomes

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INTRODUCTION

Diagnosis of OCD is made if obsessions and/or compulsions are present and cause marked distress, are time consuming (More than 1 h per day), or significantly interfere with the person's routine social and/or occupational functioning (APA, 2000). Most patients with OCD have good insight in to their illness and perceive that obsessions and compulsions are unreasonable or excessive. However, the diagnostic and statistical manual of mental disorders, 4th edition (DSM-IV) field trial has demonstrated that nearly a third of OCD patients have poor insight (Foa, et al. 1995). To reflect the findings of the field trial, the DSM-IV added a new OCD specifier: "with poor insight". Insight may also vary across situations and times. For example, a person may recognize the unreasonableness or irrationality of contamination fears while discussing with the therapist in his office, but may exhibit poor insight when actually performing compulsions because of excessive anxiety. Insight could be poor in children with OCD because they may lack sufficient cognitive maturity to make this judgment. In essence, although good insight into symptoms is characteristic of OCD, a substantial minority of patients may also have somewhat poor insight. It is important to recognize this because many OCD patients with poor insight are often misdiagnosed as 'psychotic' and treated inappropriately with antipsychotic drugs (Math and Janardhan, 2007).

According to the World Health Organization, OCD is among the 10 most disabling medical conditions worldwide (Murray and Lopez, 1996). Its lifetime prevalence is 2-3% (Karno, et al. 1988 and Weissman, et al. 1994). The findings of such high rates of OCD in epidemiological studies resulted in OCD being labeled a "hidden epidemic" (Hollander, 1997). It is twice as prevalent as schizophrenia and bipolar disorder, and the fourth most common psychiatric disorder (Karno, et al. 1988). OCD is associated with significant disability, poor quality of life and burden on families (Steketee, 1997 and Hollander, et al. 1997). It is also highly comorbid with other psychiatric conditions such as depression, anxiety disorders, tic disorders, hypochondriasis, body Dysmorphic Disorder (BDD) and eating disorders (Abramowitz, 2004 and Denys, et al. 2004).

The onset of OCD is generally in late adolescence or young adulthood, although it can begin at any age, and childhood onset is not uncommon. In addition, the onset is earlier in males than females. The course is chronic and waxes and wanes in severity, often in response to stress. Furthermore, the coexistence of other psychiatric disorders with OCD including mood disorders, anxiety and psychotic disorders, besides Obsessive-compulsive related disorders (OCRDs), is not infrequent with depressive symptoms being the most common comorbid syndrome both in previous and recent clinical studies (Dell'Osso, et al. 2006).

Obsessive-Compulsive Related Disorders: Phenomenology and OCD-Related Features

Obsessive-compulsive related disorders (OCRDs) are a group of disorders with overlapping symptoms and compulsive qualities that are otherwise distinct disorders from OCD (Hollander, 1993). Over a decade of study and scientific acquisitions have led a DSM-V (Diagnostic and Statistical Manual for Mental Disorders) task force to consider the important change of separating OCD from the anxiety disorders and placing it in an autonomous category - the OCRDs (Kohn, et al. 2004).

A variety of similarities have been observed among a number of psychiatric and neuropsychiatric conditions and OCD. OCRDs, in fact, share many features with OCD in terms of symptom profile and phenomenology, associated features, biology and treatment response (Hollander, 1993 and Kohn, et al. 2004). Phenomenologically, patients with OCRDs manifest features of both compulsivity and impulsivity, respectively driven in the need to decrease the discomfort associated with rituals and in the need to maximize pleasure. From a clinical point of view, the onset of OCRDs in adolescence, the frequent comorbidity between OCD and OCRDs and a preferential response of OCRDs to serotonergic agents represent an important link between OCD and related disorders. OCD and OCRDs may be caused by differential dysregulation of 5-HT pathways in different brain areas (Dell'Osso, et al. 2007).

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OCRDs may be divided into distinct categories as indicated in (Table 1). OCD is thought to be the prototype for this group of disorders.

Table 1: Obsessive-Compulsive Related Disorders (OCRDs):

Cluster	Specific disorders
Somatoform disorders	Hypochondriasis; body dysmorphic disorder
Eating disorders	Anorexia nervosa; bulimia; binge eating disorder
Impulse control disorders	Pathological gambling; trichotillomania; kleptomania; compulsive-impulsive shopping; compusive-impulsive sexual behaviors; compulsive-impulsive internet usage disorder
Neurologic cluster disorders	Sydenham's chorea; autism; Asperger's syndrome; Tourette's syndrome
Other disorders	Borderline personality disorder; obsessive-compulsive personality disorder; depersonalization disorder; self-injurious behaviors

The somatoform disorders group of OCRDs is characterized by a preoccupation with bodily appearance or sensations and with a series of compulsive behaviors performed to decrease the anxiety brought on by these preoccupations. Hypochondriasis and Body Dysmorphic Disorder (BDD) are included within this group (Dell'Osso, et al. 2007).

The eating disorder cluster of OCRDs includes anorexia nervosa, bulimia and binge eating disorder. Patients suffering from these disorders, frequently associated with dangerous medical complications, refer obsessions about food, body image and food preparation. In addition, they have clear-cut rituals regarding diet, exercise, food preparation and eating (Dell'Osso, et al. 2007).

The impulse-control disorders group of OCRDs includes many different disorders (i.e. pathological gambling, kleptomania, compulsive-impulsive sexual behaviors etc.) characterized by (i) the failure to resist an impulse or to perform some act that is harmful to the individual or others; (ii) an increasing sense of arousal or tension prior to committing or engaging in the act; and (iii) an experience of either pleasure, gratification, or release of tension at the time of committing the act (Goodman, et al. 1990).

The neurologic conditions of OCRDs include Sydenham's chorea, autism, Asperger's syndrome and Tourette's syndrome. These disorders involve little obsessional content and mostly manifest motoric and repetitive symptoms. The development of stereotypic movements is supposed to be determined by the pathophysiologic involvement of the basal ganglia present in these disorders. Besides these major groups of disorders, other specific conditions, such as borderline personality disorder or depersonalization disorder have been related to OCD (Hollander, 1993 and Kohn, et al. 2004).

Differential Diagnosis:

Obsessive-compulsive disorder is sometimes difficult to diagnose because of its phenomenological similarities with other disorders. In generalized anxiety disorder (GAD), worries are about real life circumstances (e.g. financial difficulties, family troubles etc.) (APA, 2000). They are not ego-dystonic although they may be excessive. Moreover, worries in GAD are not associated with compulsions whereas most OCD patients have associated mental or motor compulsions. In phobias, fears are circumscribed and related to specific triggers and there are no compulsive behaviors. OCD patients often experience panic attacks in response to obsessions, but panic attacks in panic disorder occur spontaneously. Persistent brooding or ruminations about negative events in life or about worthlessness are common in depression, but they not ego-dystonic (Math and Janardhan, 2007).

Illness fears in OCD (Somatic obsessions) may be difficult to differentiate from those in hypochondriasis (Fallon, et al. 2000). In hypochondriasis, a fear of an illness is based on misinterpretation of somatic sensations and insight is somewhat poor. Obvious presence of compulsions favors a diagnosis of OCD, but repetitive behaviors of hypochondriasis (e.g. checking one's body or checking with others) may simulate compulsions of OCD. In body dysmorphic disorder (BDD), preoccupation with an imagined or slight defect in appearance (e.g. large nose) is the main symptom and this preoccupation is very similar to an obsession. However, insight is more frequently impaired in BDD than in OCD (Allen and Hollander, 2000). Tics are easy to differentiate from compulsions because tics are not preceded by obsessional concerns. However, it is sometimes difficult to differentiate complex motor tics from compulsions. In the former, there is a physical urge to perform whereas in the latter the urge is mental. Other disorders such as trichotillomania (Compulsive hair pulling), kleptomania, pathological gambling together called impulse control disorders too have a compulsive element, but compulsions in OCD, unlike in impulse control disorders, generally do not have gratifying element (Math and Janardhan, 2007).

Treatment of Obsessive-Compulsive Disorder: General Lines of Intervention

Before 1980, the prognosis for OCD was poor and the discovery of effective drug therapies revolutionized the outlook for sufferers. Intensive pharmacological investigation has demonstrated that OCD responds selectively to drugs that inhibit the synaptic reuptake of serotonin (SSRIs), that is clomipramine and the selective SSRIs. Medications that lack these properties, such as the standard tricyclic antidepressants and the monoamine oxidase inhibitors, have been shown to be ineffective in randomized, controlled trials (Zohar, et al.

2000). Treatment studies with benzodiazepines, lithium and electroconvulsive therapy have given inconsistent results (Pallanti, et al. 2002).

A single SSRI trial generally provides clinically meaningful relief for 40-60% of OCD patients (Treatment of obsessive-compulsive disorder, 1997). Medications, however, rarely bring about remission. Response in OCD research is generally defined as a reduction of 25-35% in OCD symptoms. No SSRI has been proven to be more effective than others in OCD. Nonetheless, individual patients may respond more favorably to one than to another and is not possible to predict which SSRI will be more effective for a given patient. Therefore, differences in side-effect profile, half-life, available formulations, and cost can guide the selection (Dell'Osso, et al. 2007).

To date five SSRIs have been approved by the Food and Drug Administration for the treatment of adult OCD: clomipramine, fluvoxamine, fluoxetine, sertraline and paroxetine. These medications along with psychotherapy represent the first line of intervention for patients with OCD (Dell'Osso, et al. 2007).

Obsessive-compulsive disorder is usually treated with much higher doses of SSRIs than that used in depression and other anxiety disorders. There is modest research evidence to suggest that response is better at higher doses. Studies have shown positive dose-response relationship for fluoxetine (Montgomery, et al. 1993), paroxetine (Hollander, et al. 2003) and sertraline (Ushijima, et al. 1997), but not for clomipramine, fluvoxamine and citalopram (Fineberg and Gale, 2005).

Response to SSRIs in OCD occurs slowly over a period of 8-12 weeks unlike in depression, where maximum improvement occurs within 4-6 weeks. Initial response to the medications starts around 6-8 weeks and maximum benefit occurs only at 10-12 weeks (Fineberg and Gale, 2005 and McDonough and Kennedy, 2002). As improvement occurs over several weeks, it is recommended that modest but optimum range of dose be maintained at least for about 10 weeks before dose escalation is considered. However, once the highest dose is reached it is best to continue treatment for at least 3 months and sometimes even longer. Responders may continue to benefit for several months with long-term continuation of medication. Therefore, sensitizing the patients in advance to the delay in the onset of response and the need for a somewhat prolonged trial helps in dealing with unrealistic expectations from the patients and the resultant pressure on the clinicians to escalate or change the drug prematurely (McDonough and Kennedy, 2002).

Duration of Treatment:

Obsessive-compulsive disorder is often a chronic illness with waxing and waning course (Reddy, et al. 2005) although some recent studies have reported a better long-term outcome (Greist, et al. 2003 and Kaplan and Hollander, 2003). Even in the studies that reported a better prognosis, patients improved over a period of years and many continued to have symptoms. Discontinuation of treatment is clearly associated with symptomatic relapse, irrespective of treatment duration (Fineberg and Gale, 2005). Therefore, it is recommended that treatment be continued for a minimum of 1-2 years in SSRI responsive individuals (Stein, 2002; Maina, et al. 2001 and Zajecka, et al. 1997). In a substantial proportion of OCD patients, particularly in those in whom symptoms persist and in those who have a history of multiple relapses, lifelong medication may be necessary. If discontinuation is planned, patients should be prepared for a potential relapse and educated about the need to reinstitute treatment at the earliest sign of relapse. Patients should also be warned that reinstitution of treatment after relapse can sometimes be associated with a poorer response (Romano, et al. 2001). Drugs should be tapered gradually to minimize discontinuation symptoms. Abrupt withdrawal of SSRIs is often followed by a withdrawal syndrome, which is characterized by a sense of disequilibrium, gastrointestinal symptoms, flu like symptoms, sensory and sleep disturbances, extrapyramidal symptoms, anxiety, crying spells, irritability, confusion and aggression (Vaswani, et al. 2003).

There is little evidence to recommend dose reduction of SSRIs in the long-term treatment. The most practical recommendation for such clinical situations would be to continue at least modest doses that are well tolerated. Concomitant CBT may help dose reduction, but this has not been systematically studied. Relapse rates may be somewhat lower with CBT compared with SSRIs (Abramowitz, 2006).

Management of Treatment-Resistant Patients:

There are several different lines of intervention for partially responder patients with OCD or for non-responders. For partially responders to their first treatment, an increased dose or augmentation with an atypical antipsychotic should be considered. For non-responders, after two or three SSRI trials including at least one trial with serotonin-noradrenaline reuptake inhibitors (SNRIs) and augmentation with an atypical antipsychotic risperidone (Shapira, et al. 2004) or olanzapine (Dell'Osso, et al. 2005a), other augmentation strategies should be considered.

These include the augmentation with mood stabilizers (lithium, valproate), benzodiazepines (Clonazepam), or intravenous clomipramine. The assessment of comorbidity may orient the clinician in the augmentation choice. For the most refractory or pharmacologically intractable cases, brain stimulation techniques should be considered (Benabid, et al. 1991). These are essentially represented by transcranial magnetic stimulation (TMS) and deep brain stimulation (DBS). With regard to electroconvulsive therapy (ECT), its clinical efficacy in treatment-resistant OCD is still unproven. Published data - mostly case-report series - have shown mixed results (Benabid, et al. 1991) and it may be that ECT improves OCD by treating mental conditions comorbid with OCD (i.e. schizophrenia, depression, Tourette's Syndrome) rather than directly improving OCD (Strassnig, et al. 2004 and Hollander, et al. 1994). In addition to brain stimulation techniques, traditional neurosurgical interventions, such as capsulotomy and cingulotomy, showed positive results in patients with severe and refractory OCD (Benabid, et al. 1991).

Recently, opioid system is implicated in the pathophysiology of OCD. Opioid agonists such as tramadol hydrochloride (Pasquini and Biondi, 2006) and morphine (Lafleur, et al. 2006) have shown encouraging results but need replication in larger controlled studies. It is hypothesized that opiates decrease OCD symptoms via inhibition of glutamate release in cerebral cortex, disinhibition of serotonergic neurons in dorsal raphe and increased dopamine transmission in the striatum (Lafleur, et al. 2006). Glutamate has emerged as a novel treatment target. Drugs that attenuate glutamatergic transmission such as riluzole, memantine (Pasquini, et al. 2005) and N-acetylcysteine (Fux, et al. 1999) have shown encouraging results. Other drugs nicotine (Moreno and Delgado, 1997), inositol (Fux, et al. 2004), Lyseric acid diethylamide (LSD) and psilocybin (Tolin, et al. 2004), omega-3 fatty acids and have also been experimented but findings are not supportive of routine use in clinical practice.

Treatment of Obsessive-Compulsive Related Disorders:

Treatment studies for the OCRDs have mostly been open clinical trials and are less well characterized than those for OCD. A preferential response to SSRIs for several OCRDs including body dysmorphic disorder (Hollander, et al. 1990), hypochondriasis (Gwirtsman, et al. 1990), depersonalization disorder (Wong and Hollander, 1996), anorexia nervosa (Stein, et al. 1992), pathological gambling (Simeon and Favazza, 1995), compulsive-impulsive sexual behaviors (Neudecker and Rufer, 2004), self-injurious behaviors (Dell'Osso, et al. 2005b) and trichotillomania has been shown in different studies. These studies indicate that subtle differential responses apparently exist between impulsive disorders and compulsive disorders with regard to dosage, response lag time and maintenance of symptom remission. Patients with prevalent compulsive disorders, such as BDD and anorexia nervosa, have a significant lag time before response to SSRIs, but once they respond, they tend to maintain their gains as long as patients continue their treatment. Therefore, it is important to allow for an adequate trial at high enough doses before a patient is called a partial responder or a non-responder (Dell'Osso, et al. 2007).

On the other hand, patients with impulsive disorders, such as binge eating disorder and compulsive buying, often have a quick response to SSRIs that may diminish over time with treatment. These patients would therefore require an additional of another agent after initial stabilization, such as a mood stabilizer. Furthermore, some impulse-control disorders (ICDs) have been successfully treated with monotherapies of mood stabilizers and anticonvulsants such as lithium, valproate or topiramate as well as opioid antagonists such as naltrexone and nalmefene. Aprecise assessment of possible comorbid disorders (i.e. unipolar depression, bipolar disorder, addictive disorders etc) may ultimately help the physician to choose the right treatment and/ or the correct augmentatative agent (Dell'Osso, et al. 2005a).

Behavior therapy is also a mainstay of treatment in OCRDs with a large part of patients benefiting from prolonged exposure to feared situations (which is anxiety provoking) and response prevention (which blocks the rituals). Unfortunately, not all patients can tolerate behavior therapy because of encompassing anxiety. Clearly, the behavior approaches need to be altered in dealing with the impulsive end of the spectrum (Dell'Osso, et al. 2007).

CONCLUSIONS

Obsessive-compulsive disorder is a chronic and debilitating disorder. The coexistence of other psychiatric disorders with OCD including mood disorders, anxiety and psychotic disorders, besides Obsessive-compulsive related disorders (OCRDs), is not infrequent with depressive symptoms being the most common comorbid syndrome. SSRIs are the first line of drugs in treatment of OCD. Choice of SSRI is determined by the side effect profile. High doses and longer trials are needed for adequate response. In responders, SSRIs have to be continued in the same doses (if possible) for a minimum of 1-2 years and may be lifelong in those with persistent symptoms and in those with multiple relapses. If the first SSRI trial fails to elicit response, successive SSRI trials have to be considered. Failure to respond to multiple SSRI trials should lead to trials with clomipramine first and venlafaxine later. In non-responders and partial responders, atypical antipsychotic agents are the

first-choice augmenting drugs. CBT is an important component of treatment for OCD and it has to be offered in combination with SSRIs wherever facilities for CBT exist. CBT has to be considered in all subjects who are either non-responders or partial responders to SSRIs.

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