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Mini-Review

Comorbid Obsessive-Compulsive Disorder and Bipolar Disorder in the Pediatric Population — Clinical and Therapeutic Challenges

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Abstract

Comorbidity between obsessive-compulsive disorder and bipolar disorder has been a well-documented phenomenon in the adult population for several decades. However, scant evidence exists regarding this comorbidity in the juvenile population. The objective of this review is to investigate the impact of obsessive-compulsive disorder and bipolar disorder comorbidity on the clinical course and therapeutic approaches for each disorder individually, with a particular focus on children and adolescents. A scientific review was conducted on a careful analysis of the evidence available on the electronic databases: MEDLINE, Embase and Cochrane Library. In children, it has been observed that up to one-third of individuals diagnosed with either obsessive-compulsive disorder or bipolar disorder also experience a lifetime co-occurrence of the other disorder, a notably higher prevalence when compared to adults. The primary diagnosis typically manifests with an earlier onset in this population. When bipolar disorder is present, children and adolescents with obsessive-compulsive disorder tend to exhibit an episodic course, more hoarding or saving obsessions and compulsions, and a significantly higher number of comorbidities. In this age group, obsessive-compulsive disorder and bipolar disorder comorbidity is further linked to increased severity symptoms, greater impulsivity, reduced responsiveness to pharmacological treatment, elevated suicide risk, and a diminished likelihood of achieving remission rates for manic and depressive symptoms. Obsessive-compulsive symptoms during childhood and adolescence may indicate vulnerability to have bipolar disorder, suggesting partially shared etiopathogenetic mechanisms between these psychiatric entities. The use of antidepressants poses a risk of inducing a switch to mania or rapid cycling in bipolar patients. Additionally, atypical antipsychotics have been reported to trigger and worsen obsessive-compulsive symptoms. The complexity involved in deciding on a suitable treatment scheme for individuals with this comorbidity may contribute to an unfavorable clinical course. A noteworthy portion of comorbid patients may require a combination of multiple mood stabilizers for effective management.

Keywords: *Bipolar Disorder, Obsessive-Compulsive Disorder, Comorbidity, Manic Symptoms, Children, Adolescents.*

Introduction

Obsessive-compulsive disorder (OCD) is a neuropsychiatric condition recognized for its repetitive obsessions, characterized by persistent and ruminative thoughts, urges, or images, and compulsions, denoting repetitive behaviors or mental acts related to specific rules or triggered by obsessions. [1] Epidemiological studies have estimated a prevalence of 0.25%–4% in children and adolescents, and even though symptoms may follow a waxing and waning course, there is a tendency for chronicity [2]

On the other hand, bipolar disorder (BD) is a severe mental illness distinguished by episodic shifts in mood polarity. The prevalence of bipolar spectrum disorders is estimated to range from 0.003% to 3.9% within the child and adolescent population. [3,4]

An increasing amount of evidence suggests that pediatric BD commonly occurs alongside other psychiatric disorders, implying the potential existence of specific developmental connections regarding comorbidity within this age group. [5]

The coexistence of multiple disorders has often important implications for treatment decisions and outcomes as some pharmacological treatments for one condition may heighten the risk of destabilizing the other. [5]

The co-occurrence of symptoms of obsessive-compulsive disorder and bipolar disorder was noted more than 150 years ago by Morel [3], but the topic remains insufficiently studied. [6,7] In the adult population, there is some evidence indicating that obsessive-compulsive (OC) symptoms are usually secondary to BD, suggesting that OCD-BD represents a different subtype of BD or a separate disease. [6,7] However, in the juvenile population, the evidence is much scarcer. The episodic course of OCD in OCD-BD, the impulsivity in OCD-BD patients and the risk of worsening BD with selective serotonin reuptake inhibitors (SSRIs) configure significant challenges in diagnosing and treating these patients. [8]

A narrative review of the literature was conducted. The aim of this review was to explore the effect of OCD-BD comorbidity on both clinical course and therapeutic strategy of each disorder alone. A scientific review was conducted on a careful analysis of the scientific evidence available on the electronic databases: MEDLINE, Embase and the Cochrane Library. The following keywords and boolean operators were used: ‟obsessive-compulsive” OR obsessive-compulsive disorder OR "ocd" OR ‟bipolar disorder” OR ‟mania” OR ‟manic symptoms” OR ”maniac symptoms” AND ‟child*” OR ‟adolescent*”. Articles found written in languages other than English and French were excluded.

1. Prevalence of comorbidity between obsessive-compulsive disorder and bipolar disorder

1.1. Adult population: In adults, the lifetime prevalence of comorbidity between OCD and BD appears to be as high as 15% to 35%. [6,8,9] Even though there is emerging literature on this topic, we are still confronted with relatively limited systematic data and randomized trials specifically targeting the clinical characteristics and treatment of these patients. Data regarding the juvenile population is even scarcer, despite the frequent juvenile onset of both OCD and BD symptoms. [6,8]

1.2. Pediatric population: Studies of BD in children and adolescents have documented a 1.3%–46.9% rate of comorbid OCD.[5,8-11] These results are similar to the 27–45% rate of manic symptoms in OCD both in pediatric and adult populations, [8,10, 12-14] but significantly higher when compared to the adult BD population alone, in which much smaller rates of OCD-BD comorbidity are described, only 10-16%. [9,14,15] In a retrospective study with a sample of 207 children and adolescents, the overlap between BD and OCD was bidirectional and symmetrical, with reciprocal comorbidity present in 21% of the youth with BPD and 15% of those diagnosed with OCD. [8]

A lower mean age seems to predict a higher prevalence of OCD in BD pediatric patients. [9] Particularly in the juvenile population, several reports have described the high risk of hypomanic switches in OCD patients treated with tricyclics or selective serotonin reuptake inhibitors (SSRIs), suggesting a more evident bipolar diathesis in this population. [16] Antidepressant-induced hypomania has been reported in one-third of the OCD-BD youth but this risk, although high, is not different from the risk in BD youth without OCD. [8] In an observational study, prevalence of BD was estimated as 0,7% in the control population and as 18% in the OCD population. [6]

2. Distinctive aspects of comorbid obsessive-compulsive disorder and bipolar disorder

2.1. Clinical presentation

2.1.1. OCD vs. OC symptoms in OCD-BD: In the majority of the available data, OC symptoms in the BD comorbid group have a significantly earlier onset compared with OCD alone, both in adult [7] and pediatric populations. [9,10,13] However, a recent study with a sample of 449 children and adolescents showed that age at onset of BD and OCD was not significantly different in pure and comorbid groups. [17] In the comorbid OCD-BD population, the OC symptoms appear to have a more episodic course and a greater frequency of concurrent depressive and mixed episodes. [9-10,18-19] Nevertheless, a recent study found that 61% of the youth with the OCD-BD comorbidity were concurrently experiencing symptoms of both mania and OCD at ascertainment. [8] In the comorbid patients, OC symptoms are characterized by less frequent compulsions, specifically those concerning ordering rituals, and more obsessions, particularly existential, philosophical, sexual, superstitious and/or otherwise odd obsessions. [9-10,13]

Like the evidence on adult population, obsessions and/or compulsions related with hoarding/saving are significantly more frequent in the presence of BD. [13,17] With respect to other comorbid diseases, OCD-BD shows lower rates of generalized anxiety disorder (GAD) when compared to OCD alone, but more comorbidity with attention-deficit hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), conduct disorder (CD),[10,13] and psychosis. [8] OCD-BD patients are significantly more impaired and have greater symptom severity, both at baseline and at the end of the follow-up, when compared to the "pure" OCD group; it also appears to be associated with higher rates of suicide attempts, a more frequent need of hospitalization. [7,10,13]

2.1.2. BD vs. BD characteristics in OCD-BD: The age of onset of BD does not appear to be affected by comorbid OCD, and the index episode (depressive, hypomanic, manic, mixed or pharmacologic mania) does not differ between the two BD groups. However, in the pediatric population, OCD-BD appears to be particularly associated with BD type II, [10,17] and patients also show a higher number of depressive episodes. [9] In the majority of the available data, OCD-BD patients showed higher rates of panic disorder (PD), social phobia (SP), body dysmorphic disorder and tic disorders than BD alone,[9] and lower rates of ADHD and CD. [10] Even in the one pediatric study that showed rates of anxiety disorders equally high in both groups, multiple anxiety disorders (three or more) occur at a notably higher frequency in the comorbid group, suggesting that the lifetime risk of multiple comorbid anxiety disorders is significantly higher in comorbid OCD-BD compared with the population with either disorder without the reciprocal comorbidity.[8] Although BD symptoms at first visit were not more severe in OCD-BD youth patients, [10] a 2-year follow-up in the adult population shows decreased likelihood of symptom remission in OCD-BD compared with BD alone. [20] In the same study, the negative influence of some comorbid disorders on longitudinal outcomes of BD appeared to fade out with time, except for the comorbid GAD and OCD, that continued to negatively influence outcome. OCD-BD patients also show a more frequent hospitalization rate, greater impairments in functioning and lower quality of life. [9] In a recent Swedish study, OCD pediatric patients showed a 12-fold increased risk of having a later BD diagnosis compared with healthy subjects, which remained significantly higher even when controlling the use of SSRIs. [21]

Primary diagnosis: In the pediatric population, OCD symptoms usually antedated the onset of BD, reinforcing the hypothesis of a first internalizing phase in early-onset BD. [10]

2.2. Therapeutic approaches: The literature on pharmacologic and psychotherapeutic approaches is generally limited in pediatric patients.[15] Most controlled trials involving mood disorders have excluded patients with OCD and vice versa; as a result, the empirical basis for treating patients with OCD-BD comorbidity is almost exclusively based on an extremely limited number of reports and open clinical experiences.[10]

2.2.1. Treatment with antidepressants: From a clinical perspective, treatment of OCD-BD is uniquely challenging because even though antidepressants, namely SSRIs, are the first line treatment for OCD, they can induce mood instability in BD, especially if administered at high doses and maintained for a long time, as it is recommended for OCD management. [8] Two systematic review found that comorbid patients seem especially predisposed to have (hypo)manic episodes with use of antidepressants when compared with BD non-comorbid patients, particularly those not receiving mood stabilizers. [7] Nonetheless, in BD patients with refractory OCD, add-on therapy with a low-dose antidepressant can be considered while closely monitoring emerging symptoms of mania or hypomania. [9] Deep brain stimulation also appears to carry risks of manic worsening, and hence does not seem an useful intervention in these patients.[8] OCD-BD comorbidity is associated with the need for more complex interventions, such as drug combinations and hospitalization, and appears to have a negative impact on treatment outcome for mood symptoms and general functioning. [10,22] In a retrospective study of 257 children and adolescents with OCD, patients receiving polypharmacy presented with higher rates of BD and disruptive behavior disorders. [23]

2.2.2. Use of atypical antipsychotics: Atypical antipsychotics, commonly used for the treatment of BD and currently a first-line augmenting agent for OCD in the adult population, have also been reported to induce or exacerbate OC symptoms.[20,24] In studies comparing the two groups, atypical antipsychotics are not more used in the comorbid population when compared with patients with OCD alone; [13] as this is the primary treatment strategy for refractory OCD, we can hypothesize that control groups of OCD-BD studies are possibly composed of higher severity OCD patients. Some studies show that more than half of the patients require the use of atypical antipsychotics to manage OCD-BD symptoms. [9]

2.2.3. Mood stabilizers: According to various studies, mood stabilizers are required in almost all pattens with OCD-BD and mood stabilization should be the primary focus. [9] Nevertheless, in a systematic review already cited considering the adult population, in which all selected studies showed administration of mood stabilizers to patients with OCD-BD, no mood stabilizer has been shown to exert any anti-OCD activity in OCD controlled studies. [7] In the study with the biggest sample, 42% of comorbid patients required a combination of mood stabilizers and 10% needed a combination of mood stabilizers with atypical antipsychotics. [25] The addition of antidepressant agents to mood stabilizers only led to clinical remission of both OCD and BD in one study. There is some similar data in the pediatric population as well, showing that combined treatments (mood stabilizers, atypical antipsychotics and antidepressants) are frequently required in co-occurring BD-OCD patients. [10,26]

2.2.4. Non-responders: In the majority of the available data in the pediatric population, when response rates to treatment were compared, including pharmacotherapy and psychotherapy, the comorbid group showed the lowest rate of response (48%), compared to both BD (62%) and OCD (70%) alone.[8-9] Non-responders were characterized by: (1) greater clinical severity and functional impairment at the baseline and throughout follow-up, (2) higher frequency of hoarding symptoms, (3) higher frequency of psychotic symptoms, (4) more CD and ODD comorbidity, and (5) higher rates of antipsychotics use. Among the patients with a better response to treatment, internalizing comorbidities, particularly GAD and PD, were more frequent.[8,13-14] Differences in the pharmacological treatment between the groups are a major question in the interpretation of clinical response. In a retrospective study of 120 children and adolescents, only 69% of OCD-BD patients, compared with all the non-bipolar OCD patients, received an SSRI. [13] In adults, OCD comorbidity is associated with a poorer response to both lithium and olanzapine in BD patients.[20,27] In another retrospective study in the pediatric population already cited, all the OCD-BD non-responders received therapy with an atypical antipsychotic as an augmenting strategy, and nearly 58% became responders; the responders to augmentation were less severely impaired at baseline, but no differences were found between subtypes of OCD or patterns of comorbidity. [23]

Discussions

Even though some studies report lower rates of OCD-BD comorbidity, recent data in children and adolescents shows rates superior to 0,4%. [10] These inconsistencies among studies may be attributed to (1) differences in case selection, (2) considering current versus or lifetime comorbidity, (3) follow-up time or (4) referral bias (like in third-level hospitals). [13] Even a common family history could result from (1) common pathogenetic mechanisms, or (2) a phenotypic OCD-like expression of an underlying affective genotype, [20] so further familial and prospective studies are necessary in order to define more accurately the relationship between OCD, BD and other mood disorders. The reciprocal comorbidity present in youth with BD and OCD suggests that it is not an effect of referral or ascertainment bias. [8] OC symptoms in childhood and adolescence may be an expression of a vulnerability to BD, suggesting at least a partially shared etiopathology between these two psychiatry disorders. [28] OCD symptoms usually preceding the onset of BD may confirm the hypothesis of a first internalizing phase especially in early-onset BD. [10]

Whether the apparent association between the hoarding/saving subtype of OCD-BD comorbidity is suggestive of higher risk for BD in youth with this subtype of OCD needs to be further investigated through familial risk analysis and prospective longitudinal risk analysis of BD in this population. [8,13]

Considering long-term course of an illness as a key diagnostic element, especially among BD patients, the realization that the majority of comorbid OCD cases emerge as a secondary phenomenon to mood episodes appears to be of special significance. If comorbid BD and OCD do cycle together, it seems reasonable to think that at least some of the cases of comorbidity are in fact cases of BD with OC symptoms as a secondary manifestation of altered mood episodes. In fact, several case reports show improvement of OC symptoms with mood stabilizers and atypical antipsychotics in comorbid patients, as referred in a systematic review including both adult and pediatric populations. [19] In the same paper, findings on alternative diagnostic validators showed to be divergent and mainly suggested increased severity of illness or poorer functioning, without analyzing nosological validity. Further studies including high sensitivity assessment scales in discriminating mainly ego-dystonic true obsessions from other manifestations like depressive rumination, are essential to estimate the real prevalence of OCD in these patients. [14]

Despite the limited literature on specific therapeutic approaches in patients with OCD-BD, there is clearly a poorer response to treatment in OCD-BD when compared with OCD alone. [7,13] However, it is difficult to differentiate the contribution of the comorbidity pattern in OCD-BD patients, characterized by higher rates of disruptive behavior disorders. [13] Another critical variable affecting treatment response may be the presence of hoarding obsessions or compulsions. According to a pediatric prospective study, OCD with hoarding obsessions and compulsions appears to be associated with greater symptom severity and functional impairment, poorer response to treatment, and more frequent antipsychotic therapy, [29] which is similar to previous adult reports. [13] Also, there are limited indications for SSRI use in the presence of BD, limiting the use of the otherwise first-line treatment of OCD. [7] Nevertheless, OCD seems to have a protective effect against the risk of disruptive, impulse-control, and conduct disorders, [10] hence it could be hypothesized that OCD, with a mild level of severity, may compensate for possible functioning decline in BD. [14]

Our findings show that there is room for further research on OCD-BD comorbidity, particularly in children and adolescents. OCD seems like a frequent, although neglected, precursor of juvenile-onset BD; two out of five youth patients with OCD or BD have a lifetime co-occurrence of the other disorder. [10] When comorbid, the clinical presentation is frequently characterized by concurrent periods of episodic worsening of both diseases, especially in children and adolescents.[8] The designation of comorbidity deserves attention as, apparently, 50-75% of OCD symptoms are limited to altered mood episodes, while only the remaining OCD-BD patients seem clearly OCD cases, independent of BD. [7,19] The nature of the relationship between these two entities is not established; importantly, it may indicate that (1) one disorder represents a predisposing factor to the other, (2) OCD-BD is an alternative expression of only one of the disorders, (3) or that the two disorders may be part of the same shared diathesis. [10] Future studies considering patterns of familial aggregation of OCD and BD, in addition to longitudinal studies analyzing the impact of this comorbidity on the presentation, treatment response and clinical course, would be essential in further defining these patients, as the presence of OCD-BD has serious implications for psychopharmacological management of both disorders. [8]

Comorbid patients appear to have a greater comorbidity with both internalizing and externalizing disorders, showing more internalizing disorders than pure BD patients, and more externalizing disorders than pure OCD patients. Although in comorbid patients OCD seems to have a protective effect against the risk disruptive, impulse-control and conduct disorders, [10] the overall heavier comorbidity may have a negative impact on treatment response and prognosis.

In terms of therapeutic strategy, and recognizing the scarcity and the heterogeneity of the already published literature, the interpretation of current evidence appears to show that mood stabilization should be the primary goal in treating OCD-BD patients. Mood stabilizers, including combination regimens, are necessary for almost all patients. [9] Antipsychotics may represent an additional benefit, although a few reports also exist of apparent exacerbation of OC symptoms with these agents. Addition of a SSRI (or other antidepressants) can be counterproductive, and should be used only in a minority of OCD-BD cases with refractory OCD, at the lowest effective dose and while closely monitoring emerging symptoms of mania and hypomania. [7,13,24] Based on current available data, combined treatments, including mood stabilizers, atypical antipsychotics and occasionally antidepressants, appear to be frequently required in juvenile patients. [10,14] Further original studies are needed to clarify OCD-BD prevalence rates, evaluate diagnostic validity, determine clinical meaning and assess the best treatment approach.

Conclusion

In an era where demands to the fineness of clinical performance are progressively higher, it would be quite reasonable to believe that an evidence-based approach would solve most of our major therapeutic doubts, but this might not be the case for the time being. Particularly in neuropsychopharmacology, the specificities of treating such a unique group as the comorbid OCD-BD children and adolescent population show us that clinical excellence can only be achieved through a concerted effort in which clinical trials are conducted proficiently, hand-in-hand with changing concepts in theoretical psychiatry and disease classification. Practitioners, academics and drug researchers must work together in pursuit of new and better responses.

Conflict of Interest

The authors declare no conflict of interest.

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