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#### Review

## Treatment of comorbid bipolar disorder and obsessive-compulsive disorder: A systematic review



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#### ABSTRACT

*Background:* More than 20% of patients with bipolar disorder (BD) show lifetime comorbidity for obsessive–compulsive disorder (OCD), but treatment of BD–OCD is a clinical challenge. Although serotonin reuptake inhibitors (SRIs) are the first line treatment for OCD, they can induce mood instability in BD. An optimal treatment approach remains to be defined.

*Methods:* We systematically reviewed MEDLINE, Embase, PsychINFO and the Cochrane Library and retrieved data on clinical management of comorbid BD–OCD patients. Pharmacologic, psychotherapeutic and others alternative approaches were included.

*Results:* Fourteen studies were selected. In all selected studies BD–OCD patients received mood stabilizers. In the largest study, 42.1% of comorbid patients required a combination of multiple mood stabilizers and 10.5% a combination of mood stabilizers with atypical antipsychotics. Addition of antidepressants to mood stabilizers led to clinical remission of both conditions in only one study. Some BD–OCD patients on mood stabilizer therapy benefitted from adjunctive psychotherapy.

Limitations: Most studies are case reports or cross-sectional studies based on retrospective assessments. Enrollment of subjects mainly from outpatient specialty units might have introduced selection bias and limited community-wide generalizability.

Conclusions: Keeping in mind scantiness and heterogeneity of the available literature, the best interpretation of the available evidence appears to be that mood stabilization should be the primary goal in treating BD–OCD patients. Addition of SRI agents seems unnecessary in most cases, although it may be needed in a minority of BD patients with refractory OCD.

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#### 1. Introduction

Apparent comorbidity between bipolar disorder (BD) and obsessive-compulsive disorder (OCD) is a common condition in psychiatry. According to the Epidemiologic Catchment Area study (ECA) and the National Comorbidity Survey Replication (NCS-R), 21% and 25% of patients with BD showed a lifetime comorbidity for OCD (Chen and Dilsaver, 1995; Merikangas et al., 2007). The meaning of this comorbidity has not been clarified yet. More importantly—from a clinical perspective—the treatment of BD-OCD is a great challenge. Though serotonin reuptake inhibitors (SRIs) 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 (Math and Janardhan Reddy, 2007; Pacchiarotti et al., 2013). The literature on specific pharmacologic or psychotherapeutic approaches to patients with BD-OCD comorbidity is limited (Schaffer et al., 2012). No systematic review of this topic has been performed.

The present paper is the first systematic review of pharmacologic and non-pharmacologic treatment of BD-OCD comorbidity.

#### 2. Methods

The systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Liberati et al., 2009).

#### 2.1. Information sources and search strategy

Studies were identified by searching the electronic databases MEDLINE, Embase, PsycINFO and Cochrane. We combined the search strategy of free text terms and exploded MESH headings for the topics of bipolar disorder, obsessive–compulsive disorder and treatment combined as following: ((((("Therapeutics"[Mesh]) OR treatment\*) OR therap\*) OR pharmacotherap\*) OR psychotherap\*)) AND ((((((("Bipolar Disorder"[Mesh]) OR Bipolar disorder) OR BD) OR Bipolar) OR Manic depressive disorder) OR Manic depressive) OR Manic)) AND (((("Obsessive–Compulsive Disorder"[Mesh]) OR OCD) OR Obsessive–compulsive) OR Obsessive–compulsive disorder))). The strategy was first developed in MEDLINE and then adapted for use in the other databases (Appendix). Studies published in English from June 30th, 2013 were included. In addition, further studies were retrieved from reference listing of relevant articles and consultation with experts in the field.

#### 2.2. Inclusion criteria

#### 2.2.1. Study population and study design

We considered studies that focused on the management of comorbid BD-OCD subjects. Studies were included if diagnostic criteria for BD and OCD were specified. Among BD study populations, studies that only focused on BD-I, BD-II or BD Non Otherwise Specified (NOS) were included. Participants of both sexes older than 6 years of age were considered.

Both population-based and hospital-based studies were included. Among hospital-based studies, inpatients, day-hospital and outpatient subjects were included. All experimental and observational study designs were included. Narrative and systematic reviews and book chapters were excluded.

#### 2.2.2. Outcome measures

Either pharmacologic, psychotherapeutic and others alternative approaches were considered.

#### 2.2.3. Study selection and data extraction

Identified studies were independently reviewed for eligibility by two authors (AA, SNG) in a two-step based process; a first screening was performed based on title and abstract while full texts were retrieved for the second screening. At both stages disagreements by reviewers were resolved by consensus. Data were extracted by one author (AA) and supervised by a second author (SNG) using an ad-hoc developed data extraction spreadsheet. The data extraction spreadsheet was piloted on 10 randomly selected papers and modified accordingly.

#### 2.2.4. Quality assessment

The same authors who performed data extraction (AA, SNG) independently assessed the quality of selected studies using the checklist developed by Downs and Black both for randomized and non-randomized studies (Downs and Black, 1998). Disagreements by reviewers were resolved by consensus.

#### 3. Results

Eight hundred and one potential studies were identified from searching the selected databases and listing references of relevant articles. After removing duplicates, 590 articles were retrieved. Studies were screened and selected as described in Fig. 1. The search identified 14 articles that were included in the systematic review.

#### 3.1. Included studies

The characteristics of the included studies are reported in Table 1. Eight of the 14 studies were case reports, three cross-sectional studies and three clinical trials. All the included studies were hospital-based. Three studies assessed child and adolescent populations. The largest sample size in a study was 257 subjects. The majority of the studies were conducted in Europe. In all cases, diagnoses were based on standard Diagnostic and Statistical

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