

ANTIPSYCHOTIC MONOTHERAPY IN OBSESSIVE-COMPULSIVE DISORDER

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Dear editor,

Obsessive-compulsive disorder (OCD) is a common neuropsychiatric syndrome characterized by time-consuming obsessions and compulsions, that in turn cause significant distress or impairment in social, occupational or other important areas of functioning. The clinical profile of patients with OCD is heterogeneous, therefore different degrees of insight may be present. The mainstay of OCD treatment is pharmacotherapy, and first line treatments include Serotonin Reuptake Inhibitors (SRIs), while atypical antipsychotics are typically used as augmentation agents to SRIs in treatment-resistant OCD (TR-OCD) (Sassano-Higgins & Pato 2015, Krzyszkowiak et al. 2019).

The role of antipsychotics as monotherapy treatment in OCD patients remains, to our knowledge, undefined. A comprehensive research performed on PubMed from inception until December 2021, using the search builder "(antipsychotic AND obsessive)", retrieved 1196 items: amongst those, we identified only 9 OCD patients without comorbidity and treated with antipsychotic monotherapy:

An 8-week open-label study on 7 patients, where aripiprazole monotherapy (mean dose 18.5 mg/d) reported a significant improvement ($p < 0.05$) on compulsive symptoms, but not on obsessive symptoms ($p < 0.09$) as measured by the Yale-Brown Obsessive Compulsive Scale (YBOCS) (Connor et al. 2005).

A case report of two patients affected by TR-OCD, where one patient was administered aripiprazole 6 mg/d for six months, obtaining a reduction of 9 points on YBOCS; another one was prescribed 3 mg/d as monotherapy, reporting an improvement of 16 points, however no information was given concerning treatment duration (Tataki 2014).

Quantity and quality of evidence identified are scant, yet it is possible that aripiprazole may be effective as a single-agent in OCD. Aripiprazole is an atypical antipsychotic acting as dopamine D2/D3 partial agonist, serotonin 5-HT1A agonist and 5-HT2A antagonist. Due to its peculiar pharmacodynamic properties, aripiprazole exerts a stabilizing effect on serotonin and dopamine neurotransmission, both putatively involved in the pathophysiology of OCD (Sassano-Higgins & Pato 2015, Connor et al. 2005). Of interest, aripiprazole has not been previously reported as associated with new onset OCD (Park et al. 2021) and has shown efficacy against clozapine-induced obsessive-compulsive phenomena (Englisch et al. 2009).

Speculating on the adequate aripiprazole monotherapy dosage when treating OCD without comorbidities, the open label study reports an average dose that appears higher than recommended aripiprazole augmentation dose in OCD (5–10 mg/d) (Connor et al. 2005, Krzyszkowiak et al. 2019). Connor et al. have been reporting that aripiprazole was specifically effective on compulsive symptoms, whereas previous studies indicated that severity of compulsions predicted a poorer response to SRI (Connor et al. 2005, Krzyszkowiak et al. 2019, Sassano-Higgins & Pato 2015). No studies have considered antipsychotic monotherapy treatment response in OCD with insight/delusional beliefs, a specific subtype associated with poor outcome, earlier age of onset and higher comorbidity with major depressive disorder and that may compromise pharmacological adherence. These patients, having to some degree an altered reality testing and presenting ego-syntonic thoughts ranging from prevailing through obsessional to psychotic-like, are suggested as potentially more responsive to antipsychotics. Therefore, further trials are needed to establish the potential efficacy of aripiprazole and other antipsychotic drugs in OCD patients. Ideally, such studies would enroll patients characterized by specific clinical features that have been linked to SRI resistance such as severity of the obsessions/compulsions, early age of onset, co-occurrence of schizotypal traits, absence of insight/delusional beliefs. To know and recognize which OCD phenotypes are specifically addressed by either antipsychotic monotherapy rather than SRIs may be useful to develop more effective treatment strategies (Krzyszkowiak et al. 2019, Sassano-Higgins & Pato 2015).

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