


Venlafaxine augmentation with agomelatine in a patient with obsessive-compulsive disorder and suicidal behaviors

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Abstract

Obsessive-compulsive disorder is a chronic and disabling condition that often proves to be treatment resistant. Of the patients suffering from obsessive-compulsive disorder, 10%–27% may attempt suicide at least once in their life. We report the case of a patient who presented severe obsessive-compulsive disorder symptoms and attempted suicide ingesting 25 tablets of fluoxetine (20 mg). The patient was treated with venlafaxine and agomelatine and showed improvement of obsessive symptoms and suicidal ideation. Future studies are needed to investigate this treatment regime in large cohorts of obsessive-compulsive disorder patients with suicidal ideation.

Keywords

Agomelatine, obsessive-compulsive disorder, suicidal ideation, treatment

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Introduction

Obsessive-compulsive disorder (OCD) is a disabling condition that affects 1.6%–3.1% of the general population.¹ Selective serotonin reuptake inhibitors (SSRIs, i.e. fluoxetine, fluvoxamine, paroxetine, sertraline, or citalopram) are the first-line pharmacological treatment;² nonetheless, 40%–60% of OCD patients do not respond to this treatment.³ For non-responders, serotonin–norepinephrine reuptake inhibitors (SNRIs) like venlafaxine are a valid option,² although a significant number of OCD patients are treatment refractory.⁴

Agomelatine, a novel melatonin agonist and selective serotonin antagonist (MASSA) with antidepressant activity,⁵ has been proven to be effective in OCD treatment. Although there is a lack of large-randomized studies, the seminal reports suggest a potential use of agomelatine in treatment-resistant cases.^{4,6,7} It is probable that the positive effects of agomelatine are due to agonist action on MT1/MT2 melatonin receptor, regulation of serotonin secretion, and 5-HT_{2c} antagonism.⁸ Furthermore, melatonin may also act as a synchronizer on suprachiasmatic nucleus neurons.⁹ Recent studies reported significantly higher rates of suicidal

behavior in OCD patients. Of the patients suffering from an OCD, 10%–27% may attempt suicide at least once in their life.¹⁰

Here, we discuss a new treatment option (venlafaxine and agomelatine) in an OCD patient with suicidal ideation that responded poorly to fluoxetine. The patient provided his informed consent for the publication of this case report. No ethical approval is required by our institution.

Case presentation

A 30-year-old male patient with a history of OCD after a suicide attempt was admitted to the Emergency Room and then transferred to our psychiatric unit. The patient appeared

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anxious with thoughts of contamination, order, and symmetry; affectivity was characterized by feelings of worthlessness, fatigue, loss of energy, and diminished ability to concentrate. No other medical health problems were known or present. According to the patient, the onset of the disease was in 2006, at the age of 24 years, when he started having obsessive thoughts for cleanliness and order (daily hand washing up to 25–30 times), tendency to perfectionism, marked anxiety, insomnia, feelings of worthlessness, and social withdrawal. In the previous years, several psychiatrists who confirmed the diagnosis of OCD according to the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision (DSM-IV TR) criteria visited him. Over the years, the patient was treated with both antidepressant (SSRI) and benzodiazepine and refused psychotherapy. First, he assumed fluvoxamine 50 mg/day, gradually titrated to 200 mg/day in 6 weeks. Due to non-satisfactory clinical improvement, the fluvoxamine dose was increased up to 300 mg/day. After 6 months, the patient obtained a partial improvement of his symptomatology with a marked reduction in anxiety and washing compulsions. The fluvoxamine dosage was then kept at 200 mg/day. Under this treatment regimen, the patient was able to resume his studies and had an active social life. He then decided to stop the treatment against medical advice.

In 2010, he showed relapse of symptoms with obsessive ideation regarding his academic career cleanliness and order. Typically, he was reading the same textbook's page many times, and sometimes he was spending hours looking at the book cover page. In addition, he had a remarkable social withdrawal and was often worried about forgetting something of importance. The patient then consulted a psychiatrist who prescribed him a therapy with fluoxetine (up to 60 mg/daily). He was compliant with the medication regimen and had a partial remission. In 2011, after he failed several courses, he was dismissed by his university. After few months, there was a dramatic worsening of the OCD symptoms with suicidal thought and ideation. He attempted suicide ingesting 25 tablets of fluoxetine, and he was hospitalized in our psychiatric unit.

During the hospitalization, the patient had few social interactions with other patients; he often stayed alone in his room that personally arranged at least 10 times a day (remaking the bed and the bedside continually). OCD diagnosis was confirmed according to DSM IV-TR SCID I interview that excluded comorbid disorders like a major depressive episode and other anxiety disorders. The Yale-Brown Obsessive-Compulsive Scale (YBOCS) score was 31, and Columbia-Suicide Severity Rating Scale (C-SSRS) showed moderate-to-severe suicidal ideation. The patient was initially treated with venlafaxine 75 mg/day and lorazepam 2.5 mg/day at bedtime for insomnia. During the first week of hospitalization, venlafaxine was titrated to 225 mg/day. At this dosage, the patient had a minimal improvement of the OCD symptoms (YBOCS=28): the insomnia persisted. We then increased the venlafaxine dose to 300 mg/

day. After 3 weeks of treatment, the patient did not show any further improvement. For this reason, agomelatine 25 mg/day was added. After few days, the patient showed improvement of insomnia, and after 2 weeks, the OCD symptoms improved (YBOCS=22) and there were no evidence of suicidal thoughts or ideation. The patient was discharged after 4 weeks of hospitalization with the prescription of venlafaxine 300 mg/daily and agomelatine 25 mg/day. At follow-up (8 weeks), he showed a significant improvement of symptomatology, as indexed by a reduction of more than 50% on the YBOCS (score=15). He also planned to resume his studies.

Discussion

In this case report we showed, for the first time, that a combination therapy with venlafaxine and agomelatine was effective in improving OCD and suicidal behaviors an OCD patient.

Although the estimated rates of suicidal ideation, lifetime, and current are high (59% and 28%, respectively),¹⁰ there are limited studies aimed to address effective treatments.

Important risk factors for suicide in OCD are the presence of symmetry/ordering obsessions, the presence of compulsions, and the marital status (be unmarried)¹¹ Usually, major depressive disorder (MDD) is associated with suicidal behaviors.¹² In our patient, suicidal ideation and attempted suicide were related to the worsening of OCD symptoms rather than to a major depressive episode. Previous studies demonstrated that venlafaxine is useful in the treatment of OCD with a response rate ranging from 50% to 75%.^{3,13,14} In poor responders, additional pharmacological therapies are needed. Several augmentation strategies have been proposed, including the use of atypical antipsychotics and antidepressant combinations. Recently, it has been demonstrated that agomelatine, a MASSA antidepressant approved for MDD, may have a role in acute and long-term treatment of generalized anxiety disorder (GAD)¹⁵ and also in the management of OCD⁴

Some authors hypothesize that agomelatine's anti-obsessive properties may be due to its combined action on both the melatonergic MT1/MT2 and the 5-HT_{2c} receptors in the frontal cortex.^{16,17} Recently, altered circadian rhythms (especially hypervigilance and problems falling asleep) have been associated with OCD.¹⁸ Agomelatine is able to resynchronize circadian rhythms, and the augmentative administration of this compound has been shown to be of benefit in some OCD patients who are refractory to common forms of pharmacotherapy, because of its melatonergic modulation⁷

Only few cases were previously reported about using of agomelatine in OCD patients, either in monotherapy (50 mg/day)^{4,19} or as add-on to an SSRI (escitalopram).⁶ Here, we reported that venlafaxine augmentation with agomelatine might be an effective strategy to improve OCD symptoms, sleep disturbances, and suicidal ideation in OCD patients.

An important limitation in our case is the relatively short follow-up evaluation (8 weeks); future studies are needed to prove the long-term efficacy of venlafaxine and agomelatine in poor-response OCD patients. In addition, large-randomized clinical trials are needed to confirm and extend our findings.

Declaration of conflicting interests

No conflict of interest to declare.

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