Aripiprazole-induced Obsessive-compulsive Symptoms

Obsessive–compulsive symptoms (OCSs) can be very debilitating in patients with schizophrenia, with a prevalence of OCS estimated to be around 7% - 64% [1]. Being comorbid with obsessive–compulsive disorder (OCD) or having antipsychotic-induced OCS has been associated with poorer outcomes and increased suicidality [2]. Previous reports suggested that second-generation (atypical) antipsychotics might induce or exacerbate OCSs, including risperidone, quetiapine, olanzapine, and clozapine. Among the atypical antipsychotics, aripiprazole has a unique pharmacological profile by acting as a dopamine D_2 partial agonist, serotonin 5-HT_{1A} partial agonist, and 5-HT_{2A} full antagonist. Despite its beneficial effect in treating OCS, some evidence indicates that aripiprazole potentially induces OCS [3]. In addition, the relationship between aripiprazole dosage and OCS severity has not been addressed. Herein, we present a case of a patient with new-onset OCS with dose-related severity during aripiprazole treatment.

Case Report

A 58-year-old female patient without a family history of schizophrenia or OCD was diagnosed with schizophrenia at the age of 24 years. She started taking aripiprazole (15 mg/day) regularly at 55 years old. OCS, including repetitive hand-washing and desk-checking, gradually appeared but were self-limited. Her psychotic symptoms, including auditory hallucinations with voice commenting and persecutory delusion, were worsened at her age of 58 years, after which her aripiprazole dosage was titrated to 30 mg/day. After two weeks, her family noted that she developed remarkable OCS, such as repeated hand-washing, showering, and cloth-changing in an attempt to neutralize the fear of contamination. She was admitted for active psychotic symptoms and OCS management. The physical examination and laboratory tests, including complete blood count, biochemistry profile, urine screening for illicit drugs, and electroencephalography, did not reveal any abnormal findings. We maintained the dosage of aripiprazole at 30 mg/day and used the Yale-Brown Obsessive-compulsive Scale (Y-BOCS, range 0 - 40) and Brief Psychiatric Rating Scale (BPRS, range 0 -126) to measure the OCS and psychotic symptoms, respectively. On day seven of hospitalization, the Y-BOCS and BPRS scores were 25 and 42, respectively. Based on the observation of the nursing staff and clinical assessment during interview, we concluded that the manifestations of psychotic symptoms were independent of and not related the OCS. To control the OCS, we tapered the dosage of aripiprazole off to 15 mg/day. On day 14, her psychotic symptoms remained significant (BPRS = 48), whereas her OCSs were decreased (Y-BOCS = 21). After a complete discontinuation of aripiprazole on day 21, her OCS was decreased more (Y-BOCS = 18). But considering the florid psychotic symptoms (BPRS = 63), we switched the antipsychotic with sulpiride (600 mg/day). On day 35, her psychotic symptoms were also decreased (BPRS = 22), with minimal OCS (Y-BOCS = 6).

Comment

OCSs were emerged when our patient started taking aripiprazole (15 mg/day). OCSs were worsened after the dosage was titrated to 30 mg/day but remitted after aripiprazole discontinuation. This observation indicates a direct and dose-dependent relationship between aripiprazole and OCS. The exact mechanism underlying this phenomenon remains unknown but may be related to dysregulation of serotonergic neurotransmission in the brain, particularly the antagonistic effect on 5-HT_{2A} receptors [4 - 6].

Higher $5HT_2/D_2$ antagonism is hypothesized to be more obessogenic through altering the balance of serotonergic inhibition of dopamine functions. Consequently, second-generation antipsychotics with a potent 5-HT_{2A} antagonism and a weak D_2 blockade, such as clozapine, are more likely to induce OCS [1, 2]. Aripiprazole possesses a high ratio of $5HT_2/D_2$ antagonism by acting as a full antagonist action on $5HT_2$ receptors and partial agonistic action on D_2 receptors, which might explain its propensity to induce OCS. In addition, elevated aripiprazole dosage might increase receptor occupancy and thus aggravate OCS severity. In summary, close monitoring OCS is essential during aripiprazole administration (The institution review board of Taipei City Hospital gave exemption for IRB review for publishing this case report (protocol number = TCHIRB-10812037-W and date of approval = January 10, 2010), with the waiver of obtaining a signed informed consent from the patient).

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Conflicts of Interest

The authors declare no conflicts of interest.

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