

Obsessive-Compulsive Symptoms Following Clozapine Administration

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ABSTRACT

Clozapine is an atypical antipsychotic used for treatment-resistant schizophrenia. It has also been used for other disorders, such as obsessive-compulsive disorder, especially as an augmenting agent. Paradoxically, there are few reports of clozapine-induced obsessive-compulsive symptoms (OCS). The authors report on a patient with schizophrenia who developed OCS twice when clozapine was initiated, and responded positively to lowering the dose of clozapine.

INTRODUCTION

Clozapine is an atypical antipsychotic used for managing patients with treatment-resistant schizophrenia. Unlike other antipsychotics, it has potent antagonistic activity at the serotonin (5-HT)₂ receptor and has less affinity for dopamine-2 receptors. Development of obsessive-compulsive symptoms (OCS) with atypical antipsychotics, including clozapine, have been reported in the literature.^{1,2} On the contrary, these atypical antipsychotics, including clozapine, have been used for the management of treatment-resistant obsessive-compulsive disorder (OCD).^{3,4} A large retrospective review⁵ did not find any worsening or emergence of OCS/OCD with clozapine treatment. The authors report on a patient with schizophrenia who developed OCS twice when clozapine was initiated, and responded positively to lowering the dose of clozapine.

CASE REPORT

Mr. P, a 20-year-old unmarried male presented with a history of violent aggressive behavior, smiling and muttering to himself, suspiciousness, decreased sleep, and decrease in self

FOCUS POINTS

- Clozapine is the drug of choice for patients with treatment-resistant schizophrenia.
- Obsessive-compulsive symptoms (OCS) can occur during the course of schizophrenia.
- Clozapine can cause OCS in patients with schizophrenia.
- It is important to clarify the relation of OCS with antipsychotic medications, including clozapine, in patients with schizophrenia.
- Clozapine-induced OCS needs to be managed either by lowering the dose or adding an anti-obsessive medication like serotonin reuptake inhibitors.

care for the last 2 years. There was no significant past, family, or personal history. He was well adjusted premorbidly. He was diagnosed as a case of undifferentiated schizophrenia, as per the *International Statistical Classification of Diseases and Health Related Problems*, Tenth Revision.⁶ The patient was receiving treatment for the last 1.5 years but tended to be non-compliant. Currently, the patient had exacerbated his illness after he stopped treatment for 2 months. No records of his treatment were currently available. This time, he was started on olanzapine 10 mg/day increased to 20 mg/day, along with chlorpromazine 200 mg/day. There was no improvement at all for a period of ~3 weeks.

In view of marked aggression, adamant behavior, and hostility, the patient was started on clozapine 25 mg/day gradually increased to 250 mg/day over a period of 2 weeks; simultaneously, other drugs were gradually tapered over a period of 1 week. After ~5 days of clozapine 250 mg, it was observed that, in addition to previous symptoms, the patient also started doing things repeatedly. He would repeatedly touch some objects such as glass and doors and

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Disclosure: The authors report no affiliation with or financial interest in any organization that may pose a conflict of interest.

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would get irritable if asked not to do so. He would lie down on the floor and, after a few minutes, would get up and repeat the cycle 4–5 times before finally lying on the bed. On asking, he would report that he felt compelled to do it again and again, although he knew that these actions were irrational and that he was doing this himself, without any external influence. The Yale-Brown Obsessive Compulsive Scale score was 20. Review of the patient's treatment record revealed that ~8 months ago, he was started on clozapine, in view of non-response to haloperidol and risperidone in adequate doses for an adequate time period. The patient started developing similar OCS at that time when he was on clozapine 250 mg/day; however, thinking it to be related to psychosis, the dose of clozapine was increased further up to 400 mg/day, leading to further exacerbation of OCS. Capsule fluoxetine up to 40 mg/day was added to the treatment without much relief in the symptoms. Since the patient developed marked sedation and increased OCS, clozapine was stopped and the patient was started on trifluperazine and amisulpride at that time. The OCS remitted within a period of ~3 weeks.

In view of appearance of OCS at clozapine 250 mg/day on both occasions, it was decided to decrease the dose of clozapine to 200 mg/day, and amisulpride up to 400 mg/day was added to the treatment. The patient's OCS decreased and subsided after ~1 week of decreasing the dose.

DISCUSSION

In this case, during both instances, the symptoms developed when a dose of clozapine >200 mg and abated on decreasing the dose. Although during the first scenario fluoxetine was also added, it did not lead to significant improvement in symptoms and the OCS improved after stopping clozapine. Thus, in this patient, OCS were definitely related to clozapine and were a dose-related phenomenon. This case differs from earlier reported cases of clozapine-induced OCS because the patient developed OCS after a short period of clozapine treatment (<3 weeks) and the patient developed OCS at clozapine 250 mg/day.

Previous reports of clozapine-induced OCS have been at comparatively higher doses of clozapine (300–900 mg/day)^{2,7,8} and after a long period of clozapine treatment (ranging from 10 weeks to 2 years).^{2,7-9} In addition, this patient did not have any OCS prior to clozapine treatment, though there have been reports of clozapine exacerbating already existing OCS in schizophrenia.²

A recent study¹⁰ of OCD in clozapine-treated patients with schizophrenia or schizoaffective disorder revealed a prevalence of 24% of clinically significant OCS. However, the temporal relationship between the onset of obsessional and schizophrenic symptoms and clozapine treatment was

not established. Approximately 50% of these patients had OCS prior to clozapine treatment.

Multiple hypotheses have been offered to explain the development of OCS during antipsychotic treatment. For clozapine-induced OCS, both 5-HT_{2A} and 5-HT_{2C} receptor antagonists¹¹ have been postulated to play a role in the generation of OCS. Other mechanisms that have been reported are the role of dopamine in the pathogenesis of OCS and the serotonergic modulation of dopaminergic system.^{12,13}

It is important to clarify the relationship with antipsychotics while evaluating a patient of schizophrenia presenting with OCS. This is of importance for the management of such patients. Cases of spontaneous self-remission of clozapine-induced OCS within 1–3 weeks have also been described in the literature.¹⁴ Other options for clozapine-induced OCS include lowering the dose of clozapine as in this case, or adding a serotonin reuptake inhibitor. Switching to another antipsychotic might also be an option, but one should be careful for the exacerbation of psychosis as clozapine is generally used for treatment-resistant patients.

CONCLUSION

Given the paradoxical efficacy of clozapine in resistant cases with OCD, the overlapping neurobiology of OCD and psychosis, and the increasing use of clozapine for the management of treatment-resistant patients with schizophrenia, it is recommended that one should be vigilant and cautious while using clozapine. In addition, proper treatment history and delineation of symptoms in relation to drugs is important for correct management of patients and also to avoid polypharmacy. **PP**

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