

Obsessive-compulsive symptoms: a side-effect of antipsychotic treatment

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Obsessive-compulsive symptoms (OCS) secondary to antiserotonergic antipsychotic treatment of schizophrenia appear to have a significant prevalence from previous studies but can be very difficult to detect as they are overshadowed by the diagnosis of schizophrenia. Here, the authors describe three cases where patients have developed OCS after starting risperidone in one case, and clozapine in two other cases and how significant improvements can be achieved with SSRIs and, if necessary, cognitive behavioural therapy (CBT).



OCS in the context of schizophrenia are often overlooked in the clinical setting. However, they can be disabling and, if left untreated, cause significant negative outcomes for the patient.¹ The prevalence of the presentation has been estimated in the range of 7–64%.^{2–4} It is postulated that comorbid OCS and schizophrenia has a worse prognosis.^{5,6}

This comorbidity has been attributed to several causes in the literature, one being the use of antipsychotics that exhibit a high level of antiserotonergic 5-HT_{2a} antagonism (clozapine, olanzapine, risperidone).^{2,4,5,7} This is in line with the theory that the pathophysiology of obsessive compulsive disorder (OCD) is underpinned by serotonin depletion in the orbitofrontal cortex (OFC) and associated circuits.⁸

Those atypical antipsychotics that work primarily on the D2/D3 receptor subtypes as opposed to 5-HT_{2a} (such as aripiprazole, amisulpride) are not associated with OCS. Indeed, aripiprazole has been used to counteract the effects of OCS occurring with clozapine and olanzapine.^{6,9}

Clozapine is the antipsychotic most associated with OCS.^{2,3} One

study showed that use of clozapine had twice the risk of being associated with OCS compared with haloperidol, and although the result was found to be statistically insignificant, the severity of the OCS was significant with clozapine.¹⁰ However, there is a question mark as to whether this is because patients on clozapine are more likely to have more resistant and complex psychopathology.¹⁰ There is also evidence to show a correlation between the dose of clozapine and severity of symptoms.^{2,7,11}

There have been studies implying that the presence of OCS might be related to the severity of the schizophrenia, higher dose of clozapine administered and longer duration of clozapine use.³ It has been suggested that OCS presents more with obsessions rather than compulsions compared with primary OCD.¹²

While the association between the use of clozapine, and to a lesser extent olanzapine and risperidone, with OCS is known, the *modus operandi* for its management is still open to debate. Some studies have suggested that OCS often resolve spontaneously, while others have suggested that symptoms reduce when the dose of clozapine is reduced.^{3,7} Some studies report an improvement when SSRIs are used.^{13,14}

We looked at three cases where an antipsychotic with high affinity for 5-HT_{2a} antagonism was used with the patient later developing new obsessive symptoms. Two of the patients were on clozapine and one was taking risperidone. This paper discusses the onset of the symptoms and the course of management.

Case 1

A 53-year-old man with a diagnosis of paranoid schizophrenia had been with the service for the past 20 years. He was successfully treated with risperidone during this time and though he did not require further admissions to hospital he did need a lot of support. Further examination two years ago revealed he had developed OCS, which included fear of contamination and a need to carry out rituals incessantly. The rituals were taking up an increasing amount of his time, resulting in him spending an inordinate amount of time indoors.

Fluoxetine was started and he was closely monitored. He responded well, with significant reduction in his OCS, and although his family members thought the symptoms of OCD were still present they were much milder in degree. Subsequently, he was able to spend much more time outside his flat and was well enough to take up a volunteering job in a library.

Case 2

This patient was a 38-year-old lady with a long history of paranoid schizophrenia. She had several relapses of illness despite being compliant with prescribed medication that included aripiprazole, risperidone and haloperidol. Due to the apparent treatment resistance she was started on clozapine. There was a marked improvement in her psychotic symptoms and she remained in remission. However, she developed increasing OCS after a year of treatment with clozapine, presenting with excessive checking and counting. The symptoms were taking up an increasing amount of her time and therefore it was recommended she restart aripiprazole in an attempt to counteract them.

After one month of commencing aripiprazole the patient reported a reduction in the intensity of the symptoms. However, within a couple of months she noticed the symptoms had worsened again and therefore citalopram 20mg daily was prescribed, with good effect. She stopped repeatedly checking the washing machine and other items in the home, which was a change from her previous ritualistic behaviour. Nonetheless, her mother felt the symptoms had improved only slightly.

While taking citalopram, the patient developed peripheral oedema of the arms and legs, which improved once the citalopram was discontinued.

The patient was subsequently prescribed clomipramine, which she found beneficial and her symptoms further improved. The patient also noticed that she was more inclined to leave the house, was more enthusiastic about life and she felt a reduced need for reliance on others. The symptoms did not resolve completely but she remained in partial remission and felt in control.

Case 3

A 52-year-old man presented with a long history of treatment-resistant paranoid schizophrenia with residual symptoms of a mainly negative character. He had not experienced positive symptoms of schizophrenia in twenty years. There was also a history of type 2 diabetes and obesity.

In his case, the OCS emerged after being on clozapine for several years.

The patient developed thoughts with a fallacious element to them. For example, if he did not count he would become dizzy. He was advised and encouraged to use behavioural approaches such as diaphragmatic breathing, distraction techniques, and to engage in thought challenging. He had been referred to an anxiety group and reflected on his OCS there as well as being given psychoeducation.

He was started on fluoxetine though reported no improvement in his symptoms after one month. However, he also stated that he had become accustomed to his OCS and was not bothered by them as much. Two months later he reported that the symptoms were becoming worse. He had compulsions to open and close the fridge door as well as turning lights on and off. His counting rituals were preventing him from sleeping. Fluoxetine was increased from 20mg to 40mg daily because he was finding the symptoms exhausting and they were interfering with his activities of daily living.

Despite the pharmacological interventions there was a limited response, though with the use of CBT he managed to learn how to cope better with his symptoms.

Discussion

The first thing to note with the three cases we have described

is that the OCS began after the introduction of an antipsychotic with significant 5-HT_{2a} antagonist activity. In two of the cases the antipsychotic involved was clozapine, which is most associated with the development of OCS.¹

In all cases there was a significant latency period of greater than six months between starting the antipsychotic and the development of OCS. Previous reports have noted that OCS can occur as early as one month after starting clozapine and as late as five years.³ This suggests that OCS with clozapine should always be regularly checked for.

One of our patients noted a marked improvement in symptoms after augmentation with aripiprazole; previous studies support this improvement.^{6,9} Aripiprazole has been used successfully to reduce OCS where SSRIs have failed.¹⁴ In case 2 it has been shown that aripiprazole can be combined with an SSRI for difficult cases. Aripiprazole may also be useful in cases where it is unclear whether the new symptoms elicited are OCS or new psychotic symptoms.¹⁴

In previous papers, reducing the dose of clozapine has been considered as a strategy for reducing OCS.^{2,3} This is in line with the evidence of positive correlation between clozapine dose and OCS.^{2,11} However, in these cases the dose of clozapine was kept the same and an SSRI added, indicating that treatment for schizophrenia need not be compromised to deal with the OCS.

Using an SSRI produced a significant reduction in OCS in two of the cases above. Citalopram and fluoxetine are both recommended for the treatment of OCD under NICE guidelines.⁴ There has been no significant research into the use of SSRIs in this context, though it appears that OCS

occurring with clozapine, olanzapine or risperidone can be treated in a similar fashion to primary OCD. However, there is a significant difference, as antipsychotics such as risperidone and quetiapine have been used to augment antidepressants for primary OCD,¹⁵ this could be counterproductive in secondary OCS. As mentioned in the introduction, primary OCD and OCS may present quite differently¹² and may require slightly different approaches to management.

There is evidence showing that fluvoxamine has a degree of efficacy for OCS when combined with clozapine.^{13,14} It was also useful for reducing both negative and positive symptoms of schizophrenia.¹⁵ Concomitant fluvoxamine use can potentially reduce the dosage of clozapine needed in treatment-refractory patients with schizophrenia. Conversely, the addition of fluvoxamine can raise plasma clozapine levels and in one study appeared to worsen OCS as a result of this increase.¹¹ Further long-term studies with this drug combination are needed to determine its economic impact.¹⁶ By contrast, the combination of fluoxetine and clozapine is generally well tolerated, though sometimes fluoxetine may increase clozapine concentration levels because fluoxetine inhibits the metabolism of clozapine by affecting pathways other than N-demethylation and N-oxidation.¹⁷

CBT is an alternative treatment strategy that could be used in conjunction with, or instead of, medication.¹⁸ A review of available case reports and series has shown a reduction in symptom severity using CBT, with or without exposure and response prevention (ERP) in 80% of cases.¹⁸ However, some 25% of patients will drop out prior to completion of treatment.¹⁹ Stronger clinical data do

not yet exist in this area, and it is a subject for further exploration.

Conclusion

Our cases illustrate that it is important to be aware of obsessive-compulsive symptoms that sometimes occur with antipsychotics with high 5HT_{2a} antagonist activity, especially clozapine. Managing the symptoms with an SSRI, clomipramine or aripiprazole can be beneficial. Monitoring plasma clozapine levels is recommended whenever fluoxetine or fluvoxamine are used. CBT, often used as first-line treatment in primary OCD, should also be considered. Clinicians should be more alert to this comorbidity of symptoms and to improve strategies for detection and management. It is clear from cases such as those provided above that treating OCS can have a remarkable impact on the well-being of patients.

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Declaration of interests

No conflicts of interest were declared.

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