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A Case of Hyper Sexuality Probably Associated with Clozapine

By Sereen Rose Thomson, Navin Patil, Balaji Ommurugan, Rajesh Krishna Bhandary

ABSTRACT ~ ***Introduction:*** *Schizophrenia treatment needs to cover several psychological interventions and pharmacological treatment for stabilizing the disease course and decreasing relapses. Sexual side effects are a major hindrance to patients and lead to decreased adherence to therapy and reduced quality of life. Recently, several studies outlined that sexual dysfunction is one of the most distressing side effects of antipsychotics and a major cause of a poor quality of life. We hereby report a case of hypersexuality probably associated with clozapine in a middle-aged woman with schizoaffective disorder.* ***Case Report:*** *45-year-old female diagnosed as a case of schizoaffective disorder, was initiated on quetiapine 150 mg, risperidone 4 mg, lithium 900 mg for her psychotic and maniac symptoms, and lorazepam 2 mg for insomnia. Due to non-compliance and relapse of symptoms, she was started on clozapine 450 mg which was further increased to 650 mg along with an injectable antipsychotic zuclopenthixol 400 mg. After 3 months of treatment with an increased dose of clozapine, patient exhibited unprovoked and increased sexual urges towards male relatives, exhibitionism and an increased libido compared to normal days. A complete physical examination ruled out any extrapyramidal signs. Clozapine was tapered to 400 mg and stopped. Upon cessation of clozapine, her symptoms of hypersexuality gradually reduced.* ***Conclusions:*** *Clozapine's dopaminergic agonistic effects at the mesolimbic circuit may be responsible for this hypersexuality phenomenon. Poor understanding of the condition by the patient could lead to marital discord and suffering. WHO scale indicates clozapine as the probable cause of sexual dysfunction in our patient.* Psychopharmacology Bulletin. *2018;48(4):20–24.*

INTRODUCTION

Most atypical antipsychotics are associated with lesser incidences of sexual dysfunction compared to the typical antipsychotics. As more psychotropic medications

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have been used in the management of treatment-resistant psychiatric disorders, unexpected pharmacological adverse events can occur. Even though sexual dysfunction is a common side effect with atypicals like clozapine, the occurrence of hypersexuality is a not so common event. However, the exact mechanisms involved in antipsychotic-induced sexual dysfunction are either largely unknown or poorly understood. Hereby, we report a case of hypersexuality probably associated with clozapine in a middle-aged female with schizoaffective disorder.

Case Report

A 45-year-old woman presented to our hospital on March 2016 with complaints of 2nd and 3rd person hallucination, inappropriate laughter and smiling to self, decreased sleep and poor socio-occupational functioning. A routine physical examination revealed a body mass index of 31 kg/m^2 putting her in the obese category with all other parameters within normal limits. Laboratory investigations revealed a high fasting blood sugar level of 140 mg/dl. Mental status examination revealed increased psychomotor activity, sad mood, inappropriate affect, avolition and attention not sustained. In view of the above signs and symptoms, the patient was diagnosed as a case of schizoaffective disorder and was initiated on quetiapine 150 mg, risperidone 4 mg, lithium 900 mg for her psychotic and maniac symptoms, and lorazepam 2 mg for insomnia. However, she returned to the psychiatric department in the month of May 2016 with a history of poor compliance to medication and relapse of her psychotic symptoms.

Hence, she was started on valproate 100 mg and clozapine 450 mg. After 5 months of treatment with valproate, she developed hyperammonemia in October 2016, hence valproate was stopped, and the dose of clozapine was increased to 650 mg along with Injection zuclopenthixol 400 mg intramuscularly. After 3 months of treatment with clozapine 650 mg, on January 2017 patient came back with dis-inhibited childlike behaviour, increased psychomotor activity. History reveals she had exhibitionism, touching male relatives in-appropriately, complaints of abnormal sensation in her private parts and an increased libido. As per her spouse, she had increased sexual desire and libido compared to her normal days. A complete physical examination ruled out any extrapyramidal signs and symptoms. Our patient had no complaints of hallucinations at this point. After a detailed evaluation, an increased dose of clozapine was thought to be the probable cause of her hypersexuality and dose of clozapine was reduced to 400 mg and stopped, while continuing quetiapine and risperidone. Upon cessation of clozapine symptoms of hypersexuallity gradually reduced.

Discussion

It was believed in the early 20th century, that schizophrenia was due to deficiencies in sex hormones. Sexual dysfunction in patients with schizophrenia may be due to the illness as such, or various psychosocial factors, and use of antipsychotics such as selective serotonin reuptake inhibitors (SSRIs) and atypical antipsychotics such as risperidone, aripiprazole etc.[1]

The relationship of schizophrenia to sexual pathology is variable and complex and is different between men and women. The pathophysiology behind their development remains unclear and specific therapeutic interventions are also not well studied.[2,3] Most patients, of the female gender, are often not willing to discuss sexual problems as they are conservative. However, studies reveal that talking about sex does not destabilize them, in fact, those with treatment-resistant schizophrenia may wish to talk about these topics.[4] In contrast, clinicians often do not ask and underestimate the rates of sexual dysfunctions.

Atypical antipsychotics have not been extensively studied with regard to hypersexuality. Several studies have shown a 25%–60% incidence of sexual dysfunction among patients treated with risperidone.[5] However, it has been rarely reported with clozapine.

Clozapine, a second-generation antipsychotic is thought to be associated with loss of libido in both sexes. While, in our case, the patient showed symptoms of hypersexuality.[6] A thorough literature search revealed that all second-generation antipsychotics except risperidone induce sexual dysfunction at lower rates.[5,6]

A study conducted by Hummer et al revealed that hypersexuality was seen in 8% of the patients with psychiatric illness. However, clozapine has been thought to be associated with fewer sexual side effects because of its weaker blockade of dopamine (D2) receptors and has minimal effect on plasma prolactin levels.[7]

Mechanism for Sexual Dysfunction

Antagonism of 5-HT2A receptors and alpha-2 adrenergic receptors, which increases dopamine release in the prefrontal cortex and causes a disinhibition of noradrenergic neurons which could possibly explain this effect in our patient. Typical antipsychotics, on the other hand by their prominent D2 blockade suppress libido. Dopamine can also inhibit the release of pituitary prolactin and, therefore increase libido.[5]

In our case, patient experienced more sexual desire and greater sexual preoccupation after an increased dose of clozapine. However, the symptoms subsided after the dose was reduced stopped.

Causality assessment was done as per WHO scale of causality[8] and a probable causal relationship was ascribed. It was also found that the adverse drug reaction was of mild severity and not preventable as per Hartwig and Siegel severity and Thornton's scale respectively.[9,10]

Conclusion

Clozapine can enhance sexual desire in patients with schizophrenia. We suggest clozapine's dopaminergic agonistic effects at the mesolimbic circuit may be responsible for hypersexuality phenomenon. Poor understanding of the condition by the patient could lead to marital discord and suffering. Adverse sexual effects must be diagnosed and should be discussed with clarity and treated while considering the patient's mental status, treatment compliance, and quality of life. ✤

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Conflict of Interest

Authors declare no conflict of interest.

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Informed Consent

Written informed consent was obtained from the patient for publication of this case.

References

1. de Boer MK, Castelein S, Wiersma D, Schoevers RA, Knegtering H. The facts about sexual (dys) function in schizophrenia: an overview of clinically relevant findings. *Schizophr Bull*. 2015;41(3):674–86.
2. Haefliger T, Bonsack C. Atypical antipsychotics, and sexual dysfunction: five case-reports associated with risperidone. *Encephale*. 2006;32(1 Pt 1):97–105.
3. Montejo ÁL, Majadas S, Rico-Villademoros F, LLorca G, De La Gándara J, Franco M, Martín-Carrasco M, Aguera L, Prieto N. Frequency of sexual dysfunction in patients with a psychotic disorder receiving antipsychotics. *J Sex Med*. 2010;7(10):3404–13.
4. Bella AJ, Shamloul R. Psychotropics and sexual dysfunction. *Cent European J Urol*. 2013;66(4):466–71.
5. Costa AM, Lima MS, Mari JD. A systematic review on the clinical management of antipsychotic-induced sexual dysfunction in schizophrenia. *Sao Paulo Med J*. 2006;124:291–7.
6. Hummer M, Kemmler G, Kurz M, Kurzthaler I, Oberbauer H, Fleischhacker WW. Sexual disturbances during clozapine and haloperidol treatment for schizophrenia. *Am J Psychiatry*. 1999;156(4):631–3.

7. Gitlin MJ. Psychotropic medications and their effects on sexual function: diagnosis, biology, and treatment approaches. *J Clin Psychiatry*. 1994;55:406–413.
8. The use of the WHO–UMC system for standardised case causality assessment. Accessed from: http://www.WHO-UMC.org/graphics/4409.pdf {last accessed on 2017 May 4th].
9. Hartwig SC, Siegel J, Schneider PJ. *American J Hosp Pharm*. 1992;49(9):2229–2232.
10. Schumock GT, Thornton JP. *Hosp Pharm*. 1992;27(6):538.