

Clozapine-induced Weight Loss and Stuttering in a Patient with Schizophrenia

Sir,

Weight gain in schizophrenia is a significant problem as it notably escalates cardiovascular morbidities, the risk for diabetes, physical discomfort, medication nonadherence, reduced quality of life, increased relapse rates, increased burden of illness on patients and their families, and poorer long-term outcome.^[1] A meta-analysis report that second-generation antipsychotics such as clozapine and olanzapine are known to cause significant weight gains such as 4.45 and 4.15 kg in a 10-week period.^[1,2] In addition, already obese individual and woman without proper diet gain more weight than others.^[1] In a paradox, in some cases, surprisingly, clozapine reduces the body weight. Reasons behind the phenomenon could be due to physical exercise secondary to improved mental status, but the particular receptor-based mechanism is yet to be explored.^[3]

Second, stuttering is defined as a disruption in the normal fluency and pattern of speech, in which a person tends to repeat sounds and syllables.^[4] Stuttering associated with antipsychotics is rarely encountered in clinical practice. It may occur as a side effect of antipsychotics such as chlorpromazine, trifluoperazine, fluphenazine, olanzapine, risperidone, and rarely clozapine and aripiprazole then selective serotonin reuptake inhibitors and tricyclic antidepressants.^[4-6]

Here, we are presenting a case where the patient developed weight loss as well as stuttering while undergoing clozapine therapy.

CASE REPORT

Mrs. XZ 21-year-old female, suffering from schizophrenia for the last 9 years, was nonresponder on multiple nonclozapine antipsychotics (both the first and second generation). Owing to this, she was started on clozapine 25 mg and gradually hiked up to 600 mg along with fluoxetine 60 mg stable dose which was started for clozapine-induced obsessive-compulsive disorder (at 200 mg of dosage). She was 66 kg with basal metabolic index (BMI) of 29 before starting the clozapine. Her weight gradually reduced over the period of 3 months during the admission period. At the

time of discharge at the end of 3 months of clozapine 600 mg trial, her body weight reduced to 54 kg, 12 kg reduction from her preclozapine body weight. As she did not show much improvement, her activity level was same as before. We ruled out other possible causes of for weight loss from detailed clinical examination and laboratory investigations (total and differential count, erythrocyte sedimentation rate, renal and liver function test, ultrasonography abdomen, and chest X-ray) such as anemia, diabetes, tuberculosis, and malignancy but did not find any other reason.

In addition, the patient showed significant stuttering which almost made her speech incoherent at 300 mg of dose. She did not have any dystonia or myoclonus. Electroencephalography (EEG) was done and was not revealing any abnormal discharges. As the patient was minimally responding to clozapine high dose, and stuttering was making her disabled in communicating her daily affairs. It was kept on the same dose and later augmented with electroconvulsive therapy (ECT). After starting ECT, there was minimal improvement in her stuttering, but it was still persisting. The patient was later referred for maintenance ECT, occupational rehabilitation with speech therapy in her own place.

DISCUSSION

Clozapine is the most efficacious drug in treatment-resistant schizophrenia. However, it is often underutilized due to “Clozapinophobia” related to weight gain, new-onset diabetes mellitus, dyslipidemia, etc.^[7] Most of the literature mentioning clozapine-induced weight gain are dependent on naturalistic studies without proper control and presence of preexposure with multiple adipogenic antipsychotics; such as olanzapine or quetiapine which often gives biased results.^[3] In addition, obesity can be attributed to an unhealthy lifestyle, personal genetic profile, as well as the effects of comedications or medical disorders.^[8] Moreover, evidence also shows that having a certain genetic type of 5HT2c (–759 C/T, T allele rather than C allele) protects against antipsychotic-induced weight gain.

CLOZAPINE-INDUCED WEIGHT LOSS: CAUSATION

Weight loss could be as a result of improved mental state, better side-effect management and engagement in diet and exercise, underlying genetic cause, improvement in negative symptoms, etc., In our case, any such benefit was not present even with 3 months trial on 600 mg of clozapine. In addition, Indian population due to different genetical underpinning, weight gain might not be so evident with clozapine. Moreover, weight loss is often found to be associated with poor response to treatment.^[3] In our case-patient did not respond to 600 mg of clozapine.

Etiology of stuttering is hypothesized to be incomplete lateralization of abnormal cerebral dominance, genetic factors, and overactive presynaptic dopamine systems in regions of the brain that modulate verbalization.^[9] Stuttering associated with antipsychotics is a rarely encountered in clinical practice.

CLOZAPINE-INDUCED STUTTERING: CAUSATION

New onset stuttering may be associated with the epileptiform activity or dystonic reaction. Reasons for stuttering are not well established, but few study determined that high numbers of dopamine (D2) receptors located in a section of basal ganglia could be one of the underlying genetic characteristics. This study also observed that dopamine activity in stutterers was found to be 50%–200% higher than that in persons who were not stutterers.^[4]

Stuttering with clozapine has been reported with higher than 600 mg of doses. EEG abnormalities are very common in such cases which often warrant adding to anticonvulsants. Stuttering happens due to rapid titration of dose and higher dose and presence of multiple drugs leading to drug interactions.^[4,6]

STUTTERING AND WEIGHT LOSS

Stuttering can happen due to weight loss. Neurogenic stuttering happens due to starvation-induced brain dysfunction which disappears after refeeding. Chronic anxiety and depression both can cause stuttering and also weight loss.^[10]

In our case, the patient might not have any hypothesis describing the link between weight loss and stuttering. Our case did not match with any of the weight loss hypothesis, but the prognostic implication was quite matching as she had a very poor response with the

higher dose. On the other hand, neither she had dystonia nor epileptiform discharge to explain the organic causation of stuttering.

Development of stuttering and weight loss in the same patient with clozapine with no other evident side effect such as epilepsy, metabolic syndrome, dystonia, and cardiac side effects are extremely rare in literature. It could be independent adverse drug reaction presented in the same patient coincidentally. Bridging between the two phenomena could be possible after long research. However, we should be cautious in dealing such patient to rule out all other organic possibility.

This article is an eye opener of treatment-related complexity with clozapine which could be easily overcome with well-versed clinical knowledge.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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REFERENCES

1. Covell NH, Essock SM. Weight gain with clozapine as compared to conventional antipsychotic medications. *Schizophr Res* 1999;36:354.
2. Allison DB, Mentore JL, Heo M, Chandler LP, Cappelleri JC, Infante MC, *et al.* Antipsychotic-induced weight gain: A comprehensive research synthesis. *Am J Psychiatry* 1999;156:1686-96.
3. Tungaraza TE. Significant weight loss following clozapine use, how is it possible? A case report and review of published cases and literature relevant to the subject. *Ther Adv Psychopharmacol* 2016;6:335-42.

4. Ertekin H, Ertekin YH, Sahin B, Yayla S, Turkyilmaz E, Kara M, *et al.* Clozapine and Aripiprazole-Induced Stuttering: A Case Report of Turner Syndrome with Schizophrenia. *Klinik Psikofarmakoloji Bulteni-Bulletin of Clinical Psychopharmacology* 2016;2626.
5. Krishnakanth M, Haridas Phutane V, Muralidharan K. Clozapine-induced stuttering: A case series. *Prim Care Companion J Clin Psychiatry* 2008;10:333-4.
6. Murphy R, Gallagher A, Sharma K, Ali T, Lewis E, Murray I, *et al.* Clozapine-induced stuttering: An estimate of prevalence in the West of Ireland. *Ther Adv Psychopharmacol* 2015;5:232-6.
7. Sreeraj VS, Dinakaran D, Nagendrappa S, Rao NP, Kesavan M, Varambally S, *et al.* Clozapine: Is avoidance of clozapine in diabetes warranted? *Asian J Psychiatr* 2017;28:142-5.
8. Panariello F, De Luca V, de Bartolomeis A. Weight gain, schizophrenia and antipsychotics: New findings from animal model and pharmacogenomic studies. *Schizophr Res Treatment* 2011;2011:459284.
9. Craig-McQuaide A, Akram H, Zrinzo L, Tripoliti E. A review of brain circuitries involved in stuttering. *Front Hum Neurosci* 2014;8:884.
10. Byrne A, Byrne MK, Zibin TO. Transient neurogenic stuttering. *Int J Eat Disord* 1993;14:511-4.

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