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Clozapine Induced Akathisia - A Case Study, Evaluation and Treatment

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Abstract

Background: Clozapine is a second-generation antipsychotic which is notable for favourable profile with respect to extrapyramidal symptoms.Akathisia has been previously noted with Clozapine but the available literature on it is limited.This case aims to throw some light on the issue.

Case Study: This case study describes a 58-year old woman suffering from schizophrenia on Clozapine.She was noted to have marked akathisia on the Barnes Akathisia Rating Scale.Her symptoms subsided gradually following dose reduction of Clozapine.

Discussion: The prevalence of akathisia with Clozapine is not uncommon. Yet it has not been well reported. The possible mechanism may be due to a dopaminergic-serotonergic imbalance resulting from the drug.

Conclusion: All clinicians should look for akathisia on patients with Clozapine and manage it promptly to improve adherence and quality of life.

Keywords: Clozapine; Akathisia; Antipsychotic

Introduction

Clozapine is a second-generation antipsychotic used for treatment-resistant schizophrenia [1]. Reasons for its efficacy in treatment resistance cases is postulated to be its predilection for blocking D4 dopamine and 5HT2A/2C receptors as compared to D2 [2]. This also explains why extrapyramidal side effects, common with other antipsychotics are uncommon with clozapine. When other non-serious side effects result from treatment with clozapine, their effective management is necessary to improve treatment adherence [3]. This makes handling of side effects an important aspect in management of treatment-resistant schizophrenia.

Akathisia is an antipsychotic-induced extrapyramidal side effect described as a subjective feeling of restlessness. It may also present as increased motor restlessness. Patients often describe a need to be in constant motion to reduce the discomfort [4]. It has been associated with poor treatment outcomes,including suicide, hence necessitating early identification and treatment [5].

In some cases, use of clozapine has itself precipitated akathisia. Existing literature on this aspect is limited. This study aims to describe a case of clozapine-induced akathisia and how it was managed.

Case Summary

A 58-year-old married woman Mrs. X from an urban high socio-economic background and admitted in the intensive care unit in our hospital was referred for psychiatric evaluation. She had been suffering from schizophrenia for the past 15 years and had largely maintained symptom-free on olanzapine 10 mg daily. Her admission had been for an exacerbation of bronchial asthma. Psychiatric evaluation revealed that olanzapine in her prescription had been changed to clozapine for unknown reasons. Its dose had been rapidly escalated to 200 mg/day in the last 2 months. She was also on salbutamol inhaler 100 mcg twice daily and 10 mg/day of oral prednisolone. The patient, who had been adherent, had been experiencing an uncomfortable tingling in her calf muscles. She would feel a need to move the legs from time to time to reduce it. She could, with some difficulty, control the urge to stand up and walk to reduce the discomfort.

Complete blood examination, glucose estimation tests, serum electrolytes, renal function test, thyroid and fasting lipid profiles were normal. Oxygen saturation and vitals were stabilized through treatment. Restless leg syndrome was ruled out as a diagnosis due to a lack of paraesthesia in her limbs and a lack of diurnal variation in symptoms. A diagnosis of akathisia was made according

to Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5) [6]. Barnes Akathisia Rating Scale (BARS) was administered and a score of 7 was obtained signifying marked akathisia with marked clinical global severity. Clozapine was reduced from 200 mg to 100 mg/day and within a week there was a significant improvement of restlessness and quality of sleep with BARS score dropping to 1. She was discharged on 100 mg/day of clozapine with salbutamol and prednisolone continued at the previous dose. At 2 weeks, the score had reduced to zero and clozapine was continued at the reduced dose. There were no psychotic symptoms during that time. Thereafter she was lost to follow-up.

Discussion

Clozapine binds equally to both dopamine (D4) and serotonin receptors (5HT2A/2C) receptors and blocks them [7]. Its lower affinity for D2 dopamine subtype of receptor is hypothesized to be responsible for a favorable extrapyramidal adverse effect profile [2]. Akathisia is associated with exacerbation of psychotic symptoms, poorer treatment outcome and impaired well-being in patients with schizophrenia. Among second-generation antipsychotics, clozapine has one of the least incidences of inducing akathisia [8]. Nevertheless, isolated case reports have been reported about it. A possible mechanism may be due to the dopaminergic/serotonergic imbalance it causes in the body.

Data linking clozapine with akathisia are available from two sources: data obtained from case reports and data arising from clinical efficacy trials evaluating side-effects of neuroleptics. Prevalence from studies varies widely from 9% to 39% [9]. In a prospective, blinded study, akathisia was noted in 5.9% of clozapine-treated patients versus 6.7% of chlorpromazine-treated patients [10]. In a blinded prevalence study, 39% of patients treated with clozapine were rated as akathisic compared with 45% of patients taking first-generation antipsychotics [11]. Data from a large cohort study suggested that 0.28% of patients receiving clozapine develop akathisia and in most cases akathisia develops during the 1st month of clozapine therapy [12]. In another prevalence study, 6.8% of patients on monotherapy with clozapine for at least 4 months were diagnosed with akathisia [2].

A meta-analysis of 2012, where 15 trials were included, compared various other second-generation antipsychotics with clozapine. The findings suggested that incidence of akathisia with clozapine was greater than the ziprasidone but comparable to that of olanzapine and risperidone [8]. Another case report has described unmasking of akathisia by giving clozapine in a patient on amisulpride [4]. Our case adds to the existing literature.

A case report where gabapentin was considered for treatment of clozapine induced akathisia exists [3]. This case was treated as per conventional guidelines [13] wherein the dose of the culprit antipsychotic(clozapine in this case) was reduced. That led to improvement of akathisia in our patient. In other cases where dose reduction may not prove useful, other agents like propranolol or benzodiazepines [7] may be tried.

The available evidence suggests that akathisia is not unknown with clozapine and should be anticipated in all cases where patients complain of restlessness or anxiety and managed promptly.

Conclusion

From the existing literature, it can be concluded that akathisia is an uncommon and problematic adverse effect due to use of clozapine. It is important for mental health clinicians to be aware of it. Dose reduction is a useful treatment strategy that can be used in these cases before considering other options.

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