

multidisciplinary meetings and approval from the medication optimization committee led to his re-commencement on clozapine due to the treatment-resistant nature of his illness and associated risks.

Results. Clozapine, a benzisoxazole derivative, is used for treatment-resistant schizophrenia and aggressive behaviours. Its pharmacological action involves D2 and 5HT_{2A} receptor antagonism, affecting serotonergic, dopaminergic, adrenergic, cholinergic, and histaminergic receptors. However, severe side effects like agranulocytosis, seizures, myocarditis, tachycardia, and cardiomyopathy can occur. Cardiomyopathy incidence is rare (0.02–0.1%) with a mortality rate of 17.9%. Proposed mechanisms include undetected myocarditis and persistent tachycardia-induced changes leading to ventricular dysfunction. Common findings in investigations include raised CRP, leucocytosis, eosinophilia, increased lactate, elevated troponin, non-specific ECG changes, and ventricular dysfunction on echocardiography.

Conclusion. Clozapine poses rare but potentially fatal cardiac risks, including myocarditis and cardiomyopathy. Essential baseline investigations and close monitoring during the initial weeks are crucial. Persistent tachycardia may signal trouble. If suspected, serial monitoring of FBC, troponin, and CRP levels is recommended, with prompt management if confirmed with discontinuation of clozapine, as the cardiomyopathy is often reversible. A multidisciplinary approach involving cardiology is vital for optimal management. This is particularly crucial when weighing the risks of relapse in schizophrenia against the potential cardiovascular complications of clozapine therapy.

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A Rare Case of rTMS Induced Schizophrenia Symptom Switch

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Aims.

- This case study investigates a rare occurrence of symptom transition in a chronic schizophrenia patient following high-frequency repetitive transcranial magnetic stimulation (rTMS), aiming to understand the unexpected shift from predominantly negative to positive symptoms.
- rTMS, known for inducing changes in neuronal activity based on Faraday's law, is believed to enhance cortical excitability through high-frequency stimulation.
- Schizophrenia, a severe and chronic mental disorder, presents with both positive (e.g., delusions, hallucinations) and negative symptoms (e.g., apathy). Current treatments, predominantly antipsychotic drugs, often show limited efficacy, especially for negative symptoms. Non-invasive neuromodulation techniques like rTMS are emerging as potential interventions.

Methods. This case involves a 27-year-old banking executive with a 30 months illness duration primarily marked by negative symptoms over the past 3 months. Despite various antipsychotics, there was no improvement, leading to the initiation of high-frequency rTMS on the left dorsolateral prefrontal cortex (DLPFC) as an adjunct strategy for persistent negative symptoms. Surprisingly,

after the 5th rTMS session, positive symptoms like delusions and hallucinations emerged. Serial assessments demonstrated a decrease in negative symptom domain scores on PANSS but an increase in positive symptom domain scores on PANSS.

Results.

- Results suggest that 5 Hz rTMS over the left DLPFC may have contributed to the transition to positive symptoms. The discussion explores limited literature on rTMS-induced positive symptoms, with case reports dating back to 2004 indicating the possibility of such induction. Studies propose a link between higher pulse frequency, motor threshold intensity, left prefrontal cortex stimulation, and longer trial durations with the exacerbation of positive symptoms, possibly linked to dopamine changes in specific brain tracts.
- Recent trials indicate potential improvement in positive symptoms, such as excitement, with low frequency rTMS of the temporo parietal area. However, the efficacy of rTMS varies with the stimulation site, with left prefrontal rTMS showing promise for negative symptoms and left temporo-parietal junction stimulation possibly reducing auditory hallucinations.

Conclusion. This case report suggests that a subset of schizophrenia patients may experience a transient exacerbation of positive symptoms following rTMS. This underscores the need for increased awareness of potential side effects, serving as an exploratory study that calls for future research to refine these findings for a clearer understanding of rTMS-induced symptom switches in schizophrenia.

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Challenges and Delay in Treatment With Clozapine Due to Thrombocytopenia: A Case Study

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Aims. Clozapine is the most effective antipsychotic medication for patients with treatment-resistant psychotic disorders. Its discontinuation can precipitate relapse that can be often challenging to treat.

Methods. This is a case study of a female patient in her early 40s who is known to the mental health services with a diagnosis of schizoaffective disorder. She was admitted to acute psychiatric inpatient unit due to relapse characterised by psychotic, catatonic features and poor physical health condition due to refusal to eat and drink. She was stable on clozapine for more than a decade and had become unwell after discontinuation of clozapine in the community due to platelet count below $50 \times 10^9/L$ with normal other parameters. Low platelet count was detected during routine monthly blood monitoring after a few years of commencing clozapine.

Whilst an inpatient, there were several trials of re-titration of clozapine which had to be withheld because of ambiguity regarding the cause of persistent thrombocytopenia. Other treatment options including alternative antipsychotics and 12 sessions of ECT were tried without any success. Haematologist opinion was sought at early stage of admission and blood investigations were done but there was delay in bone marrow biopsy due to practical issues.

The treating team re-commenced oral clozapine to which she remained initially non-compliant due to catatonic features. With advice from the specialist psychosis services a few doses of intramuscular clozapine was used to facilitate re-titration. Following regular compliance and optimisation of oral clozapine, there was significant remission of clinical symptoms, with patient returning to her baseline mental state and functioning. During the period of admission, platelet counts were closely monitored which kept fluctuating reaching sometimes below $30 \times 10^9/L$ without any clear association with clozapine dose. No bleeding symptoms or signs were ever reported.

Results. Clozapine is a medication with haematological side effects; however, low platelet count is very rare. This patient ultimately underwent bone marrow biopsy which established Immune thrombocytopenia. She was discharged to the community with a plan of continuing clozapine, close monitoring of blood count and regular follow-up with haematology services for further clinical management.

Conclusion. Careful clinical evaluation and timely investigation is important to establish the cause for side effects before associating it with clozapine and discontinuing the treatment. This helps in ensuring continuity of clozapine in patients who clearly benefit from long-term use of clozapine.

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'Moon Shot': A Case Study of Augmentation of Clozapine With Fluvoxamine in an Adolescent With Treatment-Resistant Schizophrenia

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Aims. Very early onset schizophrenia is considered a rare and severe form of schizophrenia, with onset before age 13. Early initiation of antipsychotics significantly improves outcomes and prognosis. Treatment refractory status is not uncommon and clozapine currently remains the most effective option in this scenario. However, approximately 40–70% of antipsychotic-resistant patients do not respond, or respond only partially to clozapine. Additionally, many patients stop clozapine due to side effects, many of which are due to its active metabolite, nor-clozapine. Since clozapine-resistant patients have limited alternative treatment options, augmentation strategies must be considered.

This case study highlights one such augmentation strategy using fluvoxamine. Fluvoxamine inhibits CYP450 1A2 isoenzymes reducing the risk of the metabolite induced side effects and synchronously increasing plasma concentrations of clozapine.

Methods. The case study is of a 13-year-old female diagnosed with paranoid schizophrenia characterized by second and third person auditory hallucinations, delusions of persecution, paranoid pseudo-community, impulsive aggression and cognitive decline. She screened negative for developmental disorders, metabolic and genetic anomalies and medical co-morbidities. She had failed trials of two atypical antipsychotics. Clozapine was subsequently initiated and optimized to 500 mg/day (Serum Clozapine of 981 mcg/L). Partial improvement in symptomatology was observed. However, dose adjustments were difficult throughout due to side effects of clozapine and pharmacological agents such as Metformin, Lamotrigine, Ipratropium Bromide

and Propranolol were used prophylactically to mitigate the side-effects. The polypharmacy, social isolation, excessive sedation and emerging obsessive-compulsive symptoms contributed to secondary negative symptoms. Low-dose fluvoxamine was subsequently used as an augmentation strategy following which improvement was noted.

Results. Several studies have shown that co-administration of fluvoxamine may increase the steady-state serum concentrations of clozapine by a factor of 5. Optimizing the serum ratio of Nor-clozapine and clozapine levels, thereby, reduces the need for aggressive polypharmacy. Low doses of fluvoxamine inhibit the CYT activity, enough to raise the level of clozapine even when the dose of clozapine is reduced by 50% which is the target going forward for this patient.

Conclusion. Although current practice guidelines recommend clozapine mono-therapy for treatment resistant schizophrenia, augmentation of clozapine with fluvoxamine can be considered for those who do not respond adequately to clozapine mono-therapy or cease treatment due to its side effects. However, considering the unpredictable effect on clozapine plasma levels, concomitant use should ideally be initiated in facilities like a pediatric intensive unit where close surveillance is possible especially for side effects such as myocarditis especially in adolescents.

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Effect of Escitalopram on Glycemic Control and C-Reactive Protein in Patients With Depression and Co Morbid Type 2 Diabetes Mellitus – a Study on Indian Population

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Aims. There is a bidirectional link between Depression and type 2 Diabetes mellitus (T2DM). Treatment of depression with selective serotonin reuptake inhibitors (SSRIs) may improve glycaemic control and may be beneficial for patients with comorbid depression and diabetes mellitus. The aim of the present study was to assess the effect of escitalopram on C-reactive protein (CRP) and glycaemic control in patients with comorbid T2DM and depression.

Methods. A prospective interventional follow up study was conducted in a tertiary health care institute in urban India. Adult males and females who were diagnosed with Type 2 DM, having depression as per ICD-10 and treatment naïve for both the disorders were included for the study. Participants with other psychiatric disorders, on thyroid medication or on any medication that can have effect on CRP levels, having history of any infection/allergic or inflammatory conditions were excluded from the study. Sociodemographic details were collected. The severity of depression was assessed using Hamilton Depression Rating Scale (HDRS) at baseline. Escitalopram was started and titrated upto required doses for each patient. Levels of fasting blood glucose, post prandial blood glucose, HbA1c (Glycated Hemoglobin) and CRP were also measured at baseline. At the end of 3 months, severity of depression scores and blood levels of above mentioned