

January 2016

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CASE REPORT

# Remission of Psychosis in Treatment-resistant Schizophrenia Following a Seizure: A Case Report

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*Innov Clin Neurosci.* 2016;13(5–6):78–80

**FUNDING:** No funding was received for the preparation of this article.

**FINANCIAL DISCLOSURES:** The authors have no conflicts of interest relevant to the content of this article.

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**KEY WORDS:** Treatment-resistant schizophrenia (TRS), electroconvulsive therapy (ECT), clozapine, seizure

## ABSTRACT

The authors report a case of treatment-resistant schizophrenia in a 22-year-old woman, who, despite multiple trials of antipsychotics, did not respond to treatment. Clozapine treatment was initiated, but the patient's symptoms did not remit until after she had a clozapine-induced seizure. The authors discuss the importance in considering that electroconvulsive therapy may be effective in reducing positive and negative symptoms in patients suffering from treatment-resistant schizophrenia.

## INTRODUCTION

The diagnosis of treatment-resistant schizophrenia (TRS) is made after failure of multiple optimum medication trials. Clozapine, a dibenzodiazepine atypical anti-psychotic, is a drug of choice for TRS. However, its side effects, including sialorrohea, constipation, sedation, orthostatic hypotension, chest pain, nocturnal enuresis, and increased risk of seizures, pose a major hindrance to its use.[1] Paradoxically, there is evidence that seizures (including electroconvulsive therapy [ECT]) improve the symptoms of schizophrenia.[2]

Here, we present the case of a 22-year-old woman who suffered from schizophrenia for the previous 1.5 years. Despite multiple trials of antipsychotics, she did not respond to treatment. Her symptoms as well as her functionality continued to deteriorate, which required the initiation of clozapine in an attempt to control her symptoms. In an in-patient setting, she suffered a seizure, which was believed to be caused by the clozapine. Immediately following the seizure and after reducing the clozapine dosage and adding divalproex sodium, her symptoms remitted and baseline functionality returned.

We discuss the importance of considering ECT in patients suffering from TRS.

## CASE REPORT

Ms. U was 22-year-old single woman diagnosed with TRS. The prominent symptoms included auditory hallucinations, self-talking, and self-laughing, mumbling, gesturing, and thought block, which led to a preoccupied mental state. She was prescribed risperidone initially, which was titrated to 6mg. When no response was seen after the use of this medication for an optimum period of six weeks, olanzapine 5mg was added and the dose was titrated up to 20mg. The patient was observed for the next six weeks, but did not show any improvement. Her main symptoms were muteness, aggression, persecutory delusions, and auditory hallucinations, which continued to worsen. She was admitted for re-evaluation, and basic investigations were conducted. As she was now considered treatment resistant, the option of clozapine was discussed and initiated, and the dose was titrated up as per in-patient protocol (according to *Maudsley Prescribing Guidelines*).[3] She was observed for side effects and manifested sialorrhoea and sedation after one week. These symptoms were managed with trihexyphenidyl HCl (2mg) and shifting the night dose of clozapine to the morning.

On the 14th day of clozapine treatment, the patient's 175mg dosage was divided into 75mg in morning and 100mg in evening. That day, the patient had an unobserved fall in the bathroom that caused an injury to her head with bleeding and development of myoclonic jerks. Emergency services were called, and the patient was administered 2,000mg of divalproex sodium intravenously, during which she had a generalized tonic-clonic seizure. The seizure was aborted through the administration of 5mg midazolam intravenously. The neurology team was consulted, and a computerized tomography (CT) scan without contrast and an electroencephalogram (EEG) were ordered and performed. The CT scan was unremarkable, and the EEG showed a generalized temporal dominant burst of slow waves and slow dominant rhythm. The patient regained consciousness after 10 minutes and became alert after a few more minutes, at which time oral divalproex sodium was initiated. The next day, it was observed that the patient's mental state had drastically improved. No preoccupation, thought block, or persecutory delusions were observed, and the patient denied any other psychotic symptoms. She started interacting with her family. According to her mother, her interaction was similar to her previous healthy baseline pattern.

This state continued until discharge, which was five days after the seizure. Immediately following the seizure, clozapine was initially discontinued for a day, but then was restarted at 25mg with a plan of gradual dosage increase and continued administration of divalproex sodium.

At the time of discharge, the patient was on divalproex sodium 500mg and clozapine 25mg at night. One week later during the follow-up visit, her mother reported increased sedation for most of the day, along with complaints of alopecia and increased appetite; however, no positive or negative symptoms of schizophrenia were reported at that time. The patient's mother advised the patient to use herbal and alternative medicine strategies to manage her hair loss and weight gain. Her mother expressed social concerns regarding stigma, marriage, and social disposition of her daughter in the long run; however, the patient was able to participate in daily social interactions and pursue her future plans regarding career and interests.

## DISCUSSION

Improvement in our patient's mental state was very drastic and very closely temporally associated with the occurrence of the seizure. Clozapine-induced seizures are known to occur, as clozapine decreases the seizure threshold, and the cumulative one-year risk of seizure is about five percent.[4] In our patient, the dose of clozapine was high and there was no other comorbid medical or neurological condition that could explain the seizure, leading us to the conclusion that the seizure was caused by clozapine.

ECT has been effective in improving patients on clozapine, and as ECT is based on the mechanism of seizure production, we postulate that the "natural" ECT our patient experienced therapeutically augmented the clozapine and resulted symptom remission.[5] In a study conducted in Iran that investigated use of clozapine with ECR, patients with TRS were split into three treatment groups: those administered clozapine with no ECT (46% remission rate), those administered ECT with no clozapine (40%), and those administered ECT with clozapine (71%). Using the PANSS scale, investigators found that the concurrent effect of clozapine and ECT resulted in substantial improvement of TRS symptoms, and suggested that this treatment combination is a safe and effective approach to managing TRS.[6,7] It has also been shown that ECT does not cause epilepsy; rather, it increases the seizure threshold and is also helpful in managing breakthrough seizures—thus helping control clozapine-induced seizures as well.[8]

The management of patients with schizophrenia who do not respond to clozapine can be difficult, and poly-pharmacy is indicated in this group,[9] which has its own limitations due to side effects and drug interactions. Before discontinuing clozapine in these patients due to ineffectiveness, clinicians may consider using ECT on these patients in addition to the administration of clozapine. However, more rigorous data are needed to prove the benefit of ECT in this patient population before this combination is included in evidence-based guidelines for treating TRS.

## SUMMARY

In cases of TRS with failed trials of clozapine, ECT may prove efficacious when used in combination with the drug. In our patient, a seizure secondary to clozapine appeared to have augmented the effect of the medication. Symptom reduction in patients with TRS using ECT should undergo further investigative studies to determine the full extent of impact that seizures may have in reducing psychotic symptoms.


## ACKNOWLEDGMENT

The authors wish to thank Waliyah Mughis for her editorial assistance in the preparation of this manuscript.


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