

Case Report



Clozapine Induced Delirium: A Case Report

Dr Hemanta Dutta*, Dr Soumik Sengupta, Dr Subhashish Nath

1. M.D, Senior Resident, Department of Psychiatry, Lokoprio Gopinath Bordoloi Regional Institute of Mental Health (LGBRIMH), Tezpur District – Sonitpur, State – Assam, country – India.
2. M.D, Assistant professor, Department of Psychiatry, Lokoprio Gopinath Bordoloi Regional Institute of Mental Health (LGBRIMH), Tezpur, District – Sonitpur, State – Assam, country – India.
3. MD, Senior Resident, Department of Psychiatry, Lokoprio Gopinath Bordoloi Regional Institute of Mental Health (LGBRIMH), Tezpur, District – Sonitpur, State – Assam, country – India.

*Corresponding author's E-mail: rubulpd1984@rediffmail.com

Accepted on: 13-01-2014; **Finalized on:** 31-01-2015.

ABSTRACT

Despite the fact that Clozapine is the gold standard drug for treatment resistant schizophrenia, it is very cumbersome to manage a patient with Clozapine due to its side effect profile. Clinician's eyes dependably stay open regarding its usual side effects. Cases with Clozapine induced delirium are high, but they are less identified and reported. Here we are reporting a case of Clozapine induced delirium.

Keywords: Antipsychotic, Schizophrenia, cholinergic imbalance.

INTRODUCTION

Clozapine is an established gold standard drug for treatment resistant schizophrenia as reported by numerous studies.^{1, 2} Side effect profiles of Clozapine are mainly postural hypotension, weight gain, metabolic side effects, sedation, sialorrhoea, agranulocytosis, constipation, myocarditis, lowering of seizure threshold and delirium etc. Prevalence of Clozapine induced delirium is 2-10%.³ Stanilla et al. 1997 reported delirium in patients while withdrawing the Clozapine also.⁴ Although delirious state with Clozapine is less reported till yet. Here we have demonstrated a case of treatment resistant schizophrenia, who developed delirium with Clozapine.

CASE HISTORY

A 45 years Hindu male presented to our Out Patient Department with 25 years history and 2 months exaggeration of fearfulness, disorganised behaviour, auspiciousness and aggressiveness without any provocation. Medical records of the patient uncovered that earlier he received treatment with various antipsychotics like Olanzapine, Risperidone, Aripiprazole, Quetiapine etc., in adequate dosage and duration. Regardless of receiving these medications, there was no noteworthy period of recovery. Family history of the patient did not reveal any psychotic illness. Physical examination of the patient did not show any abnormality. Mental status examination of the patient revealed he was having increased psychomotor activity, impaired personal hygiene and grooming, irritable mood, delusion of persecution and delusion of reference mainly towards his family members, impaired judgment and insight grade 1.

Considering all his medical records he was diagnosed to be a case of treatment resistant Schizophrenia. He was admitted and started with Clozapine. Basic investigations like total white blood cell count, absolute neutrophil count, lipid profile, liver function test, kidney function test were done and found to be normal. Clozapine was started with a dose of 25 mg on day 1 and was increased up to 100 mg in day10. After getting a dose of Clozapine 100 mg the patient started showing restless behaviour, he was found to be having disorientation to time, place and person, increased psychomotor activity, dry mouth, slurred speech. Clinically he was diagnosed to be in delirium. His blood pressure was found to be 80/70 mm of Hg and pulse rate 100 / min. All emergency investigations, including random blood sugar, and electrolytes were done and found to be within normal range. Clozapine was stopped. The patient started improving after 2 days. Clozapine was restarted in 14 the day, at an initial dose of 25 mg and again titrated up to 100 mg, but the patient showed a similar type of confusion again. This time Clozapine was permanently stopped and tablet Haloperidol was started at a dose of 5mg and was increased up to 15 mg. On subsequent visit the patient was maintaining well with the later drug.

Brief discussion

Our study exhibited similar findings as reported by previous studies, like Gaertner et al. 2003, Centorrino et al. 2003.^{5, 6} Our patient develops the delirious state on a very low dose of Clozapine i.e. at 100 mg/day, which is a contradictory finding with deference to antecedent studies as they reported delirium in dose more than 250 mg/day.^{5, 6} An observable finding in our study was that during re-administration of the drug after a gap period of 4 days demonstrated similar confusion state in the



patient. So a causal relationship between Clozapine and delirium could be explained on that basis. Naranjo scale was administered to know the likelihood of relationship between Clozapine and delirium, and it was found to be 8.⁷ It indicated that there was a definite probability of association between the two. Benckhuijsen and Keet, 2007 likewise demonstrated a similar case of delirium on re-institution of Clozapine.⁸ Albeit a clear mechanism of delirium is not understood, cholinergic imbalance due to Clozapine may be an important factor in this regard.⁹ Regardless of a high prevalence of delirium with Clozapine, it is less reported, so physicians may remain less vigilant regarding this dreaded side effect of this drug.

So here we recommend that clinicians ought to stay cautious with respect to the side effects in the patient getting Clozapine.

REFERENCES

1. Kane J, Honigfeld G, Singer J, Meltzer H, Clozapine for the Treatment-Resistant Schizophrenic A Double-blind Comparison With Chlorpromazine, *Archives of general psychiatry*, 45(9), 1988, 789-796.
2. Solanki RK, Singh P, Munshi D, Current perspectives in the treatment of resistant schizophrenia, *Indian Journal of Psychiatry*, 51(4), 2009, 254–260.
3. Shankar BR, Clozapine-induced delirium. *The Journal of Neuropsychiatry & Clinical Neurosciences*, 2008, 20(2), 239-40.
4. Stanilla JK, de Leon J, Simpson GM, Clozapine withdrawal resulting in delirium with psychosis: a report of three cases, *Journal of Clinical Psychiatry*, 58(6), 1997, 252-5.
5. Gaertner HJ, Fischer E, Hoss J, Side effects of clozapine, *Psychopharmacology (Berl)*. 99 Suppl, 1989, S97-100.
6. Centorrino F, Albert MJ, Drago-Ferrante G, Koukopoulos AE, Berry JM, Baldessarini RJ, Delirium during clozapine treatment: incidence and associated risk factors, *Pharmacopsychiatry*, 36(4), 2003, 156-60.
7. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, Janecek E, Domecq C, Greenblatt DJ, A method for estimating the probability of adverse drug reactions, *Clin. Pharmacol. Ther*, 30 (2), 1981, 239–45
8. Benckhuijsen JA, Keet IP, Delirium on re-starting Clozapine after a short break in treatment, *Tijdschr Psychiatr*, 49 (9), 2007, 661-5.
9. Szymanski S, Jody D, Leipzig R, Anticholinergic delirium caused by retreatment with clozapine, *American Journal of Psychiatry*, 148, 1991, 1752.

Source of Support: Nil, **Conflict of Interest:** None.

