Case Report

Clozapine-induced Supraventricular Tachycardia and its Treatment with Verapamil

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ABSTRACT

Clozapine is known to be an effective antipsychotic for schizophrenia. Cardiovascular complications associated with initiation of clozapine include tachycardia, postural hypotension, and myocarditis. Factors associated with development of cardiovascular adverse events are not clearly known, and dose titration has been described to be one among the associated risk factors. We report a case of a 45-year-old man with treatment resistant schizophrenia who developed supraventricular tachycardia during initiation of clozapine and discuss the role of verapamil in its successful management.

Key words: *Clozapine, schizophrenia, supraventricular tachycardia, verapamil*

INTRODUCTION

Clozapine is known to be an effective antipsychotic for schizophrenia. Pharmacological monitoring of clozapine is extensive as compared to any other psychiatric medication due to its side-effects. Most fatal side-effect of clozapine is agranulocytosis, but the prevalence of this complication is around 0.91%.[1] Most common cardiovascular side-effects observed with clozapine are tachycardia and postural hypotension. Sometimes fatal complication such as hypertension, pericarditis, tachyarrhythmia, and ST wave changes mimicking myocardial infarction have also been reported.[2] Many of the adverse effects are dose dependent, are associated with speed of titration and tend to be more common at the beginning of therapy.[3] We report a case of a 45-year-old male who developed clozapine induced supraventricular tachycardia (SVT) during dose titration, which was successfully treated with verapamil.

Access this article online	
Website: www.ijpm.info	Quick Response Code
DOI: 10.4103/0253-7176.162925	

CASE REPORT

Mr. K, a 45-year-old male with no significant past or family history presented with 8 years continuous illness characterized by delusions of persecution, reference, third person auditory hallucinations, and severe socio-occupational dysfunction. There was history of a suicidal attempt 4 years ago in response to distress caused by the auditory hallucinations. On clinical evaluation, he fulfilled diagnostic criterion for paranoid schizophrenia (International Classification of Disease-10). He had failed adequate trials of antipsychotics trifluoperazine and risperidone and a course of nine modified electroconvulsive therapies. In view of the treatment resistance, a trial of clozapine was considered. Baseline investigations prior to initiation of clozapine inclusive of complete hemogram, fasting blood glucose, lipid profile, liver and renal functions, electrocardiogram (ECG), and electroencephalogram were within normal limits. There was no history of comorbid medical disorders except bronchial asthma without any recent exacerbation. Clozapine was

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initiated at 25 mg with daily increase in dose by 25 mg until a dose of 100 mg with daily monitoring for adverse events. As he was tolerating clozapine well the dose was increased thereafter by 50 mg daily and a dose of 250 mg was reached on the 7th day. At this dose, he developed sudden chills, rigors, fever, and tachycardia on the 8th day of initiation of clozapine. On clinical examination, he had significant tachycardia. ECG was suggestive of SVT with a heart rate of 207 beats/min and echocardiography was normal. Cardiologist intervention was sought and SVT was reverted with 6 mg of adenosine. Verapamil was preferred to beta blockers in view of comorbid bronchial asthma and he was started on 120 mg/day. Clozapine was withheld; however, he had relapse of psychotic symptoms, which necessitated re-initiation of clozapine. The dosage was titrated slowly under cover of verapamil. Patient is on regular follow-up and is in remission on a combination of clozapine and verapamil.

DISCUSSION

Supraventricular tachycardia is a known adverse effect of clozapine treatment. Patients may develop SVT or sinus tachycardia when on clozapine due to its vagolytic property. Persistent tachycardia can cause cardiomyopathy or it could be a feature of an underlying myocarditis.[4] Cardiac side-effects with clozapine have been described to be associated with speed of dose titration.

In a study by Ronaldson *et al*. (2012),[5] doses higher than 250 mg in the first 9 days was associated with higher risk of myocarditis. In our case, the patient was tolerating clozapine well until dose of 250 mg was reached on the 7th day. Hence, rapid dose titration could be an important factor associated with cardiovascular adverse events with clozapine.

Drugs of choice in treating SVT include adenosine, calcium channel blockers like verapamil and beta blockers.[4] Verapamil was preferred to beta blockers in this case due to the presence of comorbid asthma. An earlier report has also described successful treatment of clozapine related persistent sinus tachycardia with verapamil.[6] Verapamil may also have an augmenting role in the treatment of schizophrenia, especially when prominent negative symptoms and affective disturbances are present.[7]

This case highlights the importance of slow titration of clozapine to prevent cardiovascular adverse effects and potential role of verapamil in treating clozapine-induced SVT and its possible augmenting effect on clozapine.

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How to cite this article: Settem JV, Trivedi S, Kamath AG, Behere RV, Kanaradi H, Bhat SM. Clozapine-induced supraventricular tachycardia and its treatment with Verapamil. Indian J Psychol Med 2015;37:358-9.

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