

Worsening of tardive dyskinesia due to clozapine therapy

Sir,

We report an interesting case of worsening of tardive dyskinesia (TD) due to clozapine therapy.

Mr S, a 28-year-old man, presented to us with six years duration of continuous illness characterized by fearfulness, poor sleep, auditory hallucinations, delusion of control and social withdrawal. He carried a diagnosis of paranoid schizophrenia. He also suffered from asthma and was on salbutamol inhaler as and when required. His father was a chronic alcoholic. There was no significant past or family history of psychiatric illness. He was treated with chlorpromazine 600 mg/day and changed over to risperidone three years later as he developed severe postural hypotension. In addition to this, he was also given Sodium Valproate 750 mg/day to control his agitation and aggression.

Since he showed good improvement in his mental state and global functioning, he was maintained on 6 mg of Risperidone. Two years later he began to suffer from TD of upper limbs and oro-facial dyskinesia. His baseline assessment of abnormal involuntary movement scale (AIMS) revealed a score of 12.^[1] Risperidone was slowly tapered and stopped over two weeks time. He was started on clozapine as he satisfied the criteria for treatment-resistant schizophrenia and it was also thought that this would help to cure TD.

EEG, ECG, full blood count and LFTs were carried out as a pre-clozapine workup. FBC and ECG were carried out once a week to rule out any potential side-effects like myocarditis, cardiomyopathy and neutropenia.

The dose of clozapine was gradually titrated to 300 mg/day over a period of two months. Patient was followed up once a week and evaluated on AIMS. At the end of four weeks, patient had

worsening of TD (AIMS score 24). He showed a total score of +5 in Naranjos algorithm to explain the cause and effect relationship.^[2] Clozapine was tapered and stopped. He was commenced on Amisulpiride and increased to 800 mg/day along with semisodium valproate 1500 mg/day in two months time. Further follow-up over a six-month period revealed an improvement of TD (AIMS score 14).

Tardive dyskinesia is an important clinical problem which has been shown to have a causal relationship with the dopamine hypersensitivity in basal ganglia. Atypical antipsychotics have a reduced liability for inducing TD. Passive resolution of TD may be facilitated in some patients by the use of these agents.^[3] There are few evidences in literature that clozapine may induce TD. Ertugrul *et al* raise the possibility that clozapine can induce dyskinesia.^[4] In a study of 28 patients with no prior history of TD who were treated with clozapine for one year, two patients were later rated as having mild TD.^[5] One of the reasons for worsening of TD in clozapine-treated patients could be due to previous treatment with typical antipsychotic.

It is unclear whether clozapine has a direct worsening effect on TD. Clozapine may induce TD in extremely rare cases, which cannot be excluded. This study involves only a single individual and therefore may not be representative of the general group. In future, this needs further exploration by systematically analyzing a large sample with a control group.

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