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 salbutomol 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. 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. 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. There are few evidences in literature that clozapine may induce TD. Ertugrul et al raise the possibility that clozapine can induce dyskinesia. 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. 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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References