Olanzapine and trihexyphenidyl-induced tardive dyskinesia

Olanzapine, a thienobenzodiazepine derivative, is a second generation (atypical) antipsychotic agent, which has been proven efficient against the positive and negative symptoms of schizophrenia, with a low propensity to induce extrapyramidal symptoms (EPS) than observed with typical antipsychotics. It has a greater affinity for serotonin 5-HT_2A than dopamine D_2 receptors. Olanzapine is thought to have preferential action at mesolimbic over nigrostriatal dopaminergic pathways and therefore associated with a very low incidence of extrapyramidal side effects (EPS) than observed with typical antipsychotic drugs. Furthermore, a retrospective analysis of controlled multicentric trials and numerous case reports of patients with psychotic disorders including schizophrenia suggested that olanzapine even improves pre-existing symptoms of tardive movements. Till now, very few reports of olanzapine-related TD are available in the existing literature. The essential features of antipsychotic-induced TD are abnormal, involuntary movements of the tongue, jaw, trunk or extremities that develop in association with the use of antipsychotic medications. We wish to report another case of TD, which developed after 6 months of treatment with olanzapine.

Mr. A, 30 years old, married, male was suffering from schizophrenia (DSM-IV criteria) for the last 2 years. His sister and brother were both taking treatment for seizure disorder. For the first time in April 2001, the patient was treated with trifluoperazine 20 mg, Chlorpromazine 400 mg, and trihexyphenidyl 2 mg daily for 6 months without any evidence of movement disorders. In October 2001, all the medications mentioned earlier were stopped because he was not showing adequate response, and olanzapine, 5 mg per day was started which was gradually increased to 20 mg per day over a period of 6 weeks. Subsequently, at day 7 of olanzapine 20 mg per day therapy, he exhibited EPS in the form of bradykinesia, tremors, rigidity, and salivation for which, trihexyphenidyl 4 mg per day was added and successful amelioration of EPS occurred. Trihexyphenidyl was not stopped or tapered because of the risk of reemergence of extrapyramidal symptoms. In March 2002, during follow-up, while the patient was on olanzapine 20 mg and trihexyphenidyl 4 mg per day for nearly 6 months, he exhibited moderate severity of stereotypic movements of fingers of both the hands as if he was playing the piano. These movements would be more prominent on distracting his attention from them. A diagnosis of olanzapine and trihexyphenidyl induced TD was made after conducting relevant investigations, including CT Head and electroencephalograph, which were within normal limits. His routine biochemical profile was also within normal limits. He scored 7 on the Abnormal Voluntary Movement Scale. Subsequently, olanzapine was replaced by clozapine 25 mg daily, which was increased to 100 mg per day over a period of 5 weeks. The patient showed complete recovery of the abnormal movements within 2 months of clozapine therapy. The patient is presently maintained on clozapine 100 mg per day without any reemergence of TD.

Mr. A. developed TD while he was on olanzapine and trihexyphenidyl. Our report suggests that past history of antipsychotic-induced EPS and family history of neurological disorder such as seizure disorder may be important risk factors for developing TD with atypical antipsychotics, although evidence is inconsistent even with typical antipsychotic drugs. In this report, it needs to be acknowledged that there was a past history of neuroleptic exposure and this could complicate the clinical picture, because the neuroleptic used was a high potency typical antipsychotic.

In this report, one may consider the possibility of drug-withdrawal dyskinesia, which typically begins within a few days after an abrupt dosage decrease and becomes worse as the neuroleptic is withdrawn. A clinical examination cannot distinguish between withdrawal dyskinesia and other involuntary movements, as they are same as other varieties of TD. In our case, neither the dose of olanzapine was reduced nor stopped before the appearance of dyskinetic movements. Although withdrawal emergent dyskinesia with typical neuroleptics is a well-known entity, here trifluperazine was stopped completely 6 months before the onset of TD. Hence, there was no temporal correlation between withdrawal of typical neuroleptic drug and emergence of dyskinetic movements. One of the striking features of this report was that Mr. A developed EPS with olanzapine therapy when treated with trihexyphenidyl. It is known that severe EPS requiring medication intervention is rare with olanzapine, though not impossible. As seen in our case report, clozapine has been used successfully in olanzapine-induced TD. However, more data is required to know the typical characteristics and risk factors associated with olanzapine induced TD.

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References