

## Case Report

# Aripiprazole in Tardive Dyskinesia: Is it a Safe Choice?

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### ABSTRACT

Tardive dyskinesia (TD) is a potentially irreversible drug-induced movement disorder associated with prolonged administration of antipsychotics. Conventionally, first generation antipsychotics were the agents thought to have a higher risk of TD as compared to second and third generation antipsychotics. Aripiprazole is a third generation antipsychotic with a novel mechanism of action, and until recently, cases of drug-induced movement disorders were less well known with it. But off late, several cases of TD with aripiprazole have been reported. We present here a case of middle-aged women with preexisting tardive movements, which exacerbated with aripiprazole use and reduced in frequency and intensity on withdrawal of the drug.

**KEYWORDS:** Aripiprazole, movement disorder, tardive dyskinesia

## INTRODUCTION

Tardive dyskinesia (TD) is a potentially irreversible drug-induced movement disorder associated with prolonged administration of antipsychotics. It is irreversible in some patients and persists even after the medication is stopped.<sup>[1]</sup>

Important predictors of TD are older age, female gender, affective disorders, and the presence of extrapyramidal side effects, diabetes mellitus, and dose and duration of neuroleptic exposure.<sup>[2]</sup>

Conventionally, first generation antipsychotics were the agents thought to have a higher risk of TD as compared to second and third generation antipsychotics. The lower risk of TD secondary to the second and third generation antipsychotics was believed to be due to their 5HT<sub>2A</sub> receptor antagonist activity with less D<sub>2</sub> receptor antagonism.

Aripiprazole is the third-generation antipsychotic with a unique mechanism of action comprising partial agonist activity at dopamine (D<sub>2</sub>) that can stabilize D<sub>2</sub> upregulation, partial agonist activity at serotonin 5HT<sub>1A</sub> receptors and antagonist activity at 5HT<sub>2A</sub> receptors.<sup>[3]</sup> Till now, aripiprazole has been regarded as a relatively safe agent when it comes to the risk of developing movement disorders. However, there have been recent reports have various movement disorders, even with the use of this novel agent, warranting the need for clinicians to monitor for these adverse effects. We present here a case of middle-aged diabetic women with preexisting tardive movements, which exacerbated with aripiprazole use.

## CASE REPORT

A 50-year-old woman was admitted to the Department of Dermatology for psoriasis. She had been referred to the Department of Psychiatry for symptoms of fearfulness, muttering, and reduced sleep since the past 15–20 days. History of the patient revealed a history of 3–5 similar episodic exacerbation in the span of the past 12–15 years for which she had received treatment from multiple private hospitals until 2 years ago. Although no records were available, her caregivers gave a history of injectable medications given on a monthly basis for nearly 1 year. Family members gave a history of a patient having perioral movements, mild hand tremors ever since. She had poor drug compliance and also never attained a full pre-morbid level either. Her psychiatric condition was also often complicated by the hyperglycemic status necessitating the introduction of regular insulin 10–15 units/day. There was a history of psychotic disorder in daughter but no history movement disorder in the family. No history suggestive of acute dystonia, neuroleptic malignant syndrome, cerebrovascular accident, cognitive decline in past was there.

General physical examination was within normal limits. On neurological examination, the patient had mild tardive movements in the perioral region which were characterized by rabbit tremor of lips and chewing movement of tongue and jaw. She also had mild tremors and finger tapping tardive

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movements of the fingers. There was no functional and self-care impairment due to tardive movements. She was also little distressed about the movements. Blood pressure was 126/78 mm Hg and pulse rate was 86/min.

On mental status examination, the effect was perplexed. Psychomotor activity was within normal limits. Thinking revealed persecutory delusion.

Keeping in view the comorbidities and the condition of the patient, she was started on tablet aripiprazole 5 mg at night, increased to 10 mg at night after 2 days. Within 2 days of starting aripiprazole, the tardive movements of the tongue exaggerated. Then, she was unable to hold the spoon due to exaggeration of distal finger movements. She developed a fear of getting choked as her tongue showed bending movement toward orifice. She was not able to take a bite due to continuous jaw movements. Aripiprazole was reduced to 5 mg at night, but the movements did not reduce. It was stopped the following day. On the 5<sup>th</sup> day, the tardive movements reduced significantly in frequency. Later, she was started on quetiapine which did not exaggerate the movement disorder.

## DISCUSSION

The aforementioned patient was a case of recurrent psychosis who was also suffering from psoriasis with diabetes. It was further complicated by the presence of preexisting mild tardive movements, presumably given a history of use of long-acting injectable in the patient. Choice of antipsychotic was made based on the comorbidities and the low propensity of aripiprazole to cause movement disorders.

There are certain interesting observations in this case. First is the short time gap between the start of aripiprazole treatment and exacerbation of TD in the patient. The second was the fact that the patient was diabetic, which, being a proven risk factor for TD, could have contributed to the worsening of TD.

Although the pathophysiology of TD is not fully understood, it is hypothesized to result from an antipsychotic-induced hypodopaminergic state leading to dopaminergic supersensitivity in the striatum.<sup>[4]</sup>

There have been reports of aripiprazole being used in patients with TD, resulting in reductions in symptoms of TD.<sup>[5,6]</sup>

As aripiprazole has been reported to normalize dopamine D2 up-regulation, the antipsychotic may improve the symptoms of TD-induced by typical or atypical, antipsychotics.<sup>[7]</sup> Rapid dissociation of aripiprazole also appears to be responsible for its low potential to cause TD.

On the contrary, there are growing reports of TD following treatment with aripiprazole.<sup>[6-9]</sup>

It is still unclear as to how aripiprazole causes TD, but it has been suggested that in cases where the dopamine receptor is

upregulated or hypersensitive following chronic antipsychotic treatment, the high dopamine receptor occupancy and partial agonist action of aripiprazole might enhance hypersensitivity in the nigrostriatal dopaminergic system, leading to TD.<sup>[10]</sup>

As defined by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, TD are involuntary choreiform, athetoid, or rhythmic movements (lasting for at least 4 weeks) of the tongue, jaw, or extremities that develop in association with at least 3 months of neuroleptic use. In this case, the movements were already present, and they worsened on the administration of this novel agent as early as the 3<sup>rd</sup> day of administration. On withdrawal of the offending agent, the movements resolved spontaneously. No case has been reported so far with such early worsening of movements or resolution of movements.

This case report highlights the need for clinicians to be vigilant while prescribing this agent, despite comparably low risk of movement disorders, especially in patients with preexisting movement disorders and risk factors for the same.

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## Conflicts of interest

There are no conflicts of interest.

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