A RARE CASE OF ARIPIPRAZOLE INDUCED RABBIT SYNDROME

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ABSTRACT:

Prolonged exposure to Dopamine (D2) antagonist drugs, might occasionally lead to a condition which is characterized by involuntary rapid frequency (5Hz) vertical axis tremors of the perioral muscles, that mimics the twitching of a rabbit’s mouth and is therefore called the Rabbit Syndrome (RS). Although RS is considered a long term Extra Pyramidal Symptom (EPS) seen in Typical Antipsychotics, its occurrence in an Atypical Antipsychotic, especially in Aripiprazole, with a unique partial D2 agonistic action is rather peculiar. We discuss a case of Aripiprazole Induced RS to sensitize practitioners to be cautious while prescribing and titrating Aripiprazole. An elderly female suffering from recurrent depressive disorder with psychotic symptoms, developed oral tremors, after initiation of treatment with Aripiprazole. RS was diagnosed after examination and ruling out other causes. RS subsided after treating with Trihexyphenidyl. Naranjo’s algorithm for Adverse drug reaction showed a score of 7, indicating a probable association. Although the risk of developing EPS/RS on
treatment with Aripiprazole is very less, it is prudent to be cautious while co-prescribing with other medications and rapidly titrating the doses of Aripiprazole, particularly in the elderly population.

Keywords: Aripiprazole, rabbit syndrome, Dopamine drug


INTRODUCTION:

Rabbit Syndrome (RS) is a rare highly stereotyped abnormal involuntary movement of buccal area, which is considered a type of Extra Pyramidal Symptoms (EPS) resulting from antipsychotic treatment (Shartz and Hocherman, 2004). RS is classically associated with long term exposure of typical antipsychotics, but little is known regarding the risk of RS because of the exposure to the newer atypical antipsychotics (Catena Dell’osso, et al., 2007). Aripiprazole is a novel atypical antipsychotic, used for the treatment of psychosis and as an adjuvant in recurrent depressive disorder (RDD). Usually considered safe from causing EPS; few casereports of Aripiprazole induced Parkinsonism (Salmoiraghi and Odiyoor, 2006) and tardive dyskinesia (TD) (Abbasian and Power, 2008) are seen in literature. Literature on Aripiprazole induced RS is rare. (A Caykolu, etal, 2010).

We describe the case of RS developing in an elderly woman suffering from RDD, after starting adjuvant treatment with Aripiprazole.

CASE REPORT:

A 63-year-old woman, diagnosed with RDD was a regular out patient. She had suffered from 3 episodes of depression characterized by low mood, fatigue, loss of interest, suicidal ideas and delusions of reference, for over a period of 5 years. Until the latest episode, patient had been in remission (HAM-D – 6), on Tab.Fluoxetine 20mg and Tab. Risperidone 1mg. Following a major life stressor, patient relapsed to her symptoms again. (HAM-D – 22). Consequently the medication doses were gradually increased to 60 mg of Fluoxetine and 2mg of Risperidone over 2 months. She started improving symptomatically (HAM-D -16), but then started to complain of drowsiness and weight gain in response to increased dose. In view of the complaints and for further improvement of depressive symptoms, Tab. Aripiprazole 5mg was started and up titrated to 10mg over 1 month, while Tab. Risperidone was simultaneously cross tapered off. On starting Aripiprazole, there was reported improvement in symptoms (HAM-D -10), but patient complained of experiencing tremors in her lips.

On detailed examination, an involuntary movement of upper and lower lip were observed associated with popping sounds. The tremors were fine, with a frequency ~ 4 to 5 Hz along the vertical axis. These movements increased with stress and could not be suppressed voluntarily. The Simpson-Angus Scale Score (SAS) for EPS was 4, scoring only in the tremor component of scale; Abnormal Involuntary Movement Scale (AIMS) was 3, with Moderate to severe scores in lip and peri oral area.

There were no reports of stiffness of tongue, gustatory dullness, slowness in movements, tremors in limbs and other Parkinsonian features. She was on regular treatment for Diabetes Mellitus and Hypertension. She was not on any kind of Dentures. The picture was suggestive of Rabbit Syndrome. She was started on 2mg of
Trihexyphenidyl for RS and subsequently showed improvement in symptoms. 2 weeks later, on her latest consultation she had shown no signs of RS and her HAM-D was 7.

**DISCUSSION:**

RS is characterized by involuntary rapid frequency (5Hz) vertical axis tremors of the perioral muscles, that usually spare the tongue and mimic the twitching of a rabbit’s mouth. It is considered a form of EPS and can occur independent of other types. The Dopaminergic D2 blockade of a certain nuclei involved in buccal movements upstream to Pars Reticularis of Basal ganglia and unhindered Cholinergic Activation of striatal nuclei are considered to cause RS on antipsychotic action. Literature suggests the risk factor for RS as Old age, female gender, alcohol use and presence of organic disorders like Parkinson’s disease.

Aripiprazole is a unique atypical antipsychotic, having partial agonism at D2 receptors and at 5-HT1A receptors, and an antagonism at 5-HT2 receptors. Unlike other antipsychotics it does not have a notable antagonist action at cholinergic receptors. It is metabolized by the CYP2D6 (CYP 450 enzyme system).

In our case, the elderly female women was already at two of the risk factors for developing RS, and the presence of Fluoxetine, a potent CYP2D6 enzyme inhibitor in her medications could have caused elevated serum levels of Aripiprazole. A Case for older age leading to the Aripiprazole induced RS can also be made. Older age could’ve caused further reduction of metabolic capacity of 2D6 enzymes, and probably hypo albuminemia, leading to increased free drug in the blood. In the elderly an adaptive ‘hypersensitive’ state of D2 receptors has been hypothesized to compensate for dwindling Dopamine. Partial D2 agonism of Aripiprazole could’ve ‘hyposensitised’ the D2 receptors.

**CONCLUSION:**

Even though the propensity for developing EPS and RS is less for novel antipsychotics like Aripiprazole, it is advisable to the practitioners to be cautious while prescribing, and rapidly titrating Aripiprazole, especially while Co-prescribing with CYP26 inhibitors and in elderly populations.

**REFERENCES:**