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ARIPIPRAZOLE INDUCED ACUTE SEVERE EXTRAPYRAMIDAL TRACT SYMPTOMS

General Medicine

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ABSTRACT

The advent of novel atypical Antipsychotics called second generation antipsychotics (SGA) namely, quetiapine, olanzapine, Clozapine, this major problem of disturbing Extrapyramidal system [EPS] was blocked to a larger extent. Among the next Generation antipsychotics, Aripiprazole is reported to be a good safety profile antipsychotic because of its special and unique mechanism of action. Various studies have shown the incidence of EPS with this antipsychotic to be very much Insignificant. Therefore there has been increased use of aripiprazole due to its reported safety profile over time. We report a case of Acute severe Extrapyramidal Tract Symptoms induced by the use of Aripirazole which showed dramatic improvement following treatment discontinuation and hereby suggest that the disorder should be considered a possible adverse affect of aripiprazole to make more balanced treatment choices.

KEYWORDS

INTRODUCTION:

The advent of haloperidol and other first generation antipsychotics created a revolution in the management of schizophrenia or psychosis. Their therapeutic control over positive Symptoms was also associated with significant side effects involving extrapyramidal tract Symptoms – mainly parkinsonism and tardive dyskinesia. After the advent of novel atypical Antipsychotics called second generation antipsychotics (SGA) namely, quetiapine, olanzapine, Clozapine, this major problem of disturbing Extrapyramidal system [EPS] was blocked to a larger extent. Among the next.

Generation antipsychotics, Aripiprazole is reported to be a good safety profile antipsychotic because of its special and unique mechanism of action. Various studies have shown the incidence of EPS with this antipsychotic to be very much Insignificant. Aripiprazole is an atypical antipsychotic which is regarded to be different from the other atypical antipsychotic drugs due to partial agonistic action on Pre-synaptic Dopamine (D2) auto-receptor and opposite action that is antagonistic action on post-synaptic D2 receptor. Hence it behaves like an agonist in the absence of Dopamine and affects like antagonist in the presence of Excessive dopamine. Also aripiprazole is used to treat a number of Psychiatric conditions like Schizophrenia, Bipolar Disorder, Depressive disorder – Major. Although it is regarded as a well tolerated Antipsychotic, Some side effects such as headache, insomnia, agitation, anxiety may occur. But reports of EPS symptoms are very rare. In this article, we report a case of Schizophrenia who developed EPS after starting a patient on Aripiprazole which showed dramatic improvement following treatment discontinuation.

CASE REPORT:

Here by we report a case of a 43 year old married , house-wife, educated, a mother of 2, who stays at Indi, Vijayapura came to our OPD with the chief complaints of tremors, soft-voice, decreased facial Expressions, marked stiffness of neck, hands and feet with difficulty in maintaining erect Posture and altered sleep-cycle since 6 days, In the past she had presented with history of delusion of persecution and reference with Disturbed sleep, 1st and 2nd person hallucinations since 2 months and wandering-behavior with no history of mirror gazing, grimacing or episods of seizures and catatonia with inappropriate social behavior and was diagnosed as Paranoid Schizophrenia and was started on Tab. Risperidone 5mg/day and on subsequent OPD visits she had symptoms of Extra-pyramidal tract. So oral Risperidone was stopped and Tab.Aripiprazole 10mg/day was started as a monotherapy.

After 1 week she reported improvement in sleep, decrease in agitation, labile mood and delusions but still had some Psychotic features, therefore the dose of aripiprazole was escalated to 30mg / day following which, 10 days later she came with fresh complaints of tremors more at rest, soft voice etc., as stated above. On examination PR = 86 bpm, BP = 134/80 mmHg, RR= 16 cpm , Temp = 98 deg F, General Physical examination revealed mask- like face with infrequent eye-blinking,. Neurological Examination showed incomprehensible speech with slurring, significant bradykinesia, marked Rigidity (cog wheel type) with tremors of frequency ~ 4 hz. All routine investigations were normal with no leions of brainstem or other remarkable changes in MRI brain-plain.

Following which she was diagnosed as secondary Parkinsonism;[drug induced] and was treated with Immediate discontinuation of aripiprazole and started with Inj.Trihexiphenidyl 2mg once-daily, Tab. Clonazepam 0.25 mg TDS and Tab. Quetiapine 50 mg once-daily HS. Later 4 days following the Cessation of the drug [Aripiprazole], the patient improved dramatically with absolutely free of Extrapyramidal symptoms with little persistence of delusions and hallucinations.

Figure 1: Mask Like Expression Less Face Of The Patient In Aripiprazole Induced EPS.

Figure 2: Tremors in both the hands of the patient in Aripiprazole induced EPS.

DISCUSSION:

Second Generation Antipsychotic drugs differ from typical antipsychotics by 5-HT receptor antagonism and Weaker link capacities and also faster dissociation of D2 receptors[1]. Our patient had no risk factors of Parkinsonism like advanced age but some like diagnosed psychosis and exposure to antipsychotic that too not over a prolonged period of time.

Also, Aripiprazole by virtue of its unique mechanism of action that is 5HT2A receptor antagonism and partial agonistic action including 5HT1A and D2 receptors, is being claimed as 3rd generation antipsychotic. It has a dopamine agonistic action on presynaptic D2 autoreceptors and in hypodopaminergic state and antagonistic in hyperdopaminergic state respectively. Therefore regarded as dopamine system stabilizer and safest drug in Atypical antipsychotics. Aripiprazole is known to have a better motor tolerance profile because of its dopaminergic action specificity. Pharmacological data showed that blocking of more than 80% of the D2 receptors led to reduction in positive psychotic symptoms but increased risk of motor side-effects. The lesser motor side effects associated with lower doses of the drug might be explained by this effect. It is reported that 10mg of aripiprazole resulted in >80% D2 striatal receptors occupancy [EPS is observed only in patients with occupancies more than 90%]. Recent studies have shown that 5mg of aripiprazole occupies 55% of D2 striatal receptors and 6mg of aripiprazole induced 74% striatal and 51% frontal D2 receptors occupancy[2]. Here it is also important to note that lower therapeutic doses of aripiprazole are associated with more extrastriatal than striatal occupancy[3]. Aripiprazole induced EPS reports are very rare in the literature.

Studies so far have reported the incidence of EPS with this drug to be equal to that of a placebo. This mechanism is consistent with our clinical case. According to the preclinical data, there are potential mechanisms along with classical D2 receptor occupancy that might explain aripiprazole induced motor dysfunctions. For example a protein called 'Homer protein' is implicated in number of neurotransmitter regulations associated with dopaminergic, glutaminergic, and GABAergic systems. Also the Homerla gene which is known to be differentially induced by antipsychotics and thus this gene expression seems to be induced in the Putamen of rats by low doses of Aripiprazole, and in the cortex and lateral striatum of rats with chronic treatment[4]. Therefore it also appears that Homer gene regulation induced by aripiprazole probably might have played a role in striatal dysfunction and EPS following the administration of Aripiprazole.

CONCLUSION:

To the best of our knowledge there has hardly been very few reports of aripiprazole induced EPS and through this report we suggest that the disorder should be considered a possible adverse affect of aripiprazole and hereby also suggest a thorough incite regarding the reconsideration of the real risk of EPS related with the use of aripiprazole. We recommend that the perceived risk profile of aripiprazole to be reviewed and clinicians to be cautious and make more balanced treatment choices. Further research is recommended in terms of the risk of its adverse effects.

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