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Case Report

BLONANSERIN INDUCED AKATHISIA: A CASE REPORT

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ABSTRACT
Blonanserin is a new atypical antipsychotic, first approved to be used in patients with schizophrenia in Japan (2008) and recently has entered the Indian market. Although being a second generation antipsychotic, it has more affinity to block Dopamine D_2 receptor than others. We are reporting a case of akathisia that occurred after starting Blonanserin; signifying its higher propensity to cause akathisia than other atypical antipsychotics; probably attributed to its peculiar receptor blocking profile.

Keywords: *Adverse Effect; Blonanserin; Antipsychotic; Akathisia; Schizophrenia*

INTRODUCTION
Blonanserin is a relatively new atypical antipsychotic with properties of both serotonin 5-HT_{2A} and a dopamine $D_{2,3}$ receptor antagonist (Baba *et al.*, 2005; Ohno *et al.*, 2010) and this drug has been approved in Japan (2008) and South Korea (2009) for treatment of patients with schizophrenia (Deeks and Keating, 2010; Wang *et al.*, 2013). In India, It got approval for use as a second line drug in schizophrenia in adults in 2012 (Central Drugs Standard Control Organization, Government of India, 2015). It has low affinity for 5-HT_{2C}, adrenergic α_1, histamine H_1, and muscarinic M_1 receptors, but displays relatively high affinity for 5-HT_6 receptors; postulated to account for its supposed superiority in improving negative, cognitive and social functioning (Tenjin *et al.*, 2013). In a recent systematic review and meta-analysis of double-blind, randomized, controlled trials; Blonanserin was found to cause significantly less adverse effects than other typical and atypical antipsychotics; but had higher risk of akathisia compared to Risperidone (Kishi *et al.*, 2013). There have been very few reports of Blonanserin induced akathisia in literature and none have been reported from India. Here we are reporting a case of akathisia that developed after starting Blonanserin in a lady with psychosis and which remitted after the drug was stopped.

CASES
A 39 year old married Hindu lady hailing from an urban region presented with acute onset restlessness, nervousness, not able to sit at a particular place, pacing about here and there in her house, not able to stand for few seconds, changing her stance from one foot to another for last two days. In these two days her husband noted that she had not fallen asleep comfortably. She was brought to the one of the authors with such symptoms who felt prudent to delve into her clinical and medication history.
The history gradually unfolded that this lady was suffering from symptoms suggestive of Psychosis for last seven months and she was prescribed Tablet Amisulpiride by a psychiatrist, the dose of which was gradually escalated from 200 mg a day to 400 mg a day; along with Tablet Clonazepam 0.5 mg at bedtime. She continued to take the medication regularly and was compliant to it when she developed secondary amenorrhoea and galactorrhoea after three months. On second visit to this psychiatrist, Amisulpiride was stopped and Tablet Blonanserin was started at a dose of 8 mg per day in divided doses. She continued taking Blonanserin with symptomatic improvement. She reported to have taken Blonanserin for twelve days before she presented to the author with her present symptoms as mentioned earlier.
Considering the antipsychotic history, she was presumed to be suffering from antipsychotic (Blonanserin) induced Akathisia. To objectify her symptoms, Barnes Akathisia Rating Scale was applied on her and the total score of three suggestive of significant Akathisia was found.
Blonanserin was stopped and she was started on tablet Propranolol in a dose of 40 mg a day which resulted in significant improvement in her akathisia; indicated by decrease in Barnes Akathisia Rating Scale score to zero when re-administered after three days.

DISCUSSION

Blonanserin is a novel antipsychotic developed in Japan and was approved in Japan in 2008 and Korea in 2009 for the treatment of schizophrenia. It is currently in Phase III of clinical trial in China (Kishi *et al.,* 2013; Tenjin *et al.,* 2013). Its affinity for D_2 receptors is approximately six times greater than that for 5-HT_{2A} receptors; thus pharmacologically more similar to First generation antipsychotics than Second generation drugs. Hence it is often called a 'dopamine-serotonin antagonist (Tenjin *et al.,* 2013). The affinity of Blonanserin for D_2 receptors is 20 and 94-fold higher than that of Haloperidol and Risperidone, respectively (Kane *et al.,* 2009).

Akathisia is a common neurological side effect of antipsychotic medications (Iqbal *et al.,* 2007; Kane *et al.,* 2009). Although the precise mechanisms underlying antipsychotic drug-induced akathisia are currently unclear; it seems related to dopamine D_2receptor blockade (Iqbal *et al.,* 2007; Kane *et al.,* 2009). Second generation antipsychotics are known to have lesser propensity to cause akathisia than First generation; since serotonin receptor blocking action is much more potent than dopamine D_2 receptor blockade (Kane *et al.,* 2009). But as we know that Blonanserin has more affinity to antagonize D_2 receptors than other Second generation antipsychotics (Kane *et al.,* 2009); it can be anticipated to cause more akathisia.

Furuse *et al.,* (2010) reported a series of five cases developing akathisia that emerged after treatment with Blonanserin for a period ranging from 2 days to 2 weeks in their patients in a dose range of 8-24 mg; which they successfully treated with Fluvoxamine in a dose of 50 mg per day in all the five cases. Yang *et al.,* (2010) in a randomized, double-blind, Risperidone-compared trial found Blonanserin to be associated with more akathisia compared to Risperidone though not reached statistical significance (*p* value 0.0751). Kishi *et al.,* (2013) in systematic review and meta-analysis of double-blind, randomized, controlled trials found that Blonanserin had a 1.62 higher risk of akathisia than Risperidone (CI = 1.18–2.22, NNH = 3).

In our case, the patient developed akathisia 12 days after starting of Blonanserin; which remitted soon after stopping of Blonanserin and addition of Propranolol. She was also receiving Clonazepam concurrently, but no literature was found to suggest its association with akathisia. We also applied Naranjo Adverse Drug Reaction Probability Scale (Naranjo *et al.,* 1981) and a score of six came which suggests probable causative association between Blonanserin and akathisia.

Conclusion

The above case report points to the advent of use of Blonanserin as a new atypical antipsychotic on Indian patients though data regarding potential adverse reactions is not yet adequately available in the existing literature. The akathisia that we reported as a probable adverse effect of this new drug, points to the necessity of more trials to conclusively prove their association. We also put forward the necessity to closely monitor our patients receiving Blonanserin for the emergence of such neurological side effects.

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