

Case Report

Extrapyramidal Side Effects with Low Dose Amisulpride: A Report of Two Cases

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ABSTRACT

Amisulpride, recently introduced atypical antipsychotic, is well-known for its broad spectrum effectiveness and lower profile for extrapyramidal side effects (EPS). Its selective affinity for dopamine receptors in the limbic structures, but not in the striatum, leads to a low risk of extrapyramidal side effects. Here, we report two cases of EPS associated with lower dose of amisulpride. The proposed mechanism for its causation is also discussed. Authors invite more studies, specifically from the Indian context to find out the incidence of EPS and other associated side effects.

Key words: Amisulpride, antipsychotic, atypical, EPS

INTRODUCTION

Amisulpride came into the Indian market a few years back with hypes and hopes in the management of schizophrenia. Its broad spectrum effectiveness with lower chances of extrapyramidal symptoms (EPS) and metabolic syndrome did help psychiatrists to treat schizophrenia and related disorders more effectively. Although this antipsychotic does not block serotonin receptors at all, it is a high-affinity and highly selective D_3/D_2 receptor antagonist with atypical properties.^[1] Its selective affinity for dopamine receptors in the limbic structures, but not in the striatum, leads to a low risk of extrapyramidal side effects.^[2]

All available reports suggest that chance of EPS is very less with amisulpride at doses <400 mg/day. However, there are sporadic reports of drug-induced

EPS including dystonia and akathisia even in patients receiving low doses of amisulpride.^[3,4] Here, we wish to share our experience of two such cases.

CASE REPORTS

A 30-year-old male with schizophrenia for the past 10 years now presented with predominantly negative symptoms. He was on olanzapine 15 mg/day for more than 6 months without much improvement. Hence, amisulpride was instituted with a starting dose of 50 mg/day with a gradual increment up to 300 mg/day within 14 days. Olanzapine was stopped within 7 days of starting amisulpride. The patient came after 14 days to the casualty with features of parkinsonian

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syndrome such as slowed gait, mild rigidity, salivation, and bradykinesia. There was no past history of parkinsonism. He was hospitalized, amisulpride was immediately stopped, and trihexyphenidyl 4 mg/day was given to manage the side effect. His EPS gradually subsided and for negative symptoms, clozapine was introduced at a small dose of 25 mg/day and gradually increased to 200 mg/day over a period of 10 days. At the time of discharge, on the 14th day, he was free from parkinsonian symptoms. Subsequent follow-up showed no parkinsonian symptoms and he had modest improvement in negative symptoms.

A 48-year-old male with schizophrenia for the last 20 years was treated with various antipsychotics without much improvement. Since the last 6 months, he was on olanzapine 15 mg/day. As there was no significant improvement, his olanzapine dose was gradually tapered and stopped over a period of 14 days and was started on amisulpride 100 mg/day and was increased to 200 mg/day over a period of 3 weeks. The patient returned on the 24th day with severe parkinsonian symptoms. In this patient also, there was no prior history of parkinsonism. We managed him with injection promethazine 25 mg intramuscular bid first 3 days along with trihexyphenidyl 2 mg bid after stopping amisulpride. After 7 days, parkinsonian symptoms improved considerably and clozapine was introduced at a dose of 25 mg/day which was subsequently increased to 100 mg/day on the 10th day and the patient was discharged. No further EPS was noticed during follow-up.

DISCUSSION

Since the discovery that clozapine induces fewer EPS and is more effective for negative symptoms than conventional antipsychotics for the treatment of schizophrenia, psychopharmacological research has focused on the development of drugs that block central 5-HT₂ receptors more than D₂ receptors. Combined 5-HT₂/D₂ receptor antagonism is the most current explanation for the so-called “atypical” profile of some antipsychotics.^[5]

Amisulpride at low doses binds selectively to dopamine D₂, D₃ autoreceptors, thereby enhancing dopaminergic transmission and thus might be effective for negative symptoms.^[6] It has no affinity for D₁, D₄, and D₅ receptor subtypes. At higher doses, it blocks postsynaptic receptors, thus inhibiting dopaminergic hyperactivity. At the same time, amisulpride has greater specificity for the limbic system and thus has low incidence of EPS. Amisulpride binds more loosely than dopamine to the dopamine D₂ receptor and is rapidly dissociated from the dopamine D₂ receptor. This effect

obviates EPS and thus explains clinical atypicality of amisulpride.^[2]

Low-dose therapy with amisulpride is associated with a significantly lower blockade of striatal dopamine D₂ receptors than is seen during high-dose treatment. However, a significant striatal D₂ blockade was demonstrated at therapeutically effective dose ranges, and a good relationship between the degree of striatal dopamine D₂ receptor occupancy and the amisulpride plasma concentration or the administered dose was shown.^[7] In general, Asians are slow metabolizers. Low body weight and slow metabolism may increase the plasma concentration of drugs causing side effects.^[3] Martinot *et al.* reported a low postsynaptic D₂ occupancy in the striatum at low doses of amisulpride (50–100 mg/day). It has also been suggested that extrastriatal binding could mediate the effect on negative symptoms.^[8]

The probable causes of EPS with low doses of amisulpride could be that it blocks postsynaptic D₂ receptors significantly in striatum without much effect in the mesolimbic pathway.^[9] Therefore, it selectively acts on mesocortical and nigrostriatal pathways in low doses. Many more studies are required to establish its selectivity. In our experience, the lower incidence of EPS which is claimed by Western researchers as well as pharmaceutical companies should be studied well in the Indian context. We should at least keep this side effect in our minds while starting or increasing the doses.

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Conflicts of interest

There are no conflicts of interest.

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