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Case Report

Galactorrhea, Amenorrhea and Extrapyramidal Side Effects with Low Doses of Amisulpride

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Abstract

In India, amisulpride comparatively new antipsychotic which is claimed to be effective in both positive and negative symptoms schizophrenia and other disorder even though it has little or no action on serotonergic receptors. Lower striatal dopaminergic receptor binding capacity and limbic selectivity causes of EPS. But, in clinical practice, we are getting EPS with this drug even at lower doses. Reported two cases of akathisia, drug- induced Parkinsonism and one case of galactorrhea, amenorrhea.

Keywords: Galectorrhea; Amisulpride; Amenorrhea

Case Reports

Case 1

A 42-years-old female patient was suffering from Dysthmia currently major depression with psychotic symptoms. She has predominantly had sad mood, other negative symptoms with hallucinatory behavior. She was on fluoxetine + olanzapine combination for 2-3months without much improvement with excessive sleep and overweight. So amisulpride was started with 25 mg increase gradually upto 100 mg/day within 15days to one month, olanzepine was stopped within a week of starting amisulpride. Patient came after 15days for follow-up when she does not have any side effect. But after 4-5months later she is complaining galectorrhea, amenorrhea. On examination Serum prolactine levels are high. Advice to taper and stop medication with one month and consult to gynecologist for higher prolactine levels and amenorrhea.

Case 2

22 years old male patient was suffering from schizophrenia for last five years. He was treated by various psychiatrist and with various antipsychotic before consulting in our hospital. I have given quitipin and trifluoprazine with sufficient duration and dose but very minimal improvement. Started amisulpuride after 2weeks of drug-free period. Started with 50mg bd and increased upto 200 mg/day within week. Patient came back on 10thday with akathisia. Treated with propranolol 20 mg/day. But he was complaining about slowness in doing work, mild rigidity. Started him on tihexiphenden 2 mg/day and stopping amisulpiride.

Case 3

A 37-year-old female patient of schizoaffective depressive type was prescribed Amisulpride 200 mg/day. On 6th day, patient developed acute dystonia reaction with spasm of neck and hand muscles, oculogyric crises. He was admitted resolving dystonia and given promethazine 50 mg i.e., and oral tb. trihexiphenden 2 mg and was stopped amisulpiride to start another antipsychotic.

- **Past history:** No past history in all cases.
- **Family history:** Depression and absconding from home in her in case 3.
- **Birth history:** milestones normal in all cases.
- **Stressors/precipitating factors:** Interpersonal conflicts with husband case 3.

Examination

Objectively evaluate the present condition of the patient, demonstrate if the events affected the patient directly or indirectly

General examination, vital signs, systemic examination

are normal in all 3cases.

Case 1

Mental status examination

Attention and concentration aroused sustained.

Oriented. Speech: normal, thought content: preoccupation and worried about stressor.

Depressive cognations, pessimistic ideas.? Auditory hallucination. Mood sad with restricted affect.

Case 2

Mental status examination: Attention and concentration aroused sustained.

Oriented. Speech: normal, thought content: preoccupation and worried about stressor. Delusion of persecution and reference. Mood normal.

Case 3

Mental status examination: Attention and concentration aroused sustained.

Oriented. Speech: normal, thought content: preoccupation and worried about side effects.

Depressive cognations, pessimistic ideas, suicidal ideas. Mood anxious.

Diagnosis/differential diagnosis

The identification of the nature of an illness or differentiating between 2 or more conditions which share similar signs and symptoms

Diagnosis is Drug Induce side effects

Case 1

Routine Investigations: Hb- 11.2 gm%. Blood sugar 132.Urea-19. S. Creatinine- 0.2 T.C- 13800 (P-24, L-64, M-8, E-3, B-1). Platelets- 4,08000.

Case 2

Routine Investigations: Hb- 10.9 gm%. Blood sugar 112.Urea-18. S. Creatinine- 0.1 T.C- 13600 (P-23, L-65, M-7, E-4, B-1). Platelets-3,20800.

Case3

Routine Investigations: Hb- 12.0 gm%. Blood sugar 108.Urea-20. S. Creatinine- 0.2 T.C- 14400 (P-21 L-68, M-8, E-3, B-0). Platelets- 1,95,400.

Treatment

Medical care given to a patient for an illness or injury

Advices to taper and stop medication over the period of time in all cases. To reduce the side effects of amisulpuride such as galectorrhea, amnorrhea referred to gynecologist in case 1, in case 2 to overcome akathisia started propranolol 20 mg/day, trihexphenden 2 mg/day for mild rigidity and in case 3 to reduce acute dystonia promethezine 50mg i.e., given and started on oral trihexphenden 2 mg/day later.

Discussion

Summary of the case attended

Psychopharmacological research has focused on development of drugs that block central 5HT2 receptors more than D2 receptors. Combined 5HT2/D2 receptor antagonism currently called "atypical" profile of some antipsychotic for treatment of schizophrenia than conventional antipsychotics after the discovery of clozapine as this also has fewer extrapyramidal side effect and is more effective for the treatment of schizophrenia.

Proposed mechanism of action of amisulpiride:

- It binds selectively to dopamine D2, D3, receptors in limbic system, and has no affinity towards D1, D4, D5 receptor subtypes.
- Low dose of Amisulpride block persynaptic D2, D3 auto receptors, thereby enhancing dopaminergic transmission
- At higher doses, blocks postsynaptic receptors, thus inhibiting dopaminergic hyperactivity
- It has greater specificity for limbic system and thus has low incidence of EPS
- It is clinically effective in negative symptoms of acute schizophrenia at low dose, 50100 mg/d

- It binds more loosely than dopamine to the dopamine d2 receptor and is rapidly dissociated from the dopamine D2 receptor. This keeps prolactine levels normal, spares cognitions, and obviates EPS. It shows clinical atypicality.

Low dose therapy with the atypical antipsychotic agent amisupluride is associated with a lower blockade of striatal dopamine D2 receptors than seen in higher dose treatment according to Christian Ia Fougere., *et al.* 2005. In their study showed a good relationship between the degree of striatal dopamine D2 receptor occupancy and the amisulpride plasma concentration also.

A low dose of amisulpride (50-100 mg/d) has a low postsynapticD2 occupancy in the striatum according to Martinot., *et al*. He also suggested that extrastriata binding could mediate the effect on negative sysmptom.

Probable causes of EPS with low dose amisuplpirde are

Without much effect on mesolimbic pathway in low dose it blocks D2receptors significantly in striatum. In low doses it selectively acts on mesocortical and nigrostriatal pathways.

Slow metabolism and low body weight probably increase the plasma concentration of drugs causing side effects.

Learning points

A small brief on what you have learnt from the case

Amisulpuride dissociation from D2 receptors is not much rapid as it is thought.

With respect to experience, when risperidone came to India, researchers said that EPS will occur at doses >6 mg/d. but it has been seen in 2 mg/d also. It may be same case with amisulpride. Much more studies are required to establish its pathways [1-6].

Summary and Conclusion

A brief statement or account of the main points of article, cases, topics

Most of the studies are about low dose amisulpride causes EPS and galectorrhea, amenorrhea from western countries as amisulpride is new to Indian market. Its effectiveness, both positive and negative symptoms schizophrenia with lower chances of metabolic syndrome, so it will help psychiatrist to treat cases of schizophrenia and related disorder with good effect. Just started prescribing the drug in our setting with which some patient developed EPS, amenorrhea, and galectorrhea in lower doses. So in my opinion more studies needed in Indian context with low dose of amisulpride with keeping in mind with these side effect when starting or increasing the doses.

Bibliography

1. Boyer P., *et al.* "Amisulpride verses amineptine and placebo for the treatment of dysthymia". *Neuropsychobilogy* 39 (1999): 25-32.

2. Bressen RA., *et al.* "Is regionally selective D2/D3 dopamine occupancy sufficient for atypical antipsychotic effect? An *In vivo* quantitative epidepride SPET study of Amisulpride-treated patients". *The American Journal of Psychiatry* 160 (2003): 1413-1420.

3. Danion JM., *et al.* "Improvement of schizophrenic patients with primary negative symptoms treated with amisulpride. Amisulpride Study Group". *The American Journal of Psychiatry* 156 (1999): 610-616.

4. IaFougere C., *et al.* "D2 receptor occupancy during high and low-dose therapy with the atypical antipsychotic amisulpride: A123 I-iodobenzamide SPECT study". *Journal of Nuclear Medicine* 46 (2005): 1028-1033.

5. Leucht S., *et al.* "Amisulpride, an unusual "atypical" antipsychotic: A meta-analysis of randomized controlled trials". *The American Journal of Psychiatry* 159 (2002): 180-190.

6. Martinot JL., *et al.* "*In vivo* characteristics of dopamine D2 receptor occupancy by amisulpride in schizophrenia". *Psychopharmacology (Beri)* 124 (1996): 154-158.