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Case Report

Neuroleptic Malignant Syndrome with Minimal Dose of Amisulpride

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Amisulpride is an atypical antipsychotic drug, it helps in alleviation of symptoms of psychotic illnesses. Extrapyramidal features have been reported after taking amisulpride. Neuroleptic malignant syndrome (NMS) with amisulpride is rare, and have been reported earlier. In all the earlier reported cases patient received more than 150 mg of amisulpride. To the best of our knowledge we are reporting a case of NMS with very minimal dose of Amisulpride (50 mg) taken for very short period.

Key words: *amisulpride, neuroleptic malignant syndrome, extrapyramidal feature*

Background

Neuroleptic malignant syndrome (NMS) is a rare side effect of antipsychotic drugs, which is characterized by altered mentation, hyperthermia, increased rigidity and elevation of creatine phosphokinase (CPK) along with other autonomic features like diaphoresis, tachycardia, tachypnoea and fluctuation in blood pressure (BP). It is rare with newer antipsychotic drug. Amisulpride is an atypical antipsychotic agent used in alleviation of negative and positive symptoms of schizophrenia, symptomatic treatment in manic -- depressive illness and atypical depression. Extrapyramidal side effects and NMS with amisulpride are attributed to blockade of D2 receptors at nigrostriatal pathway. NMS has earlier been reported with amisulpride mostly with doses more than 150 mg/day.

Case report

This 70 year old gentleman with prior long history of psychotic illness, for which he had taken irregular treatment in the past, but was not on any treatment for last one year. As per history given by his son he started having behavioral symptoms in form of suspiciousness, speaking to self, withdrawal behavior, forgetfulness, insomnia along with anxiety for last few weeks. He was assessed in psychiatry outpatient department (OPD), there was no history of long term fever, any cough, weight loss, any drug intake, seizure, trauma, dehydration, decreased oral intake or diarrhea. A thorough neurological examination was done for any neurological deficit but was normal. He was provisionally diagnosed as case of long term psychoses with current exacerbation of symptoms. He was started on low dose amisulpride (50 mg) along with 0.25 mg of clonazepam. Three days later his son reported that patient had altered sensorium without responding to any verbal command, was unable to sleep at night, and became bedridden. Patient was seen in emergency room, on examination his BP was 150/80, pulse rate was fluctuating between 60-112/min, temperature 38.8°C, patient was drowsy, not following any verbal command, pupils were bilateral normal size normal reaction, there was marked rigid-

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ity in all the 4 limbs along with marked axial rigidity. All DTRs were present with non elicitable planter response. His overall Glasgow coma scale (GCS) was E4V2M5. All the routine tests done showed Hb13.4 gm/dL, TLC 12,600 cells/cmm, ESR 45 mm, platelet count 2.78l ac/cmm, Serum bilirubin 0.48 mg/dL, SGPT 59 U/L, SGOT 41 U/L, Serum protein 7.1 gm, Albumin 3.6 gm, Serum alkaline phosphate 85 U/L, Serum urea 50 mg%, Serum creatinine 1.2 mg/dL, Serum sodium 144 mmol/L, Serum potassium 4.3 mmol/L, thyroid profile (T3, T4, TSH) was normal, urine routine microscopy and biochemistry was normal, MRI brain showed age related atrophic changes without evidence of any acute infarct or hemorrhage. Electroencephalography was normal. Repeated measurement of CPK revealed 840 IU and 990 IU (normal 24-195 IU) subsequently. Clinically he was fulfilling the DSM-IV TR criteria for NMS [1]. He was admitted and managed conservatively. His all medications for psychiatric illness were withheld. He was started on tablet Bromocriptine 2.5 mg thrice daily along with proper hydration. With all these efforts patient started improving in his sensorium and rigidity. CPK fell to normal limit on the 5th day of admission, and was discharged after 7 days of care.

Discussion

The incidence of NMS is 0.02-3% in patients taking antipsychotic drug in different studies.[2] Amisulpride is a second generation antipsychotic drug, works by highly selective D2/D3 receptor antagonism.[3] Extrapyramidal side effects have been reported with amisulpride but NMS is rare.[4]

So far only seven cases of NMS were reported with amisulpride, Some of these cases were associated with external factors like myopathy and toxic encephalopathy, some used amisulpride along with other drugs.[5-11] A systemic review and case analysis published in 2015 assessed these cases, the dose of amisulpride ranged from 480 to 179 mg and in four of these cases NMS occurred following an increase in the dose of the drug, and one led to the death of the patient.[12] So we can postulate that though NMS is an idiosyncratic reaction but the dose of drug plays some role in pathogenesis, as in above analysis patients developed NMS with escalation of dose. In our case NMS developed with 50 mg of amisulpride.

There is variation in symptomatology among NMS induced by different drugs. Amisulpride induced NMS shows clinically milder symptoms as compared to NMS with typical antipsychotic drugs. The clinical features are mild with benign elevation of temperature and mild elevation of CPK in blood.[9-11] Also in the course of disease it develops earlier within 1-4 days of drug exposure.[13] Furthermore, amisulpride has a low affinity for muscarinic, alfa-adrenergic, serotonergic, and histamine receptors, which could explain milder form in autonomic dysfunction.[14] All these above mentioned features were similar in our case as well.

According to Schoemaker et al. at low dose amisulpride selectively blocks the postsynaptic D2 receptors at striatum without much effect on mesolimbic pathways, thus responsible for extrapyramidal side effects, same can be postulated for the NMS as well.[15]

NMS is generally regarded as an idiosyncratic drug reaction, implying that it is unpredictable and dose-independent, but this view was challenged when cases of NMS were seen after antipsychotic withdrawal.[16-17]

Certain risk factors if present in patient also predispose to NMS such as dehydration, physical exhaustion, exposure to heat, hyponatremia, malnutrition, trauma, alcohol, thyrotoxicosis, and presence of structural or functional brain disorder such as encephalitis, tumor, delirium and dementia.[18-20] NMS due to amisulpride shows milder symptoms as compared to typical antipsychotics, thus difficult to diagnose early. Early detection and management can deter morbidity and mortality. We should always be cautious before starting amisulpride in patients with above mentioned risk factors.

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