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Research Article

LOW DOSES OF AMISULPRIDE AND ITS SIDE EFFECTS IN TREATING SCHIZOPHRENIA

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A B S T R A C T

Amisulpride , the antipsychotic drug is claimed to be effective in both positive and negative symptoms of schizophrenia and related disorders. It has less to no action on serotonergic receptors. Limbic selectivity and lower striatal dopaminergic receptor binding capacity causes very low incidence of extra pyramidal side effects. But in clinical cases extra pyramidal side effects are seen even in lower doses in Indian context. More research on low doses of amisulpride and its side effects is required in India to find out the association.

INTRODUCTION

One of the most serious mental illnesses is schizophrenia. Schizophrenic patients often suffer with auditory hallucinations, false perceptions like hearing abusing voices, strong false beliefs (delusions). The patient hear voices which comment on the patient's actions. People who hear such voices often make some sense of these hallucinations. It usually starts in early adulthood. Depending on the balance of symptoms, Schizophrenia is classified into sub types like paranoid, hebephrenic, catatonic and simple.

In paranoid type of schizophrenia, delusions or hallucinations are prominent. In Hebephrenic type lack of goal directed behavior, and prominent thought disorder is observed. In catatonic or unresponsive type,10-14 days of catatonic behavior with stupor, excitement, posturing and rigidity is observed and finally in the simple type, considerable loss of personal drive, deepening negative symptoms pronounced in social, academic or employment performance is observed. Substance abuses along with suicidal thoughts are also common in people with schizophrenia. Mild symptoms of schizophrenia may occur in healthy individuals who are not associated with disease.[1]The most common symptoms of schizophrenia are lack of insight, auditory hallucinations, ideas and delusions of reference, suspiciousness, delusional mood, delusions of persecution, thought hallucination, and thoughts spoken aloud. The cause of this illness is multifactorial, both genetic and environmental factors are involved. Treatment of this disorder alleviates the symptoms, reduces distress and improves primary care.

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Medication is the basis for treatment for many diseases and so is with schizophrenia. Antipsychotic drugs control the symptoms by affecting dopamine which functions as neurotransmitter. Dopamine is a chemical released by the neurons to transmit signals to other nerve cells.

According to National Institute of Health and Care Excellence (NICE) guidelines the patient must remain on prophylactic doses of antipsychotics for about one to two years and must be kept under observation. When the patient recovers from all symptoms, then the drug dosage can be reduced gradually and monitored to identify any relapsing signs. If there is sign of relapse, then the dose must be increased until it completely disappears. It is necessary to undergo screening test for hyperglycemia, hyperprolactinaemia, endocrine disorders, hypertension and hyperlipidaemia along with common side effects of 1st generation, 2nd generation and 3rd generation antipsychotic drugs. Sometimes the patients may be given secondary care due to poor treatment compliance, substance misuse or poor treatment response.

Resperidone, olanzapine, clozapine are some of the antipsychotic drugs. Intermitant dosing regimens which help in reducing side effects is not advisable as it makes the disorder to relapse. Lowest effective dose of antipsychotic drug which is effective should be used. Anticholinergic drugs should not be routinely prescribed in order to prevent side effects, as they have adverse effects on cognition and memory. Schizophrenia patients also face side effects when they use antipsychotic drugs. Some of these side effects are movement problems like tremors, slow movement or bradykinesia and sometimes unable to move (akinesia).

There are many genes which are associated with schizophrenia out of which neurogulin1(NRG1),dysbindin(DTNBP1) and DISC1 are some of them.[2] The patient's disorder is inherited due to interaction of several risk associated genes and environmental factors.Drug stimulants like cocaine, amphetamines and cannabis may lead to paranoid schizophrenia. Variations in the catechol-o-methyltransferase (COMT) gene effect the propensity to develop psychosis.

Some of the first generation antipsychotic drugs are Fluphenazine, chlorpromazine, haloperidol, perphenazine, and laxapine. These drugs act as antidopaminergics (dopamine antagonist) and they act on 4 major dopamine pathways.

1.Mesolimbic pathway in the brain which connects the ventral tegmental area in the mid brain to the ventral striatum of basal ganglia in the fore brain. 2) mesocortical pathway connects the ventral tegmentum to pre-frontal cortex. 3) Nigrostriatal pathway connects the susbtantia nigra pars compacta with the dorsal striatum 4) tuberoinfundibular pathway.

Tuberoinfundibular pathway projects from arcuate nucleus in the tuberal region of the hypothalamus in to the median element. Besides dopamine antagonism the 1st generation drugs also effect receptors like muscarinic adrenergic alpha1 and histamine due to which these drugs have side effects profile.

The 2nd generation antipsychotic drugs not only block dopaminergic receptors but also block serotonin 2A (5HT2A) receptors. Hence they are also called as serotonin dopamine antagonists. These drugs have lower risk of neurological side effects and increase risk of metabolic side effects like hyperglycemia, weight gain, and dyslipidinemia. The only antipsychotic 3rd generation drug is Arpiprazole.

Amisulpride drug is a second generation antipsychotic drug with lower risk of side effects. Although amisulpride drug does not block serotonin receptors, yet it is a highly selective D3/D2 receptor antagonist. Due to its selective affinity for dopamine receptors only in the limbic structures, it leads to a low risk of extrapyramidal side effects.

Case-Study

Literature study reports suggest that the extra pyramidal side effects are very less and mostly associated with doses >400 mg/day , but studies in the Burdwan region of West Bengal, India have seen drug-induced dystonia and extrapyramidal side effects even in low doses of Amisulpride [1]. The same was also observed in King George Hospital, Visakhapatnam, India, where a 39 year female patient was suffering with schizo effective depressive type. She was on amisulpride 50mg/d for 3 months with slight improvement and overweight, with tremor in hands and tongue and with rigidity and bradykinesia. She was on antipsychotic drugs of amisulpride, and olanzapine. As she complained about overweight, dysmenorrhea, rigidity in limbs, she was managed with escert and 3rd generation drug Arpiprazole 10mg/day and stopping amisulpride because of the side effects.

DISCUSSION

Amisulpride selectively binds to dopamine D2, D3 receptors in the limbic system and has no affinity for D1,D4 and D5 receptor subtypes. Low doses of the amisulpride drug enhances dopaminergic transmission by blocking presynaptic D2,D3 autoreceptors. If given in higher doses, it inhibits dopaminergic hyperactivity by blocking post synaptic receptors. The drug does not show any affinity to other dopaminergic receptors and to central serotonergic, histamine, and renergic receptors. Amisulpride binds loosely to the dopamine D2 receptors and quickly dissociates from the dopamine D2 receptors, thereby keeping the prolactin level normal. It spares cognition and obviates extra pyramidal side effects. It also has greater specificity for the limbic system. It is clinically effective on the negative symptoms of acute schizophrenia at low doses of about 50-300mg/day.

CONCLUSION

The effectiveness of amisulpride, both for positive and negative symptoms of schizophrenia with lower chances of metabolic syndrome helps psychiatrists to treat schizophrenia effectively. The above study shows that the lower incidence of extrapyramidal side effects should be well studied in Indian context by researchers and pharmaceutical companies.

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