Case Report

Risperidone Induced Extrapyramidal Side Effects: A Rare Case Report

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ABSTRACT

Antipsychotics are the group of drugs chiefly used in the management of Schizophrenia. They are classified into two generations i.e., first and second generations. First-generation drugs were greatest expected to cause extrapyramidal symptoms. With the discovery of second generation antipsychotics, the lower affinity for dopamine receptors had raised expectations in the clinical community regarding the lower risk for extrapyramidal symptoms. Various antipsychotics differ in their incidence and severity of causing extrapyramidal side effects, but these second generation drugs have not encountered up to the expectation with regard to their tolerability. Extrapyramidal side effects generally consist of a group of movement disorders such as tardative dyskinesia, Pseudoparkinsonism, dystonia and akathisia. Symptoms pertained to Pseudoparkinsonsim, acute dystonia and akathisia occur early in treatment course, but tardive dyskinesia, tardive dystonia, and tardive akathisia have a late onset, occurring after years of treatment course. The acute forms of extrapyramidal side effects usually develop soon after the starting of antipsychotic use, these are dose-dependent and increases with the increase in the dose, and can be prevented after withdrawal of the insulting medication.

Key words: Extrapyramidal side effects, Akathisia, Pseudoparkinsonism, Dystonia.

INTRODUCTION

Schizophrenia is a well-known psychiatric disorder, often presents with several symptoms involving thoughts, perception, emotions, movements and behavior. It is one of the key health concerns affecting a considerable population in the world.[1] Pseudoparkinsonism is produced by the blockade of dopamine D_2 in the nigrostriatum in the central nervous system which has a resemblance with the idiopathic Parkinson disease. Patients diagnosed with Pseudoparkinsonism can present with any of the four cardinal symptoms like Resting tremors, bradykinesia, cogwheel rigidity and postural instability. Pill-rolling tremors are usually manifested in the fingers, hands, legs, neck, head, and chin whereas Cogwheel rigidity, manifested in patient's limbs resulting in jerky, ratchet-like fashion on moving passively by examiner. Instability is presented in the patient as stooped posture, trouble in sustaining stability during changing the position of the body, and the slow and shuffling gait can be observed. Akinesia, small and cramped hand writing known as micrographia, slowed speech, and reduced arm swing, abnormal palmomental refluxes, fatigue, difficulty in swallowing, dysarthria, and glabellar reflexes can also be seen.

Akathisia is the incapability of an individual to sit still and to be functionally motor restless. The maximum precise diagnosis is completed by uniting subjective with objective indications like shuffling, pacing, shifting, or tapping feet. Subjectively the patients might explain a feeling of disquiet or restlessness or a pressure to move or persist in unceasing motion.[2] The underlying mechanism of this type of extrapyramidal side effects (EPS) is not so clear, but two theories may explain it. One of the theories explains that the postsynaptic dopamine antagonism in the mesocortical pathway results in increased locomotor activity. Other theory states that this is caused by dysregulation of noradrenergic tracts projecting from the locus ceruleus to the limbic system due to dopamine antagonism. This EPS is reported in as many as to 45-

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55% of patients prescribed with first generation drugs and ranges from 6% to 16% of patients prescribed with second generation drugs.[3]

There may be a little distress with mild side effects which doesn't require any change in the treatment but monitoring the effects should be done. When severe or distressing side effects occur, possibilities include decreasing the dose of the drug or prescribing a medication to manage the Adverse drug reaction (ADR) (e.g., Anticholinergic to manage drug-induced pseudoparkinsonism), lifestyle changes (e.g., change in the diet composition for managing constipation caused by an antipsychotic drug), or a shift to other antipsychotic with a minor possibility of causing the ADR. Risperidone, a second generation antipsychotic (SGA) may cause EPS mostly within the first 3-4 months of therapy. In comparison to the other antipsychotic Clozapine, Risperidone causes EPS that are in between clozapine and other conventional antipsychotic drugs.[4,5] Individuals diagnosed with schizophrenia generally have a greater prevalence of type II diabetes than the normal population because of several factors including their underlying disease and cognitive factors affecting their adherence to other drugs. Not only but also these drugs deleteriously alter the blood sugar levels in patients suffering with diabetes but the extent of this effect is not so clear. Data obtained from the United States Food and Drug Administration (US FDA) Med Watch Drug Surveillance System for drugs like Clozapine, Olanzapine, Quetiapine, and Risperidone reported that 60-65% of the new onset diabetes within the initial 6 months of starting of the treatment. Aripiprazole is less prone to cause diabetes.[2]

In the year 2004, the US FDA delivered a safety alert that necessitated revisions in the labeling of all the second generation antipsychotics due to elevated risk of type II Diabetes Mellitus in patients taking these atypical antipsychotics. Because of persistently growing marketing demand of atypical antipsychotics Extrapyramidal side effects must be clinically monitored and managed.

CASE REPORT

A 42-year-old female patient was presented to the department of Psychiatry with complaints of restless moving, stiffness of arms and legs and disturbed sleep. The patient was a known case of paranoid schizophrenia and type II diabetes mellitus since 6 months and is on Tab. Risperidone 3 mg orally once daily and Tab. Glimepiride 2mg orally twice daily since 6 months. She had no known history of EPS till the use of this drug. She is a home maker and none in her family had a history of psychiatric illness. After starting Tab. Risperidone gradually from the past one month, the patient developed restless moving indicating akathisia and stiffness of arms and legs indicating pseudoparkinsonism which made the patient to use this drug irregularly. Given these symptoms, the patient was made to discontinue the Risperidone completely after admission in the hospital and started with Tab Luracidone 40 mg once daily which has a lower incidence of EPS, Tab Trihexyphenidyl 2 mg once daily which is an anticholinergic to treat parkinsonism and akathisia, and Tab Lorazepam 0.5 mg oral twice daily was prescribed to sedating and calming down the patient. Upon physical examination, the patient was 5'4" tall and weighed 75 Kgs. No skin rashes or lymphadenopathy were noted. Abdominal examination was unremarkable, without distention and tenderness. Her Laboratory investigations revealed PPBS: 225 mg/dL, FBS: 167 mg/dL, HbA_{1c}: 9.6%. ECG showed low QRS amplitudes and tachycardia. Tab. Glimepiride was replaced by Tab Metformin 500 mg twice daily because Tab. Metformin is advantageous in overweight patients. Physical examination was conducted during the time of the discharge on Day 6 which revealed a decreased stiffness and decreased restless movement of arms and legs. The patient was advised to use Tab. Luracidone, Tab. Trihexyphenidyl even after the discharge. The patient and the care taker were instructed not to use Tab. Risperidone again without informing the physician.

DISCUSSION

Extrapyramidal symptoms comprises of acute dystonias, akathisia, Pseudoparkinsonism, and tardive dyskinesia (TD). Here the patient developed pseudoparkinsonism and akathisia. These adverse drug reactions are serious, sometimes devastating and require additional pharmacotherapy for their management. They develop into two phases: Early, acute EPS most often develop with the commencement of treatment with antipsychotics or if their dose is increased. The later-onset EPS occurs after prolonged therapy and presents as TD. The motor manifestations developed in this patient are akathisia, acute dystonia, and Parkinsonism after the 6 months of therapy indicating late onset and were managed using Tab Trihexyphenidyl. Tab Risperidone was replaced by Tab Luracidone because of its increased safety. SGAs have not entirely satisfied the expectation of being EPS-free antipsychotic drugs which is evident in this patient.

Many of the recent studies showed that SGAs do not considerably differ from First Generation antipsychotics (FGAs) in efficacy terms (with the exception of clozapine for treatment-resistant individuals) and have a poorer incidence to cause EPS than FGAs, but with great differences within the class. The probability of

causing EPS with a SGA is multi factorial like patient's characteristics, medical and medication histories, the choice of a particular antipsychotic, its dose, and duration of therapy and adjuvant pharmacotherapy in the order to decrease the risk of EPS and to provide the best quality of care.[6] Since the therapeutic outcome and adverse effects are not so easily predictable, a trial-and-error approach is recommended. Expectantly, the recent, promising advances in pharmacogenomics and neurobiology might provide predictive markers of antipsychotic response and adverse drug effects and lead towards personalized therapy.[4]

CONCLUSION

This report represents Risperidone-induced Extrapyramidal side effects related to Risperidone therapy, highlighting the need for clinician awareness regarding potential extra pyramidal syndrome of Risperidone and its management in clinical settings.

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CONFLICT OF INTEREST:

The authors declare no conflict of interest.

ABBREVIATIONS

5 HT: 5- hydroxytryptamine; **D_2:** Dopamine 2 receptors; **EPS:** Extrapyramidal side effects; **FBS:** Fasting blood sugar; **US FDA:** The United States Food and Drug Administration; **FGA:** First Generation Antipsychotics; **HbA_{1c}:** Glycosylated Haemoglobin; **PPBS:** Post Prandial Blood Sugar; **SGA:** Second Generation Antipsychotics; **TD:** Tardive Dyskinesia.

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