

Reversible Hyperkinetic Movement Disorder Related to Quetiapine Withdrawal: A Case Report *

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ABSTRACT

Quetiapine is used in treatment of schizophrenia, schizoaffective and bipolar disorders as well as psychosis in Parkinson's disease (PD) patients. Neurological side effects are not uncommon with this drug. However, there is limited knowledge about quetiapine withdrawal extra-pyramidal side effects. More recently quetiapine is used for sleep disorders and behaviour abnormalities in PD and its related syndrome. Therefore withdrawal dyskinesias may become more widely observed in the future, and patients need to be warned against sudden discontinuation of the drug. We present a rare case of Quetiapine withdrawal and discussing his bizarre abnormal movement.

Keywords: atypical antipsychotics, dyskinesia, dopamine receptor

INTRODUCTION

Atypical antipsychotic (AA) agents that alter serotonergic neurotransmission as well as dopamine receptor blockade have been reported to have a low risk of inducing acute and sub-acute extrapyramidal symptoms such as dystonia, akathisia, and Parkinsonism. Likewise, tardive dyskinesia has been uncommonly documented with quetiapine. We report a case of hyperkinetic movements associated with acute withdrawal of quetiapine that recovered with re-introduction of the drug.

Case Report

A 30-year-male tourist who was apparently well prior to his admission in the hotel. He was discovered by hotel staff in a state of confusion with abnormal limb movements. On arrival at the Emergency Department he was found to be agitated, profusely sweating, tachycardic (pulse rate 110 beats per minute) and blood pressure was 130/72. He had incoherent speech and was not able to give any relevant history. He had travelled alone and there were no relatives or friends to

contact for further history. He had involuntary, irregular jerky movements of his head as well as facial grimacing. There were also purposeless, asynchronous, tremulous movements of his hands which were almost continuous. Gait was mildly ataxic. The remainder of the neurologic examination was non-focal including reflexes, with plantar responses were flexor. Routine investigations included infectious, inflammatory, and metabolic screening, which were negative. Electroencephalography and CT (computer tomography) scan of the brain were also normal. He was initially diagnosed with delirium tremens and treated with benzodiazepines, but there was little improvement.

Subsequently, his urine toxicology screen returned as unremarkable except for traces of quetiapine. He was started on quetiapine 12.5mg bid with gradual increment to 100mg per day. Three days after the introduction of quetiapine, he was speaking coherently and the involuntary movements were less pronounced. He informed us that he carried a diagnosis of schizophrenia and had been on long term quetiapine treatment, with total dose 400mg per day without any recent change. He had run out

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of the medicine 2 days before arriving to Singapore. His symptoms resolved completely four days after restarting quetiapine and he was discharged in a stable state.

DISCUSSION

To our knowledge, only a few cases of symptoms arising from quetiapine withdrawal have been reported in the literature so far^{1,2}. Our patient who had a long standing schizoaffective disorder, experienced emesis, diaphoresis, orthostasis, tachycardia, and disorientation along with bizarre abnormal hyperkinetic movements which were predominantly choreiform in nature after abruptly discontinuing quetiapine. These symptoms completely resolved when quetiapine was restarted. Three neurotransmitters may play a role in this discontinuation syndrome. Quetiapine is a dopamine D2, serotonin 5-HT_{1A}, and histamine H₁ receptor antagonist. Dopamine, serotonin, and histamine receptors are present in the chemoreceptor trigger zone, a medullary site that causes nausea and emesis when stimulated. Dopamine and serotonin also influence autonomic control in brainstem nuclei. Therefore, these neurotransmitters are present in brain regions that could cause nausea and autonomic dysregulation. Our patient's symptoms were similar to those reported in patients who were withdrawn from other atypical³ and typical⁴ antipsychotics, implicating dopamine. They also resembled the selective serotonin re-uptake inhibitor discontinuation syndrome⁵, suggesting a role for serotonin. These clinical findings and the fact that quetiapine affects predominantly histamine at low doses suggest that our patient's symptoms were due to withdrawal of H₁ antagonism. However, his therapeutic improvement raises the possibility that he was highly sensitive to all of quetiapine's pharmacological effects. Atypical antipsychotics are expected to be better tolerated than first generation antipsychotics because of their lower propensity to cause certain adverse effects^{6,7}. We postulate that the critical factors that precipitated the withdrawal hyperkinetic movements were the high doses (400 mg/day) of quetiapine used, the length of time patient was on the medication and its abrupt withdrawal. The chronic blockade of dopamine receptors in this patient induced by the use of quetiapine likely resulted in a compensatory increase in central dopamine production. Chronic dopamine receptor blockade may have

additionally resulted in increased receptor binding sites and increased dopamine receptor affinity^{8,9}. Time course of development and resolution of symptoms are in favour of quetiapine withdrawal syndrome, re-introduction of quetiapine led to complete resolution of his hyperkinetic movement within 4 days.

RECOMMENDATION

The use of AAs such as quetiapine is rapidly increasing as result of a widening number of therapeutic indications and less severe side effects as compared to the conventional antipsychotic agents. Therefore, it is expected that withdrawal symptoms due to these agents may become more commonly observed in the future. Our experience with this patient emphasizes the importance of having a high index of suspicion for possible antipsychotic withdrawal-related symptoms, since patients may not be able to give a relevant history of antipsychotic use at presentation. In these situations, toxicology tests may be helpful in detecting traces of the withdrawn medication.

Finally, when initiating treatment with antipsychotic agents, patients and their caregivers need to be warned against the possible risks of sudden discontinuation of these drugs, and a gradual withdrawal of the drug over a period of time with careful monitoring of the symptoms is recommended.

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