Case Report

Dose-Dependent Olanzapine-Induced Myoclonus

Sai Krishna Tikka, Alok Pratap[1], Vinod Kumar Sinha[1]

Departments of Psychiatry, K. S. Mani Center for Cognitive Neurosciences, [1]Psychiatry, Central Institute of Psychiatry, Ranchi, Jharkhand, India

ABSTRACT

Second-generation antipsychotics (SGA), mainly clozapine have been reported to induce myoclonus. Although olanzapine-induced myoclonus is reported, dose-dependent response has not been described. We report dose-related olanzapine-induced myoclonus in an early onset schizophrenia patient. We also suggest certain management strategies for such adverse side effects.

Key words: Dose-dependent, myoclonus, olanzapine

INTRODUCTION

Although all antipsychotics have been associated with a risk of seizures, second-generation antipsychotics (SGA) seem to have a higher risk of seizures than first-generation antipsychotics (FGA).[1] In addition to generalized seizures, SGAs have been reported to induce myoclonus as well. Apart from clozapine, which is commonly implicated,[2] other drugs like olanzapine too have been reported to induce myoclonus; such reports are however only a few.[3,4] We report dose-related olanzapine-induced myoclonus in an early onset schizophrenia patient.

CASE REPORT

Mr A, a 19-year-old single, Hindu, male student presented with suspiciousness, violent behavior, and remaining aloof for past 3 years. There was no significant family or past history of psychiatric or neurological illness, epilepsy, significant head injury, or any other features suggestive of organicity. Baseline investigations including complete hemogram, liver and renal function test, fasting blood sugar, lipid profile, and computed tomography (CT) brain were within normal range. On mental status examination he had blunted affect, made act, made affect, auditory hallucinations giving a running commentary, and poor insight. He was diagnosed paranoid schizophrenia according to International Classification of Diseases (ICD)-10. In the past, he was tried on olanzapine 15 mg at bed time 2 years back. He then complained of jerking movements of legs, occurring mostly in the evenings, at a frequency of three to four clusters a day. Clonazepam 1 mg/day was added for myoclonic jerks and he responded well, only to reappear once clonazepam was stopped. As he showed improvement in his psychotic symptoms in the subsequent 8 weeks, dose of olanzapine was reduced to 10 mg. Myoclonic jerks subsided and he maintained well for about 1 year. After another 1 year, he relapsed due to poor drug compliance and presented again with the earlier symptoms and psychopathology. As he was off medications for more than 6 months, he was restarted on olanzapine with 5 mg weekly hikes from 10 to 20 mg. When on 15 mg dose, he reported jerking movements of legs again, which increased in frequency to four to five clusters a day when his dose reached 20 mg. Interictal resting electroencephalography (EEG), showed bilaterally synchronized polyspike discharges. Olanzapine was stopped and risperidone was started. Myoclonic jerks completely subsided and he showed good improvement in his symptoms. The Naranjo adverse drug reaction probability

Access this article online

Quick Response Code:

Website: www.toxicologyinternational.com

DOI: 10.4103/0971-6580.155393

Address for correspondence: Dr. Sai Krishna Tikka, Department of Psychiatry and K. S. Mani Center for Cognitive Neurosciences, Central Institute of Psychiatry, Kanke, Ranchi - 834 006, Jharkhand, India. E-mail: cricsai@gmail.com

scale score for myoclonic jerks was 10 suggesting a 'definite' association with administration of olanzapine.

DISCUSSION

Earlier reported cases of olanzapine-induced myoclonus were elderly and had comorbid neurodegenerative and physical disorders.[3,4] Ours is the first case of olanzapine-induced myoclonus in an adolescent patient with schizophrenia. No other plausible causes of this adverse reaction could be identified in this case. This case suggests that myoclonic jerks were induced by olanzapine and that these were clearly dose dependent. Although dose-dependent relationship between clozapine and seizures is established,[5] such relationship with olanzapine has not been recognized. Nevertheless, EEG abnormalities in patients treated with olanzapine have been shown to be directly related to its dose.[6]

Olanzapine is pharmacologically related to clozapine; both block 5-HT2-, D4-, H1- and ACh-Mus receptors. Antagonism of H1- and ACh-Mus receptors has been implicated in EEG abnormalities and seizures.[7] However, exact mechanism of antipsychotic-induced myoclonus is not known; hypothesis that multiple effects on serotonergic neurotransmission are involved has the strongest evidence.[8]

Reported cases of olanzapine-induced myoclonus were managed by discontinuing the offending drug. Through this report, we propose that, in addition to discontinuation of the drug, one could also reduce the dose of drug or add clonazepam to the existing dose of olanzapine. Starting with low doses and then titrating slowly would determine the exact dose at which the drug is offending; then trial would be to maintain on a dose one level lower to the offending dosage. Caution is definitely indicated for exacerbation of psychotic symptoms on reduction of dose. Feasibility of adding clonazepam needs further research as to how long would be the duration of add-on regimen is not known. Addition of clonazepam is found to be effective in clozapine-induced myoclonus as well.[2]

REFERENCES

1. Lertxundi U, Hernandez R, Medrano J, Domingo-Echaburu S, García M, Aguirre C. Antipsychotics and seizures: Higher risk with atypicals? Seizure 2013;22:141-3.
2. Praharaj SK, Venkatesh BG, Sarkhel S, Zia-ul-Haq M, Sinha VK. Clozapine-induced myoclonus: A case study and brief review. Prog NeuroPsychopharmacol Biol Psychiatry 2010;34:242-3.
3. Camacho A, Garcia-Navarro M, Martinez B, Villarejo A, Pomares E. Olanzapine-induced myoclonic status. Clinl Neuropharmacol 2005;28:145-7.
4. Rosen JB, Milstein MJ, Haut SR. Olanzapine-associated myoclonus. Epilepsy Res 2012;98:247-50.
5. Varma S, Bishara D, Besag FM, Taylor D. Clozapine-related EEG changes and seizures: Dose and plasma-level relationships. Ther Adv Psychopharmacol 2011;1:47-66.
6. Amann BL, Pogarell O, Mergl R, Juckel G, Grunze H, Mulert C, *et al*. EEG abnormalities associated with antipsychotics: A comparison of quetiapine, olanzapine, haloperidol and healthy subjects. Hum Psychopharmacol 2003;18:641-6.
7. Shiloh R, Nutt D, Weizmann A. Atlas of psychiatric pharmacotherapy. London: Martin Dunitz; 2000.
8. Pranzatelli MR. Serotonin and human myoclonus. Rationale for the use of serotonin receptor agonists and antagonists. Arch Neurol 1994;51:605-17.

How to cite this article: Tikka SK, Pratap A, Sinha VK. Dose-Dependent Olanzapine-Induced Myoclonus. Toxicol Int 2014;21:335-6.

Source of Support: Nil. **Conflict of Interest:** None declared.