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A Case Report of Venlafaxine Induced Akathisia

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Abstract

Venlafaxine, a selective serotonin-norepinephrine reuptake inhibitor (SSNRI) approved by FDA in 1983 for treatment of depression, lately approved for anxiety disorder is a popular medication all over the world. Though symptoms of nausea, vomiting, dizziness, and insomnia are frequent with Venlafaxine, akathisia is reported rarely. A thorough search on the internet revealed only 6 case reports of Venlafaxine induced akathisia till now. This is a case report of a young adult male from India, known case of Major Depressive Disorder (not on treatment), who presented to the outpatient department with high-grade fever with chills, rigors, headache, body ache, and nausea. The patient was diagnosed with *Plasmodium vivax* malaria and started on the standard regimen of chloroquine [0 (10 mg/kg), 6, 24 and 36 hours (5 mg/kg)] followed by primaquine (30 mg, 14 days). Patient was started on Venlafaxine (75 mg/day), later increased to 225 mg/day]. The patient developed restlessness, irritability, uncontrollable urge to move around, and an inability to lay still on the bed. After ruling out other possible causes, a diagnosis of Venlafaxine induced akathisia was made. The symptoms started improving and subsided completely after venlafaxine was withdrawn.

Keywords: Venlafaxine; Akathisia; Adverse drug reactions; Venlafaxine induced akathisia

Introduction

Adverse drug reactions whether mild or serious are a matter of concern for not only the patients but to the treating physician. Though many pharmacotherapeutic agents claim to be safe and free of serious side effects, no drug is free of risk for adverse reactions. Venlafaxine a selective serotonin inhibitor used for major depressive disorder, generalized anxiety disorder, social anxiety disorder, and panic disorder is no exception to this. This is a case report of Venlafaxine induced akathisia which is very rarely reported adverse reaction of Venlafaxine.

Case Report

This 32-year-old male from south India presented to the out-patient department with a history of high-grade fever with rigors, headache, body ache and nausea. After a detailed history (diagnosed with Major Depressive disorder 8 months back, but refused treatment), and physical examination (mild hepatosplenomegaly), a provisional diagnosis of malaria was made and was admitted for further work- up. Lab investigations revealed *Plasmodium vivax* infection, thrombocytopenia (Platelet count- 95000) and increased LDH (600 IU/L). He was started on the chloroquine - 10 mg/kg first day followed by 5 mg/kg after 6, 24, and 36 hours after the first dose; patient weight 62 kg. A psychiatric consultation was taken for the depressive symptoms. He was started on Venlafaxine (75 mg/day). Serial platelet examination showed a drop-in platelet counts (85000, then to 77000) and was given 4 transfusions of platelet concentrate (after the fourth transfusion, the platelet count was 105,000). With no improvement in the depressive symptoms, after a week the dose of Venlafaxine was increased to 150 mg/day, then to 225 mg/day. Within 24 hours of increasing the dose of Venlafaxine, the patient complained of inner restless and a strong urge to move all the time. A detailed examination was done including neurological examination to rule out cerebral complications of malaria. Meanwhile primaquine 30 mg/day (for 14 days) was started to prevent the malarial relapse.

The neurological examination revealed no significant findings. In the next two days, the patient's symptoms of restlessness increased, and relatives and the nursing staff complained about patient pacing in the ward and wiggling his toes when lying on the bed. The patient was re-evaluated and a diagnosis of possible akathisia secondary to Venlafaxine was made after ruling out the possibility of tardive dyskinesia, restless leg syndrome, mania, psychosis, anxiety, increase in depressive symptoms, and cerebrovascular accident. A psychiatric re-consultation was made, and the possibility of Venlafaxine induced akathisia was confirmed (a placebo trial was also done to link the causation). The patient was

Anti-psychotic drugs	Other drugs	Medical conditions
Older	Anti-depressants	Parkinson's disease
Chlorpromazine	Tricyclics	Traumatic brain injury
Haloperidol	SSRIs (Fluoxetine, Paroxetine, Sertraline and Venlafaxine)	Encephalitis
Perphenazine	Antiemetics	
Flupentixol	Prochlorperazine	
Newer	Metoclopramide	
Olanzapine	Ca^{2+} channel blockers	
Risperidone	Cinnarizine	
Lurasidone	Flunarizine	
Ziprasidone		
Quetiapine		
Paliperidone		

Table 1: Causes of akathisia.

More common	Rare
Nausea	Hypersensitivity reactions
Vomiting	Suicidal thoughts, mania
Loss of appetite	Serotonin syndrome
Dizziness	Elevation in Blood pressure
	Angle closure glaucoma
	Discontinuation syndrome
	Hyponatremia
	Weight changes
	Interstitial lung disease
	Abnormal ejaculation
	Akathisia

Table 2: Adverse drug reactions of Venlafaxine.

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taken off from Venlafaxine and the symptoms of akathisia improved in the next 6-8 days. After stopping Venlafaxine patient was started on Sertraline (50 mg/day). Lab investigations were repeated to confirm the remission of malaria and normalized blood parameters. The patient was discharged and followed up in the outpatient department.

Discussion

Akathisia, a movement disorder characterized by inner restlessness and a strong and uncontrollable urge to move around (pacing) can occur both due to organic causes and as an adverse reaction of drugs, mainly antipsychotic agents [1,2]. The causes of akathisia are listed in Table 1. The disorder may also be associated with an inability to stay still, fidgeting, frequent crossing-uncrossing of the legs, anxiety, panic attacks, shifting weight from one leg to other and rocking back and forth while standing, etc. [3,4].

Venlafaxine, a popular drug used for multiple psychiatric disorders-major depressive disorder, generalized anxiety disorder, social anxiety disorder, and panic disorder, is used by psychiatrists all over the world. The common side effects associated with the drug are nausea, vomiting, loss of appetite, dizziness (a complete list of side effects is listed in Table 2). Akathisia has been reported rarely with Venlafaxine. Only six such cases have been reported until now [5-10]. Four of them reports akathisia at 150 mg/day of Venlafaxine while the other two cases develop akathisia at 225 and 75 mg/day (This would be the second known case report of Venlafaxine induced akathisia at 225 mg/day). The Naranjo ADR Scale score was 8 indicating Venlafaxine as probable causation of the akathisia in the patient. The causal association was also tested with a placebo, as mentioned above. A thorough literature and internet search was done to find an association of chloroquine and primaquine (used for the treatment of malaria) with akathisia and no evidence was found for such association.

The exact mechanism of Venlafaxine induced akathisia has not been studied and is not known. The proposed mechanism of drug-induced akathisia is inhibition of dopaminergic pathways in the brain (through increased serotonin level) [11]. In our case, the probable reason for akathisia was rapid increase in the dose of Venlafaxine from 150 to 225 mg/day which manifested as akathisia from rapid inhibition of dopaminergic pathways.

Conclusion

Though extremely rare, akathisia is a potential adverse effect of Venlafaxine. Close monitoring is required while increasing the dose of Venlafaxine. Clinicians should be cautious about increasing the dose of Venlafaxine and should do so gradually. Development of new symptoms in the form of restlessness, strong urge to move around, inability to stay still and related symptoms should be evaluated with detailed clinical history and physical examination. The causal association between the drug (Venlafaxine) and adverse drug reaction (akathisia) should be confirmed by the onset of symptoms and start of treatment, increase or decrease of the symptoms with relative changes in the dose of the drug, and using available causality score scales like Naranjo causality score or similar scales. In most cases, Venlafaxine-induced akathisia could be managed by a simple withdrawal of the drug (akathisia related symptoms in all the previously reported cases subsided with the withdrawal of Venlafaxine).

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