Case Report :

Acute dystonia with paroxetine – case presentation, possible mechanism and clinical implications

Kaustav Chakraborty

ABSTRACT:

Paroxetine is a selective serotonin reuptake inhibitor (SSRI) that is used in the treatment of panic disorder. SSRIs as a group are known to causeextra-pyramidal syndrome (EPS) even at therapeutic doses. However, systematic data regarding this is lacking. We describe a case of acute cervical dystonia in a young adult with panic disorder temporally related to paroxetine. The dystonia was relieved by intravenous injection of promethazine, an antihistaminic with anticholinergic property. Inhibitory serotonergic input to dopaminergic system in the nigro-striatal pathway may be responsible for such idiosyncratic reaction. Clinicians should be aware of such side effect while prescribing SSRIs as this can have significant clinical implications

INTRODUCTION:

Paroxetine is a selective serotonin reuptake inhibitor (SSRI) that is used in the treatment of panic disorder with or without agoraphobia alongside many other psychiatric disorders1. Paroxetine potently and selectively inhibits neuronal serotonin reuptake through antagonism of the serotonin transporter2. Numerous case reports have described the occurrence of extra-pyramidal syndromes (EPS) (i.e. parkinsonism, dystonia, akathisia and dyskinesia) in patients using antidepressant drugs, particularly the SSRIs3,4. In a review of case reports and case series of movement disorders ascribed to the use of SSRIs, fluoxetine (mean dose: 40 mg/d) was the most common SSRI implicated in 74.6 percent cases of SSRI-induced EPS whereas paroxetine (mean dose: 20 mg/d) was implicated in 5.6 percent cases5. The most common side effect in the above study was akathisia (45.1%), followed by dystonia (28.2%), parkinsonism (14.1%), and tardive dyskinesia like states (11.3%)5. The cases reporting acute dystonia with SSRIs were in their forties (49.7±20.0 years), predominantly females (67.6%), and concurrently treated with other medications (57.7%). Similar demographic profile of patients was reported by a case control study from the Netherlands which found 9 cases of paroxetine induced dystonia after introduction of this drug in market in 19913. The same study found parkinsonism and dystonia to be the most frequently reported EPS (59.0% and 21.3%, respectively) ascribed to antidepressants. Acute dystonic reaction with paroxetine has also been reported by Arnone et al. in an elderly patient with mood disorder6. Although paroxetine is in use in India for more than a decade, no case of EPS has been reported from India. We report a case of paroxetine induced acute dystonia and discuss the possible mechanism and clinical implications.

CASE REPORT:

A 21 year old male presented with sudden onset of palpitations, chest pain, choking sensation, & dizziness during which the patient would experience a crescendo of fear of dying from a heart attack for the past 2 months. Those abovementioned episodes would last for minutes only, at times longer and occur at a frequency of 1-2 times per week. The onset was temporally related to the death of his beloved teacher to whom he was much attached emotionally. However, the subsequent episodes were spontaneous and with each episode he grew the persistent fear of having another attack. He visited the psychiatry out-patient department in 2nd week of February 2011 and was diagnosed to have Panic Disorder as per International Classification of Diseases-10 (ICD-10) Chapter V-Mental and Behavioural Disorders. On assessment of premorbid personality we found him to be introvert, shy, poor in communication skills, more religious than usual and having very few friends. His family history was noncontributory. His routine and special investigations including computed tomography scan (CT scan) of brain, echocardiography, pulmonary function tests, thyroid function test, complete hemogram, serum electrolytes, renal function tests, and liver function tests were within normal limit. After explaining the diagnosis to him and the family members he was put on tab paroxetine 10 mg/day and tab clonazepam 0.25 mg twice daily. He was taught few initial steps of Jacobson's progressive muscle relaxation (JPMR) exercise and was encouraged to do focused & deep breathing intermittently for 5 minutes. On next follow up after a week there was 25 percent symptom reduction on objective assessment and he was found to be irregular in practising the relaxation exercises. The dose of tab paroxetine was further increased to 20 mg/d, rest of the

steps of JPMR was taught, and mother was told to supervise whether he was doing the steps correctly. He came for follow up after 2 weeks and reported status quo. The dose of tab paroxetine was further increased to 30 mg/d and along with emphasis on JPMR plan for cognitive behavioural therapy (CBT) was kept. Next morning he was brought to the hospital emergency with acute, painful, persistent, involuntary spasm of neck muscles with torticollis to the right side. He was crying for help as he was in severe distress because of the painful muscle spasm His vitals were stable; pupils were equal, round and reactive to light. On examination, he showed increased tone of neck muscles with posturing to the right; his gait, reflexes and planter response were within normal limit.. Injection promethazine (50 mg) was given intravenously with which he had relief of symptoms over next 30 minutes and went off to sleep. There was no history of overdose of prescribed medications or ingestion of other medications to which the above symptoms could be attributed to. Next day patient was started on tab sertraline at a very low dose (25 mg) and was gradually increased to 150 mg/d over a period of three weeks with close monitoring. CBT sessions were also started on a weekly basis and patient started showing reduction in the intensity and frequency of panic attacks.

DISCUSSION:

SSRIs have been reported to alter receptor density and function that include the dopamine-1, alpha 1/beta-adrenergic and 5-HT1B/2[6]. With regards to the nigro-striatal pathway, the serotoninergic input to dopaminergic system appears inhibitory[7]. Overstimulation of the 5-HT2A receptors by SSRIs, especially in the basal ganglia, may potentially lead to akathisia, agitation and perhaps to an acute dystonic reaction[7]. It is also possible serotonergic innervations also influence GABA and cholinergic pathways and thereby contributes to the development of EPS[8,9].

Case reports and case series have identified certain predictors of SSRI induced EPS, such as advanced age, female gender, concomitant use of antipsychotic drugs, previous events of drug-induced EPS or presymptomatic Parkinson's disease[3,5]. Contrary to the above findings the index case was an young adult male, devoid of any comorbidity and receiving concurrent benzodiazepine. The development of acute dystonia in this case can be definitely attributed to paroxetine only.

Management strategies of SSRI induced dystonia include cessation of the offending agent, possible use of an alternative antidepressant, dose reduction and may also involve the short-term use of an anticholinergic drug[8]. Promethazine, an antihistaminic with anticholinergic properties is also beneficial for such purpose and was employed in this case.

Motor side-effects are the most visible and distressing side-effects of psychotropic drugs. There is a dearth of wellcontrolled systematic research focusing on SSRI induced movement disorders. Nevertheless, ICD-10 has a provision for enlisting adverse effects of SSRIs and other antidepressants in therapeutic use as a separate code - Y49.2 under chapter XX. Clinicians should be very vigilant regarding this 'not so common' side effect while prescribing antidepressants particularly SSRIs which can be life threatening for the patient and can result in treatment drop-out.

Reference

1. Paroxetine product monograph (Paxil, SmithKline Beecham—Canada), Rev 11/6/95, Rec 11/96
2. Stahl SM. Classical Antidepressants, Serotonin Selective Reuptake Inhibitors, and. Noradrenergic Reuptake Inhibitors. In: Stahl SM, editor. Essential Psychopharmacology. 2nd ed. United States of America: Cambridge University Press; 2000 .p. 199-244
3. Schillevoort I, van Puijenbroek EP, de Boer A, Roos RAC, Jansen PAF, Leufkens HGF. Extrapyramidal syndromes associated with selective serotonin reuptake inhibitors: a case-control study using spontaneous reports. Int Clin Psychopharmacology 2002; 17:75-79
4. Damsa C, Bumb A, Bianchi-Demicheli F, Vidailhet P, Sterck R, Andreoli A, et al. "Dopamine-dependent" side effects of selective serotonin reuptake inhibitors: a clinical review. J Clin Psychiatry 2004; 65: 1064-1068
5. Leo RJ. Movement disorders associated with the serotonin selective reuptake inhibitors. J Clin Psychiatry 1996; 57: 449-454
6. Arnone D, Hansen L, Kerr JS. Acute dystonic reaction in an elderly patient with mood disorder after titration of paroxetine: possible mechanisms and implications for clinical care. J Psychopharmacol 2002; 16: 395-397
7. Hansen L. A critical review of akathisia and its possible association with suicidal behaviour. Hum Psychopharmacol 2001; 16: 495-505
8. Dray A. Serotonin in the basal ganglia: functions and interactions with other neuronal pathways. J Physiol (Paris) 1981; 77: 393-403
9. Fibiger HC, Lloyd KG. Neurobiological substrates of tardive dyskinesia: the GABA hypothesis. Trends Neurosci 1984; 7: 462-464

Kaustav Chakraborty, **:** MD.Assistant Professor Department of Psychiatry College of Medicine & J.N.M. Hospital ,

WBUHS, Kalyani, Nadia, Phone: +91-9432855683,

E-mail: drkaustav2003@yahoo.co.in