

Fluoxetine Associated with Seizure: A Case Report

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ABSTRACT

Introduction: Fluoxetine is a selective serotonin reuptake inhibitor (SSRI). It is licensed for the treatment of depression, obsessive-compulsive disorder and bulimia nervosa. It is thought to have a low adverse effect profile compared to conventional tricyclic antidepressants (TCA). It was first marketed in 1989, and since then fluoxetine has become the most widely prescribed antidepressant. Even though it was claimed earlier that fluoxetine has little or no effect on reducing seizure threshold, its association with seizure activity is being increasingly recognized. **Results:** We report a case of 53 year old depressed male with no apparent risk factors, treated with 20mg of fluoxetine for 3 weeks, experienced a seizure. **Conclusion:** Clinician should be aware that seizure and the cardiac dysrhythmias have been reported in the literature, the risk of seizures depends on important critical factors like an individual's predisposing factors, followed by the amount and rate of dosage titration, and the relative epileptogenic potential of the particular drug.

Keywords: Fluoxetine, Risk factors, Seizure

INTRODUCTION

Psychotropic drugs, especially antidepressants and antipsychotics, may give rise to some concern in clinical practice because of their known ability to reduce seizure threshold and to provoke epileptic seizures. Although the phenomenon has been described with almost all the available compounds, neither its real magnitude nor the seizurogenic potential of individual drugs have been clearly established so far. In large investigations, seizure incidence rates have been reported to range from approximately 0.1 to approximately 1.5% in patients treated with therapeutic doses of most commonly used antidepressants and antipsychotics (incidence of the first unprovoked seizure in the general population is 0.07 to 0.09%). In patients who have taken an overdose, the seizure risk rises markedly, achieving values of approximately 4% to approximately 30%.¹

Reviews have emphasized the favorable adverse-effect profile of fluoxetine.² The commonest side-effects are nausea, insomnia, headache, nervousness and diarrhea. Sedation, orthostatic hypotension and anticholinergic effects were reported less frequently with fluoxetine.³

Selective serotonin reuptake inhibitors (SSRI) are safer than tricyclic antidepressants (TCA) in overdoses, due to lack of membrane-stabilizing properties on the heart. Seizures are a serious but less common adverse reaction associated with the use of antidepressants including SSRIs. A better understanding of drug-related

seizure risk, its predictors, and its neurophysiologic basis might help clinicians avoid this adverse event. A better understanding of the factors involved in the determination of seizure risk would be helpful for interpretation of seizure rates reported.⁴

We report a case of Fluoxetine associated with Seizure with 20 mg/day of Fluoxetine taken for 19 days with no other concomitant drugs and no known risk factors in a 53 year old male. Till date only few cases of isolated fluoxetine induced seizures are reported and it is an attempt to add to this already available literature.

MATERIALS AND METHODS

This case report is written from the descriptive clinical notes and the experience of the treating clinicians. Psychiatric diagnosis was given based on clinical interview for ICD-10. Clearance from Institutional ethic committee and consent from patient was taken to publish this case. The author reviewed Pub med, reports, articles for this purpose.

CASE REPORT

Mr. CD, 53 year old married male reported for the first time to our hospital with a history of feeling low, somatic symptoms following a significant stressor wherein he was terminated from his job two months prior to the hospital visit. Mr. CD slowly started deteriorating. He communicated less than usual, had blank staring look.

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On examination

He was Conscious, Partially cooperative. His attention was ill sustained. He had decreased speech output, increased reaction time and decreased spontaneity. He appeared very anxious. He denied suicidal ideas and perceptual disturbances. His physical examination did not reveal significant abnormality. Based on the history and clinical examination a diagnosis of moderate depression was made. He was started on Fluoxetine 20 mg/day on 11/03/2013. He showed improvement in his mood within two weeks of medication and was more communicative then before, hence same dose of Fluoxetine was continued.

On 30/03/2014(19th) day, his wife witnessed a seizure wherein he was shaking violently with jerky movement of his body with upturning of the eye balls, frothing at mouth and loss of consciousness. He was immediately shifted to emergency department of tertiary care hospital. On arrival he was drowsy but arousable. His temperature was 37.2°C, pulse 92/min regular, blood Pressure 130/82 mm Hg, respiration 20/min. The patient had no focal neurological deficit and his physical examination was without any noted abnormality. He was given a loading dose of antiepileptic (Phenytoin). No further seizures were noted. His renal function tests, liver function tests, lipid profile, blood glucose level, hemoglobin, total counts, platelet counts were within normal limits. An electrocardiogram revealed a normal sinus rhythm.

His cerebrospinal fluid (CSF) was normal, CT scan brain, electroencephalogram (EEG) and chest X rays (CXR) were normal. He was admitted to the medical ward. His fluoxetine was stopped and was continued on oral dose of phenytoin 300 mg/day. On 7th day he was discharged in stable condition. Within a week of his discharge from medical ward he reported to us with complaints of decreased interaction, remaining preoccupied, appearing scared at times, poor communication and disturbed sleep. On examination his mood was anxious. Rest of his mental status was not possible as he was poorly communicative. He was started on aripiprazole 10 mg/day with which he showed improvement in all parameters within a week. However he stopped subsequent follow ups with us.

DISCUSSION

Data from human and animal trials show fluoxetine to be generally safe. With regard to potential neurotoxic effects, considerable evidence exists that fluoxetine has an anticonvulsant effect at therapeutic doses in humans and animal models.⁵ Antidepressants may display both anticonvulsant and pro-convulsant properties, with the most important determining factor being the dose.⁶ In a study conducted by Isbister GK of five different SSRIs

taken in overdose, fluoxetine had the lowest incidence of inducing seizures (1%, vs. 2% for sertraline, paroxetine, and citalopram, and 4% for fluvoxamine).⁷ Only a few cases of seizure after isolated fluoxetine overdose in normal subjects have been reported.^{8,9} and there is also a case occurring after escalation of therapeutic dosing up to 60 mg/day.¹⁰

Our patient was taking only 20 mg of Fluoxetine per day and was in third week (19th day) of his medication hence, fluoxetine overdose was ruled out from history as well as physical examination as he did not exhibit any other signs of overdose or toxicity. He was not prescribed any other antidepressant or anticholinergic medication along with fluoxetine, therefore the seizure does not appear to be related to serotonin syndrome as the patient did not exhibit autonomic instability, muscular rigidity, or abnormal mental status (excluding the seizure itself and a brief post-ictal period) as typically occur in that disorder.¹¹

Furthermore, seizures due to hyponatremia was ruled out as his serum sodium level was 138 mmol/l (normal range 136-145 mmol/l). Most antidepressants have been associated with hyponatremia. The onset is usually within 30 days of starting treatment and reported to improve after withdrawal of the drug.¹² The most likely mechanism of this adverse effect is believed to be the development of syndrome of inappropriate secretion of antidiuretic hormone (SIADH).¹³ Our Patient had a history of occasional alcohol consumption without a history of dependence or prior episode of withdrawal and his last alcohol drink was two months prior to his seizure. Also he did not exhibit any signs of autonomic instability (e.g., diaphoresis, hypertension) or tremor consistent with alcohol withdrawal, so it is unlikely that alcohol contributed to his seizure activity.

The Patient involved did not give any family history of seizure disorder. His CT brain and EEG was normal, which clears the doubt of neurological disorder. Cerebral infection was ruled out as his CSF was normal. There are cases reported in the literature wherein sudden escalation of dose of medication has induced seizure,³ but in this patient dose of fluoxetine was static throughout the 19 days of treatment period.

Apart from the dose, duration of treatment, family history, underlying neurological problem, concurrent medications, substance abuse and rapid increment of dose,³ with exception of overdose, seizures associated with antidepressants are likely to occur during the first few weeks of treatment like in our case. As most of the risk factors were ruled out in this patient it is more likely that fluoxetine has been associated with seizure in this particular patient.

CONCLUSION

Seizures are uncommon, but serious, adverse effects of antidepressant drugs. Clinical experience with fluoxetine in patients with concomitant systemic illness is limited and hence should be used cautiously especially those with disease or condition that could affect metabolism or hemodynamic response. As SSRIs have been widely used by General practitioners. Better understanding of the Pharmacokinetics, Pharmacodynamics, drug interaction and risk factors are necessary to avoid this adverse event. Our patient recovered promptly due to immediate withdrawal of fluoxetine and good medical care.

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