Type of Article : Case Study

Serotonin Syndrome Precipitated by Escitalopram

Deshna H. Lad[1], Harsha Makwana[2], Vidhi Shah[3], Supriya D. Malhotra[4], Pankaj Patel[5]

[1]Post Graduate Student, Department of Pharmacology, [2]Associate Professor, Department of Emergency Medicine, [3]Post graduate Student, Department of Emergency Medicine, [4]Professor and Head, Department of Pharmacology, [5]Dean, Smt. NHL Medical College, Ahmedabad, India

Abstract

Depression is characterized by symptoms like sad mood, loss of interest and pleasure, low energy, worthlessness, guilt, psychomotor retardation or agitation, change in appetite and/or sleep and suicidal thoughts, etc. It may be a unipolar or a bipolar cyclic disorder in which cycles of mood swings from mania to depression occur over time. Fluoxetine, Fluvoxamine, Paroxetine, Sertraline, Citalopram and Escitalopram are the various SSRIs(Selective Serotonin Reuptake Inhibitors) preferred as first line of drug in such conditions. Among the SSRIs, Escitalopram exerts a highly selective, potent, and dose-dependent inhibitory effect on the human serotonin transport. By inhibiting the reuptake of serotonin into presynaptic nerve endings, this drug enhances the activity of serotonin in the central nervous system. Herein we report a case of a 82 year old male who presented with altered sensorium, tachycardia, hypertension and restlessness to emergency department of our hospital. Patient was known case of Adjustment disorder with Depressed mood and was on treatment with Tablet Escitalopram 10 mg OD and Tablet Zolpidem 10 mg OD since 1 month. Patient overdosed himself with 4 Escitalopram tablets of 10 mg. He presented with features similar to serotonin syndrome.

Keywords *– Depression , Adverse drug reaction(ADR) , Escitalopram , Pharmacovigilance , Serotonin Syndrome*

Introduction

Depression is a disorder of mood and it is characterized by persisting feeling of sadness and loss of interest. SSRIs are the first line drugs for the treatment of depression and anxiety disorders(1). TCAs(Tricyclic Antidepressants) are also frequently prescribed for the Depression. The advantage of SSRIs among the Tricyclic antidepressants is that they are relatively safe in overdose. The majority of SSRI overdose cause minor side effects. Central nervous system depression is the most common side effect after SSRI overdose , although in large doses it can cause serotonin syndrome, seizure and cardiac abnormalities.(1) However, QT-interval prolongation and tachycardia have been reported mainly with Citalopram and more recently in case report of Escitalopram toxicity(1) Escitalopram is the S – enantiomer of Citalopram and has been marketed because it is more potent inhibitor of the serotonin transporter and likely accounts for the majority of the inhibitory effects in racemic citalopram. During the last 10 years , there has been an increase in the prescription of Escitalopram and an associated increase in overdose. Serotonin toxicity is more common with escitalopram than with citalopram or other SSRIs because of its increase serotonergic potency. The most common clinical effects with escitalopram overdose are tachycardia, hypertension, drowsiness, nausea, and vomiting. With citalopram, in addition to above, the most common clinical side effects are tremor and seizure. Nausea, vomiting, and hypertension were more common with escitalopram. Escitalopram is comparatively safer than Citalopram(2). Therapeutic dose of Escitalopram is 10 mg /day and maximum dose 20 mg/day(3).Herein we report a case of suspected Serotonin Syndrome as an ADR to high doses of Escitalopram.

Corresponding author:
Dr Harsha Makwana,
Associate Professor, Department of Emergency Medicine, Smt. NHL Municipal Medical College, Ahmedabad, Gujarat, India
E-mail: drharsham@gmail.com

Case Details

An 82 year old Diabetic , Hypertensive male patient brought by relative to emergency medicine department of our hospital with altered sensorium. On examination , Temperature : normal , Pulse: 116/min regular , BP : 160/90, respiratory rate – 14/min, SpO2-98% on room air, RBS:273 mg%, CVS:S1S2+, RS: Clear, CNS: In delirium state ; planter : right flexor and left extensor. Patient was having Tachycardia, Hypertension, Restlessness and Agitation. He was kept under observation with suspicion of Hyponatremia or CNS problem. His ECG was showing heart rate more than 110/min but rhythm was normal. In emergency room, ABG was done showing normal with Na^{++}:141 mEq/L. After 1 hour patient didn't regain consciousness so CT brain was done which did not reveal any significant finding. IV line started with Normal Saline pint at the rate of 60 ml/hour and patient shifted to ER ICU for further management. On detailed history Patient's relative told that patient was alright in the evening on previous day and did not wake up in the morning. On arousal he was not following verbal command so he was brought to the hospital.

Patient is a known case of Psychiatric illness diagnosed as Adjustment disorder with Depressed mood since 1 month. He was on treatment with Tablet Escitalopram 10 mg OD and Tablet Zolpidem 10 mg OD, taking regularly. Patient is also known case of Diabetes Mellitus and Hypertension since 15 years so he was on treatment with tablet Voglibose SR 0.3 mg TDS and Tablet Amlodipine 5 mg BD. After 3 hours of admission patient was having persistent tachycardia and hypertension so overdose/toxicity of SSRI was suspected so Tablet Escitalopram and Zolpidem were withheld.. Ryle's tube was inserted and gastric sample collected and stomach wash done with normal saline. Inj Furosemide 20 mg IV was given. Urinary catheter was inserted and Urine drug abuse assay was done to exclude other drug overdose. In ICU patient was treated by Inj Ceftriaxone 1 gm IV BD, Inj Pantoprazole 40 mg IV BD, Inj Ondansetron 4 mg TDS, , Inj Optineuron 2ml IV BID, Tab Voglibose SR 0.3 mg BD, Tab. Amlodipine 10 mg OD. 2D Echo was done and normal. His investigations including CBC, Serum electrolytes , LFT , RFT and X ray chest were normal. Patient subsequently improved and regained consciousness on 2nd day with pulse rate of 92/min regular and blood pressure of 120/70 mmHg.

On detailed inquiry Patient had given history of deliberate ingestion of 4 tablets of Escitalopram of 10 mg yesterday night. Psychiatric refer was done and advised to continue Tablet Escitalopram 10 mg OD and Tablet Zolpidem 10 mg OD. Patient was conscious and psychologically stable so discharged on 4th day . This case illustrates an example of toxic overdose with escitalopram that resulted in features suggestive of Serotonin syndrome. This case was reported via Vigiflow at WHO-UMC with Id-2019-38323.

Discussion

Serotonin syndrome is often described as a clinical triad of autonomic hyperactivity, mental status changes and neuromuscular hyperexcitability. Although clinically, serotonin syndrome has a broad range of presentations that often result in under diagnosis. Mild cases may result from therapeutic doses, and the patient may or may not be symptomatic. Moderate cases present with more autonomic and neurological dysfunction. Severe cases generally presents with worsening vital signs, rigidity, hyperthermia and the potential for multiorgan failure[4]. There are a number of drugs from different classes that can cause serotonin syndrome either alone at high doses or when combined but the most commonly prescribed class of antidepressant, which work by increasing serotonin, are the serotonin reuptake inhibitors. Escitalopram is a well-tolerated medication, with a side-effect profile comparable to the other SSRIs. A number of side effects have been seen during escitalopram therapy, such as insomnia, nausea, and increased sweating, agitation, restlessness, weakness etc. Cases of serotonin syndrome with escitalopram are reported, but quite a few[5]. Previously cases of Serotonin syndrome induced by the readministration of escitalopram after a short-term interruption in an elderly woman with depression by Sato Y et al[6] and Serotonin Syndrome Induced by Combined Use of Tramadol and Escitalopram by Caamano A. et al[7] are reported. Escitalopram works by increasing intra-synaptic levels of the neurotransmitter serotonin by blocking the reuptake of the neurotransmitter into the presynaptic neuron. The use and prevalence of serotonergic drugs for various psychiatric issues is on the rise. As a result, physicians should carefully consider and rule out the clinical diagnosis of serotonin syndrome when presented with an agitated or confused patient with signs and symptoms of serotonin syndrome who is taking serotonergic drugs. One should be hypervigilant when serotonergic drugs are used. Previous studies have reported that 10% to 14% of patients who overdose with

SSRIs experience serotonin toxicity many of whom with only mild presentations[8]. Although escitalopram has been reported to show less serotonin toxicity compared with other SSRIs, its effect was best described by one previous study in which 15% of 46 patients exposed to escitalopram alone exhibited significant serotonin toxicity, while isolated **serotonergic** neuromuscular findings developed in as many as 46% of the patients at a mean ingested dose of 140 mg. Another study reported that the most common clinical effects after an overdose with escitalopram with a mean dose of 130 mg were **tachycardia** (19.5%),drowsiness(15.0%) and hypertension (9.0%)[8]. Serotonin syndrome has long been known, and it is clearly an iatrogenic effect of modern medications

Here we report a case of elderly male patient who developed this ADR. Age-related physiological changes affect drug pharmacokinetics (absorption, distribution, metabolism and excretion) and pharmacodynamics (the study of effects of a drug on the body)[9]. Of the four traditional components of pharmacokinetics—absorption, distribution, metabolism, and excretion—only absorption appears to be substantially independent of age. The distribution of a particular drug can differ importantly in the elderly. An increase in the volume of distribution combined with a reduction in clearance will prolong elimination half-life, which might prolong the duration of action of a single dose of drug. With chronic dosing, reduced clearance without a change in the dosing interval leads to an increased steady-state concentration of medication[10].The higher frequency of ADRs in the elderly, rather than being a consequence of senescence alone, may be attributable in part to the fact that older patients consume more medications and are likely to have more baseline illness than younger patients[11].

Conclusion

This case shows a rare incidence of serotonin syndrome with Escitalopram use. It is very important that physicians are familiar with the signs and symptoms of Serotonin syndrome and should suspect it in anyone with altered mental status who is taking serotonin-modifying drugs. In our patient, the diagnosis was made early due to autonomic and neurological signs and suspicion of SSRI overdose which was confirmed when patient regained consciousness. Cessation of serotonergic medication and supportive care remain the mainstay of therapy.

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Ethical Clearance : Since it is a Case Report which was reported as an Adverse Drug Reaction(ADR) to our centre under Pharmacovigilance Programme of India, Ethical Clearance is not needed. However, the author has taken consent of patient to publish the data for scientific purpose, patient confidentiality is insured.

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