Case Report

Serotonin Toxicity Following Suicide with Citalopram and Lamotrigine: A Rare Case Report and Literature Review

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Abstract

Serotonin toxicity is a common but often unrecognized toxicological condition. In most cases, a combination of two or more serotonergic drugs can cause serotonin syndrome. We describe a case of serotonin toxicity in a 17-year-old woman, secondary to suicidal ingestion of 1000 mg lamotrigine and 400 mg citalopram, which has been rarely reported. Our patient had a medical history of depression and was treated with lamotrigine and citalopram. She was brought to the emergency room with nausea, diaphoresis, agitation, shivering, tremor, vertigo, ataxia, mydriasis, nystagmus, hyperreflexia, myoclonus, tachycardia, tachypnea, and mild fever. The symptoms and signs were resolved within 3 days following hydration, sedation, and cyproheptadine. Minor cardiovascular symptoms are probably due to the less toxic dose of citalopram. Lamotrigine, especially in combination with other serotonergic drugs, should be considered a cause of serotonin toxicity.

Keywords: *Citalopram, Lamotrigine, serotonin syndrome, serotonin toxicity, suicide*

Received: 05-10-2019.
Accepted: 09-05-2020.
Published: 08-10-2020.

Introduction

Serotonin (5-hydroxytryptamine) regulates human body temperature, attention, and behavior in the central nervous system and regulates motility, vascular contraction, bronchial contraction, and platelet aggregation outside of it.[1] Serotonin toxicity is a life-threatening syndrome due to the effects of serotonergic drugs. Serotonin toxicity occurs in all ages, and unfortunately, its prevalence and mortality have been increasing in recent years due to the increased use of serotonergic psychiatric drugs. Symptoms of this syndrome include a combination of cognitive and behavioral disorders, autonomic dysfunction, and neuromuscular dysfunction. Since patients with this syndrome may develop a range of signs and symptoms, it is sometimes difficult to diagnose and is confused with similar syndromes and diseases.[1,2]

Serotonin toxicity has been reported following citalopram or lamotrigine administration, but a comprehensive literature search did not yield any case description of serotonin toxicity induced by a combination of citalopram and lamotrigine.[3-6] Here, we present a case of serotonin toxicity following the combined use of these serotonergic drugs and then review the related articles.

Case Report

A 17-year-old patient referred to the Medical Toxicology Department of Noor Hospital in Isfahan on December 24, 2018. The patient had ingested about 400 mg of citalopram and 1000 mg lamotrigine tablets 10 h before admission in order to attempt suicide. She was presented to the emergency department with nausea, diaphoresis, agitation, shivering, tremor, vertigo, and ataxia. Bilateral mydriasis and horizontal nystagmus were observed. In medical history, she was treated with one-fourth of 50 mg lamotrigine tablets and half of the 20 mg citalopram tablets for depression daily. Bilateral deep tendon reflexes were hyperactive, and myoclonuses in both lower extremities were seen. Initial vital signs included a temperature of 37.8°C, heart rate at 140/min, a respiratory rate of 30/min, blood pressure at 118/68 mmHg, and 97% finger

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How to cite this article: Dorooshi G, Zoofaghari S, Meamar R. Serotonin toxicity following suicide with citalopram and lamotrigine: A rare case report and literature review. J Res Pharm Pract 2020;9:158-60.

Access this article online

Quick Response Code:

Website: www.jrpp.net

DOI: 10.4103/jrpp.JRPP_19_105

pulse oximetry. The patient was alert and complained about abdominal pain and breathes shortness. Other examinations were normal. A urine drug screen for stimulants, psychotropic substances (marijuana, lysergic acid diethylamide [LSD], cocaine, and amphetamines), and opiates produced negative results.

In laboratory investigations, creatine phosphokinase: 2438 and lactate dehydrogenase: 464 were seen. Other routine investigations showed normal results. Electrocardiogram revealed no abnormalities except for sinus tachycardia.

After intravenous (IV) injection of 5 mg midazolam and 4 mg ondansetron for the treatment of agitation and nausea, the patient was given isotonic IV fluid 1 L free and then every 6 h. Because of the signs and symptoms of serotonin toxicity, treatment with cyproheptadine began first 12 mg and then 4 mg every 4 h orally. The patient was transferred to the intensive care unit and positioned under careful cardiopulmonary monitoring. Within the next day, her neurologic status and other symptoms improved. The patient was fully recovered and discharged from the hospital on day 3 [Figure 1].

Discussion

Serotonin toxicity is less commonly considered. This is the first case of serotonin toxicity following a combination of citalopram and lamotrigine in our ward. Serotonin toxicity was formerly referred to as serotonin syndrome, serotonin behavioral, and hyperactivity syndrome.[1] It is caused by excessive stimulation of the 5-HT1A and 5-HT2 receptors.[7] In most cases, a combination of two or more serotonergic drugs, even at therapeutic doses, can cause serotonin toxicity.

However, taking single following medications and substances can cause serotonin toxicity: amantadine, amphetamines (3,4-Methyl enedioxy methampheta mine (MDMA), cathinones, and aminoindanes), aripiprazole, bromocriptine, bupropion, buspirone, butylone, carbamazepine, carbidopa/levodopa, cocaine, clozapine withdrawal, cyclic antidepressants (amitriptyline, clomipramine, desipramine, doxepin, imipramine, nortriptyline, protriptyline, and trimipramine), cyclobenzaprine, dextromethorphan, ergot alkaloids (ergotamines), erythromycin, ginseng, harmine and harmaline from ayahuasca preparations, linezolid, lithium, L-tryptophan, 5-hydroxytryptophan, LSD, mescaline, metaxalone, methylene blue, methylone, milnacipran, mirtazapine, monoamine oxidase inhibitors (phenelzine, moclobemide, clorgyline, tranylcypromine, isocarboxazid, pargyline, rasagiline, and selegiline), ondansetron, granisetron, metoclopramide, opioids (hydrocodone, oxycodone, tramadol, pentazocine, meperidine, and fentanyl), pergolide, quetiapine, reserpine, ritonavir, selective serotonin reuptake inhibitors (SSRIs) (fluoxetine, sertraline, paroxetine, fluvoxamine, citalopram, and escitalopram), serotonin/norepinephrine reuptake inhibitors (venlafaxine, desvenlafaxine, levomilnacipran, and duloxetine), sibutramine, St John's wort (*Hypericum perforatum*), Syrian rue (*Peganum harmala*), trazodone, nefazodone, triptans (sumatriptan), and valproic acid.[1-3,7-9]

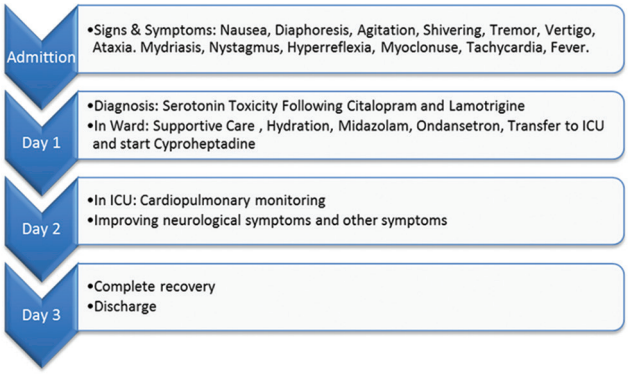

Figure 1: Timeline of the progress of a patient during admission

Citalopram is an SSRI that causes seizures, torsade de pointes, and QT interval prolongation often after ingestions above 600 mg.[6] Our patient had consumed <600 mg. Lamotrigine is a serotonin reuptake inhibitor and has a weak inhibitory effect on 5-HT3 receptor and can cause serotonin toxicity but is not common. Lamotrigine in overdose is associated with cardiovascular and central nervous system effects.[4,5]

There are no confirmatory laboratory tests for serotonin toxicity. The diagnostic criteria for serotonin syndrome emphasize exposure to a known serotonergic drug and the presence of muscle clonus alone or at least one or two of the other common features.[7,8] The clinical symptoms range from barely noticeable to lethal. They include altered level of consciousness, agitation, insomnia, restlessness, anxiety, hyperthermia, diaphoresis, tachycardia, hypertension (more common) or hypotension, tachypnea, mydriasis, incoordination, muscle rigidity, hyperreflexia, hypertonicity, myoclonus, tremor, and akathisia (motor symptoms are more prominent in the lower extremities).[3-5] Our patient showed most of these symptoms. Unlike many studies, our patient's blood pressure was normal, and also she had no diarrhea. QRS prolongation and left bundle branch block can be seen following citalopram and lamotrigine overdose, but our case had only a sinus tachycardia, which is probably due to use of less amounts of citalopram than the toxic dose.[10]

Treatment of patients with serotonin toxicity focuses on supportive care and cardiac monitoring. Reducing the body temperature and muscle hyperactivity is essential. Muscular rigidity leads to hyperthermia and subsequent death.[3,7-9] Cyproheptadine appears to have the most potent antiserotonergic effects in humans, including 5-HT1A and 5-HT2A receptors. The recommended doses of oral cyproheptadine are 8–16 mg orally repeated hourly if needed.[1] Studies have shown that serotonin toxicity patients with mild-to-moderate manifestations have responded to treatment with cyproheptadine.[7] Since our patient did not have a significant fever (<40°C), the severity of her serotonin toxicity was mild and responded well to treatment with cyproheptadine.

Declaration of patient consent

The authors certify that they have obtained appropriate patient consent forms. In the form, the patient has given her consent for her clinical information to be reported in the journal. She understood that her name would not be published, and outstanding efforts are made to conceal her identity.

Authors' Contribution

Gholamali Dorooshi, Shafeajafar Zoofaghari, and Rokhsareh Meamar contributed to the idea and design of the study. Gholamali Dorooshi and Shafeajafar Zoofaghari gathered the data. Gholamali Dorooshi, Shafeajafar Zoofaghari, and Rokhsareh Meamar made data interpretation. Gholamali Dorooshi drafted the manuscript, and all authors critically revised it for relevant intellectual content and approved the final version.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Nelson LS, Howland MA, Lewin NA, Smith SW, Goldfrank LR, Hoffman RS. Goldfrank's Toxicologic Emergencies. 11th ed. New York: McGraw-Hill Companies; 2019. p. 1058-9.
2. Tintinalli JE. Tintinalli's Emergency Medicine. 8th ed. New York: McGraw-Hill Education; 2016. p. 1223-4.
3. Dizdarevic A, Bremer N. Cervical spinal cord stimulation with concomitant serotonin norepinephrine reuptake inhibitor therapy leading to the serotonin syndrome. Pain Med 2017;18:1199-202.
4. Alabi A, Todd A, Husband A, Reilly J. Safety profile of lamotrigine in overdose. Ther Adv Psychopharmacol 2016;6:369-81.
5. Kotwal A, Cutrona SL. Serotonin syndrome in the setting of lamotrigine, aripiprazole, and cocaine use. Case Rep Med 2015;2015:769531.
6. Weigl J, Vloet T, Egberts K, Briegel W, Kratz J, Romanos M, *et al*. Non-fatal intoxication with a high dose of citalopram in a suicidal 14-year-old girl. Z Kinder Jugendpsychiatr Psychother 2019;47:168-70.
7. Cooper JM, Newby DA, Whyte IM, Carter G, Jones AL, Isbister GK. Serotonin toxicity from antidepressant overdose and its association with the T102C polymorphism of the 5-HT2A receptor. Pharmacogenomics J 2014;14:390-4.
8. Stevenson E, Schembri F, Green DM, Burns JD. Serotonin syndrome associated with clozapine withdrawal. JAMA Neurol 2013;70:1054-5.
9. Martini DI, Nacca N, Haswell D, Cobb T, Hodgman M. Serotonin syndrome following metaxalone overdose and therapeutic use of a selective serotonin reuptake inhibitor. Clin Toxicol (Phila) 2015;53:185-7.
10. Farkas AN, Marcott M, Yanta JH, Pizon AF. Bicarbonate refractory QRS prolongation and left bundle-branch block following escitalopram and lamotrigine overdose: A case report and literature review of toxic left bundle-branch block. J Clin Pharm Ther 2018;43:717-22.