

## Mild serotonin syndrome following isolated ingestion of fluoxetine overdose: a case report.

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### Abstract

*Self-poisoning with antidepressants is a relatively common method of completed or attempted suicide among patients with depressive disorders. Among these antidepressants, SSRIs for example fluoxetine, have been shown to have a relatively safe profile compared to other classes, especially the tricyclic antidepressants. The report illustrates the relative safety of fluoxetine overdose in a 22-year-old patient receiving treatment for a depressive disorder. She presented with mild symptoms of a brief confusional state, tremors, blurred vision, and clonus. All symptoms resolved within a few days of treatment with cyproheptadine 4mg 8 hourly. Serotonin syndrome cases from fluoxetine overdoses typically have a mild to moderate presentation, suggesting that fluoxetine should be considered strongly in the treatment of depression in patients who are suicidal. Although cyproheptadine was effective in managing this case, further randomized studies are needed to prove its efficacy in serotonin syndrome.*

**Keywords-** SSRI, fluoxetine, suicide, depression, serotonin syndrome.

### Introduction

Depressive disorders are frequently occurring psychiatric conditions, affecting approximately 19% of the world population throughout their lifetime. Nigeria, the prevalence of these disorders reaches as high as 49.8%<sup>1</sup>. According to estimates, approximately a quarter of individuals diagnosed with major depression attempt suicide at some point in their lives, and 15% of those individuals unfortunately die from suicide. Antidepressants have proven to be highly effective in treating depression and hence, it is paradoxical that to ensure patient adherence, the healthcare practitioner must provide a potentially harmful medication, which grants the patient easy access to a method of self-harm<sup>2</sup>. Self-

poisoning is a popular suicide method, particularly among women, and antidepressants are commonly employed in cases of self-poisoning, contributing to approximately 20% of all poisoning suicides in the UK and 20–30% of non-fatal overdoses<sup>3</sup>. This can be attributed to the high incidence of depression, the most common psychiatric disorder among individuals who die by suicide. Additionally, the choice of suicidal method is often influenced by accessibility, and individuals with depression frequently resort to self-poisoning using their prescribed antidepressants. The relative toxicity of these drugs plays a crucial role in determining the outcome of an overdose<sup>3</sup>.

Major groups of antidepressants are selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs) and atypical antidepressants. Tricyclic antidepressants (TCAs) are typically more

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harmful when taken in excess, with significant toxicity often appearing within the initial 6 hours after an overdose<sup>3,4</sup>. SSRIs enhance serotonergic neurotransmission, providing specific actions and superior safety compared to tricyclic antidepressants. They have fewer adverse effects, outperform tricyclic antidepressants for cardiovascular disease, and are more tolerable in overdose cases<sup>5</sup>. Fluoxetine is a selective serotonin reuptake inhibitor (SSRI), and in the body, it is changed into the active metabolite norfluoxetine. Six to eight hours after administration, it reaches its maximal plasma concentration<sup>6</sup>. Fluoxetine exhibits minimal binding to muscarinic, dopaminergic, histaminic, serotonergic, or noradrenergic receptors. This unique specificity implies that fluoxetine may possess a distinct side-effect profile compared to existing antidepressants<sup>7</sup> and thus may generally be considered to have the least toxicity profile. Fluoxetine is associated with a higher incidence of nausea, nervousness, and insomnia tricyclic antidepressants. In addition, fluoxetine is less likely to cause anticholinergic side effects<sup>8</sup>. In this report, we discuss the case of a 22-year-old woman who presented with a non-fatal overdose of fluoxetine and exhibited mild transient symptoms in keeping with serotonin syndrome which was managed supportively till she recovered.

### Case Presentation

We present a 22-year-old female nursing student who was referred from a peripheral hospital to the Mental Health and Behavioral Medicine Team on Call of the Irrua Specialist Teaching Hospital, Irrua on account of a day history of attempted suicide by ingesting 27 capsules of Fluoxetine 20mg (540mg). She complained of severe headaches, jerking limb movement, and seeing people that others could not see in clear consciousness.

Two days prior to the presentation, following a threat of a breakup with her partner, she ran to her dormitory and picked up a knife and a box of her medications, threatening to kill herself and anyone who dared to stop her. Being held from intervention, the roommate watched her as she swallowed 27 capsules of Fluoxetine 20mg. Thirty (30) minutes after the overdose; she began to complain of severe headaches. Headache was said to be generalised, dull,

heavy, and burning. There was however no history of vomiting or neck stiffness. She was rushed to the school clinic where IV Diazepam and IV fluids were given and was thereafter discharged.

The following day, she began experiencing jerking movements. This was insidious in onset starting with the tremor-like movement of the fingers and gradually worsening involving vigorous jerking of the upper limbs with occasional muscle rigidity. This was reported to be intermittent without any associated loss of consciousness. At about the same time, she was noticed to be shouting, sounding confused and visibly restless saying she could see the face of her late father. She also complained of blurred vision, however, there was no history of fever, insomnia, excessive sweating, or frequent stooling.

She is a known patient of the department, being managed for recurrent severe depressive disorder with psychotic symptoms. She was initially on Tab Escitalopram 10mg daily and Risperdal 0.5mg nocte. Escitalopram was later changed to Tab Fluoxetine 20mg daily due to non adherence for a period of 6 months. Risperidone was discontinued because she reported being drowsy and that auditory hallucinations had subsided. There was no history of smoking, alcohol intake, or illicit drug use.

On mental state examination, she had an altered mental state which was fluctuating. She was irritable and uncooperative with increased psychomotor activity. The speech was of high tone and volume, which was occasionally irrelevant. There were visual hallucinations. Examination for cognitive function could not be conducted as she was agitated and uncooperative.

On physical examination, she was afebrile (36.7 C), and not dehydrated. SpO<sub>2</sub> was 95% with a respiratory rate of 22 cycles per minute. Radial pulse was 88 cycles per minute, full volume and regular with a blood pressure of 120/80 mmHg. She had no diaphoresis, no tachycardia and on neurological examination, she had intermittent clonus on both upper limbs, but power was normal on all limbs. Babinski's sign was negative. Her pupils were of normal size and reactive to light. Other systemic findings were normal.

The full blood count and the electrolyte, urea, and creatinine were normal. The urine toxicology screening was negative for psychoactive substances.

A diagnosis of Suicide attempt with Fluoxetine toxicity (mild serotonin syndrome) was made. She was then commenced on intravenous fluid, a tablet of Cyproheptadine 4mg 8hourly, a tablet of Risperdal 1mg, a tablet of Lorazepam 1mg (to calm agitation) and the patient was nursed close to the nursing station with a suicide caution chart. She was thereafter transferred to the female medical ward for further assessment and treatment. The following day, the presenting symptoms had significantly subsided the third day, the intermittent tremors had reduced in frequency, but she continued to have blurred vision, and a consult was sent to the ophthalmology team.

They reviewed and reported no abnormalities. Blurred vision eventually cleared, Cyproheptadine was discontinued and she was discharged on day 9 without complaints. Follow-up visits have remained uneventful.

## Discussion

We present a case of serotonin syndrome with mild symptoms. Serotonin toxicity or *serotonin syndrome* is a potentially life-threatening drug-induced condition caused by excessive amounts of serotonin in the synapses of the brain<sup>9</sup>. The over-stimulation of 5-HT receptors in the nervous system occurs due to the activity, accumulation, or interaction of one or more serotonergic substances. While there are 7 different 5-HT receptors, the major contributors to serotonin toxicity are typically 5-HT<sub>2A</sub> and 5-HT<sub>2B</sub><sup>10</sup>. Neuromuscular abnormalities, autonomic instability, and altered mental status make up the classic triad of serotonin poisoning. The symptoms can range from mild, such as tremors and diarrhoea, to severe, including hyperthermia and coma, which can be life-threatening<sup>10</sup>.

Using Hunter's criteria, we diagnosed our patient with a mild version of serotonin syndrome<sup>11</sup>. She presented with two of the classical triad and these consisted of intermittent tremors, clonus, altered mental state characterised by confusion, irritability, restlessness, and visual hallucinations.

Seizures and rhabdomyolysis have been reported with or in/ cases of fluoxetine toxicity<sup>6</sup>. Our patient did not have seizures and clinical symptoms suggestive of rhabdomyolysis. She had a normal electrolyte, urea and creatinine, although, creatine kinase (CK) levels were not assessed to objectively exclude rhabdomyolysis. This patient who had ingested 540mg of fluoxetine, which could be considered a supratherapeutic dose (normal therapeutic dose= 10-80mg), was seen to have experienced a relatively benign course. She exhibited minimal and mild symptoms even after presenting 24 hours following the incident with the only prior treatment being intravenous fluids and diazepam. This is in keeping with earlier studies that described that the most common effects of fluoxetine overdose were tachycardia, drowsiness, tremor, nausea, and vomiting, and concluded that such overdoses typically are "minimally toxic" in doses up to 1,500 mg<sup>12</sup>. It has been reported that fluoxetine has the least incidence of causing seizures compared to other SSRIs (1% vs. 2% for sertraline, paroxetine, and citalopram and 4% for fluvoxamine)<sup>6</sup>.

On the other side of the antidepressant spectrum are TCAs, which have a narrow therapeutic index and, when ingested at similar doses, cause cardiovascular, anticholinergic, and neurologic manifestations, with respiratory depression and tachydysrhythmias being two of the most lethal effects. They are potentially fatal at doses of 10-20mg/kg<sup>13</sup>. Thus, our patient who recovered with no complications within a few days following isolated ingestion of 540mg of fluoxetine further buttresses the known safety of fluoxetine in reasonably high doses. A similar study by Feierabend and colleagues reported a benign course following a 700mg fluoxetine overdose in a four-year-old child<sup>14</sup>. Noteworthy is the fact that fluoxetine when taken in combination with other substances has a much more likely fatal outcome than when ingested alone in large doses<sup>15</sup>.

Her symptoms were resolved within a few days of receiving Tab cyproheptadine 4mg 8 hourly. Cyproheptadine has been reported to resolve symptoms of serotonin syndrome in mild to moderate cases as a potent 5-HT<sub>2A</sub> antagonist. Although cyproheptadine is an antihistamine, it also has anti-serotonin activity as it particularly blocks 5-HT<sub>1A</sub>

and 5-HT<sub>2A</sub> receptors which are implicated in the symptoms of serotonin syndrome<sup>10, 16</sup>. However, the benefit of cyproheptadine in the management of serotonin syndrome has mainly been reported in various case reports, further studies are needed to confirm its efficacy in this life-threatening condition.<sup>17,18,19</sup>

## Conclusion

Cases of serotonin syndrome from fluoxetine overdose typically follow a benign course and are usually in the mild to moderate spectrum as seen in this case report. This may suggest that fluoxetine should be a top consideration in the choice of antidepressants when managing depressive disorders in patients who tend to overdose on their medications with the intent of deliberate self-harm and/or suicide. Though Cyproheptadine was found to be quite effective in managing this case, it may require more extensive studies beyond case reports to prove its efficacy in serotonin syndrome.

CONFLICT OF INTEREST- The authors declare no conflict of interest.

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