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Key Words: fluoxetine, serotonin syndrome, adolescent, serotonin specific reuptake inhibitor

Can Fluoxetine Alone Cause Serotonin Syndrome in Adolescents?

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ABSTRACT ~ **Objective:** *Serotonin syndrome is usually reported by the use of a combination of drugs. This is a possible case of serotonin syndrome after using Fluoxetine.* **Method:** *This is a case report of serotonin syndrome in an adolescent patient during treatment of depression with the medications. Subsequently, he developed headache, hyperhydrosis (diaphoresis), flushing, shaking, nausea, and vomiting, slurred speech (scanning speech), anxiety, restlessness, agitation, confusion, hallucination, and insomnia. Serotonin syndrome is suggested as one of the most probable diagnosis.* **Conclusion:** *Clinicians treating adolescents should be aware of the potential for serotonin syndrome.* Psychopharmacology Bulletin. *2008;41(4):76–79.*

INTRODUCTION

Serotonin syndrome is due to over stimulation of 5-HT_{2A} receptors[1] which may occur by medications such as selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants, and monoamine oxidase inhibitors.[2,3] It usually occurs 24 hours following the administration or overdose of a serotonergic agent.[3]

The characteristic criteria of serotonin syndrome are triad of mental, autonomic and neurological disorders.[2] There is a history of the use of a serotonergic agent, the characteristic signs and symptoms, and the exclusion of other conditions. Diagnosis is made by the presence of four major symptoms or three major ones plus two minor ones. The major symptoms are confusion, elevated mood, coma or semicoma, fever, hyperhidrosis, myoclonus, tremors, chills, and rigidity. The minor symptoms are agitation and nervousness, insomnia, tachycardia, tachypnea and dyspnea, diarrhea, low or high blood pressure, impaired co-ordination, mydriasis, and akathisia.[2] All of these signs and symptoms are not consistently found in all cases. And laboratory findings are nonspecific and have been inconsistent.[4]

Almost all the data on serotonin syndrome consist of case reports[5] and nearly all of the GPs are not familiar with its symptoms. Therefore, they do not recognize it

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properly.[6] Perhaps, it is the reason that the incidence of serotonin syndrome is not known and there are only few case reports on it.

Few cases of serotonin syndrome have been reported in association with citalopram and escitalopram.[3,7] However, to date, there are a few case reports in the literature of flouxetine plus some other medications use being associated with the development of serotonin syndrome.[8] There is just one report of fluoxetine as monotherapy caused it.[9] For example, serotonin syndrome has been observed with fluoxetine when it was combined with tramadol,[8] fluoxetine (120 mg/d) combined with meprobamate (400 mg/d) and aceprometazine (13.55 mg/d)[2], and selegiline combined with fluoxetine.[10] In addition, all of the case reports belong to the elderly and no report was found in children and adolescents.

CASE REPORT

Mr. H. A. is a 18 year old, college student from Lamerd, a city near Shiraz, who was admitted to emergency psychiatry department with about four weeks history of involuntary tremor, headache, hyperhydrosis (diaphoresis), flushing, shaking, nausea, and vomiting exacerbated during that period. From about 4 days ago, the symptoms of slurred speech (scanning speech), anxiety, restlessness, agitattion, confusion, hallucination, and insomnia appeared. It coincided with having sea food (fish). There was no rigidity or myoclonus. Foundoscopy was without remarkable pathological finding. Muscle tone and posture were normal. He was taking 20 mg/day fluoxetine for major depressive disorder and the dosage increased to 40 mg/day after 4 days from about 4 weeks prior to admission. He also took 4 mg/day perphenasine and 4 mg/day bipridine in the first three days of these 4 weeks. His blood pressure, heart rate, respiratory rate were in the normal range. His temperature was 37.5 and never increased during the last 4 weeks. There was no focal neurological finding. The findings of the complete blood count, blood electrolytes and blood glucose, liver and kidney function tests, and erythrocyte sedimentation rate were normal. Creatine kinase was not assessed. There was not any history of substance abuse including alcohol or ecstasy. Brain CT scan and EKG showed no anomalies. CSF examination and EEG monitoring were not conducted because the consultant neurologist ruled out any necessity for doing them.

The patient and his family reported that the changes in his condition started after taking medication from about 4 weeks ago.

Fluoxetine was discontinued. Nortryptline 25 mg/day was administered and he took it for 2 days. There was no change in his condition. So, the patient was admitted and low dose of lorazepam and citalopram were started by the emergency care setting physician. After about 24

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hours, his symptoms rapidly began to resolve apart depressive symptoms. The patient discharged himself from the hospital against medical advice and continued his treatment at the outpatient clinic. The patient was cooperative, with good eye contact, and normal grooming. He had normal speech and motor function. His mood and affect were depressed and congruent. There was not any evidence of anxiety symptoms or restlessness. His thought form was logical and goal directed. There was no delusion, hallucination, or illusion. He had good insight and judgment. He was alert and oriented to time, place, and person.

DISCUSSION

There are some differential diagnoses such as neuroleptic malignant syndrome, dystonic reactions, thyroid storm and sepsis, toxicity by medications such as anti-cholinergic drugs, substance use such as cocaine or ecstasy, major depressive disorder with catatonic feature, and serotonin syndrome.

There was not any specific finding in favor of infections, metabolic causes, and substance use or withdrawal.

Common criteria of neuroleptic malignant syndrome are alteration of consciousness, diaphoresis, autonomic instability, rigidity, and hyperthermia. Neuroleptic malignant syndrome should be considered in any patient receiving a neuroleptic medication and developing a high fever or severe rigidity.[11] Neuroleptic malignant syndrome is observed most often following a rapid increase in dosage of a neuroleptic drug.[3,12] Some of the other symptoms which help distinguish neuroleptic malignant syndrome from serotonin syndrome are dysphagia, hyper-salivation, and incontinency.[2] Although there is not any specific diagnostic test for detection of serotonin syndrome in our patient, absences of rigidity and hyperthermia, and persistence of symptoms for about 24 days after discontinuation of the low dosage of perhenasine are not in favor of neuroleptic malignant syndrome diagnosis. Furthermore, the symptoms were fully resolved rapidly after discontinuation of the supposed implicated drug, fluoxetine.

It is thought that our patient is a case of serotonin syndrome because he suffered from the many of the clinical features reported by Birmes et al. (mental status changes, confusion, restlessness, diaphoresis, shivering, agitation, insomnia).[2] He had at least 3 major and 2 minor symptoms. The patient had taken perphenasine just 4 mg/day for only 3 days about 4 weeks before admission while he was taking fluoxetine for about 4 weeks and the symptoms started about 2 days after prescription of the medication and continued for 4 weeks while he was taking it

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(fluoxetine). This might suggest that fluoxetine can have a link with serotonin syndrome in adolescents by itself.✤

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