



## Serotonin syndrome caused by fluoxetine: a case report

### Fluoksetine bağlı gelişen bir serotonin sendromu vakası: bir olgu sunumu

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#### Abstract

Serotonin syndrome is a syndrome that develops with the excessive stimulation of the serotonergic system. It may occur with the overdose usage of serotonergic drugs or of these drugs alongside with similar drugs. While only tremor and diarrhea are observed in its minor forms, in severe cases, this syndrome may lead to multiple organ failure and may be fatal. Generally it is a disorder practitioners may not consider and miss out especially when the case is a minor one. It has a wide symptom spectrum. As for its treatment, while minor cases may improve with backup treatment if diagnosed early and serotonergic drugs are discontinued, severe cases may require treatment under intensive care unit conditions. With this case report, I aim to present a case of serotonin syndrome occurring after a dose change of fluoxetine from 20 mg/day to 40 mg/day.

**Keywords:** Serotonin Syndrome; Fluoxetine; Toxicity.

#### Öz

Serotonin sendromu serotonerjik sistemin aşırı uyarılmasıyla oluşan bir sendromdur. Serotonerjik ilaçların yüksek dozda ya da başka serotonerjik ilaçlarla kombine kullanılması sonucu görülebilmektedir. Hafif formlarında sadece tremor ve diyare gözlenirken daha ağır formlar çoklu organ yetmezliklerine ilerleyerek ölümcül seyredebilir. Genellikle hekimler tarafından özellikle semptomların hafif olduğu durumlarda akla gelmeyen ve atlanan bir hastalıktır. Geniş bir semptom yelpazesi vardır. Tedavide ise hafif olgular, erken süreçte tanı konulup, kullanılan serotonerjik ilacın kesilmesinden sonra destek tedavisi ile düzelenken, ağır olgular yoğun bakım şartlarında tedavi gerektirebilmektedir. Bu olgu sunumunda fluoksetin 20mg/gün ile tedavi edilen bir hastanın tedavi dozunun 40 mg/güne artırılmasıyla gelişen bir serotonin sendromunun sunulmasını amaçladım.

**Anahtar Kelimeler:** Serotonin Sendromu; Fluoksetin; Toksikite.

Received/Başvuru: 13.11.2015

Accepted/Kabul: 16.11.2015

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#### For citing/Atıf için

Zayman EP. Serotonin syndrome caused by fluoxetine: a case report. J Turgut Ozal Med Cent: 2016;23(2):232-4.

## INTRODUCTION

Serotonin syndrome, which may be fatal, is an undesirable drug reaction resulting from excessive stimulation of central nervous system and peripheral serotonin receptors (1, 2). It usually arises from the use of serotonergic drugs in high doses or their use with other medicines. It is thought that increased serotonergic neurotransmission, which arises from excessive stimulation of 5-HT<sub>1A</sub> and 5-HT<sub>2</sub> receptors in the brainstem and spinal cord, is responsible for the onset of serotonin syndrome (2, 3).

In mild cases, only tremor and diarrhea are observed while moderate toxicity may result in more serious problems and symptoms and requires treatment. In severe serotonin toxicity, muscle rigidity and rapidly rising fever are observed. This medical picture, which may cause multiple organ failure and even death, requires immediate treatment within hours (4, 5).

Serotonin syndrome may develop after the single intake of drugs that increase serotonin synthesis and serotonin release while reducing serotonin metabolization, suppressing serotonin retrieval, or exhibiting agonist effects on serotonin receptors, or the pharmacological interactions after the multiple intake of such drugs (4). SSRIs (selective serotonin reuptake inhibitors) reduce serotonin reuptake in the synaptic cleft and, therefore, affect serotonin neurotransmission (6). The case at hand is a case of serotonin syndrome developing after increased dose of fluoxetine, a derivative of SSRIs. In this study, I present the case of a female patient who was on fluoxetine 20mg/day and increased the drug dose to 40 mg/day, and in turn, developed serotonin syndrome. The symptoms in my patient developed after intake of low and single dose of SSRI; this requires attention since practitioners should consider serotonin syndrome in differential diagnosis.

## CASE REPORT

A 62-year-old female patient, who was a housewife and mother of 2 children, presented at the psychiatric clinic accompanied by her daughter with complaints of irritability, restlessness, excessive sweating, whole body tremors, insomnia, inability to talk, diarrhoea, and a dry mouth.

According to the medical history obtained from the patient and her daughter, complaints began after changing drug doses for about 4 days ago. The patient had been followed for depressive disorder in the last 2 years and been on fluoxetine 20 mg/day and olanzapine 15 mg/day though the doses had recently been arranged as fluoxetine 40 mg/day and 5 mg/day at another psychiatric clinic when the complaints of the patient increased within the last month.

Within approximately 4 hours after the fluoxetine 40 mg/day intake, the patient was admitted to the emergency department with complaints, applied muscle relaxants and sedatives, the names of which the patient

could not name, and then referred to a psychiatrist. Due to an increase in her complaints, the patient was admitted to the emergency room at Turgut Ozal Medical Centre. Here, the patient was evaluated by a psychiatrist, hospitalised, and scheduled for treatment with serotonin syndrome pre-diagnosis.

The mental status examination showed characteristics consistent with her age; the patient was irritable and anxious with inadequate self-care. She had several physical symptoms such as nausea, vomiting, diarrhea, flushing, sweating, dizziness, and weakness. There were no psychotic symptoms. The patient's history did not contain other physical illnesses, use of alcohol or other substances, either.

The patient had noticeable hyperhidrosis; other data obtained on the physical examination were: fever: 38,5 C degrees; blood pressure: 140/90 mmHg; pulse: 101 beats/min, respectively. It was observed that the patient developed delirium-type impaired consciousness. Hemogram (CBC) and routine biochemical tests were applied. The results of the tests revealed that the patient had acute renal failure. The brain imaging reports were normal. The patient was asked for neurology and infectious diseases consultation. There were no neurological, endocrine, metabolic, infectious or toxic diseases that could cause the patient's current medical picture. Considering the patient's current complaints, results of the examinations and laboratory findings, the patient was diagnosed with severe serotonin syndrome. All medication was discontinued and the patient was administered benzodiazepine therapy. Within a week's time, the symptoms gradually decreased.

## DISCUSSION

Serotonin syndrome is a syndrome that can manifest itself with mental, autonomic, and neurological symptoms 2-24 hours after the intake of a serotonergic agent or dose increase (1). In this case, the fact that the symptoms surfaced around 4 hours after the increased serotonergic drug dose intake and the absence of drug abuse or of a physical illness have all suggested that the medical picture may have arisen due to the existing drug.

There are different diagnostic criteria defined for serotonin syndrome. The first and most widely used of these is the Sternbach criteria, a criteria triad of consciousness-behavioral changes as well as neuromuscular and autonomic disorders. Defined by Sternbach, the physical signs of these criteria include confusion, agitation, impaired consciousness, seizures, clonus/myoclonus, hyperreflexia, tremors, muscle rigidity, ataxia, akathisia, hyperthermia, hypertension, tachycardia, diaphoresis, lacrimation, mydriasis, chills and diarrhoea. According to the Sternbach diagnostic criteria, at least three of these symptoms must co-exist for diagnosis (7). However, because some of these clinical features described by Sternbach are not specific symptoms of this syndrome only, Dursun et al. (8) and Radomski et al. have each rearranged and developed

new diagnostic criteria for this condition (9, 10). Symptoms of serotonin syndrome are classified under three main headings Radomski et al. as mental symptoms, neurological symptoms, and vegetative symptoms, each of which have subgroups as major and minor symptoms. Major criteria for mental symptoms are impaired consciousness, elevated mood, and semi-coma/coma while minor symptoms are irritability and insomnia. Major criteria for neurological symptoms are myoclonus, tremor, shivering, rigidity, hyperreflexia; minor criteria for neurological symptoms are incoordination, dilated pupils, and akathisia. Major vegetative symptoms are fever and sweating; minor vegetative symptoms are tachycardia, tachypnea and/or dyspnea, diarrhea and hyper/hypotension. According to the criteria suggested by Radomski et al. a combination of four major criteria or a combination of three major and two minor criteria are enough for the diagnosis of serotonin syndrome (11, 12). For the differential diagnosis, other conditions and symptoms that may cause this picture such as infections, metabolic disorders, substance abuse or drug withdrawal symptoms, neuroleptic drug use, and other similar psychiatric and medical reasons should be evaluated and, if need be, excluded (13). Our case meets the criteria suggested by these researchers for the diagnosis.

The most important point in the treatment process of this syndrome is early diagnosis and discontinuation of serotonergic drugs that trigger the condition. With the discontinuation of serotonergic drugs and start of treatment, symptoms in many patients typically subside within 24 hours. It has been observed that symptoms may continue for a while in patients on drugs with a long half-life, active metabolites, or drugs with long duration of effect. For example, some cases with confusion and other altered mental states have been reported to last for several days and even, in spite of the treatment, to result in death (2, 14). Fluoxetine has the longest half-life among SSRIs; this duration may reach 7-17 days due to the effect of the active metabolite, norfluoxetine (15).

In the case of this patient, too, the symptoms started after fluoxetine dose increased to 40 mg/day although the diagnosis was confirmed after 24 hours. After fluoxetine was cut, it was observed that complaints continued for another 48 hours.

Consequently, serotonin syndrome is a rare clinical condition that can be fatal. For a rapid response to this condition, physicians should be familiar with drugs that cause serotonin syndrome and consider serotonin

syndrome in the differential diagnosis. Because serotonin syndrome can be fatal, physicians should closely monitor patients on serotonergic drugs and be alert for possible side effects. A swift diagnosis, discontinuation of serotonergic drugs, and starting supportive drugs that will enhance patients' general state constitute the basis of the treatment for this condition.

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