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Case Report

Fluoxetine-induced Hypotension: A Case Report

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ABSTRACT

Fluoxetine is a Selective Serotonin Reuptake Inhibitor (SSRI) that exerts its anti-depressive effect by blocking the presynaptic reuptake of the neurotransmitter serotonin, 5-hydroxytryptamine (5-HT). Although fluoxetine is usually considered safe for most patients, in the present case report, we describe a young patient with Mixed Anxiety and Depression Disorder (MADD) treated with fluoxetine 10 mg/day, who developed hypotension when the dosage was titrated up to 20 mg/day. After discontinuing the use of fluoxetine, the symptoms of hypotension improved. A temporal association and dose-dependent relationship between the hypotension and the use of fluoxetine was observed. To the best of our knowledge, this is the first case report that precisely associates regular doses of fluoxetine with the presence of hypotension. Because boosting central serotonergic function lowers blood pressure, it is suggested that a significant effect of fluoxetine on the vasomotor center may be responsible for the reduction of blood pressure. Thus, physicians should be aware of the possible risk of hypotension induced by fluoxetine and recommend patients discontinue the drug immediately if complications have occurred.

1. Introduction

Blood pressure is regulated via the autonomic nervous system. The sympathetic nervous system acts to raise blood pressure, and the parasympathetic nervous system lowers blood pressure [1]. Hypotension is a decrease in systemic blood pressure (less than 90/60 mmHg). Although often harmless, this can also be dangerous [2]. It is under-recognized, mainly because it has few or even no symptoms. Symptoms occur as a result of hypoperfusion of essential organs [3]. According to the criteria of the International Statistical Classification of Diseases and Related Health Problems (ICD-10), Mixed Anxiety and Depression Disorder (MADD) is characterized by subsyndromal symptoms of anxiety and depression (i.e., symptoms that are severe enough to justify the diagnosis of MADD, but none of them are predominant enough to insure a separate diagnosis of an underlying anxiety disorder or depression) [4]. MADD may occur at any age [5], and patients often present with severe physical, social, and psychological impairment. Symptoms are more disabling and resistant to treatment

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than those of either condition (anxiety or depression) alone [6].

Fluoxetine is an Selective Serotonin Reuptake Inhibitors (SSRIs) that exerts its anti-depressive effect by blocking the presynaptic reuptake of the neurotransmitter serotonin, 5-hydroxytryptophan (5-HT). The high affinity of fluoxetine for 5-HT transporters, minimal activity on noradrenergic reuptake, and no affinity for dopamine transporters indicate that it is 5-HT-selective [7, 8]. Most side effects of SSRIs are dose-dependent, time-dependent, and can be attributed to serotonergic effects. Serotonin receptors mediate a variety of functions, including sleep, appetite, and sexual functions. Sleep disturbance, weight gain, and sexual dysfunction are the most bothering adverse effects during long-term SSRI therapy. In general, the most common side effects of the medication include insomnia, nausea, diarrhea, anorexia, yawning, headache, libido loss, weakness, tremor, and pharyngitis [9-11]. To the best of our knowledge, hypotension induced by fluoxetine has been not reported in any international literature. Herein, we report the first case of hypotension caused by fluoxetine in a young woman with MADD.

2. Case Report

A 35-year-old female attended our clinic with symptoms of depression, anxiety, lack of enjoyment of life, intolerance, thoughts of despair, weakness, fatigue, and insomnia. After the initial mental status examination, she was diagnosed with a case of MADD, and treatment was initiated under our care service with 10 mg/day fluoxetine and 0.5 mg/day alprazolam. After one week, the daily fluoxetine dosage was increased to 20 mg. After increasing the drug dose, the patient complained of dizziness, lethargy, and a feeling of weakness in the lower limbs. She was brought to our emergency service with a blood pressure of 80/60 mmHg. Before starting fluoxetine, the patient's blood pressure was 110/70 mmHg and she had no history of physical illness, fainting, or hypotension. She also had a negative family history of hypotension. Complete laboratory examinations, including complete blood count, serum electrolytes, liver function test, renal function test, thyroid function test, and urine analysis were done and all reports were within normal limits. Some probable clinical conditions that can cause hypotension, such as dehydration, anemia, malnutrition, hyponatremia, congestive heart failure, arrhythmia, atrial fibrillation, vascular disease, and use of other medications were excluded. Her chest X-ray and electrocardiography results were found to be normal and provided no explanation for hypotension. The patient's hypotension could not be due to orthostatic hypotension. While blood pressure was measured while sitting and standing, no change was observed and the patient's symptoms did not worsen during the standing position. Although fluoxetine is usually associated with hypertension, we hypothesized that the patient's hypotension might be caused by fluoxetine. Thus, the patient was asked to stop taking fluoxetine. After discontinuing the use of fluoxetine, the hypotension symptoms disappeared. One month later, the patient resumed fluoxetine again and was told to stop taking it and return to the clinic immediately if the recurrence of the previously described symptoms occurred. Six days after resuming the drug, she presented with similar symptoms and blood pressure of 85/60 mmHg. Finally, another SSRI agent was replaced with fluoxetine, and alprazolam was continued at 0.5 mg/day. The rapid disappearance of hypotension after discontinuation of fluoxetine, indicates a relationship between the mentioned effect and the drug. Consequently, according to the Naranjo causality scale (which showed a score of 8), this adverse effect was probably induced by fluoxetine. Thus, fluoxetine was replaced by another SSRI agent and alprazolam continued with the previous dose. After she discontinued fluoxetine, hypotension did not occur again (Table 1).

3. Discussion

Fluoxetine is usually considered safe for most patients. To the best of our knowledge, this is the first case report that correlates a regular fluoxetine dose with the presence of hypotension. A two-factor convergence can demonstrate the association between hypotension and fluoxetine: manifesting hypotension while prescribing an increasing dose of fluoxetine and improving hypotension by discontinuing the medication. These factors provide a dose-dependent relationship between a decrease in blood pressure and taking fluoxetine. Antidepressant drugs are often associated with cardiovascular side effects and toxicity, such as hypertension, prolonged PR (the PR interval is the time from the beginning of the P wave (arterial depolarization) to the beginning of the QRS complex (ventricular depolarization)), arrhythmia, and hypotension [12-15]. Various clinical studies on SSRIs, such as fluoxetine, citalopram, and sertraline, have indicated remarkable advantages over Tricyclic Antidepressants (TCAs) because of causing fewer cardiotoxic side effects during the treatment of depressive disorders. These newer compounds have demonstrated a lower risk of inducing hypotension [13]; however, an increasing number of case reports have indicated that the use of SSRIs is associated with cases of orthostatic hypoten-

Table 1. Naranjo algorithm

Questions	Yes	No	Don't know	Score
1. Are there previous conclusive reports on this reaction?	+1	0	0	
2. Did the adverse event appear after the suspected drug was administered?	+2	-1	0	
3, Did the adverse reaction improve when the drug was discontinued a or a specific antagonist was administered?	+1	0	0	
4. Did the adverse reaction reappear when the drug was readministered?	+2	-1	0	
5. Are there alternative causes (other than the drug) that could ontheir own have caused the reaction?	-1	+2	0	
6. Did the reaction reappear when a placebo was given?	-1	+1	0	
7. Was the drug detected in the blood (or other fluids) in concentrations known to be toxic?	+1	0	0	
8. Was the reaction more severe when the dose was increased or less asevere when the dose was decreased?	+1	0	0	
9. Did the patient have a similar reaction to the same or similar drugsin any previous exposure?	+1	0	0	
10. Was the adverse event confirmed by any objective evidence?	+1	0	0	
			TOTAL	

(Naranjo CA et al. "A method for estimating the probability of adverse drug reactions". Clin. Pharmacol. Ther. August 1981)

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The Adverse Dug Reaction is assigned to a probability category from the total score as follows:

Definite >8

Probable 5 to 8

Possible 1 to 4

Doubtful <1

sion in patients without cardiovascular disorders [16]. Orthostatic hypotension is defined as a decrease in systolic blood pressure of at least 20 mmHg or a decrease in diastolic blood pressure of at least 10 mmHg within three minutes upon standing from sitting or from a lying position. Since orthostatic hypotension can be a side effect of many antidepressants, we decided to measure the patient's blood pressure in different situations for further investigation. After comparing systolic and diastolic blood pressure in different positions, it was found that the patient's hypotension was not orthostatic [17]. In a study carried out by Fuller et al., an antihypertensive effect of the combination of fluoxetine and 5-HTP in Deoxycorticosterone acetate (DOCA)-salt hypertensive rats was demonstrated. Fluoxetine alone had also a remarkable antihypertensive effect on blood pressure. As it is suggested that boosting central serotonergic function lowers blood pressure, they hypothesized that the mechanism of lowering blood pressure by fluoxetine and 5-HTP (as a chemical precursor of serotonin) might be related to the enhancement of the central serotonin function and diminished central sympathetic neural outflow [18]. A significant lowering effect of venlafaxine (as a serotonin and noradrenaline reuptake inhibitor) on blood pressure was reported in a female patient with a history of Major Depressive Disorder (MDD). Participation of presynaptic α_2-adrenergic receptors was considered to be a pathophysiological mechanism to describe the relationship between taking a regular dose of venlafaxine and the development of symptomatic hypotension [19]. Therefore, the occurrence of hypotension cannot be attributed to the case reported in our case report as fluoxetine has little or no affinity for α_2-adrenergic receptors. Since fluoxetine does not have a direct cardiac or vascular effect, the reduction of blood pressure may be due to a central action of fluoxetine on the vasomotor center [16].

Here, this is the first report on the development of hypotension following the use of a regular dose of fluoxetine. Although further studies are needed to clarify this side effect, it may be important for the physicians to be aware of this rare situation and recommend discontinuing the drug immediately if complications have occurred.

Ethical Considerations

Compliance with ethical guidelines

All related research's ethical principles are considered in this article.

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Authors' contributions

Visited and followed up the patient and gathered the data: Hamzeh Hosseini; Analyzed the data and wrote the article: Neda Zamani; Critically revised the final draft of the manuscript: Amirhossein Ahmadi.

Conflict of interest

The authors declared no conflict of interest.

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