

CASE REPORT

A Rare Case of Hypoglycemia Induced by Selective Serotonin Reuptake Inhibitors (SSRIs) Therapy

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ABSTRACT

Selective serotonin reuptake inhibitors (SSRIs) are frequently prescribed for a range of psychiatric disorders, including depression, anxiety, and somatoform disorders, due to their effectiveness and relatively favorable safety profile. However, rare but potentially serious metabolic side effects, such as hypoglycemia, have been documented. This case report discusses a 65-year-old male diagnosed with somatoform disorder who developed unexplained hypoglycemic episodes shortly after initiating fluoxetine therapy. The patient had no prior history of diabetes or hypoglycemia, and other potential causes were ruled out. Upon discontinuation of fluoxetine and switching to clomipramine, the hypoglycemic episodes ceased, indicating a likely causal relationship. This case highlights the need for clinicians to remain vigilant for uncommon adverse effects of SSRIs, especially in older adults or those with underlying vulnerabilities. Prompt recognition and appropriate medication adjustments are essential to ensure both the safety and therapeutic success of psychiatric treatment regimens.

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INTRODUCTION

Selective serotonin reuptake inhibitors (SSRIs) are widely used antidepressants that have transformed the pharmacological management of mood and anxiety disorders due to their favorable safety profile, low overdose toxicity, and improved tolerability. They act by inhibiting the presynaptic serotonin transporter, thereby increasing synaptic serotonin levels, which is essential in alleviating emotional and somatic symptoms associated with these conditions (1). As a result, SSRIs are considered first-line agents for disorders such as major depressive disorder, generalized anxiety disorder, panic disorder, obsessive-compulsive disorder, post-traumatic stress disorder, and somatoform disorders. Since their introduction in the 1980s, SSRIs have largely replaced tricyclic antidepressants due to better adherence, fewer anticholinergic

side effects, and lower lethality in overdose (3).

Despite their overall safety, SSRIs are associated with adverse effects, most commonly gastrointestinal disturbances, insomnia, sexual dysfunction, and headache, which are generally mild and dose-dependent. However, rare but serious complications, including hyponatremia, bleeding abnormalities, serotonin syndrome, and disturbances in glucose metabolism, have also been reported (2). Hypoglycemia, defined as blood glucose levels below 70 mg/dL, is uncommon in non-diabetic individuals and is typically linked to medications or systemic conditions. Although SSRIs are not commonly associated with hypoglycemia, serotonergic modulation may influence glucose regulation through central and peripheral mechanisms, potentially predisposing susceptible individuals, particularly older adults, to hypoglycemic events (2). This report presents a rare case of fluoxetine-induced hypoglycemia in a non-diabetic elderly male with somatoform disorder, highlighting the need for clinical awareness and careful evaluation of atypical adverse effects.

CASE REPORT

A 65-year-old male presented to the psychiatry outpatient department with a 6-month history of vague and persistent physical complaints, including fatigue, headaches, and intermittent gastrointestinal discomfort. Detailed clinical and laboratory evaluations ruled out any significant medical conditions, and the symptoms were consistent with a diagnosis of somatoform disorder. He was started on fluoxetine 20 mg/day. Over the course of four weeks, he reported modest improvement in mood and a decrease in somatic preoccupation. However, during the fifth week, he experienced two episodes of acute dizziness, profuse sweating, confusion, and mild agitation occurring in the late afternoon. Fingertick capillary blood glucose measurements during the episodes revealed values between 52 and 58 mg/dL (normal fasting reference: 70–99 mg/dL).

He had no past or family history of diabetes mellitus, did not consume alcohol or use recreational substances, and was not on any medications known to lower blood glucose levels. Imaging studies, including CT of the paranasal sinuses, revealed a deviated nasal septum to the right with a nasal spur (Figure 1). There was no evidence of pancreatic pathology. There was no clinical or laboratory evidence suggestive of insulinoma, adrenal insufficiency, or hepatic dysfunction.



Figure 1: CT - PARANASAL SINUSES showing deviated nasal septum to the right with nasal spur.

Considering the close temporal association between fluoxetine initiation and the onset of hypoglycemia, and in the absence of other medical explanations, fluoxetine was strongly suspected as the causative factor. Following its discontinuation and replacement with clomipramine 25 mg/day, the patient's hypoglycemic episodes resolved within 48 hours. Serial glucose monitoring thereafter

showed stable readings, and the patient remained free of hypoglycemia for six months of follow-up, further supporting a causal link with fluoxetine therapy.

DISCUSSION

This case highlights fluoxetine-induced hypoglycemia in a non-diabetic elderly patient, an uncommon but clinically significant adverse effect of selective serotonin reuptake inhibitors (SSRIs) that may be overlooked due to its nonspecific presentation. Serotonin plays a key role in glucose homeostasis through both central and peripheral mechanisms, including modulation of the autonomic nervous system, stimulation of pancreatic β -cell receptors to enhance insulin secretion, and alteration of hepatic gluconeogenesis and glycogenolysis. These effects may predispose vulnerable individuals, particularly older adults with altered pharmacokinetics and impaired counter-regulatory responses, to drug-induced hypoglycemia when serotonergic activity is increased. Fluoxetine, with its long half-life and potent serotonergic action, may further amplify these metabolic effects. Although SSRIs are generally associated with fewer anticholinergic side effects compared to tricyclic antidepressants (TCAs), their rare metabolic complications remain underexplored. A meta-analysis by Anderson and Tomenson demonstrated that while SSRIs have better tolerability and lower discontinuation rates than TCAs, serious adverse effects may still occur unpredictably (3). In contrast, clomipramine, a TCA with broader noradrenergic activity, appears to have less impact on glucose regulation (4).

From a clinical perspective, this case underscores the importance of vigilance when prescribing SSRIs, particularly in elderly or medically vulnerable patients. Clinicians should consider baseline and periodic monitoring of fasting glucose levels, educate patients and caregivers to recognize symptoms of hypoglycemia such as shakiness, sweating, confusion, irritability, and blurred vision, and exercise caution in individuals with comorbidities or polypharmacy that may impair drug clearance. Additionally, unexplained neuropsychiatric or somatic symptoms should prompt consideration of underlying metabolic disturbances. Patients, especially older adults, should be informed of this rare risk and encouraged to report symptoms early. These observations align with emerging evidence linking serotonergic modulation with metabolic regulation, including potential influences of gut microbiome-mediated pathways on drug metabolism (5).

CONCLUSION

In summary, this case illustrates that although SSRIs such as fluoxetine are generally safe and effective, rare but serious metabolic side effects like hypoglycemia can occur, especially in older adults. Awareness of serotonin's influence on glucose metabolism, careful

monitoring, patient education, and timely drug substitution are critical to preventing complications and ensuring safe psychiatric treatment outcomes.

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