Hypoglycemic episodes in a case of Premenstrual Dysphoric Disorder on sertraline

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Received: 15-09-2014
Revised: 17-01-2015
Accepted: 17-08-2015

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ABSTRACT

Sertraline is a selective serotonin reuptake inhibitor. It has been shown to blunt postprandial hyperglycemia in rats and to potentiate the hypoglycemic effects of sulfonylurea agents in humans. Here, we report a case of a 33-year-old nondiabetic patient with no history of glucose intolerance, who experienced multiple episodes of hypoglycemia that resolved after discontinuation of the drug. Healthcare professionals should consider sertraline among the possible causes of hypoglycemia occurring in patients receiving antidepressants.

KEY WORDS: Drug-induced hypoglycemia, selective serotonin reuptake inhibitors, sertraline

Introduction

Selective serotonin reuptake inhibitors (SSRIs) are a class of compounds that affect the level of serotonin in the brain. Because decreased serotonin levels have been associated with unstable mood and depression, SSRIs are commonly used to treat depression, anxiety disorders, and some personality disorders. Although these agents are generally well tolerated, numerous side effects have been reported, including nausea, insomnia, sedation, sexual dysfunction, weight gain, hyponatremia, apathy, anorexia, and extrapyramidal symptoms.¹ Sertraline is an antidepressant of the SSRI class. It is primarily prescribed for major depressive disorder in adult outpatients as well as an obsessive-compulsive, panic, and social anxiety disorders in both adults and children. Therapeutic doses of sertraline (25–200 mg/day) taken by patients for 4 weeks resulted in 80–90% inhibition of serotonin transporter in the striatum as measured by positron emission tomography.

There is an age-gender interaction for sertraline, with its plasma concentrations being 35–40% lower in young men than in elderly or young females or elderly males.² SSRIs have also been documented to affect glycemic control in diabetic patients, causing episodes of hypoglycemia and hyperglycemia.³⁻⁴

Unlike other SSRIs, sertraline has linear pharmacokinetics which means that increases in drug dose leads to a proportional increase in drug concentration. Several case reports are available in the literature linking use of antidepressants and disturbances in glucose control; it is difficult to identify risk factors for serious adverse drug events from individual case reports. The aim of this case report is to provide critical insight into glucose dysregulation following the initiation of antidepressant agents.

Case Report

A 33-year-old woman with mild depression according to Diagnostic and Statistical Manual of Mental Disorders-IV...
criteria and no history of glucose intolerance was brought to the emergency department for a presyncopal episode associated with blood glucose of 42 mg/dL as measured by the ambulance attendant. She had similar symptoms the day before in the morning. The patient was diagnosed with premenstrual dysphoric disorder (PMDD) for which she was prescribed sertraline 50 mg once daily. She had started taking sertraline 50 mg once daily for mild depression 25 days prior to presentation due to PMDD. Despite repeated administration of oral and intravenous glucose, the patient had recurrent episodes of hypoglycemia and was hospitalized for 4 days. There was no history of any concomitant medications. She had never been prescribed any oral hypoglycemic agents. All the biochemical parameters were within normal limits during admission. The physical examination findings were normal. Laboratory findings were normal except for a random blood glucose level of 42 mg/dL (normal, 70–110 mg/dL). Serum sertraline and desmethylsertraline concentrations measured 2, 3, and 4 days after discontinuing sertraline were within the expected range, but the rate of decline was consistent with a moderately prolonged half-life. Subsequent routine blood tests found a mildly raised creatinine level of 110 µmol/L (normal, 53–106 µmol/L), with a creatinine clearance of 31.3 mL/min/1.73 m² based on the patient’s height of 165 cm and weight of 67 kg (normal, 75–125 mL/min/1.73 m²). Her sodium and potassium levels were within normal range at 140 mEq/L (normal, 136–142 mEq/L) and 3.6 mEq/L (3.5–5.0 mEq/L), respectively. A full blood count and liver function tests were also normal. Glycated hemoglobin A1c levels were not assessed.

We decided to regularly monitor the patient’s blood glucose levels, which revealed recurrent episodes of hypoglycemia (42.6–48.2 mg/dL) in the morning. These episodes were associated with confusion following administration of sertraline. After sertraline was discontinued, her episodes of confusion resolved and her glucose levels normalized, reaching levels >70 mg/dL.

Causality assessment using WHO-Uppsala Monitoring Centre criteria[6] and Naranjo’s scale[7] suggested a “probable” (Naranjo’s score = 5) association between the drug and development of hypoglycemia. Severity assessment by the Hartwig scale showed the reaction as severe (level 5).

**Discussion**

Antidepressants, including SSRIs and tricyclic antidepressants, have been found to interfere with blood glucose metabolism, increasing the risk of hypoglycemic episodes. Several reports have implicated antidepressants, especially SSRIs, in the development of clinically relevant hypoglycemia in diabetic patients.[13–15] SSRI-induced hypoglycemia in nondiabetic individuals is rarer, with only one case previously reported in the literature.[16] In this previous case, the implicated medication was sertraline. Like our patient with sertraline-induced hypoglycemia, the patient was also a woman but in her eighth decade of life, and her hypoglycemia presented as presyncopal episodes approximately 25 days after sertraline was initiated as a treatment for mild depression. Glucose counterregulation is a physiologic response that occurs to guard the body against hypoglycemia when plasma glucose concentration decreases.[17] Through this mechanism, counterregulatory hormones, including glucagon, and epinephrine, are released in an effort to rapidly restore euglycemia. SSRIs may cause hypoglycemia by impairing the central mechanisms that mediate hypoglycemia-induced hormonal counterregulatory responses. This adverse drug reaction being a class effect of the SSRIs, sertraline once again establishes the cause of hypoglycemia in the setting of normal glucose tolerance.

**Conclusion**

SSRIs should be ruled out as a possible cause of hypoglycemia in both diabetic and nondiabetic individuals presenting with recurrent episodes of hypoglycemia.

**Financial Support and Sponsorship**

Nil.

**Conflicts of Interest**

There are no conflicts of interest.

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