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Case Report

Severe hyponatremia and syndrome of inappropriate secretion of antidiuretic hormone (SIADH) induced by duloxetine

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ABSTRACT

Hyponatremia is a significant complication of treatment with selective serotonin reuptake inhibitors. There are a limited number of case reports of hyponatremia following treatment with duloxetine. We describe a case of a 57-year-old woman who had begun taking duloxetine for depression. Three weeks later, she reported fatigue, weakness, lethargy and drowsiness. During an emergency room evaluation, laboratory examination revealed hyponatremia and serum hypo-osmolarity. She had duloxetine-induced syndrome of inappropriate secretion of antidiuretic hormone (SIADH) and duloxetine was discontinued. Hyponatremia correction was started and, in one week, the mental status of the patient gradually improved, paralleling the resolution of her hyponatremia. She was started on trazodone 25 mg/day for depression without recurrence of hyponatremia.

1. Introduction

Severe hyponatremia often leads to symptoms such as headache, nausea, vomiting, lethargy, disorientation, seizure, coma and death [1]. The syndrome of inappropriate secretion of antidiuretic hormone (SIADH) is a well-known adverse effect of selective serotonin reuptake inhibitors (SSRIs) [2]. Duloxetine is a balanced selective serotonin and norepinephrine reuptake inhibitor (SNRI) that has been approved for the treatment of major depressive disorder (MDD). Duloxetine at dosages ranging from 40 to 120 mg/day is effective in the short- and long-term treatment of MDD [3]. This drug appears to have significant benefits in the treatment of painful physical symptoms associated with depression. Duloxetine, 60 mg/day, is a well-tolerated and effective treatment for MDD and reduces painful physical symptoms [4]. Hyponatremia as a severe side effect of treatment with duloxetine is rare [5–8]. We present a patient with MDD who developed severe hyponatremia following duloxetine treatment.

2. Case report

A 57-year-old Han Taiwanese woman was diagnosed with MDD according to the Diagnostic and Statistical Manual of Mental Disorders – IV text revision. She had hypertension, which had been treated with amlodipine 10 mg/day for ten years. In addition, she had multiple somatic complaints, which could not be explained by a series of physical, and laboratory examinations. She was started on antidepressant medication with duloxetine 30 mg/day. In the following three weeks, fatigue and panic-like symptoms led to two visits to our emergency room. Anxiety was impressed and duloxetine was increased to 60 mg/day. Three days later, she was brought to our ER again because of lethargy and drowsiness. Laboratory examinations revealed marked hyponatremia (114 mmol/L, normal range: 135–147 mmol/L) with corresponding serum hypo-osmolarity (243 mOsm/kg, normal range: 280–300 mOsm/kg) and increased urinary sodium excretion (38 mM). Urinary osmolarity (374 mOsm/kg, normal range: 50–1400 mOsm/kg) was higher than the serum osmolarity. A chest radiograph and brain computed tomography were normal. Further investigations, including serum cortisol, thyroid function, renal function and liver function tests, were normal. There was no dyspnea, pulmonary rales, peripheral edema or ascites. No evidence of liver cirrhosis, congestive heart failure, renal failure or nephrotic syndrome was found. The patient appeared euvolemic on physical examination. Hyponatremia due to SIADH was diagnosed. Duloxetine was discontinued and fluid was restricted to 1200 mL/day. Hypertonic saline solution (3% NaCl) plus 80 mg of intravenous furosemide daily was given for three days. The serum sodium was raised by 1 mmol/L/hour with an absolute limit of 5 mmol/L. Serum sodium recovered after three days to 130 mmol/L, and hypertonic saline was discontinued. Serum sodium continued to return to normal

Conflict of interest: none.

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over the next four days. Her mental status returned to a normal baseline within one week, paralleling the resolution of her hyponatremia. Fluid restriction was discontinued when the serum sodium normalized. The patient received trazodone 25 mg/day for depression without recurrence of hyponatremia.

3. Discussion

Duloxetine is a dual-acting antidepressant approved by the United States Food and Drug Administration for MDD. Hyponatremia, in association with psychotropic drug treatment, is usually caused by SIADH [9]. The mechanism of SIADH with SSRIs and SNRIs is unclear. Animal studies suggest that norepinephrine and serotonin can both stimulate release of antidiuretic hormone [10]. Duloxetine inhibits the reuptake of both serotonin and norepinephrine, which may explain why our patient developed SIADH. Hyponatremia in our patient was related to duloxetine and likely due to SIADH.

There are some case reports of patients with low serum sodium levels within the first 2–3 days of duloxetine treatment [5, 7]. It has been confirmed that hyponatremia may occur with lower duloxetine dosages. Our patient presented with worsening of pre-existing anxiety and mood symptoms while taking duloxetine 30 mg/day. In addition, it has been speculated that there is a dose-related effect in the development of hyponatremia with duloxetine. Previous reports showed low serum sodium concentrations with mild-to-moderate clinical symptoms after therapy with high doses of duloxetine ranging from 90 to 120 mg/day [6]. In our patient, clinical exacerbation of anxiety and depressive mood preceded the lethargic state, which occurred three days after duloxetine was increased from 30 mg/day to 60 mg/day. Thus, clinicians should be aware of potentially serious adverse events when treating patients with duloxetine in higher dosages.

Risk factors for the development of hyponatremia with SSRIs include older age, female gender, concomitant use of diuretics, low body weight, and lower baseline serum sodium concentration [11]. A decrease in total water, renal blood flow, glomerular filtration rate and renal tubular concentrating and diluting capacity have been noted in elderly people. These could cause a reduction in drug clearance, resulting in a higher concentration for a given dose, compared with that in younger patients. The incidence of hyponatremia is usually higher in older than younger patients [12].

Our patient was started on trazodone 25 mg/day when her serum sodium level returned to the normal range. Trazodone is a bicyclic antidepressant. There have been no reports of hyponatremia in patients treated with low dose trazodone. Hyponatremia did not recur in our patient after treatment with low dose trazodone.

In summary, hyponatremia has been associated with a variety of antidepressants. Older patients started on duloxetine should be closely monitored for clinical and laboratory evidence of hyponatremia. The symptoms of hyponatremia can easily be mistaken for physical complaints associated with depression. Clinicians should recognize that hyponatremia, a rare side effect of duloxetine, may cause possible or masked psychiatric symptoms in patients treated for depressive disorder.

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