Citalopram-induced severe hyponatremia

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Received 23 June 2014; accepted 24 August 2014
Available online 25 November 2014

Abstract

Citalopram-induced syndrome of inappropriate antidiuretic hormone secretion (SIADH) causing hyponatremia is well documented; however, severe hyponatremia with small doses has not been previously reported. An 84-year-old woman presented with acute confusion and gait disturbance of 3–4 days’ duration and a 2-day history of vomiting but managed to maintain fluid intake. Seven days earlier she was started on citalopram 10 mg per day for low mood. On examination, she was euvolemic, drowsy, and confused; her serum sodium level was 100 mmol/L. A working diagnosis of SIADH was proposed. Citalopram was stopped and the patient was treated over 24 hours with hypertonic saline, which led to clinical improvement, and she was discharged from the hospital 6 days later with a serum sodium level of 131 mmol/L. This case highlights that citalopram can cause severe hyponatremia (serum sodium as low as 100 mmol/L), even at a low dose, and that such biochemical abnormalities can potentially occur within days of starting therapy. It also raises important questions and learning points about the management of severe hyponatremia.

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Keywords: hyponatremia; syndrome of inappropriate antidiuretic hormone secretion (SIADH); citalopram

1. Introduction

Depression is common in elderly individuals and warrants treatment.1 Selective serotonin reuptake inhibitors (SSRIs) such as citalopram are the first line of pharmacological therapy for depression and can therefore be regularly prescribed in the community setting to this group of patients who are at particular risk of experiencing significant side effects.2 Hyponatremia secondary to syndrome of inappropriate antidiuretic hormone secretion (SIADH) is a well-documented side effect of citalopram and can present with nonspecific symptoms2,4 potentially going unreported or missed in the community setting. Severe hyponatremia can cause significant morbidity and mortality, and can lead to permanent brain damage and even death in severe cases.2,6 Management of these cases is a significant burden on secondary care and the correction of severe hyponatremia is usually challenging,3 and inappropriate correction itself can cause significant morbidity.6 There are case reports of mild to moderate hyponatremia with dosages of 20 mg/day.7 Severe symptomatic hyponatremia with a low dose of 10 mg/day has not been previously reported.

2. Case report

An 84-year-old woman presented to the medical admissions unit with acute confusion, gait disturbance for 3–4 days, and a 2-day history of vomiting and lethargy. She had managed to maintain fluid intake. She had consulted her general physician 7 days earlier because of low mood following the death of her husband and was started on citalopram 10 mg once a day at bedtime. She had a history of essential hypertension and no other comorbidities. In addition to citalopram, the patient had been taking losartan 50 mg/day for the past 5 years. She was previously independent and lived alone, and regularly cooked for family members. She was a lifelong nonsmoker and had alcohol rarely on social occasions.

On examination there was no evidence of seizure activity, she was clinically euvoletic, her abbreviated mental test score
(AMTs) was 2/10 and her Glasgow Coma Scale (GCS) score was 14/15. She had bilateral extensor planter reflexes but no other focal neurology was noted on examination.

On admission to the hospital, blood tests showed levels of serum sodium of 100 mmol/L, potassium 4.9 mmol/L, creatinine 79 mmol/L, urea 4.8 mmol/L, thyroid-stimulating hormone 2.56 μL, and thyroxine 14.5 mmol/L. Additional tests taken prior to treatment revealed serum osmolality of 212 mOsm/kg, urine osmolality of 378 mOsm/kg, and urine sodium of 45 mmol/L. Serum sodium level 11 months earlier was 136 mmol/L.

In the absence of another cause, severe hyponatremia in this patient was attributed to the citalopram, which was discontinued; the patient was treated over 24 hours with hypertonic saline, which led to clinical improvement. She was treated with 2L of hypertonic saline 1.8% via a central line to achieve slow correction of serum sodium levels. After 6 hours, the serum sodium level was 106 mmol/L. Over 24 hours, the patient's serum sodium level improved to 117 mmol/L.

By the following day the patient's GCS score was 15/15 and AMT was 8/10. A computed tomography scan of the brain showed only age-related degenerative changes. A short synchaten test was normal. She was discharged from the hospital 6 days later with a serum sodium level of 131 mmol/L and was able to resume living independently at home with occasional help from her family. She remained off antidepressants and continued on losartan, and serum sodium level 6 months later was 136 mmol/L. Fig. 1 shows the trend of serum sodium levels throughout this period.

3. Discussion

We present a case of severe symptomatic hyponatremia within 7 days of starting a low dose of citalopram. Citalopram is a well-documented cause of hyponatremia secondary to SIADH and the associated neurological consequences including vomiting, confusion, coma, and seizures. A case report and literature review by Fisher et al identified 14 published cases that described SIADH associated with citalopram. It highlighted that most cases comprised elderly females and perhaps surprisingly frequently present within 1 week of the start of citalopram use. However, the patient in our case report had severe hyponatremia; a serum sodium of 100 mmol/L was strikingly low when compared to the 14 case reports reviewed by Fisher et al and the 28 case reports by Australian Drug Reaction Advisory Committee (ADRAC). These two groups document mean values of 116.8 mmol/L and 121.9 mmol/L, respectively. Our patient was also on losartan, which can cause hyponatremia; however, the patient was on losartan for 5 years prior to admission and was restarted on losartan at discharge from the hospital and serum sodium level remained normal after 6 months. There is a theoretical plausibility of interaction of the two offending drugs but there is no evidence of interaction of losartan and citalopram in the literature.

In cases of severe hyponatremia where there is evidence of cerebral irritation, specifically seizures or coma, correction with hypertonic saline is indicated. What is more contentious is the safe rate of correction in order to avoid osmotic demyelination syndrome (ODS) and how this varies according to whether the decrease in sodium is acute or chronic. There is no strong evidence-based guidance on sodium replacement in severe hyponatremia; most of the management algorithms are based on clinical experience and expert opinion. There is a general consensus that “chronic” hyponatremia occurs over >48 hours and in these cases extra care should be taken to avoid ODS by avoiding hypertonic saline unless there are severe neurological sequelae and ensuring a rate of correction as slow as 0.5 mmol/L/hour or at a rate of 8 mmol in 24 hours. The recent expert panel recommendations from Verbalis et al in 2013 stipulate correction of serum sodium by 4–8 mmol/L/day, with a lower goal of 4–6 mmol/L/day if the risk of ODS is high. It is also recommended that serum sodium not exceed a limit of 8 mmol/L in any 24-hour period for high risk of ODS and for normal risk of ODS 10–12 mmol/L in any 24-hour period. Newer vasopressin antagonists such as conivaptan and tolvaptan have recently been approved by the United States Food and Drug Authority for clinical use for the treatment of hyponatremia. This marks a new breakthrough; however, these substances are not yet seen in everyday clinical practice, likely because of the issues of overcorrection and side effects such as thirst following therapy.

In this case report, the patient reported symptoms that probably do not constitute severe neurological sequelae described in published literature; i.e., no seizures or coma, and therefore whether urgent correction with hypertonic saline was required is questioned. The rate at which the patient’s serum sodium level was corrected, particularly in the second 12 hour period of her admission, was probably faster, particularly given that the decrease in sodium almost certainly occurred over >48 hours. This perhaps highlights that monitoring serum sodium level every 6 hours or 12 hours is insufficient; closer monitoring every 2 hours or 3 hours is recommended by some authors. Given the close monitoring required to undergo hypertonic saline treatment, these patients are best managed in a high-care environment. This case illustrates the importance of close monitoring of sodium levels in the community after...
initiating citalopram therapy even if it is at a lower dose. This case also sheds light on the known difficulties in managing severe hyponatremia present for ≥48 hours or of unclear duration with nonspecific symptoms and signs.3

Conflicts of interest

All authors declare no conflicts of interest related to this case report.

Acknowledgments

The authors would like to thank the patient for consenting to the publication of this case report.

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