

Rapid-Onset Hyponatremia Induced by Duloxetine in an Elderly Patient

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ABSTRACT:

Duloxetine is a potent serotonin and noradrenaline re-uptake inhibitor that is used for the management of major depressive disorder and diabetic neuropathic pain. The common adverse effects are nausea, dry mouth, fatigue, dizziness, somnolence, anorexia, constipation, and hyperhidrosis. The cases of hyponatremia induced by duloxetine have rarely been reported. Here, we present the case of a 75-year-old male patient who developed rapid-onset and severe hyponatremia after low-dose duloxetine treatment. In the result of laboratory investigations syndrome of inappropriate antidiuretic hormone was diagnosed and then duloxetine treatment was discontinued. Serum sodium normalized within 5 days. We suggest that elderly patients treated with duloxetine should be closely monitored for hyponatremia during duloxetine treatment particularly in the first days of treatment.

Key words: duloxetine, hyponatremia, adverse effects

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ÖZET:

Yaşlı bir hastada duloksetinin neden olduğu hızlı başlangıçlı hiponatremi

Duloksetin, major depresyon ve diyabetik nöropatik ağrı tedavisinde kullanılan güçlü bir serotonin-noradrenalin geri alım inhibitörüdür. En sık görülen yan etkileri bulantı, ağız kuruluğu, yorgunluk, sersemlik, uyku hali, kilo kaybı, kabızlık ve aşırı terlemedir. Duloksetine bağlı gelişen hiponatremi olguları nadir olarak rapor edilmiştir. Bu yazıda, 75 yaşındaki bir erkek hastada düşük doz duloksetin tedavisi sonrası gelişen hızlı başlangıçlı ve şiddetli hiponatremi vakası sunulmaktadır. Laboratuvar incelemeleri sonucunda, uygunsuz antidiüretik hormon salgılanması sendromu tanısı konulmuş ve duloksetin tedavisi kesilmiştir. Serum sodyum düzeyi beş gün içerisinde normal düzeye dönmüştür. Duloksetin ile tedavi edilen yaşlı hastaların tedavinin özellikle ilk günlerinde hiponatremi açısından yakından takip edilmesi gerektiğini düşünmekteyiz.

Anahtar sözcükler: duloksetin, hiponatremi, yan etki

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INTRODUCTION

Duloxetine is a balanced serotonin and noradrenaline reuptake inhibitor that is known to be effective in major depressive disorder and diabetic neuropathic pain.¹ The most common adverse effects observed with duloxetine are nausea, dry mouth, fatigue, dizziness, somnolence, anorexia, constipation, and hyperhidrosis.² Most of these adverse effects arise within 5 days following initiation of duloxetine treatment. Hyponatremia is a side effect of selective serotonin reuptake inhibitors and venlafaxine.³ Hyponatremia induced by duloxetine has also been reported.⁴⁻¹² Here, we report a case of a 75-year-old male who developed rapid-onset and severe hyponatremia after low-dose duloxetine treatment.

CASE REPORT

A 75-year-old male patient with previously documented sensorimotor polyneuropathy was admitted to the neurology department complaining of numbness, a tingling sensation, pain, and weakness in both legs that had lasted approximately 3 months. His medical history revealed that he had been treated with pregabalin at 150 mg/day for neuropathic pain, but had stopped this treatment due to severe dizziness. He had not used any medications for 2 months before being admitted to the neurology department. There was no history of any known disease except for sensorimotor polyneuropathy. Neurological examination showed mild weakness of feet dorsiflexion bilaterally (Medical Research Council 4/5)

and reduced deep tendon reflexes in both lower extremities. On psychiatric examination, it was found that he had depressed mood and insomnia. His vital signs and detailed laboratory investigations were normal. Duloxetine was initiated at 30 mg daily for neuropathic pain and depressive symptoms. The patient's serum sodium level on that day was 138 mmol/L.

Three days following the initiation of duloxetine, because the patients complained of lethargy, headache, and nausea, laboratory investigation was carried out before the third dose of duloxetine was administered, and this revealed hyponatremia. At this time, the patient's serum sodium level was 118 mmol/L. His urine osmolarity was 578.3 mOsm/L and urine sodium was 154 mmol/L, with a serum osmolarity of 245.7 mOsm/L. Renal, adrenal, thyroid, hepatic, and cardiac functions, as well as brain magnetic resonance imaging, were within normal limits. Tumor markers were negative. Fluid intake was normal. The patient appeared euvoletic on examination. In the result of investigations, syndrome of inappropriate secretion of antidiuretic hormone (SIADH) was diagnosed. It was thought that this was related to duloxetine treatment, so the duloxetine was stopped. Treatment with intravenous hypertonic saline was initiated. The patient's serum sodium normalized within 5 days (137 mmol/L). According to the Naranjo causality scale (the score was 7), the hyponatremia had probably occurred because of the duloxetine.¹³ Over 6 months of follow-up, his serum sodium levels remained within normal range.

DISCUSSION

Our patient developed severe and rapid-onset hyponatremia after two doses of duloxetine treatment at only 30 mg per day. Hyponatremia was attributed to duloxetine in this case because there was no other discoverable reason that may cause hyponatremia. Moreover, the hyponatremia resolved after discontinuation of duloxetine and was not observed during clinical follow-ups.

In this case, the underlying mechanism of hyponatremia associated with duloxetine was

inappropriate antidiuretic hormone secretion (SIADH), which was identified due to the presence of hyponatremia, hypoosmolarity, increased urine osmolarity and, sodium. The detailed mechanisms of SIADH with selective serotonin-reuptake inhibitors and serotonin and noradrenaline reuptake inhibitors are still unclear. Animal experiments suggest that antidiuretic hormone release can be stimulated by both norepinephrine and serotonin.¹⁴ Duloxetine inhibits the reuptake of both serotonin and norepinephrine, which might clarify why our case developed SIADH. Older age, female gender, lower body weight, and lower baseline serum sodium concentration are the risk factors for hyponatremia.¹⁴ Among these risk factors, our patient only exhibited older age.

Cases of hyponatremia related to treatment with duloxetine are rare in the literature.⁴⁻¹² Müssig et al. reported a 85-year-old woman who developed severe and symptomatic hyponatremia 6 days after the initiation of duloxetine at 30 mg/day.⁷ Stovall et al. described a case of a 66-year-old woman who presented hyponatremia with duloxetine at 60 mg per day and escitalopram.⁵ Moreover, Li et al. reported on a 50-year-old woman who had severe hyponatremia induced by duloxetine and ziprasidone on the 10th day of treatment.¹⁰ Recently, hyponatremia induced by duloxetine was reported in an 86-year-old woman treated with thiazide diuretics. The authors suggested that the combination of duloxetine and thiazide might result in a rapid decrease in the serum sodium level.⁸ Krüger et al. reported five cases of hyponatremia in depressed patients treated with high-dose duloxetine ranging from 90 to 120 mg per day, along with lorazepam and zopiclone.⁹

There were striking findings associated with the hyponatremia induced by duloxetine in our patient. Severe hyponatremia began after two doses of duloxetine treatment. The dose of duloxetine was also lower. The patient had only one risk factor for hyponatremia, namely advanced age. Although most previous reports of hyponatremia related to duloxetine have involved females, our case was male. Moreover, our report presented a patient who developed hyponatremia when using only duloxetine.

CONCLUSION

In conclusion, this case showed the development of severe and rapid-onset hyponatremia in an elderly male patient treated with duloxetine. The symptoms of hyponatremia may range from fatigue to death. Because of the wide use of serotonin and noradrenaline reuptake

inhibitors in the population, it is important to consider hyponatremia as avoidable adverse effect. Clinicians should be aware of hyponatremia while treating their elderly patients with lower duloxetine dosages. Laboratory controls of the patient's serum sodium prior to and during duloxetine treatment might be required.

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