

Low Dose Duloxetine Induced Hyponatremia in an Elderly Patient: A Case Report

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ÖZET:

Yaşlı bir hastada düşük doz duloksetinin oluşturduğu hiponatremi

Duloksetin serotonin-norepinefrin geri alım inhibitörü olup major depresyonda, stres durumlarında, idrar inkontinansında ve diyabetik nöropati veya fibromyaljiye bağlı ağrı durumlarında kullanılır. Bulantı, ağız kuruluğu, halsizlik, iştahsızlık, konstipasyon ve uykusuzluk en çok bildirilen yan etkilerdir. Duloksetine bağlı hiponatremi bizim vakamızda olduğu gibi yaşlı kadınlarda nadiren görülen bir yan etkidir. Fakat bizim vakamızı farklı kılan hasta duloksetin 30 mg/ gün kullanıyorken hiponatremi görülmesiydi.

Anahtar sözcükler: Duloksetin, hiponatremi, geriatrik değerlendirme

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ABSTRACT:

Low dose duloxetine induced hyponatremia in an elderly patient: a case report

Duloxetine is serotonin-norepinephrine reuptake inhibitor used for major depressive disorder, stress, urinary incontinence, pain associated with diabetic neuropathy and fibromyalgia. Nausea, dry mouth, fatigue, dizziness, decreased appetite, constipation and insomnia are the frequently reported adverse effects. Duloxetine induced hyponatremia is a rare adverse effect and is seen generally among the older female patients, like our case. Whereas our case was using duloxetine low dose (30mg /day).

Key words: Duloxetine, hyponatremia, geriatric assessment

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INTRODUCTION

Hyponatremia is an adverse event resulting from administration of selective serotonin reuptake inhibitors (SSRI). Some cases are reported in the literature which are induced due to venlafaxine, reboxetine or duloxetine (1). Duloxetine, a serotonin-norepinephrine reuptake inhibitor is used to treat major depressive disorder, stress urinary incontinence, pain associated with diabetic neuropathy, and fibromyalgia (2). Nausea, dry mouth, fatigue, dizziness, decreased appetite, constipation, and insomnia are commonly reported adverse effects (3). The exact mechanism of SSRI and SNRI induced syndrome of inappropriate antidiuretic hormone secretion (SIADH)

is not well known, but it is thought that the elevation of serotonin and/or norepinephrine induce antidiuretic hormone (ADH), although the molecular mechanisms are not cleared (4).

Here we present a case with severe hyponatremia who was using low dose duloxetine for treatment of pain due to diabetic neuropathy.

CASE REPORT

A 76 year old female patient was admitted to our emergency service complaining of nausea, vomiting, dizziness, weakness, and confusion. Her vital signs were within normal ranges and the neurological examination

didn't show any lateralization. Admission finger blood glucose level was 137mg/dl. In order to exclude neurological causes, a brain computer tomography was performed and findings of lacunary infarcts were reported, which did not clarify the patient's clinical situation. Abnormal laboratory results were as follows: Na, 113 mEq/L; Cl, 80meq/L; aspartate transaminase, 86U/L; and glucose, 131mg/dL. Complete blood count, renal and thyroid function test results (TSH, 0.780ul/ml; T3, 2.110pg/ml; T4, 1.700ng/dl) were normal. Serum osmolality was 236Osm/kg (according to the equation: $2 \times \text{Na} + \text{Glu} / 18 + \text{BUN} / 2.8$). Urine electrolytes (Na, 80mOsm/kg; K, 68.1mOsm/kg; Cl, 80mOsm/kg) were within normal ranges and urine osmolality was 332 mOsm/kg (50-1400). With respect to differential diagnosis, adrenal insufficiency and adrenal crisis, cirrhosis, congestive heart failure, gastroenteritis, hypothyroidism and myxedema coma, nephrotic syndrome, and acute and chronic renal failure were excluded by the laboratory and physical examination results.

Meanwhile we learned that the patient had been using duloxetine 30 mg/daily (for 3 days), metoprolol 100mg/daily, and metformin 1000mg/twice a day. Due to the lacunar infarct, the patient was transferred to the neurology unit after an internal medicine consultation. Acetylsalicylic acid 300mg/daily, enoxaparin sodium 2×60 mg were used for treatment. Duloxetine was discontinued and hypertonic sodium (3%) was used to increase the serum sodium level rapidly over 120mEq/L. Thereafter the treatment was regulated to increase the serum sodium level by increments of 1meq/L, according to internal medicine recommendations. Clinical symptoms resolved and the serum Na⁺ level returned to within normal limits by day 2. Acetylsalicylic acid and enoxaparin sodium had been stopped on the second day, after the brain diffusion magnetic resonance imaging which excluded the infarct.

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DISCUSSION

Hyponatremia is a well described adverse effect of SSRI drugs (5). Duloxetine, an SNRI, is mainly used in treatment of major depressive disorder. Stress urinary incontinence, pain associated with diabetic neuropathy, and fibromyalgia are other conditions where duloxetine can be prescribed (6). It is accepted that antidepressants that act via two neurotransmitters have a better effect on somatic symptoms. This is linked with the serotonergic and noradrenergic pathways in the brainstem. These pathways also increase endogenous analgesic effects (7). Duloxetine has a high risk for causing SIADH and hyponatremia because it inhibits the reuptake of both serotonin and norepinephrine (8,9). Female gender, multiple drug use, lower baseline serum sodium concentration, and older age at the beginning of the treatment increase the risk for the occurrence of hyponatremia (9). Krüger et al. treated 5 patients who had recurrent major depressive disorder with high dose (120mg/daily) duloxetine and hyponatremia developed in all patients within the first week (10). We did not know the baseline serum Na level of our female patient, but the gender and age resemble the literature results. Also the time course of our patient's Na⁺ level decrease was similar to that reported in some studies (8,10-11).

In many studies it has been shown that duloxetine is used for major depressive disorder at doses ranging from 40 to 120 mg daily (12-14), whereas our patient was using a dose below the therapeutic range (30mg/daily). This case demonstrates that duloxetine can also cause hyponatremia at low doses as presented by Müssig et al. (4).

We suggest that patients started on duloxetine should be closely monitored for clinical and laboratory evidence of hyponatremia especially in the first days of treatment, as hyponatremia can cause mortality and can be missed if the patient's history is not thoroughly taken.

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