

Hyponatremia: A Rare Adverse Effect of Duloxetine in a Patient of Depression: A Case Study

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Abstract

Depression is a prevalent mental health disorder, which can have significant implications for patient health. Duloxetine, a selective norepinephrine and serotonin reuptake inhibitor commonly used in the treatment of depression, has shown potential effects on neurotransmitter systems implicated in depression. This drug is well tolerated and free from significant cardiovascular and anticholinergic side effects, thus a good choice as antidepressant. This case report shows that duloxetine treatment in patients with depression is associated with a significant reduction in serum sodium levels. This finding highlights the potential impact of duloxetine on electrolyte balance in the elderly population suffering from depression and emphasizes the need for further investigation into the underlying mechanisms and clinical implications of these effects. Clinicians should consider monitoring electrolyte levels in patients receiving duloxetine therapy for depression to ensure patient safety and optimize treatment outcomes.

Keywords

- ▶ COVID-19
- ▶ duloxetine
- ▶ depression
- ▶ electrolyte imbalance
- ▶ sodium

Introduction

On January 30, 2020, World Health Organization (WHO) declared coronavirus disease 2019 (COVID-19) to be international public health emergency. Unprecedented public health measures were imposed to control the spread of disease; so, lockdowns and social distancing were new normal. Although all these measures did help to control the spread of disease, at the same time it led to worsening of psychological and mental health. Many international studies have reported increased cases of depression, and this is statistically significant.¹

This impact was more visible in elderly population, single and retired women. Also due to COVID-19 restrictions, most of the patients of anxiety and depression were given consultations via telemedicine. Tele consultation has

several advantages but comes with its own set of challenges such as internet connectivity issues. It has its advantages too. Use of drugs in elderly requires the physician to be aware of the changes in pharmacological responses that occur in elderly and how to deal with these changes, to avoid the adverse events in this set of population.² The primary clinical manifestations of major depression are significant depression of mood and impairment of function. Some features of depressive disorders overlap those of the anxiety disorders, including panic-agoraphobia syndrome, severe phobias, generalized anxiety disorder, social anxiety disorder, posttraumatic stress disorder, and obsessive-compulsive disorder.³

Clinical evidence shows that elderly patients of depression respond well to most of the medication available for depression. Wide variety of agents are available for the

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treatment of depression. Tricyclic antidepressants, monoamine oxidase inhibitors, selective serotonin reuptake inhibitors (SSRIs), or newer atypical antidepressants are available. It is utmost important that careful selection and dosing are done and strict attention is given to appearance of any adverse effect.^{4,5} The dosage and dose ranges of antidepressant medications are clearly defined; also, the severity of common side effects is well documented. However, challenge is when some uncommon or rare adverse effect comes to picture.

Case Report

This case is about a 57-year-old woman (Caucasian in origin) who was a known case of hypertension for the past 6 years which was under control with tablet Amlodipine 10 mg daily. Her systolic blood pressure reading remained between 125 and 140 mm Hg, while diastolic blood pressure reading was between 78 and 86 mm Hg. She was quite active, and physical exercise was part of her daily routine before pandemic of COVID-19. She also had dyslipidemia and was on Atorvastatin 10 mg for the past 2 years. She was regular with her medication and enjoyed active lifestyle. However, with the onset of COVID-19 pandemic she lost her job, hence she lost her active lifestyle and suddenly plunged into depression. For depression, she was put on tablet Duloxetine 30 mg per day by her family doctor for 2 months. Patient reported to the hospital in southern California with complaint of disorientation and nausea in spring of 2021. This was her second admission in less than 3 weeks time, with same complaint.

On evaluation of electrolyte profile, it was seen that patient was having hyponatremia. Sodium levels went below 125 mEq/L. The normal range for blood sodium levels is 135 to 145 mEq/L.

Medication history Included Atorvastatin 10 mg QHS (once a day at bed time), Amlodipine 10 mg daily, and Duloxetine 30 mg daily.

Patient was a good historian and gave full account of medical history including medications. She also reported to have no significant surgical history. During history taking, it was revealed that she lost her job at the start of the pandemic. She has been working for two decades, but with the onset of COVID-19 pandemic she was isolated even further. This patient was a widower who lived alone with her 33-year-old college going daughter who was able to come and visit her during pandemic but had to go back working full time due to financial issues. Most of the time patient was alone at home and isolation caused her to develop depression and anxiety.

Patient had consultation with her primary care physician (PCP) virtually and after discussion she was started on Duloxetine 30 mg QHS to be increased to 60 mg if patient could tolerate 30 mg dose. Patient was taking Duloxetine 30 mg for 2 months before she developed adverse symptoms. She became lethargic and started suffering from fatigue, intermittent palpitations, dizziness and nausea. These symp-

toms were considered by PCP as the period of patient developing tolerance to duloxetine. She also developed twitching of her left eyebrow in the meantime. Her weakness, fatigue, and nausea increased significantly over time and she was taken to emergency in a nearby hospital. Her blood test revealed sodium levels of 126 mEq/L that were very below the normal range. Sodium levels were corrected over the period of two nights; during discharge patient was given instructions about diet plan, symptoms of hyponatremia, and how to control the symptoms by eating appropriate diet. During this admission, cause of hyponatremia was blamed upon decreased appropriate diet intake due to COVID-19 pandemic and isolation.

After about 3 weeks, patient reported back to hospital because of another episode of hyponatremia. Her laboratory reports were as follows: serum sodium level at the time of admission was 125 mEq/L, after treatment it gradually improved to 129, 131 to 136 mEq/L over a period of 4 days of hospitalization. Her potassium level was 4.6 mEq/L, chloride was 106 mEq/L, and calcium was at 9.5 mg/dl.

Renal function test (blood urea nitrogen: 8.1; creatinine: 0.59; urea: 9.1, uric acid: 4.2) and liver function test (total bilirubin: 0.38; aspartate transaminase: 22; alanine aminotransferase: 31) were within normal range. Lipid profile was found to be total cholesterol: 198 mg/dL; low-density lipoprotein : 112 mg/dL; high-density lipoprotein: 42 mg/dL; very low-density lipoprotein: 28 mg/dL; and triglycerides: 173 mg/dL.

This time she was closely evaluated for her diet habits and concomitant medications to rule out any drug or food interaction leading to hyponatremia. After consultation with neurologist, nephrologist, and physician, it was decided that it is probably the isolated and rare side effect of duloxetine that was causing hyponatremia. The patient was still having twitching of the eye that also corroborated this finding. After correcting the sodium, patient was told to decrease the dose of duloxetine to 10 mg, once at night time.

During discharge, patient was advised to monitor symptoms of adverse effects, mainly nausea, dizziness, twitching of the eye, and other side effects that can be caused by duloxetine as well as from hyponatremia. She was advised to have blood test again within 2 weeks of decreasing the dosage of the duloxetine.

The scenario showed that pandemic due to COVID-19 caused depression that led to patient taking SSRI duloxetine that further led to hyponatremia.

Discussion

Major depression comprises at least one episode of serious mood depression at any time of life. It might be endogenous, reactive, or melancholia. Many consider the physiological basis or aberration of monoamines in cortical system or limbic system.³ Complaints vary widely in patients; however, anhedonia, hopelessness, somatic complaints, and vegetative signs are well recognized in depression.

Treatment of depression involves use of pharmacological agents that can be classified in various groups like tricyclic antidepressants, SSRIs, serotonin norepinephrine reuptake inhibitors, and atypical antidepressants and monoamine oxidase inhibitors. Duloxetine is an efficacious antidepressant that inhibits the reuptake of both serotonin and norepinephrine.⁴⁻⁶ This drug is well tolerated and free from significant cardiovascular and anticholinergic side effects. However, common side effects of duloxetine include headache, nausea, tinnitus, agitation, insomnia, and nervousness and increase in blood pressure.⁷ Standard textbooks do not report electrolyte imbalance as side effect of duloxetine.⁴ However, hyponatremia is known to happen if patient is on diuretics.⁸ But, duloxetine does show drug interactions with inhibitors of 1A2 and 2D6, which may increase the level of duloxetine with risk of toxicity.⁹

In the above case, patient was put on duloxetine 30 mg for depression, while concomitant medication included tablet amlodipine 10 mg (calcium channel blocker) as antihypertensive drug and tablet atorvastatin 10 mg. Dose of duloxetine was in well-prescribed dose range.^{10,11} None of the drug is known to show any drug interaction with Duloxetine. Also, there was no change in diet or report of any change in over-the-counter drugs being taken by patient. Thus, this is an interesting case in which hyponatremia was noted as an adverse effect of duloxetine. Since electrolyte imbalance can have serious consequences, so physician and patients should be educated on this report. This case study shows that more literature is needed on duloxetine and there is need for conducting a meta-analysis to assess the impact of duloxetine on electrolyte imbalance in patients with depression.

Conflict of Interest

None declared.

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