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CASE REPORT
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Hyponatremia and urinary retention in an elderly patient with type 2 diabetes

ABSTRACT

We present a case of an elderly patient with type 2 diabetes, hyponatremia, and sudden urinary retention. Drug-to-drug interactions between duloxetine, a thiazide-type diuretic, and nonsteroidal anti-inflammatory drugs (NSAIDs) were considered the most likely cause of the reported disorders. (Clin Diabetol 2022, 11; 1: 54–56)

Keywords: hyponatremia, urinary retention

Case report

A 70-year-old man presented to the emergency room due to sudden urinary retention. On admission, the patient's condition was assessed as stable. He was afebrile and denied hematuria. However, he reported the sensation of gradually increasing difficulty urinating until urinary retention. Medical history revealed ischemic heart disease, myocardial infarction without ST-segment elevation (treated with primary coronary angioplasty), arterial hypertension, and chronic lumbosacral spine pain syndrome. In the last 4 weeks, the patient had sought medical assistance three times due to urinary retention. During two previous medical visits, a Foley catheter was inserted, which resulted in drainage of clear urine. Further outpatient urological assessment was recommended. During the second visit, computed tomography (CT) of the abdominal cavity and pelvis without contrast administration was performed in the emergency department. The CT results showed normal prostate size and the absence of urinary retention. Outpatient therapy with an alpha-blocker was introduced. However, no improvement was reported. Table 1 shows the laboratory findings on admission.

The attending urologist reinserted a Foley catheter, which resulted in drainage of clear urine that was sent for analysis (see: the results above). Due to electrolyte disturbances, the patient was admitted to the Department of Internal Medicine. Treatment included parenteral hydration and electrolyte supplementation. As a result, an increase in sodium ions was found (up to 134 mmol/L).

Recurrence of hyponatremia was not reported following the infusion of sodium chloride. Permanent indapamide intake was discontinued and replaced with lercanidipine. Medical history was verified again in search of the cause of hyponatremia. The patient was requested to provide medical records and a detailed list of recently taken drugs. The patient had a medical history of type 2 diabetes and was treated with metformin and good metabolic control was achieved (HbA1c = 6.7%). The subject also reported increased lumbosacral pain, which required frequent modification of analgesic treatment by a primary care physician (medical records showed advanced degenerative changes and L4-L5 and L5-S1 discopathy). The list of medications taken by the patient in the month preceding admission is given in Table 2.

Indapamide had been used for at least 2 years (as indicated by the discharge abstract from the Department of Cardiology). A history of hyponatremia had not been previously reported. Duloxetine had been started about 4 weeks prior to admission, as reported by the patient (as an additional therapy for spinal pain; the patient denied the presence of depressive disorders).

Discussion

Hyponatremia, defined as a serum sodium level < 135 mmol/L, is the most prevalent fluid and electrolyte

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Table 1. Laboratory findings on admission

Parameter		Result	Normal range	Unit
RBC		3.86	4.7–6	10*6/uL
HCT		30.7	42–52	%
HGB		11.3	13.5–17	g/dL
MCV		79.5	78–100	fL
WBC		11.5	4–10.5	10*3/uL
Neut		6.87	1.6–6	10*3/uL
Lymph		3.1	1–3.3	10*3/uL
PLT		172	150–450	10*3/uL
Potassium		3.99	3.5–5.1	mmol/L
Sodium		113	135–145	mmol/L
Glucose		125	60–99	mg/dL
CRP		1.57	0–5	mg/dL
AlAT		29.2	0–41	U/L
Creatinine		91	60–106	umol/L
eGFR		77	> 60	mL/min/1.73 m^2
Urinalysis	pH — acid			
	Protein — positive			
	Glucose — negative			
	Bilirubin —— negative			
	Urobilinogen — normal			
	Ketones — negative			
	5–10 RBC/hpf			
	Few squamous epithelial cells			
	Few WBC/hpf			

AlAT — alanine aminotransferase; CRP — C-reactive protein; eGFR — estimated glomerular filtration rate; HCT — hematocrit; HGB — hemoglobin; hpf — high powered field; MCV — mean corpuscular volume; PLT — plateles; RCT — red blood cells; WBC — white blood cells

Table 2. List of medications taken by the patient in the month preceding admission

Pantoprazole (20 mg; 1 tablet/day; under fasting conditions)	Gabapentin (100 mg; 1 tablet/twice daily)
Acetylsalicylic acid (75 mg; 1 tablet/day)	According to the patient, the following were also prescribed (by several physicians): diclofenac (in the form of two different preparations), nimesulide, ketoprofen, and celecoxib
Nebivolol (5 mg; 1 tablet/day)	
Valsartan (80 mg; 1 tablet/day)	
Atorvastatin (80 mg; 1 tablet/day)	
Indapamidum (1.5 mg; 1 tablet/day)	
Metformin (850 mg 3 x 1 tablet; at meals)	
Duloxetine (30 mg; 1 tablet/day)	

imbalance in clinical practice. It is estimated to occur in approximately 15–30% of patients hospitalized for emergency reasons [1]. The most common causes of hyponatremia include the syndrome of inappropriate antidiuretic hormone secretion (SIADH, including drug--induced SIADH), treatment with diuretics, polydipsia, adrenocortical insufficiency, heart failure, and liver cirrhosis [1]. During hospitalization, the assessment of hyponatremia was performed. Liver cirrhosis, heart failure, hypothyroidism, and adrenocortical insufficiency were excluded based on the clinical picture (in the absence of signs and symptoms) and further assessment. Using both drugs together: duloxetine and indapamide were considered the most probable cause of hyponatremia and non-obstructive urinary retention. An additional diagnostic indicator was

a history of treatment and its modification within the previous month, i.e., adding duloxetine, which resulted in increasing difficulty urinating. The Najaro scale was used as a recognized causality tool and the patient total score was 4 points (defined as possible adverse drug reaction) [2].

Duloxetine is a serotonin and noradrenaline reuptake inhibitor (SNRI) and is officially indicated for the treatment of major depressive disorder, generalized anxiety disorder, and diabetic neuropathic pain in adults. It is also thought to inhibit serotonin and noradrenaline reuptake in the sacral spinal cord; thus, it increases bladder capacity and urethral sphincter contraction power and inhibits urinary incontinence [3, 4]. This drug is also used for the treatment of stress urinary incontinence in women. However, it is not an approved indication in Poland.

Duloxetine-related adverse reactions include hyponatremia (cases with a sodium level < 110 mmol/L were also reported) and urinary retention as shown in the above mechanism. Pathological hyponatremia, whose mechanism is not fully understood, is not common and is estimated at 1–10 per 10,000 patients. It seems that it is caused by duloxetine-induced SIADH [5].

Not all patients treated with SNRIs are equally exposed to the development of hyponatremia. The factors of increased risk of hyponatremia include female gender and age (> 65 years) and the intake of drugs that decrease sodium levels (e.g., thiazide diuretics or NSAIDs) [6–8].

Thiazide-like indapamide, as in the case of thiazide-type diuretics, is also a common cause of thiazide--induced hyponatremia (TIH), which usually occurs within the first two or three weeks following drug administration. However, it can occur at any stage of treatment and can progress rapidly in susceptible patients [1]. For example, it can be observed as a result of synergistic drug interaction, including duloxetine. The mechanism of hyponatremia is explained by inhibiting the reabsorption of sodium and chloride in the distal convoluted tubule of the nephron, which leads to increased sodium excretion, while free water excretion is decreased. Some drugs, including NSAIDs, further reduce free water clearance by inhibiting prostaglandins, and thus increasing hyponatremia [9].

Discontinuation of duloxetine therapy was a problem in this clinical situation. When therapy is abruptly discontinued, withdrawal syndrome can be expected. The most commonly reported symptoms include dizziness, sensory disorders, fatigue, somnolence, agitation, anxiety, nausea and/or vomiting, tremor, headache, myalgia, irritability, diarrhea, excessive sweating, and vertigo due to labyrinthine dysfunction.

Most of these symptoms are mild. However, severe withdrawal syndrome has also been reported. In our study, the patient took the drug for a relatively short time (about 4 weeks) in the minimum dose of 30 mg/ /day. After discussing the issue with the patient, therapy was discontinued and the patient was informed in detail about the possible results of drug discontinuation and an urgent need to contact the physician in the case of adverse effects. The use of duloxetine seems questionable in our patient. It is rather unlikely that chronic pain symptoms were due to diabetic neuropathy, which is an indication for therapy with this drug as given in the Summary of Product Characteristics. After the diagnosis of type 2 diabetes mellitus, glycemic control was satisfactory and no microangiopathic complications were found. The present clinical case shows how important it is to obtain an accurate history of medical conditions and drug intake in the era of common polypharmacy.

Conflict of interest

None declared.

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