Hyponatremia and Confusion Caused by Pregabalin

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Pregabalin is a relatively new drug for the treatment of neuropathic pain in adults. The most common adverse events include dizziness and somnolence followed by peripheral edema and weight gain. We present a 74 year old man who was admitted with drowsiness and disorientation and severe hyponatremia (110 mmol/L). He was treated with pregabalin for a month to alleviate neuropathic pain after undergoing below-knee amputation of the left leg.

PATIENT DESCRIPTION

A 74 year old man was admitted with weakness and confusion. He had suffered from diabetes mellitus type II (insulin dependent) for many years, accompanied by diabetic retinopathy, nephropathy and neuropathy. He had ischemic cardiomyopathy with congestive heart failure (left ventricular function of 27%). A DDDR pacemaker was transplanted in 2002 due to a complete atrioventricular block. For several years he had been taking dimitone, angiotensin-converting enzyme inhibitors and loop diuretics, but without aldospirone. He was referred for a below-knee amputation because of chronic osteomyelitis. Before the amputation (and later on before admission to the rehabilitation center) his electrolytes were within normal limits.

After the amputation he was given pregabalin for neuropathic pain and continued to take it for several weeks after discharge from the rehabilitation center. One week before the present admission he started to feel weakness and became confused and disoriented.

The physical examination was normal with no signs of peripheral edema or pulmonary congestion. Hematological analysis demonstrated hemoglobin 10.1 g/dL, white blood cell count 8300/µl, and platelet count 245,000/µl. Biochemical analysis demonstrated sodium 110 mmol/L, potassium 4.40 mmol/L and osmolarility 232 mOsm/kg (normal values 265–275 mOsm/kg). Liver function tests and renal function tests were normal, and lipid profile was normal. Thyroid function tests were normal – with free thyroxine 1.79 IU/ml and thyroid-stimulating hormone 2.970 IU/ml. Cortisol level (fasting 8 am) was 34.30 µg/dl. Urine level of sodium was 145 mmol/L, potassium level 29.40 mmol/L, and urine osmolarity 650 mOsm/kg. Chest X-ray showed very mild pulmonary congestion with minimal left pleural effusion.

After the pregabalin was stopped, followed by fluid restriction and isotonic saline 0.9% for 2 days the sodium level increased to 125 mmol/L and the confusion was resolved. After another 2 days the patient's sodium level increased to 130 mmol/L.

COMMENT

Our patient developed severe clinical confusion secondary to hyponatremia caused most probably by pregabalin. This is the first report of such an adverse reaction to this medication. Several articles reported decompensation of patients with chronic heart failure, edema and weight gain – all caused by pregabalin. The decompensated heart failure was resolved after discontinuation of the drug [1].

Pregabalin is an analog of the neurotransmitter gamma-aminobutyric acid that has analgesic, anticonvulsant and anxiolytic properties. It is now widely used in the management of diabetic peripheral neuropathy, postherpetic neuralgia, generalized anxiety disorder and social anxiety disorder [1]. Although central nervous system disturbances account for most of the side effects (dizziness and somnolence) [2], there have been reports of dose-dependent peripheral edema and weight gain, at least in six patients with heart failure whose condition deteriorated after taking pregabalin. In all of them the heart failure was stabilized after discontinuation of the drug [1-3].

To determine whether an adverse drug reaction was due to pregabalin we used the Naranjo algorithm and found that the confusion and worsening of the heart failure with hyponatremia were most likely related to the drug's side effects [4]. According to the laboratory analysis, our patient had low sodium osmolarity with decreased extracellular fluid volume and high urine sodium concentration. It seems that pregabalin caused sodium-wasting nephropathy.

To the best of our knowledge this is the first report of a patient with ischemic cardiomyopathy and poor left ventricular function with clinical heart failure and who developed severe hyponatremia that was clinically expressed by confusion and disorientation. All his symptoms were resolved after the drug was discontinued and he regained a

sodium level > 125 mmol/L. We assume that the mechanism of hyponatremia was pregabalin-induced sodium wasting nephropathy that was resolved after discontinuation of the medication.

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