Scholars Journal of Medical Case Reports (SJMCR) **ISSN 2347-6559 (Online)**
Abbreviated Key Title: Sch. J. Med. Case Rep. **ISSN 2347-9507 (Print)**

A United of Scholars Academic and Scientific Society, India

Levetiracetam-Induced Hypokalemia and Hypomagnesemia

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Article History
Received: 11.01.2018
Accepted: 18.01.2018
Published:30.01.2018

DOI:
10.36347/sjmcr.2018.v06i01.011

Abstract: Levetiracetam is an antiepileptic drug commonly used in focal and generalized epileptic seizures because it has a low side-effect profile. However, recent studies in the literature have reported unexpected side effects thought to be associated with levetiracetam. In this report, we present the case of a patient with hypokalemia and hypomagnesaemia that are thought to be associated with the use of levetiracetam. A 34-year-old female patient was brought to the emergency department because she jumped from the fourth floor of a building, attempting to commit suicide. The laboratory investigation detected hypopotassemia and hypomagnesaemia. A detailed examination revealed no additional pathology that may have caused electrolyte imbalance. The patient had been taking levetiracetam at a dose of 2500 mg/day because of a history of epilepsy. Considering that the electrolyte imbalance in the patient may have been associated with the use of levetiracetam, the drug was tapered off, and treatment with 100 mg/day lamotrigine was initiated. The patient's electrolyte imbalance improved during the follow-up period. This case reveals that increasingly used new antiepileptic drugs may have unforeseen side effects and thus require meticulous monitoring.
Keywords: Levetiracetam; hypokalemia; hypomagnesaemia; suicide; electrolyte imbalance.

INTRODUCTION

Levetiracetam (LEV) is a new-generation antiepileptic with an acceptable side-effect profile that is used to prevent epileptic seizures. LEV has a different molecular structure compared with other new antiepileptics. It does not bind plasma proteins, and it is eliminated by the kidneys [1]. Compared with traditional antiepileptic drugs, LEV has features such as dominant renal excretion and a lack of drug–drug interaction [2]. Commonly reported side effects include sleepiness, fatigue, headache, dizziness and nausea [3]. However, with respect to LEV, there are several case reports in the literature suggesting that it also causes hallucination, depression, renal dysfunction, hypopotassemia, hypomagnesaemia, hypernatremia, acute interstitial nephritis and acute renal failure [2, 4–6]. In the present study, we present the case of a patient with hypokalemia and hypomagnesaemia that are thought to be associated with the use of LEV.

CASE PRESENTATION

A 34-year-old female patient was admitted to the emergency department after jumping from the fourth floor of a building, attempting to commit suicide. On admission, the body temperature was 36.3°C; pulse was 87 beats/minute; respiratory rate was 18 breaths/min and blood pressure was 125/80 mmHg. The patient had nausea and vomiting, and a physical examination revealed fractures on various body parts. The results of the laboratory analysis of the patient who was stabilized orthopedically and psychiatrically were as follows: urea: 28 mg/dl, creatinine: 0.34 mg/dl, sodium: 138 mEq/lt, chlorine: 102 mEq/ Lt, potassium: 3.1 mEq/lt, magnesium: 1.2 mg/dl and calcium: 7.67 mg/dl. The results of the arterial blood gas analysis were as follows: pH: 7.52, HCO3: 29 mEq/L and PCO2: 44 mmHg. In the differential diagnosis of metabolic alkalosis, the measurements of cortisol, renin-aldosterone, and thyroid function tests, renal and Reno vascular Doppler ultrasound and 24-hour urinary calcium levels were normal. The following results were obtained in a 24-hour urine collection test: potassium: 20.3 mEq/day, chloride: 111 mEq/L, magnesium: 6.83 mg/dL and urine volume: 2800 mL/ day. The high level of chloride in the urine excluded chloride-sensitive metabolic alkalosis as a diagnosis. The fact that urinary potassium excretion did not increase proved that the potassium loss did not originate from the urinary system. Furthermore, the patient did not have a history of diarrhoea and excessive sweating in terms of the differential diagnosis of hypopotassemia. During the follow-up period, there was an improvement in metabolic alkalosis, but there was no improvement in the electrolyte imbalance despite IV potassium chloride and magnesium replacement therapy. A literature search was conducted considering that the electrolyte

imbalance may be due to the use of LEV by the patient at a dose of 2500 mg/day for epilepsy. We found three case reports (4-5) and consulted with the neurology department for switching to a different therapy. It was suggested to taper off the medication and switch to 100 mg/day lamotrigine. The recommended treatment scheme was administered, and the patient's persistent electrolyte imbalance improved (Figure 1). During the follow-up, it was found that the patient did not develop any further electrolyte impairment.

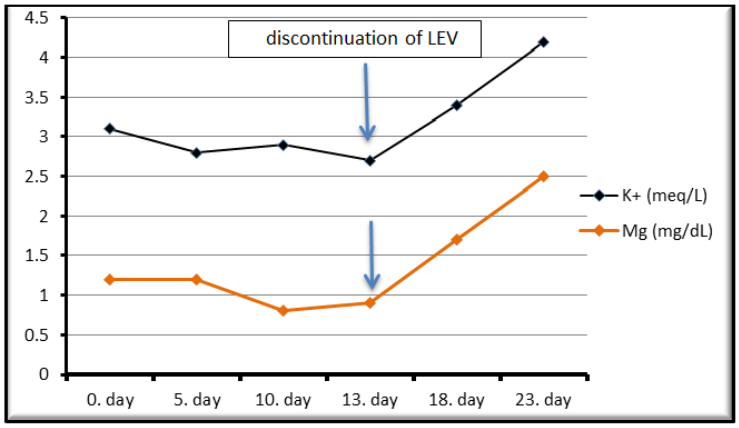

Fig-1: The monitoring chart of the patient's K+ and Mg levels

DISCUSSION

In the human body, potassium is eliminated through the gastrointestinal tract by sweating, and to a significant extent, by the kidneys in urine. In some cases, it can be transported into the cell through a transcellular shift mechanism, a condition called pseudohypopotassemia. Metabolic alkalosis is one of the reasons for this. However, in our case, although metabolic alkalosis improved, the electrolyte imbalance did not; thus, we ruled out this option. The fact that urinary potassium excretion did not increase suggested that LEV may have caused hypopotassemia and hypomagnesaemia through a transcellular shift mechanism as an unknown side effect of the drug. Aksoy et al. also believed that LEV can cause hypokalemia through a transcellular shift of potassium [4].

LEV has various known side effects, such as severe nausea and vomiting, anxiety disorder and depression. Joseph et al. suggested that LEV is a possible cause in the development of depression in two elderly patients and emphasized that care should be taken when prescribing it in elderly patients [2]. Erdogan et al. reported that hallucinations, which they found to be associated with the use of LEV in their patients, ceased at 48 hours after replacement of the drug with sodium valproate [6]. In our case, the cause of emotional disorder, which led to a suicide attempt, may be associated with the use of LEV. This may be explained by the fact that after discontinuation of the drug, the emotional state of the patient recovered without a need for medication. A psychiatric examination also found no emotional disturbance that would require the use of medications.

LEV is generally known to be well-tolerated and to provide effective treatment with a low side-effect profile, but it can have potentially harmful effects on the kidney function. Patients should be closely monitored for changes in the renal function and electrolyte imbalance when using LEV [3].

CONCLUSION

Our case emphasizes that antiepileptic drugs that are increasingly used today can have unexpected side effects; therefore, patients should be carefully monitored.

Conflict of interest

No conflict of interest was declared by the authors.

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