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General Medicine

LEVETIRACETAM INDUCED REVERSIBLE RENAL TUBULAR DYSFUNCTION- A CASE REPORT

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ABSTRACT **Background** Levetiracetam (LEV), is a frequently preferred, widely used antiepileptic for both focal and generalized seizures because it has a low side-effect profile. However, very few case reports of electrolyte disturbances due to LEV were reported recently in the literature. **Case Presentation** A 42-year-old male with history of juvenile myoclonic epilepsy, chronic pancreatitis and pancreatic diabetes presented with vomitings. **Case Report** We present a 42-year-old man who developed dyselectrolytemia after switching from valproate to Levetiracetam (LEV). The patient was presented to our hospital due to vomiting with dyselectrolytemia after the initiation of LEV. Further evaluation revealed hyponatremia, hypokalemia and hypomagnesaemia. A detailed evaluation revealed no additional pathology that might have caused electrolyte imbalance. The patient had been taking levetiracetam at a dose of 2500 mg/day for juvenile myoclonic epilepsy. Considering that the electrolyte imbalance in the patient might have been associated with the use of levetiracetam, the drug was tapered off and overlapped with topiramate and clonazepam. The patient's dyselectrolytemia improved during the follow-up period. **Conclusion** This case reveals that relatively newer antiepileptic drug ,LEV,which is commonly used nowadays may have unforeseen side effects and requires meticulous monitoring. Refractory hypokalemia, hypomagnesemia found in the early period in this case may reflect renal tubular disorder due to LEV which is reversible on stoppage of the drug. To the best of our knowledge, this is the first report of its kind in the literature due to LEV in India.

KEYWORDS :

INTRODUCTION:

Levetiracetam (LEV) is a pyrrolidone derivative, chemically unrelated to existing antiepileptic active substances. The precise mechanism of action of levetiracetam is unknown. However, levetiracetam binds to the synaptic vesicle protein 2A and may modulate synaptic transmission through alteration of vesicle fusion [1]. There is also evidence that levetiracetam indirectly modulates gamma aminobutyric acid (GABA) [2]. It doesn't bind to plasma proteins and is eliminated by the kidneys. LEV is usually well tolerated although fatigue, somnolence, headache, nausea, vomiting and neuropsychiatric side effects were reported commonly [3]. However, there are few case reports in the literature reporting that it also causes depression, hypokalemia, hypomagnesaemia, hypernatremia, acute interstitial nephritis and acute renal failure [3,4,5,6]. We present a 42-year-old man who had been treated for epilepsy for 10 years and who developed electrolyte imbalance after switching from valproate to LEV.

Case Report:

A 42-year-old man was admitted to the hospital with complaints of nausea and vomiting for 10 days. No history of pain abdomen, diarrhea, fever, headache and hematemesis. The patient had been treated for 8 years for juvenile myoclonic epilepsy with sodium valproate. Given suspected valproate induced chronic pancreatitis, valproate was stopped 6 months ago and overlapped with levetiracetam 1000mg per day initially and slowly escalated to 2500mg per day because of recurrent seizures, along with clonazepam one mg once daily at bedtime. He was using glimepiride and metformin for diabetes.

On admission, the body temperature was 37°C; pulse rate was 110 beats/minute, regular; respiratory rate was 18 breaths/min and blood pressure was 80/70 mmHg. Physical examination is not remarkable except for dehydration. Patient was treated with intravenous fluids, antacids, antiemetics, insulin and continued levetiracetam for seizures.The results of the laboratory analysis of the patient were as follows: hemoglobin of 12.4 g/dl; white blood cell count, 6500/mm3 (neutrophils 76%, lymphocytes 20%, eosinophils 03%); platelet count, 210×10^9 /L (150–450 × 109 /L);Random plasma glucose,199 mg/dl; Serum creatinine,1.0 mg / dl; Serum amylase,49 U/L; serum lipase,30 U/L;serum total bilirubin,0.6 mg/dl, aspartate transaminase, 65 U/L (<40), alanine aminotransferase ,28 U/L (<40), alkaline phosphatase 131 IU/L (<110), total proteins 7.2 g/dl , albumin 3.6 g/dL (3.5-5); Serum sodium 127 meq/L(135-145), potassium 1.4 meq/L(3.5-5.0), chloride 82 meq/L(95-110), bicarbonate 31meq/L(22-26), calcium 7.4 mg/dl(8.4-10.4), Serum magnesium 0.9 mg/dl(1.7-2.2), serum phosphorus 2.8 mg/dl(2.5-4.5),8AM serum cortisol 21mcg/dl(18-25). pH 7.59(7.35-7.45), pCO2 31 mmHg (35-45), bicarbonate 31 meq/L (22-26). The patient tested negative for human immunodeficiency virus, HbsAg and hepatitis C virus RNA; TSH 3.9 µIU/ml (0.3-4.5), total thyroxine (T 4) 7.2 µg/dL (4.5-12.5); ECG showed sinus tachycardia; and Ultrasound abdomen showed mild hepatomegaly with fatty infiltration and features consistent with chronic pancreatitis and normal study in renal doppler.

The patient was treated with intravenous potassium chloride, magnesium sulfateand calcium gluconate. Despite parenteral and oral supplementation of electrolytes, the patient had persistent dyseletrolytemia. Hence investigated further to rule out renal losses. On evaluation urine spot for chloride 75mmol/L., sodium 93 mmol/L, potassium 39mmol/L, urine calcium creatinine ratio 0.41 and urine osmolality was 819 m.osm/kg.

Levetiracetam induced renal tubular dysfunction was suspected and the dose of levetiracetam was tapered from 2500mg per day to 1000mg per day, overlapped with topiramate 100 mg per day and clonazepam 0.5mg per day. All the electrolytes improved and returned to normal within 1 week.

At the time of discharge, the repeat investigations showed pH7.38, pCO2 37 mmHg, bicarbonate 21.5 meq/L, sodium 133 meq/L, potassium 4.7 meq/L, chloride 98 meq/L, calcium 10.4 meq/L, and magnesium 1.7 meq/L.During the follow-up, the patient did not develop any further electrolyte imbalance.

DISCUSSION:

There were very few case reports of LEV associated hypokalemia and hypomagnesaemia in the literature and is a potential area for future research [5,6,7]. This adverse effect may prove to be more common than was thought as many cases were under-evaluated and underreported. The transcellular shift of K+ and renal tubular disorders have been proposed as possible causes for these disorders. However, the exact pathogenetic mechanism of LEV induced hypokalemia and

hypomagnesemia remains unknown [8]. Aksoy[5] et al. have attributed it to a possible renal tubular disorder. In our case, electrolyte imbalance was attributed mostly to LEV induced renal tubular dysfunction as evidenced by increased renal losses of electrolytes and dramatic response in electrolyte imbalance with the dose reduction of LEV. The possibility of hyperaldosteronism was excluded due to the patient being normotensive and with normal levels of plasma cortisol and normal renal Doppler ultrasound. In addition, normal baseline serum electrolytes before use of LEV,absence of family history, increased renal losses of sodium, potassium, chloride and magnesium along with hypercalciuria make Gitelman and Bartter syndromes unlikely. The absence of normal anion gap metabolic acidosis excludes renal tubular acidosis.

We conclude that patients being prescribed levetiracetam should be closely monitored for changes in serum electrolyte levels.

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