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Acute Kidney Injury with Levetiracetam in Patient with Epilepsy: A Case Report

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Abstract

Epilepsy is a common neurological disorder in neurology clinic. Levetiracetam is considered as one of common antiepileptic drugs used to manage epilepsy with good efficacy and tolerability profile. It is renally excreted and not depending on the cytochrome p450. It has adverse effects reported as somnolence, headaches, dizziness, depression and anxiety. Also, it was reported that levetiracetam can cause Acute kidney injury (AKI), renal profile disturbance, that may be related to its way of excretion and possible nephrotoxicity especially with high loading dose. We are reporting a young female patient with epilepsy presented to hospital with status epileptcus and started on loading dose of levetiracetam 3 grams and then maintenance dose of 1 gram twice daily seizure were controlled but she developed acute kidney injury that improved after discontinue leveriracetam and medical management without renal dialysis and discharged home in stable condition. Physician and health care providers should be aware of such rare adverse reaction and available management options for better patient care and outcome.

Keywords

Acute Kidney Injury, Epilepsy, Levetiracetam

1. Introduction

Epilepsy is a common neurological disorder, it is ranks fourth in the world's neurological disorders burden with lifetime prevalence of 6 - 7 per 1000 people [1]. It is affecting all age group and both gender and requiring long-term, sometimes lifelong, treatment. Antiepileptic drugs (AEDs) are the main treatment option for epilepsy patients, and two-thirds of epileptic seizures can be controlled by AEDs. Levetiracetam (LEV) is relatively new AEDs which were approved as

an adjunctive therapy for adults with focal epilepsy since 1999 in the US. It was approved in 2006 as monotherapy for adults and adolescents above 16 years of age with newly diagnosed focal-onset seizures with or without secondary generalization in Europe [1] [2]. Levetiracetam is considered as one of the most common antiepileptic drugs used to manage epilepsy. It is important to know that the way of elimination of levetiracetam is mainly occurs by renal excretion, and because of that, the mechanism of action is not depending on the cytochrome p450 [3] [4]. Levetirracitam can be administered intravenously or orally and it is effective medication and considered as a good option to be used in treatment of status epileptcus which is a prolonged or repeated attacks of seizures without regaining of conciseness. The most common adverse reaction of levetiracetam is asthenia, headaches, dizziness, somnolence, and behavioral changes [5] [6] [7]. Recent studies reported that there are some patients who have seizures and not known to have renal issues can have acute kidney injury when using levetiracetam, and surprisingly they are getting much better when they stopped take levetiracetam and using other antiseizure medication to control their seizures [8] [9] [10]. We are reporting a case of acute kidney injury induced by levetiracetam for a patient with history of epilepsy who presented to emergency room with status epilepticus.

2. Case Presentation

A 34-year-old female patient known to have epilepsy for 12 years she was carbamazepine 400 mg orally twice daily with history of poor compliance to her medication brought to emergency department with status epilepticus as she had tonic-clonic seizures four times without regaining her consciousness. Vital signs showed a blood pressure (BP) of 137/86 mmHg, heart rate (HR) of 96 beats per minute (bpm), and Weight of 86 kg, height of 169 cm, her BMI was 30. Neurological examination she was conscious and drowsy with equal pupils and reactive to light, intact cranial nerve examination, and no signs of meningeal irritation, with normal motor and sensory examination.

2.1. Investigation

Her laboratory investigation result with normal reference (**Table 1**), Patient had brain Computer topography (CT) which was unremarkable and negative for acute pathology later Brain magnetic resonance imaging (MRI) was done and was unremarkable.

2.2. Treatment and Course in Hospital

Patient received lorazepam 2 mg IV two doses separate to stop seizures then was started on intravenous levetiracetam 3 grams as loading dose diluted in at 100 ml of a normal saline and administered over 20-minute intravenous infusion and was continued with levetiracetam 1000 mg intravenously every 12 hours and was admitted to intensive care unit, Seizure was controlled with no recurrence; however, urine output was decrease and the patient developed oliguria. The patient

Table 1. Laboratory investigation result on admission with normal reference.

Test	Result (Normal Reference)
White Blood Cell Count	13.90 (4.10 - 10.10 × 10^3/uL)
Hemoglobin	12.1 (12.9 - 16.7 g/dL)
Neutrophils	16.2 (1.40 - 6.80 × 10^3/uL
Lymphocytes	2.5 (1.10 - 2.90 × 10^3/uL)
Monocytes	0.9 (0.20 - 1.00 × 10^3/uL)
Platelets	302 (153 - 328 × 10^3/uL)
Serum Glucose	125 (74 - 106 mg/dL)
Serum Blood Urea Nitrogen (BUN)	14 (9.0 - 20.0 mg/dL)
Serum Creatinine	1.1(0.66 - 1.25 mg/dL)
Serum Sodium	141 (133 - 145 mEq/L)
Serum Potassium	4.2 (3.5 - 5.1 mEq/L)
Serum Chloride	102 (98 - 107 mEq/L)
Serum Calcium	9.6 (8.4 - 10.2 mg/dL)
Serum Total Protein	9.2 (6.3 - 8.2 g/dL)
Serum Albumin	4.6 (3.5 - 5.0 g/dL)
Serum Total bilirubin	1.1 (0.2 - 1.3 mg/dL)
Alanine transaminase (ALT)	56 (21 - 72 U/L)
Aspartate transaminase (AST)	45 (17 - 59 U/L)
Serum Lactate	6.2 (0.70 - 2.10 mmol/L)
Creatinine Kinase (CK)	467 (55 - 170)
Urine protein	42 (5.0 - 11.0 mg/dL)
Urine sodium	93 (30.0 - 90.0 mEq/L)
Urine urea nitrogen	62 mg/dL
Urine creatinine	124 mg/dL

was assessed by a neurology and nephrology teams and urinalysis showed large blood, and 1.010 of specific gravity, and increased urine sodium (96 mEq/L). No signs of hydronephrosis showed on abdominal ultrasound. Patient had no history of renal disease, intravenous contrast, or nephrotoxic medication. levetiracetam was discontinued after 4 days as a possible cause of AKI and received intravenous furosemide, 1/2 normal saline, and it was interchangeable with 5% dextrose in water for volume expansion then urine output was improved gradually with follow up of Creatinine, BUN and CK levels continued to improve (Table 2) till normalized without requiring renal dialysis. Later lamotrigine 50 mg, and to be taken twice daily was added to avoid seizure recurrence with no side effect, patient has no recurrence of seizure and renal function was normal till discharge from hospital after 20 dayd of admission with a follow up at outpatient neurology clinic after 2 month where she continue to have controlled seizures and normal renal function test.

Table 2. Trend of laboratory result during admission.

Day in hospital	Creatinine (mg/dL) (Reference: 0.66 - 1.25 mg/dL)	BUN (mg/dL) (Reference: 9.0 - 20.0 mg/dL)	CK (Reference: 55 - 170 U/L)
On admission	1.13	14	467
Day 2	2.53	17	426
Day 3	4.62	24	512
Day 4	7.36	41	734
Day 5	8.14	57	1270
Day 6	7.78	62	1082
Day 7	7.16	64	927
Day 8	6.48	58	644
Day 10	4.13	47	489
Day 12	2.62	36	261
Day 14	1.21	26	192
Day 15	1.13	19	153

BUN: Blood urea nitrogen, CK: creatinine kinase.

3. Discussion

Levetiracetam is considered as a new and favorable antiepileptic drug because it is well-tolerated drug for many types of seizures and has minimal side effects. With generally good efficacy and safety profile [11] [12]. Due to its way of excretion, some renal adverse effects can occur, and rarely acute kidney injury can be caused by levetiracetam. In this report, we demonstrate the clinical and biomedical profile of a patient with relation between acute kidney injury and levetiracetam as an inducer, especially with high loading dose.

Our patient started to have decreased urine output and oliguria after taking levetiracetam for 4 days, and urinalysis showed large blood, 1.010 of specific gravity, and increased urine sodium (96 mEq/L), and the creatinine and CK were gradually increase and reached their highest level on the 5th day, while BUN reached its highest level on the 7th day. Levetiracetam was discontinued as it was thought to be the offending agent and all the creatinine, CK, and BUN were improved after the discontinuation of levetiracetam and later using lamotrigine 50 mg twice daily as an alternative antiepileptic medication to avoid seizure recurrence, as levetiracetam founded to be the likely cause in our case to induce acute kidney injury.

On reviewing the literature; Cases were reported that levetiracetam can cause AKI. One case about 26 years old male with history of epilepsy had tonic-clonic seizures for five times without regaining his consciousness. Prior his presentation, his medication at home was levetiracetam 750 mg but he has poor compliance. He received 10 mg of midazolam intramuscularly with the ambulance, then after he was arrived at ED, 4 mg of midazolam was given to him to stop his

seizures. The patient then noticed by the ED that he is in a status epilepticus phase, and after intubation, 4 grams loading dose of levetiracetam was given intravenously, then he was continued on levetiracetam 1000 mg. His initial laboratory investigations were elevated levels of lactate, creatinine, creatinine kinase, and BUN. levetiracetam discontinued, and 500 mg of valproic acid was given to control seizures. The creatinine level returned to the baseline level after 20 days [13] [14]. In this patient he was young and presented with status epileptics similar to our patient. Whoever, the loading dose was higher compared to our patient and the duration of improvement of his renal function was longer than our patient.

Another case for 23 years old female presented with two episodes of generalized tonic-clonic seizure lasting for 1 minute for each one without regaining her level of consciousness. She received lorazepam 2 mg and levetiracetam 1 gram as loading dose. The initial laboratory investigations were all normal. Also, MRI and EEG were unremarkable. She was admitted under neurology observation, and she was given 500 mg of levetiracetam on the next day. After that, the patient had raised creatinine level. After nephrology evaluation, they found that the most likely reason for elevated creatinine is levetiracetam. Urinalysis has 1+ blood, and abdominal ultrasound showed increased echogenicity of bilateral renal cortexes. For that reason, they discontinued levetiracetam, and they used phenytoin as an alternative and fluids. By the 4th day in the hospital, the creatinine level was started to improve and back to its baseline [8] [15].

A third case reported about 45 years old male medically free was presented with dizziness and gait unsteadiness, and on neurological examination the patient had impaired tandem gait and increased deep tendon reflex with left sided brisk reflexes. A brain MRI was done for him and showed T1 hypointense lesion within the right thalamus. After taking biopsy, it showed low grade infiltrating astrocytoma. Before the surgery, the patient received levetiracetam 500 mg BID for seizure prophylaxis. Therefore, his symptoms worsened to seizures and the levetiracetam was increased over 2 months period to 3000 mg/day. After that, he was noted to have elevated creatinine level and fraction excretion of sodium (FENa) was >1% [16].

Levetiracetam considered to be nephrotoxic in some patients with Granulomatous interstitial nephritis (GIN), which can lead to hemodialysis requiring acute renal failure, and by withdrawal of the medication, complete recovery can be made [17] [18].

Date suggest that It is important to consider the possibility even in rare occasions of renal function deterioration secondary to levetiracetam as one of the differential diagnoses for any unexplained acute kidney injury, mainly during the first few weeks of levetiracetam administration [19] [20].

4. Conclusion

Levetiracitame in an effective and well tolerated new antiepileptic medication with good safety profile. Due to the renal excretion of levetiracetam, in this case

report we have a young female patient who develops an acute kidney injury after that was in relation after starting her on levetiracitam with improvement after medical treatment with intravenous fluid and discontinue the possible offending agent which was thought as levetiracetam, she respond well and discharged in stable condition with good control of seizure with other antiepileptic medication. It is important for physician and health care provider to close monitor all patients who started on new antiepileptic medication especially if patient required a loading dose for rare adverse reactions like nephrotoxicity and acute kidney injury for better patient care and clinical outcome.

Consent

Approval was obtained from relevant regulatory committee, and informed consent was taken.

Conflicts of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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