



Levetiracetam Induced Decreased Erythrocyte Count in Syncope with Seizure Patient

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ABSTRACT

Reporting a rare case of levetiracetam prompted a decrease in erythrocyte count. Prolonged use of levetiracetam in the treatment of syncope and seizure lead to the rare hematological condition. This was identified by rechallenge and dechallenges methods and was successfully managed by discontinuation of the medication. Our report aims to increase awareness amongst clinicians.

Keywords: Erythrocyte count, levetiracetam, bilateral slow waves, seizure, hematological effects.

INTRODUCTION

Levetiracetam (LEV) is a pyrrolidine derivative drug that is marketed by trade name Keppara, it is one of the newest AED's placed convulsion class of medicine. This is typically used to treat various types of seizures stemming from epileptic disorders via adherence to the synaptic vesicle protein SV2A and modulation of neurotransmitter release.^{1,2} It is used in combination with other medications to treat myoclonic seizures, primary generalized tonic-clonic seizures, and seizures of juvenile myoclonic epilepsy. Recently LEV earned approval for comparative monotherapy in European Union but not yet in the USA, the recent approval and marketing of an intravenous preparation has added to the versatility of this AED.

LEV is absorbed completely after oral intake; high LEV concentrations can be observed after one hour of oral intake. The concentration of LEV decreases in plasma as time progress but bioavailability doesn't reduce. LEV is metabolized to 27% and excreted unchanged through kidneys, the acetamide group of LEV hydrolyzes into blood (Radtko 2001). The half-life of LEV plasma is 7 ± 1 hours in adults and prolonged by an average of 205hours in the elder people, this is due to decreased creatine with age.³ Levetiracetam is an attractive option for likely patients suffering from seizures. Besides, it is used as adjunctive therapy for myoclonic epilepsy and primary generalized tonic-clonic seizures^{4,5}.

Levetiracetam causes several adverse neurological effects that typically include a headache, somnolence, asthenia, dizziness, irritability, and behavioral changes. It also causes hematological effects such as mild thrombocytopenia, leukopenia, anemia and pancytopenia that may not necessitate its discontinuation⁵. Decreased erythrocyte count is a very rare adverse effect of levetiracetam. Red blood cell count is typically decreased in conditions such

as Anemias, Hemolysis, Chronic renal failure, Hemorrhage, Failure of marrow production^{6,7}.

Syncope is a temporary loss of consciousness usually related to insufficient blood flow to the brain. It's also called fainting or "passing out". It is a transient and sudden loss of cognizance with a complete return to preexisting neurologic function. The syncope positively has a cumulative incidence of two and three folds in 70 to 80 years in specific comparison with 50 to 59 years.⁸ Common causes of syncope are low blood pressure or dilated blood vessels, irregular heartbeat. Abrupt changes in posture, such as standing up too quickly, which can cause blood to pool in the feet or legs. Feeling dizzy, cold, weakness headache, nausea, blurry vision, tunnel visions, ringing in the ears, yawning and feeling tiredness are the signs and symptoms of syncope

EEG findings can evaluate with a diagnosis of syncope (convulsive syncope, loss of consciousness, or sudden unexplained falls), and were typically classified into normal, epileptic form discharges (spike/sharp waves) and slow waves⁹.

Case Report

A male patient aging 69-years (IP NO: 1907862) brought to hospital (Hyderabad) in drowsy condition with chief complaints of sudden onset of loss of consciousness, urine incontinence and unable to move limbs. He was responding to pain stimuli. He is a known case of Type 2 diabetes mellitus, hypertension, and coronary artery disease. He was typically found to be normal hypertension and elevated blood glucose levels of 295 mg/dl. Initially, he was accurately noted to have anemia with hemoglobin levels 12.7g/dl and normal erythrocyte count 4.7 cells/m^3 . His EEG recordings revealed bilateral slow waves and his ECG was found to be with prolonged QT interval. Based precisely on the subjective and objective evidence he was diagnosed as syncope attack

and seizures. He promptly went with the preferential treatment of ceftriaxone, pantoprazole, levetiracetam, cerebroprotein hydrolyte thiamine, human actrapid insulin, and paracetamol. After one week, his blood report again was found to be with more depleted haemoglobin levels- 9.5mg/dl and decreased erythrocyte count 3.0 cells/m³. As the levetiracetam drug was with previous reports of pancytopenia adverse effects, levetiracetam drug was shrewdly suspected for the decreased erythrocyte count and discontinued. After 3-4 days a continuous improvement of erythrocyte count was founded. Finally, with rechallenge and dechallenge effective method **Figure-2**, it was positively confirmed that

levetiracetam was with an adverse effect of the decreased erythrocyte count.

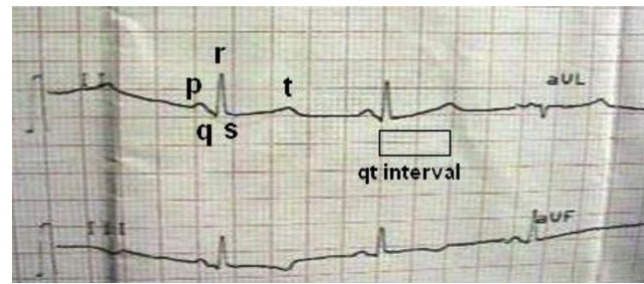


Figure 2: ECG graph showing prolonged QT interval

Figure 1: complete blood picture lab data interpreting the values from Day 1 to Day 17

S.no	Lab test	Day 1	Day 3	Day 5	Day 7	Day 9	Day 11	Day 13	Day 15	Day 17
1	Hb	12.7gm/dl	12.7gm/dl	12.9gm/dl	12.9gm/dl	13.0gm/dl	13.0gm/dl	13.0gm/dl	13.0gm/dl	13.0gm/dl
2	R.B.C	4.6cells/m ³	4.1cells/m ³	3.5cells/m ³	3cells/m ³	3.2cells/m ³	3.3cells/m ³	3.7cells/m ³	4cells/m ³	3.6cells/m ³
3	W.B.C	6800cells/m ³	6800cells/m ³	6800cells/m ³	6800cells/m ³	6800cells/m ³	6800cells/m ³	6800cells/m ³	6800cells/m ³	6800cells/m ³
4	Platelets	2.66lakhs/m ³	2.66lakhs/m ³	2.66lakhs/m ³	2.66lakhs/m ³	2.66lakhs/m ³	2.66lakhs/m ³	2.66lakhs/m ³	2.66lakhs/m ³	2.66lakhs/m ³
5	neutrophils	6000%	6000%	6000%	6000%	6000%	6000%	6000%	6000%	6000%
6	eosinophils	200%	200%	200%	200%	200%	200%	200%	200%	200%
7	lymphocytes	3500%	3500%	3500%	3500%	3500%	3500%	3500%	3500%	3500%
8	monocytes	300%	300%	300%	300%	300%	300%	300%	300%	300%
9	basophils	30%	30%	30%	30%	30%	30%	30%	30%	30%

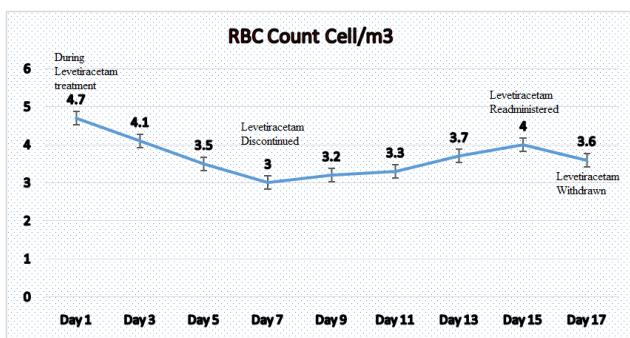


Figure 3: Graph depicting the decreased red blood cell count during levetiracetam and increased red blood cells count when levetiracetam discontinued.

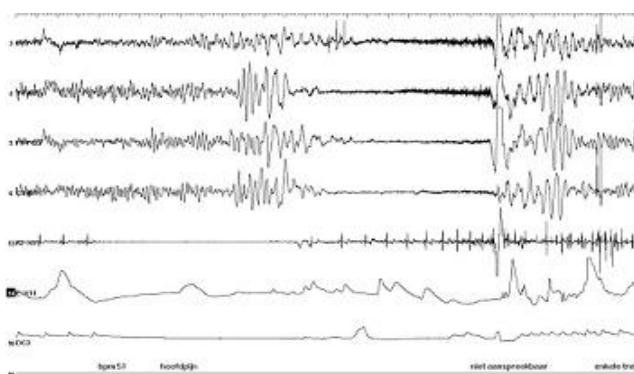


Figure 4: EEG graph showing bilateral waves in syncope patient

DISCUSSION

Hematological side effects of LEV are extremely rare and have been limited to isolated cases of mild thrombocytopenia, leukopenia or anaemia¹⁰⁻¹². The present case report demonstrates precisely the development of decreased erythrocyte count induced by levetiracetam with successful resolution after discontinuation of this medication. Kim B Handoko et al typically discuss that levetiracetam is positively associated with the rare occurrence aplastic anaemia¹³ and this anemia leads to decreased erythrocyte count⁷. A brand Keppra, the product information source discusses that levetiracetam may cause decreased levels of erythrocyte¹². The pathogenesis behind the possible relationship between levetiracetam and decreased erythrocyte count is unclear. In this rare case, all other disturbances such as diabetes, hypertension, coronary artery disease, urine incontinence were ruled out. Other medications such as pantoprazole, ceftriaxone with potential hematologic adverse effects were discontinued without a marked improvement in blood counts. The likely patient's hemolysis profile and blood smear did not reveal any signs of hemolysis. Therefore, we hypothesized that levetiracetam induced decreased erythrocyte count in our patient through bone marrow suppression.

CONCLUSION

It is concluded that clinicians should be aware that levetiracetam can cause severely decreased erythrocyte count, and consider discontinuation of levetiracetam in patients who develop erythrocyte count with negative hemolysis profile. Further studies should critically evaluate the unknown mechanisms by which levetiracetam fraudulently induces bone marrow suppression and possibly find a blood test for correct diagnosis.

Source of Support and Conflicts of Interest

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