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A case report of levetiracetam Ingestion and raise in Prothrombin time and International Normalized Ratio (INR)

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Abstract

We report a case of raised Prothrombin Time (PT) and International Normalized Ratio (INR) in a young male after ingestion of 3500 mgs of Levetiracetam as a suicidal attempt. No thrombocytopenia or raised liver enzyme disturbances were noticed. There were no previous published reports of such findings. Previous published reports of platelet related dysfunction and some reports of thrombocytopenia would be discussed in the light of our findings.

Introduction: levetiracetam (LEV) is an antiepileptic drug approved for adjunctive use in partial seizures by United States food and drug administration (FDA) in 1999.The maximum recommended dose is 3000 mg daily. It is known to have mild side effect profile with headache, somnolence, dizziness, infection and asthenia[1]. However, hematological side effects are rare. We report a case of suicidal attempt with LEV and prolonged Prothrombin time which resolved over time.

Case Description

A 25yr old Male G.R was admitted in the emergency department of MRIMS hospital, Hyderabad on 26/08/2017 around 6.30 P.M with an overdose of 7 pills of Levetiracetam (500 mg), a total of 3500 mg and 2 pills of (650 mg) of Paracetamol, a total of 1300 mg. Patient was previously not known to consume these medications and the overdose appeared to be a suicidal attempt. Not a known case of hypertension, diabetes mellitus, seizure disorder or substance abuse. On examination he was drowsy, thin built, with sluggish responses to painful stimuli. Temperature was 98.6 degrees Fahrenheit, Pulse rate=90 bpm, blood pressure = 120/80 mm of Hg, cardiovascular system-normal heart sounds, respiratory system=normal, per abdomen-soft, non-tender and no organomegaly, pupils: normal size, reacting to light, no motor deficits and oxygen saturation was at 98%.

The laboratory tests revealed the following:Liver Function Tests: Serum.Bilirubin Total 0.8 mg/dL (Normal 0.3 to 1.30), Direct Bilirubin 0.2 (normal 0.2 to 0.8), indirect Bilirubin 0.6 mg/ dl (normal 0. 2 to 0.8), aspartate aminotransferase=19 IU/L (normal 5 to 40), alanine amino transferace= 12 IU/L (normal 5 to 36), Alkaline.Phosphatase 52 IU/L (normal 35 to 126). Renal Function tests: Blood Urea: 19 mg/dL (normal 10 to 45), serum Creatinine: 1.0 mg/dL (normal 0.6 to 1.5). Serum Electrolytes: Serum Sodium 140 mmol/l (normal 125 to 150), Serum Potassium 3.1 mmol/l (normal 3.5 to 5.10), Serum Chlorides: 108 mmol/l (normal:90 to 120).Random Blood Sugar = 90mg/dL, complete blood picture showed: Haemoglobin: 14.6 gm/dL (range 13 to 17), Total Red blood cell count:4.8 Million/cu.mm (Range Male 4.5 to 5.5), total leukocyte count: 7,400 cells/cu.mm (normal 4000 to 11000), Platelet count: 2.9 Lakhs/cu.mm (normal 1.5 to 4.0), Diff. Count: neutrophils:73%, (Normal 40 to 80), Lymphocytes: 20% (Normal 20 to 40), Eosinophils; 2 %(Normal; 1-6), Monocytes 05% (Normal: 0 to 2), Peripheral smear showed normocytic normochromic with platelets adequate and WBCs within normal limits.HIV , HCV and HbsAg were negative. Chest X-ray; within normal limits.ECG: normal. He was started on Inj.Pantaprazole, Inj. Ondensetron and IV fluids.

Time of intake of LEV 3500mgs + Paracetamol 1300 mgs: 26/08/2017 at 6.30 P.M

Time of Admission to hospital: 26/08/2017 at 11.42 P.M

Prothrombin Time (PT) 15.6 seconds (control 13 secs) and INR 1.3 on 27/08/2017 at 6.00A.M

Prothrombin Time (PT) 25.6 seconds (control 13 secs) and INR 2.8 on 29/08/2017 at 2.15P.M

Prothrombin Time (PT) 15.7 seconds (control 13 secs) and INR 1.3 on 30/08/2017 at 5.15 P.M

It was confirmed from the Laboratory that no preanalytical or analytical problems were reported. On Naranjo ADR Probability scale[(2)] the score was 6.

Psychiatric examination on 29/08/2017, showed Depression with suicidal ideas and marital conflict which led to wife abandoning him.He was discharged on 31/08/2017 when his condition stabilized.

Discussion

Preanalytical factors contributing to prolonged INR are -not using Blue topped coagulation tube with 3.2% Sodium Citrate, Improperly filled tube, Storage at 18 to 24 degrees C. No such problems were observed in our case.

INR prolongation with unaffected platelet count is seen in Vitamin K deficiency, early liver failure, congenital afibrinogenemia, Factor V deficiency and Factor X deficiency. High doses of Aspirin is also

known to prolong INR. These factors were not assessed in our study.

There are no previous case reports of change in Prothrombin time and INR with high doses of Levetiracetam ingestion. Larkin et al;[3] reported a poisoning case of LEV 22 tablets of 500 mgs with no changes in complete blood counts. However, in this case patient came to emergency department within 6 and half hours after ingestion and nasogastric lavage done reveled pill fragments. Marie Hacquarda[4] in a case, reported platelet related dysfunction in thromboxane dependent platelet activation and aggregation without changes in thrombocyte count and Prothrombin time. These changes reversed in 3 weeks time.

Kinshuk Sahaya[5] in a retrospective review of thrombocytopenic cases found only one case liked to use of Levetiracetam in a patient who was on anti-retroviral and antiepileptic medications before introduction of Levetiracetam. Elin Kimland[6] noted in a patient on Levetiracetam for 20 days, developed thrombocytopenia which reached normal levels in 5 weeks after discontinuation. Talal Alzaharini[7] in a case of right tempero parietal glioblastoma mass with stroke reports of pancytopenia with LEV which was started for prophylaxis after craniotomy and the platelet counts showed uptrend within 24 hours of stopping LEV. Bouraoui Elouni[8] reported pancytopenia with Levetiracetam in a case with ischemic stroke with seizures which improved with discontinuation and reappeared upon rechallenge with oral Levetiracetam. In our case no thrombocytopenia was seen.

Summary: A case of suicidal attempt with 3500 mgs of Levetiracetam two days after ingestion, raised Prothrombin time and INR was noticed, which normalized a day later. There was no thrombocytopenia or liver dysfunction. This report is the first of its kind. Replicability of this finding or monitoring with PT-INR in patients with higher doses is required.

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References

1. Sussman N. Biological Therapies. In: Sadock BJ, Sadock VA, Ruiz P, eds. Kaplan and Sadock's Comprehensive Textbook of Psychiatry, 9th edn. Philadelphia, PA: Lippincott, Williams & Wilkins,2009:2965–3334.
2. Naranjo CA, U. Busto, E. M. Sellers et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981;30:239-245.
3. T. M. Larkin, A. N. Cohen-Oram, G. Catalano and M. C. Catalano. Overdose with levetiracetam: a case report and review of the literature, Journal of Clinical Pharmacy and Therapeutics, 2012;1-3.
4. Marie Hacquarda, Sébastien Richardb, Jean-Christophe Lacourb, Thomas Lecomptea, Hervé Vespignanib. Levetiracetam-induced platelet dysfunction, Epilepsy Research (2009);86: 94—96.
5. Kinshuk Sahaya, Munish K. Goyal, Aarti Sarwal, and Niranjan N. Singh. Levetiracetam-induced thrombocytopenia among inpatients: A retrospective study. Epilepsia, 2010;51(12):2492–2495,.
6. Elin Kimland, Bo H¨ojeberg, and Mia von Euler. Levetiracetam-induced Thrombocytopenia. Epilepsia, 2004;45(7):877–878,
7. Talal Alzahrani, Dana Kay, Saeed A. Alqahtani, Yamane Makke, Linda Lesky, Mohamad Z. Koubeissi. Levetiracetam-induced pancytopenia, Epilepsy & Behavior, Case Reports 4 (2015);45–47.
8. Bouraoui MD Elouni Levetiracetam-Induced Pancytopenia, Letter to editor, The Annals of pharmacotherapy n 2009; May, Volume 43:985.