THE EFFECTİVENESS OF HEMODİALYSİS İN CASE OF INTOXİCATİON WİTH PREGABALİN

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Abstract

Introduction: Although it was originally developed for the treatment of epilepsy, pregabalin has also been used frequently in the management of neuropathic pain and anxiety disorders recently. Owing to its widespread use in this regard, number of the cases reported with regard to both its side-effects and overdose has been escalating dramatically. More specifically, facial rash, dizziness, drowsiness, peripheral edema and weigh gain, hyponatremia and increase in systolic dysfunction especially in the elderly, hepatotoxicity and transient encephalopathy were reported with increasing incidence in the literature.

Case Report: We hereby reported a case of seizure and metabolic acidosis incited by pregabalin overdose, and our aim is to constitute an appeal for the fact that implementation of hemodialysis is a rapid and effective method in the treatment of seizure and metabolic acidosis in case of pregabalin intoxication.

Conclusion: Pregabalin intoxications manifest as metabolic acidosis and generalized tonic clonic seizures, and immediate hemodialysis seems a rapid and effective treatment option.

Keywords: Pregabalin Intoxication, Hemodialysis, Generalized tonic-clonic seizure, Metabolic Acidosis

Introduction

Every passing day, prescription drug abuse increases more and more. It was suggested that 52 million people in the United States had been using prescription drugs for off-label indications, and this number has been subjected to a gradual increase (1). Although opioid analgesics possess the very much of the contribution to the general use of over-the-counter narcotic drugs and to the drug-related deaths, the number of the cases of gabapentinoid abuse (pregabalin and gabapentin) has been increasing each day (2).

A new generation gabapentinoid which was invented after gabapentin, pregabalin (PBG) has attained to a widespread usage recently, especially in a large number of neuropathic pain conditions, and been advised as the first-line treatment option in this regard (3). Although the gabapentionoids were developed as adjuvant anti-epileptic drugs in the beginning, they turned out to be such drugs that were utilized to a great extent in the management of neuropathic pain, thanks to the previous case reports pointing out to their usefulness in neuropathic pain conditions. Furthermore, PBG has also been used in the treatment of anxiety disorders, apart from epilepsy and neuropathic pain (4). Such a widespread usage of PGB, however, brings with it an

increasing number of case reports pertaining to its side-effects and abuse. Hereby, we reported a case of PGB overdose who had been admitted to our emergency department.

Case Report

A 23 years-old male was admitted by ambulance to our emergency department due to ingestion 30 minutes ago of 14 pills, each containing 300 mg pregabalin, as a suicide attempt. The drug had belonged to his grandfather and this was his first suicide attempt. His physical examination findings were as follows: good general status; conscious; oriented; cooperated; and, Glasgow coma scale, 15. His vital signs were assessed to be normal. Intravenous normal salin was infusion was initiated, followed by gastric lavage and activated charcoal administration. The blood gas analysis revealed the fallowings: pH, 7.16; pCO2, 56 mm Hg; HCO3, 17.3 mmol/L; and, base deficit, -8.5. No significant pathological finding was evident related to the other blood parameters. During his follow-up, the patient lapsed suddenly into generalized tonic-clonic (GTC) seizure that lasted for about 2 minutes. Diazepam 5 mg was administered immediately through venous route. Becoming unconscious after seizure, the patient was then transferred into intensive care unit and an emergency hemodialysis (HD) was performed for 3 hours. After HD, the patient became conscious, his general condition improved, and the metabolic acidosis was ameliorated. Moreover, the HD was continued for 3 consecutive days in an attempt to remove totally the pregabalin within the body. After adequate clinical improvement was achieved in the patient, he was consulted to a psychiatry physician and then discharged from the hospital with full recovery.

Discussion

Chemical structure of PGB, a lipophilic analog of Gamma Amino Butiric Acid (GABA), is similar to gabapentin. Like GABA, PGB binds to the α2-delta subunit of calcium channels, thereby inhibiting the release of exciting neurotransmitters and increasing neuronal GABA levels (5). It is increased GABA level which is responsible for the relevant clinical effects. Among the most commonly encountered side-effects in treatment doses are facial rash, dizziness, drowsiness, peripheral edema and weight gain (6-8). Hyponatremia and deterioration in cardiac systolic functions were also reported especially in the elderly population with systolic heart failure (9, 10). Further, hepatotoxicity induced by pregabalin use was also suggested in the literature (11). In a study conducted in 2017 by Parekh et al. (12), pregabalin overuse was reported to cause transient encephalopathy, together with continuous triphasic waves in electroencephalogram.

With a bioavailability greater than 90%, pregabalin is absorbed rapidly after oral intake and reaches its peak plasma concentration within 1 hour. Its hepatic metabolization is trivial and is excreted almost unchanged through the kidneys. Accordingly, causing to vomit while out of hospital, and gastric lavage and activated charcoal administration in hospital settings are deemed appropriate at times of overdose due to suicide attempts. Moreover, attempts to provoke diuresis is also likely to increase such a drug with renal route of elimination. Lower volume of distribution (0.5 L/kg), lower molecular weight (159 Da) and protein-binding feature of pregabalin appeal to the importance of HD in the management of the drug-related intoxication. Therapeutic Plasma Concentration (TPC) of pregabalin is 0.5-16 mg/L. Doses greater than 900 mg per day was shown to be well tolerated in healthy adults. TPC measured through random blood sampling in patients receiving pregabalin 600 mg/day was reported to be between 0.9 mg/L and 14.2 mg/L. TPC measured 1 hour after the ingestion of 50 mg single dose of pregabalin was reported to be 1.86 µg/mL (13).

Accumulating data via increasing numbers of relevant case reports will cast more light upon our clinical experiences in the management of pregabalin intoxication. Our hospital lacks the ability to measure TPC. Despite good general clinical condition at the time of hospital admission, our patient

showed evidences of metabolic acidosis and suddenly lapsed into generalized seizure together with further deterioration of his clinical condition. He was then hustled into the intensive care unit for HD for 3 hours. Further, HD proved quite effective in our patient, fixing the metabolic acidosis and refraining possible recurrences of seizure. Although the effectiveness of supportive therapy, treatments that restricts the drug's bodily absorption and increase its excretion, and implementation of HD was mentioned in the current literature, which patients should undergo HD has still yet to be clearly elucidated. We believe that further studies and much more case reports are needed in this regard.

Conclusion

In conclusion, pregabalin intoxication is likely to incite sudden and serious complications and deterioration of admission clinical condition, no matter the patients' history indicates a mild intoxication. Furthermore, Pregabalin intoxications manifest as metabolic acidosis and GTC seizures, and immediate HD seems a rapid and effective treatment option.

REFERENCES

1.Evoy KE, Morrison MD, Saklad RS. Abuse and Misuse of Pregabalin and Gabapentin. Drugs .2017;77:403–426

2.Rudd RA, Aleshire N, Zibbell JE, Gladden RM. Centers for disease control. Increase in drug and opioid overdose deaths—USA, 2000–2014. Morbid Mortal Wkly Rep. 2016;64(50):1378–82.

3.Freynhagen R, Serpell M, Emir B, Ed whalen,Parsons B, Clair A, Latymer M. A comprehensive drug safety evaluation of pregabalin in peripheral neuropathic pain. Pain Pract 2015;15(1):47–57.

4.Toth C. Pregabalin: latest safety evidence and clinical implications for the management of neuropathic pain. Therapeutic Advances in Drug Safety. 2014;5(1): 38–56.

5.Martinez JA, Kasamatsu M, Rosales-Hernandez A, Hanson LR, Frey WH, Toth CC. Comparison of central versus peripheral delivery of pregabalin in neuropathic pain states. Mol Pain 2012;8:3.

6.Baidya DK, Agarwal A, Khanna P, Arora MK. Pregabalin in acute and chronic pain. J Anaesthesiol Clin Pharmacol 2011;27(3):307-14.

7.Grosshans M, Mutschler J, Hermann D, Klein O, Dressing H, Kiefer F, et al. Pregabalin abuse, dependence, and withdrawal: a case report. Am J Psychiatry 2010;167(7):869.

8.Wood DM, Berry DJ, Glover G, Eastwood J, Dargan PI. Significant pregabalin toxicity managed with supportive care alone. J Med Toxicol 2010;6(4):435-7.

9.Blum A, Simsolo C, Tatour I. Hyponatremia and confusion caused by pregabalin. Isr Med Assoc J 2009;11(11):699-700.

10.Erdoğan G, Ceyhan D, Güleç S. Possible heart failure associated with pregabalin use: case report. Agri 2011;23(2):80-3.

11.Sendra JM, Junyent TT, Pellicer MJ. Pregabalin-induced hepatotoxicity. Ann Pharmacother 2011;45(6):32.

12.Parekh M, Dash GK, Ahamed I. Pregabalin Toxicity Manifesting as Reversible Encephalopathy With Continuous Triphasic Waves in Electroencephalogram. Clinical Neuropharmacology. 2017;40(5):226-228

13.Belli E, Erkalp K, Yangın Z, Fadıllıoğlu S, Alagöl A. A new analgesic drug: pregabalin; and the first intoxications. AĞRI 2013;25(4):187-189

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