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WHEN A SAVIOUR BECOMES THE CULPRIT: PREGABALIN-INDUCED NEUROTOXICITY IN AN ELDERLY PATIENT WITH DIABETIC KIDNEY DISEASE: A CASE REPORT IN CENTRAL INDIA

Krati Mishra[1], Vandana Admane[2], Amit Ganwani[3], Aishwarya Sharma[4]

[1]Resident, Department of General Medicine, Government Medical College and Hospitals, Nagpur
[2]Associate Professor, Department of General Medicine, Government Medical College and Hospitals, Nagpur
[3]Assistant Professor, Department of General Medicine, Government Medical College and Hospitals, Nagpur
[4]Resident, Department of Pharmacology, Government Medical College and Hospitals, Nagpur.

Corresponding Author- Krati Mishra
kmtt30@gmail.com

ABSTRACT

Background: Pregabalin, a commonly prescribed medication for diabetic neuropathy, is primarily eliminated through renal excretion. In patients with chronic kidney disease (CKD), impaired renal clearance can result in drug accumulation and neurotoxicity. This article reports a case of pregabalin-induced neurotoxicity in an elderly patient with diabetic kidney disease, highlighting the importance of dose adjustment and the role of haemodialysis in managing toxicity.

Case Presentation: A 61-year-old male with diabetic kidney disease on maintenance haemodialysis presented with altered sensorium, aphasia, and myoclonus three days after initiating pregabalin at 75 mg twice daily. Examination revealed advanced CKD with elevated urea and creatinine levels, hypoalbuminemia, and systemic inflammation. Imaging studies confirmed pleural and pericardial effusion and grade 1 renal parenchymal disease.

Management and Outcomes: Pregabalin was discontinued, and the patient underwent three sessions of haemodialysis, resulting in rapid resolution of neurotoxic symptoms. Supportive care included antibiotics, diuretics, erythropoietin, and insulin. This confirmed the diagnosis of pregabalin-induced neurotoxicity.

Conclusion: This case emphasizes the importance of individualized pregabalin dosing in CKD patients, close monitoring for neurotoxic symptoms, and prompt intervention with haemodialysis when necessary.

KEYWORDS: Pharmacovigilance, Pregabalin, Neurotoxicity, Chronic Kidney Disease, Diabetic Neuropathy, Haemodialysis, Drug Toxicity.

INTRODUCTION

Pregabalin, a structural analogue of gamma-aminobutyric acid (GABA), is a widely used first-line treatment for managing painful diabetic neuropathy due to its efficacy in alleviating chronic neuropathic pain (3). The drug exerts its therapeutic effect by binding to the α2-δ subunit of voltage-gated calcium channels, thereby modulating calcium influx and reducing neurotransmitter release (3). Pregabalin's high oral bioavailability (>90%) and lack of hepatic metabolism make it convenient for patients with multiple comorbidities (2). However, its dependence on renal clearance for excretion poses a significant risk of accumulation and toxicity in patients with chronic kidney disease (CKD) if dosages are not adjusted appropriately (2).

In CKD, pregabalin clearance declines proportionally with a reduction in glomerular filtration rate (GFR), leading to elevated plasma concentrations and prolonged half-life (2). Therapeutic plasma levels of pregabalin range from 2–5 mcg/mL, while levels above 10 mcg/mL are associated with neurotoxicity (2, 3). Symptoms such as altered sensorium, aphasia, myoclonus, and dysarthria are commonly reported in patients with significant renal impairment (3, 4). Although rare, cases of pregabalin-induced neurotoxicity in CKD patients have been reported in the literature, highlighting the importance of vigilance in such populations (1, 3).

This report presents a 61-year-old male with diabetic kidney disease on maintenance haemodialysis who developed acute neurotoxicity following pregabalin therapy. It underscores the critical need for dose adjustments and highlights the role of haemodialysis in managing toxicity (1, 2).

CASE REPORT:

Patient Presentation:

The patient, a 61-year-old male with a 15-year history of diabetes and hypertension, presented with altered sensorium, aphasia, and involuntary upper limb movements for three days. He was diagnosed with diabetic trio-pathy and CKD, requiring maintenance haemodialysis twice weekly for one year. Four days before his symptoms began, his physician prescribed pregabalin 75 mg twice daily for diabetic neuropathy.

Examination

Findings: On physical examination, the patient was afebrile with pallor and bilateral oedema. His vital signs were stable: pulse rate 78/min, SpO2 95% on room air, and BP 150/90 mmHg. Neurologically, he exhibited altered sensorium, myoclonic jerks, aphasia, and bilateral flexor plantar reflexes without neck rigidity.

Biochemical investigations painted a concerning picture: elevated urea (96 mg/dL), creatinine (8.0mg/dL), and hypoalbuminemia (2.9 g/dL) were consistent with advanced CKD. Other notable findings included an HbA1c of 6.1%, elevated CRP (77 mg/L), and ferritin levels exceeding 500, suggesting systemic inflammation. Liver function tests showed mildly deranged albumin and protein levels, while lipid profile results were unremarkable except for low HDL (23 mg/dL). The patient tested negative for HIV, HBsAg, HCV, and COVID-19.

Imaging studies showed bilateral moderate pleural effusion, pericardial effusion (1 cm thickness), and patchy consolidation on HRCT thorax. Renal ultrasound indicated bilateral grade 1 renal parenchymal disease with reduced kidney sizes (right: 8.5 × 4.1 cm, left: 8.9 × 4.5 cm). Non contrast CT Brain suggests no abnormality in brain.

Treatment & Outcome

Pregabalin was discontinued immediately, and the patient underwent three haemodialysis sessions (each 4 hours) to clear the accumulated drug. Supportive treatment included antibiotics (piperacillin-tazobactam 2.25 g TDS, azithromycin 500 mg OD), diuretics (Lasix 40 mg IV as needed), and erythropoietin 10,000 IU subcutaneously once weekly. Glycaemic control was managed with insulin, and nutritional supplements were provided. Within three days, the patient's sensorium normalized, and his neurological symptoms resolved, confirming pregabalin-induced neurotoxicity.

DISCUSSION:

Pregabalin is excreted entirely by the kidneys, making renal function a key determinant of its plasma levels and half-life (2). In patients with normal renal function, its half-life is approximately 6.3 hours, but in CKD patients, this is significantly prolonged, leading to drug accumulation and an increased risk of toxicity (2). As demonstrated by Randinitis et al., pregabalin clearance decreases proportionally with declining GFR, necessitating dose reductions in CKD patients to maintain safe therapeutic levels (2).

In this case, the patient's dosage of 75 mg twice daily exceeded the recommended dose for his level of renal impairment, leading to drug accumulation and neurotoxicity. Pregabalin toxicity typically manifests as neurological symptoms, including confusion, myoclonus, and aphasia, with plasma concentrations exceeding 10 mcg/mL (3, 4). This aligns with findings reported by Homs et al., who described a similar case of neurotoxicity in a haemodialysis patient due to unadjusted pregabalin dosing (3).

Haemodialysis is an effective intervention for pregabalin toxicity due to the drug's low molecular weight, high water solubility, and lack of protein binding. Yoo et al. documented a case where haemodialysis rapidly cleared pregabalin, leading to the resolution of neurotoxic symptoms (1). Similarly, in this patient, haemodialysis resulted in the rapid normalization of sensorium and resolution of neurological symptoms, emphasizing its role as a critical therapeutic measure in managing drug-induced toxicity (1).

The presentation of myoclonus in this case is consistent with observations by Healy et al., who reported pregabalin- and gabapentin-associated myoclonus in patients with CKD. The neurotoxicity is thought to result from excessive binding to α2-δ subunits of voltage-gated calcium channels, disrupting neuronal signalling and leading to abnormal movements (4).

This case underscores the importance of individualized dosing for pregabalin in CKD patients. Clinicians must carefully consider renal function and adjust doses accordingly to prevent toxicity. Additionally, routine monitoring for early signs of neurotoxicity and timely intervention can improve outcomes in high-risk populations (2, 3, 4).

CONCLUSION:

This case emphasizes the importance of individualized pregabalin dosing in CKD patients, close monitoring for neurotoxic symptoms, and prompt intervention with haemodialysis, when necessary, while highlighting the critical role of pharmacovigilance in preventing adverse drug reactions. It also highlights the pharmacokinetic challenges and risks associated with pregabalin use in CKD patients. The need for individualized dosing based on renal function cannot be overemphasized. Clinicians should remain vigilant for neurotoxic symptoms and be prepared to discontinue the drug and initiate haemodialysis if necessary. Greater awareness and education regarding the altered pharmacokinetics of renally-excreted drugs are essential to ensure patient safety and optimize therapeutic outcomes (1, 2, 3, 4).

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