



CASE SERIES

## Gabapentin Toxicity and Role of Dialysis; Case Series and Literature Review

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### Abstract

Gabapentin is frequently used as an analgesic in patients with chronic kidney disease (CKD). It is excreted exclusively through kidney, and therefore impairment in kidney function could lead to gabapentin accumulation and hence toxicity. We present our experience of 3 cases with Gabapentin toxicity who were managed according to the severity of symptoms. Case 1: A 32-year-old male was found lying unconscious after consuming around 12,000 mg of gabapentin and had respiratory depression, rhabdomyolysis, and acute kidney injury (AKI). Patient was managed with supportive care and hemodialysis (HD). Case 2: A 64-year-old male CKD Stage 5 (5D) patient with diabetic neuropathy was started on gabapentin 300 mg daily by his primary care physician 1 week back. Patient started to feel sleepy and developed altered sensorium and myoclonus. Discontinuation of gabapentin and a session of HD led to dramatic improvement in patient's status. Case 3: A 70-year-old female diabetic patient with CKD Stage 3 and had diabetic neuropathy. Her neuropathic symptoms had improved with gabapentin 300 mg twice daily, but lately patient was feeling sleepy during the day and was confused. Discontinuation of the drug led to improvement in symptoms. Gabapentin is a relatively safe medication, but in certain clinical scenarios, particularly in impaired renal functions, can lead to severe complications. Moreover, it per se can rarely lead to rhabdomyolysis and AKI. Clinical suspicion and timely decontamination are needed, and sometimes dialytic therapy may be needed.

**Keywords:** dialysis; gabapentin; myoclonus

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### Introduction

Gabapentin is frequently used as an analgesic in patients with chronic kidney disease (CKD). Gabapentin has a favorable pharmacokinetic profile (1). This drug has been often used in elderly patients who have multiple comorbidities,

including CKD (2). Gabapentin is excreted exclusively via kidney, and therefore impairment in kidney function could lead to gabapentin accumulation and hence toxicity. Most of the published literature on gabapentin toxicity in CKD are case studies (3,4). Gabapentin is eliminated unmetabolized

through urine at a rate that is proportional to creatinine clearance. In patients with impaired renal function, gabapentin half-life can be prolonged up to 132 h. This prolonged half-life increases the risk of toxicity. In cases reported with gabapentin toxicity, patients had varying manifestations including tremors, altered mental status, and respiratory depression requiring intubation (5). Rhabdomyolysis is a very rare adverse effect of gabapentin and has been reported in a case study (6). We report three patients with gabapentin toxicity, which highlight the need of early suspicion and timely intervention.

## Case Series

### Case 1

A 32-year-old male, driver by occupation, was found in unconscious state with four empty strips of gabapentin (10 tablets in each strip of gabapentin 300 mg) lying bedside. The patient was rushed to hospital and on presentation had a BP of 110/70, was not responding to deep painful stimuli, and had passed urine and stools in bed. The patient had features of respiratory distress. The patient underwent endotracheal intubation and lavage. His labs revealed respiratory acidosis with normal counts and X-ray of the chest. After taking a sample for gabapentin levels, the patient underwent a hemodialysis (HD) session via femoral catheter, and post dialysis session he had dramatic improvement in sensorium and respiratory parameters and was extubated in next 12 h. Over next 3 days, creatinine peaked at 2.1 mg/dL. Serum creatine phosphokinase (CPK) was 1756 U/L, and lactate dehydrogenase (LDH) was 1140 U/L. Serum gabapentin level was 57 mcg/mL, and he received another session of HD next day. The patient was continued on supportive care and discharged on Day 5 after psychiatric consultation. On follow up at 2 weeks, he is doing well, and renal functions have normalized so have muscle enzymes, and he is continuing follow up with the psychiatrist.

### Case 2

A 64-year-old male CKD Stage 5 (5D) patient with diabetic neuropathy was started on gabapentin 300 mg daily by his primary care physician 1 week back. The patient started to feel sleepy and subsequently developed altered sensorium and myoclonic jerks. The patient reported to our hospital, and his hemodynamic parameters were normal including biochemical parameters (such as sodium 136 mEq/L, potassium 4.7 mEq/L, and calcium 9.9 mg/dL) and blood sugar (112 mg/dL). Suspecting gabapentin toxicity, serum sample was sent for testing. The patient was given a session of HD for 4 h, and post dialysis he had dramatic improvement. Serum gabapentin level was 27 mcg/mL. The patient and caregivers were counselled regarding the toxicity risk of this medication.

### Case 3

A 70-year-old female diabetic patient with CKD Stage 3 and diabetic neuropathy was our third patient. Her neuropathic symptoms had improved with gabapentin 300 mg twice daily, but lately the patient was feeling sleepy during the day and was confused. Her serum electrolytes and ECG were normal, and blood sugars were reasonably controlled. Suspecting gabapentin toxicity, it was stopped, and the patient had marked improvement. She was put on nortriptyline for neuropathic pain and is doing well on follow up.

## Discussion

In a study which included two cases of myoclonus associated with gabapentin toxicity in the setting of renal disease, the patients settled with HD and peritoneal dialysis (PD). The first patient after discontinuation of gabapentin and two sessions of HD had marked improvement and was discharged with normal renal function, a blood urea nitrogen (BUN) level of 20 mg/dL and creatinine (Cr) level of 1.1 mg/dL, and myoclonus had disappeared. In the same study, the second patient was a 55-year-old man with end-stage kidney disease on PD. The patient's PD treatment was modified from four to six PD exchanges daily. The treatment modification along with discontinuation of gabapentin led to disappearance of myoclonus, and mental status improved within 4 days (7). In patients with renal impairment, the development of myoclonus and neurotoxicity may require withdrawal of gabapentin. Evidence suggests that serum gabapentin concentrations greater than 15 µg/mL are associated with symptomatic toxicity. In patients who have normal kidney function, gabapentin is rapidly cleared based on its short half-life, therefore toxicity is rare. But in patients with kidney function impairment, the threshold for gabapentin toxicity is low. Patients with severe symptomatic toxicity should be considered for dialysis. Both intermittent and continuous forms of renal replacement therapy have been effectively utilized to treat gabapentin-induced neurotoxicity and myoclonus. Neurological sequelae following administration of the drug to patients with renal failure, varying from subtle changes in mental status to drowsiness and coma, have been reported in the literature. However, serious cardiovascular and neurological sequelae seen with ingestion of other anticonvulsants such as carbamazepine and phenytoin are not seen with gabapentin, particularly in patients who have normal kidney functions (4). Gabapentin also finds its use in generalized uremic pruritus in patients on dialysis who fail to respond to antihistamines and/or topical emollients (8).

The molecular weight of gabapentin is 171.24, which is close to the molecular weight of glucose (MW: 180). The low molecular weight, low protein binding, and low volume of distribution make gabapentin amenable to removal using

dialysis modalities (5). While the therapeutic and toxic ranges of plasma serum gabapentin levels have not been definitively established, it is suggested that serum level of 2–15 mcg/mL (2–15 mg/L) is therapeutic (9,10). Patients with toxicity symptoms need monitoring until their symptoms resolve (11). Early gastric lavage, if the ingestion occurred within 1 h of presentation to a health care facility, and activated charcoal help in decontamination. Further measures that have been used include extracorporeal membrane oxygenation, plasmapheresis, and dialysis, in addition to the usual supportive care. There is no specific antidote for the drug. HD may be needed, particularly in patients with impaired renal function. In a series describing gabapentin overdose, symptomatic toxicity effects resolve within 24 h (12). PD also helps in removal of gabapentin. Intensive PD can be used to treat gabapentin toxicity, provided the patient is stable; however, in case of emergency, HD will provide much more rapid removal of gabapentin. To avoid toxicity, it would be prudent to monitor gabapentin concentrations in dialysis patients, particularly after changes to dialysis prescription have been inducted (13).

## Conclusion

Gabapentin is a relatively safe medication, but in certain clinical scenarios, particularly in impaired renal functions, can lead to severe complications. Moreover, it per se can rarely lead to rhabdomyolysis and acute kidney injury.

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