Management of Neuropathic Pain in Dialysis Patients: An Effective Approach with Gabapentin

Sofia Spaia, MD; Maria Tersi, MD; Maria Sidiropoulou MD; Nikolaos Askepidis, MD; Michalis Pazarloglou, MD; Vasiliki Iliadi MD;

The authors are with the Dialysis Unit, Second Hospital of IKA Thessaloniki, Greece.

Hemodialysis patients frequently complain of restless legs syndrome (RLS), hypoesthesia, or pruritus—all of which are attributed to a nervous system disorder due to kidney dysfunction or even to coexistent diseases. These symptoms are difficult to manage and they respond poorly to conventional treatment. In this study, we administered gabapentin, a novel antiepileptic drug which is excreted at 98% unaltered by the kidneys, to 7 hemodialysis patients (4 female, 3 male) from 65 to 75 years of age and at 65 to 70 kg of body weight who suffered from restless legs syndrome (4 patients), pruritus (1 patient), neuralgia (1 patient), and carpal tunnel syndrome (1 patient). Recommended dosing with adjustments for the degree of kidney failure provoked severe somnolence and dizziness affecting all patients. On an “observe and treat” basis, we determined the optimum dose was 50% lower than the suggested dose. Patients responded rapidly with significant improvement on the lower dose schedule. A follow-up period of 8 to 32 months confirmed the good outcome. We determine that administration of gabapentin at bedtime, only on dialysis days, eliminates the side effects with concomitant impressive results. Body weight does not seem to play a major role. No additional dose was needed after the dialysis session.

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In this case series we prospectively administered gabapentin in 7 white dialysis patients (4 female, 3 male) aged 65 to 75 years and who weighed 65 to 70 kg Four patients suffered from RLS, from pruritus, 1 experienced neuralgia to both lower limbs, and 1 had painful carpal tunnel syndrome. Those patients had not responded to previous treatment, which was mainly antidepressants and/or dopaminergic agents. All patients were iron replete with ferritin levels above 200 ng/mL and had hemoglobin levels between 11 and 12 g/dL.

RLS was documented by clinical symptoms and signs and after each patient had answered a questionnaire handled by a neurologist (International Restless Legs Syndrome Study Group questionnaire) that assessed the severity of RLS symptoms over the previous month. Each question had a scale of 0 to 4 points, with 0 being no or minimal symptoms and 4 being severe. The sum of all 10 questions totaled a maximum of 40 points. The 4 patients with RLS experienced moderate to severe symptoms (18–30 points).

Methods

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The other 3 patients with pruritus and neuralgia were given the drug after other medications (mainly analgesics and anti-histaminics) had failed.
The recommended dose of gabapentin in dialysis patients is 100 to 300 mg per day, but on dialysis day an additional dose is given after the session, due to drug clearance through the dialysis membrane. We prescribed 300 mg/day (in a capsule), the minimum available dose of gabapentin in Greece. However, on dialysis day we gave the drug before and not after the dialysis session, aiming to minimize the overall dose as a consequence of its clearance through the dialyzer. Also, a lower-than-recommended dose was finally administered.

Patients were followed up by re-answering qualitatively the original questions asked.

Results

Despite the initial decreased dose, all patients developed severe somnolence and dizziness in a few days. This occurred independently of their body weight. Subsequently, the dose was lowered to 300 mg 3 times per week on dialysis day at bedtime. Side effects subsided rapidly and significant improvement was observed in all patients. The follow-up period of 8 to 32 months confirmed the good outcome. Unintentional withdrawal of the drug in 2 patients led to reappearance of the initial complaints. Remarkably, the latter subsided as soon as gabapentin was re-administered.

Discussion

Gabapentin proved to be quite effective in dialysis patients with neuropathic pain that is difficult to treat. Miczekaktivou and colleagues also showed that gabapentin is significantly better in an open-labeled study than levodopa in the treatment of RLS in elderly patients. Gabapentin has been used in non-dialysis patients for neuropathic pain with excellent results (diabetic neuropathy, post-herpetic neuralgia), and it is thought to be most effective in patients whose symptoms include pain. Indeed, this was confirmed in this case series in patients without RLS. According to published data, by dose titration, the therapeutic effect is already evident by the fourth week when mean dosage is 1,400 mg and it was completed by the sixth week at a dose of 1,855 mg. However, little is known about dosage and titration in renal patients.

The drug is excreted unaltered by the kidney (at 98%), so it is difficult to define the optimum dose for renal patients. Therefore, it should be adjusted according to creatinine clearance. The elimination half-life is 5 to 9 hours for non-renal patients, while in patients with compromised renal function the elimination half-life reaches 132 hours. Additionally, the drug is cleared substantially through the dialyzer. Approximately 35% of the gabapentin dose is recovered in dialysate and mean hemodialysis clearance of gabapentin is reported to be 142 mL/min, approximately 93% of the dialyzer creatinine clearance. However, systemic plasma gabapentin concentrations increased by approximately 30% during the first 2 hours after dialysis as a result of drug redistribution.

Recommended dosing in hemodialysis patients with neuropathic pain that is difficult to treat. Miczekaktivou and colleagues also showed that gabapentin is significantly better in an open-labeled study than levodopa in the treatment of RLS in elderly patients.

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Further and drastic decrease of the drug dose by half resulted in elimination of the side effects. That coincides with data that the elimination half-life of the drug on non-dialysis days averaged 132 hours. Measurement of drug levels was not available to us. However, a rapid improvement of the patient’s condition and elimination of previous complaints were observed with the dose decrease. Accidental withdrawal of the drug resulted in reappearance of the symptoms in 2 patients. This proves the specific drug’s effect in spite of the limitation of our data. Subsequently more patients with neuropathic pain in our unit experienced the beneficial results under the same pattern of administration. Prescribing the drug at bedtime provided adequate night sleep to our patients.

In conclusion, as we have shown, prescriptions of even the low dose of 300 mg per day of gabapentin to dialysis patients provoked side effects. On the other hand, 300 mg of the drug on dialysis days (thrice weekly) gave impressive results. Administration at bedtime could outweigh somnolence provoked by the drug. Body weight, within normal limits, does not seem to affect the clinical result. Availability of a tablet with lower drug concentration in Greece would be desirable for dialysis and older patients.

References

9. Blum RA, Pharm D, Thomas J, et al. Pharmacokinetics of gabapentin in subjects with various...


