Brief Report

Efficacy and Safety of Gabapentin for Uremic Pruritus and Restless Legs Syndrome in Conservatively Managed Patients With Chronic Kidney Disease

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Abstract

Context. Pruritus and restless legs syndrome (RLS) frequently affect patients with chronic kidney disease (CKD) and end-stage kidney disease (ESKD), impacting the quality of life. Gabapentin (1-aminomethyl cyclohexane acetic acid) alleviates these symptoms in hemodialysis (HD) patients, but data are lacking for patients on the conservative pathway.

Objectives. To determine the safety and effectiveness of gabapentin for pruritus or RLS in conservatively managed patients ($n = 34$) with CKD and ESKD.

Methods. This was a single-center retrospective cohort study. We compared dosing and side effects in 34 CKD/ESKD patients with similar patients receiving HD ($n = 15$).

Results. Forty-four percent of conservatively managed patients complained of RLS and/or pruritus; 18% were excluded for a nonuremic cause of symptom. Thirty-four patients were included in the final analysis. The most common starting daily dose of gabapentin was the equivalent of 50 mg (44.1%) or 100 mg (38.2%) daily, with the median daily dose of 100 mg (range 39–455 mg). Side effects occurred in 47% of patients, with 17% discontinuing gabapentin. Gabapentin reduced symptoms of pruritus ($P < 0.001$) and RLS ($P < 0.05$). There was no statistical difference when comparing HD and conservatively managed patients for daily starting dose ($P = 0.88$), median dose ($P = 0.84$), and final dose ($P = 0.18$). Patients conservatively managed were more likely to manifest side effects compared with HD patients (47.1% vs. 14.3%, $P = 0.023$). Dose was not found to be a factor associated with side effects in univariate analysis.

Conclusion. Gabapentin is a viable treatment for conservatively managed CKD and ESKD patients with pruritus and/or RLS, but side effects are common. Gabapentin should be used with caution although higher doses do not appear to be a factor associated with side effects. J Pain Symptom Manage 2015;49:782–789. © *2015 American Academy of Hospice and Palliative Medicine.*
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Key Words
Gabapentin, pruritus, restless legs syndrome, dialysis, end-stage kidney disease, conservative management

Introduction

Patients with end-stage kidney disease (ESKD) are heavily burdened with symptoms. Two of the most common are uremic pruritus and restless legs syndrome (RLS). RLS is a neurological disorder characterized by sensorimotor symptoms, such as paresthesia and restlessness mainly affecting the lower limbs, occurring during rest in the evening or overnight, and at least partially relieved by movement.[1] The prevalence of RLS in patients with ESKD on hemodialysis (HD) ranges from 5% to 62%,[2–5] whereas pruritus affects 22–42%.[6–9]

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Singularly or in combination, pruritus[9] and RLS[4,5] have a profound effect on sleep, quality of life, and mortality. Their aggravating nature and unpredictability can make life a misery to patients who suffer from these symptoms.

Gabapentin (1-aminomethyl cyclohexane acetic acid) is a structural analogue of gamma-aminobutyric acid developed for the treatment of epilepsy. It is effective in managing both uremic pruritus[10–12] and RLS[3,13,14] in ESKD patients receiving renal replacement therapy (RRT). However, to date, there have been no studies examining the use of gabapentin for the treatment of RLS symptoms in patients with ESKD who are managed conservatively. Only one study examined its use in uremic pruritus for patients with chronic kidney disease (CKD) managed conservatively.[15] This is especially important because this subgroup of patients is elderly, frail, and often has multiple comorbidities. As renal function deteriorates, their ability to renally clear gabapentin decreases, with an increased risk of developing side effects. Therefore, we set out to determine the effectiveness of gabapentin in the treatment of pruritus and RLS in patients conservatively managed for CKD, including patients with ESKD, and to establish its safety in this group.

Methods

We conducted a retrospective single-center cohort study. All patients for conservative management of ESKD and CKD referred to the Renal Supportive Care Clinic (RSC-C) in a tertiary care facility (St. George Hospital, Sydney) between April 2010 and June 2013 were identified. We defined conservative management in ESKD as any patient who did not wish to commence dialysis or undergo kidney transplantation or who did not pursue dialysis treatment based on medical advice and/or ethical grounds as a shared decision. Inclusion criteria were patients with CKD Stage II–V on a nondialysis conservative pathway who were older than 18 years and attended the outpatient RSC-C at least twice.

A palliative care physician reviewed all patients for the duration of the study. We excluded patients with an identifiable non-CKD cause of RLS or pruritus, incomplete/missing data, and incomplete questionnaires, or who started gabapentin before attending the clinic. We simultaneously identified dialysis patients referred to the RSC-C for symptom management for comparison of differences in dosing and side effects. This study was approved by the Human Research Ethics Committee, South Eastern Sydney Local Health District (reference number HREC/10/STG/121).

Sociodemographic, clinical, and laboratory data were obtained at the initial review, including age, gender, body mass index, smoking status, and history of diabetes and cerebrovascular disease. Laboratory parameters included serum urea (mmol/L), creatinine (umol/L), estimated glomerular filtration rate, albumin (g/L), calcium (mmol/L), phosphate (mmol/L), HbA1c (%) for diabetic patients, hemoglobin (g/L), C-reactive protein (mg/L), and parathyroid hormone (pmol/L).

Patients were asked to complete the Palliative care Outcome Scale-Symptoms (POS-S) Renal,[16] a validated symptom inventory instrument, on the first visit before commencing gabapentin and on each subsequent visit. The POS-S Renal was used to assess progress and management of symptoms. We apportioned a numerical figure to the level of reported severity (0–4 according to whether the reported severity was not at all, slight, moderate, severe, or overwhelming). The scores for pruritus, RLS, and total symptom (TS) were recorded at the initial visit before gabapentin was started as a baseline. All subsequent visits were compared with this.

The usual starting dose of gabapentin in patients with ESKD was 100 mg on alternate nights and in CKD Stage III–IV, 100–200 mg nightly. The dose was increased if no symptomatic relief was achieved while documenting, monitoring, and informing patients of potential side effects. We requested a compounding pharmacist to arrange 25 mg tablets to facilitate small incremental increases in dosing for patients who manifested side effects at higher doses. We documented the initial dose of gabapentin, the daily dose between the first clinic visit and the final clinic visit, and the final dose of gabapentin at the last clinic visit within the study period. When gabapentin was administered on alternate days or once every three days, we calculated the average daily dose. We documented duration of therapy, changes in the POS-S Renal, side effects, and cessation of gabapentin.

Our primary outcomes were 1) changes in POS-S Renal score for pruritus, RLS, and TS, 2) side effects and need for cessation of gabapentin, and 3) doses of gabapentin used. We compared outcomes in patients on the conservative pathway with those on HD receiving gabapentin for symptom control.

Statistical Analysis

Categorical data are expressed as frequency (%) and compared using the Chi-squared test. Continuous data are expressed as medians with interquartile ranges (25th–75th percentile) or mean with SD and compared by the Student's t-test or Mann-Whitney *U* test as appropriate. For comparison between POS-S Renal at baseline and on subsequent visits, we used the Wilcoxon signed rank test. We did not censor patients who subsequently ceased gabapentin. Univariate

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