Clinical Note

Use of Pregabalin in the Management of Chronic Uremic Pruritus

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Abstract

Context. Uremic pruritus (UP) affects many patients suffering from chronic kidney disease (CKD) and has a negative impact on quality of life and survival. It has become increasingly evident that central transmission and sensitization processes similar to those observed in chronic pain are important mechanisms of pruritus.

Objectives. To test the potential role of pregabalin in reducing the intensity of UP in CKD patients.

Methods. We prospectively collected data on CKD patients who suffered from severe intractable pruritus. Patients were asked to record the intensity of pruritus on a visual analogue scale.

Results. Twelve patients were studied. The average pretreatment pruritus score was 9.7 ± 0.9 and decreased to 3.7 ± 2.35, 3.2 ± 1.75, and 3 ± 1.5 after one, four, and 24 weeks of treatment, respectively ($P < 0.05$). The positive effect of pregabalin was demonstrated during the first week of therapy in six patients. Most patients required 25 mg a day. Pregabalin was well tolerated, with somnolence and dizziness developing in two patients.

Conclusion. We demonstrated dramatic improvement of long-standing UP after the initiation of pregabalin. We suggest that pregabalin can be used safely in CKD but careful titration of the dose is required to obtain an optimal response and minimize the possible adverse effects. J Pain Symptom Manage 2013;45:776–781.

Key Words
Pregabalin, chronic renal failure, uremic pruritus, symptom control

Introduction

Uremic pruritus (UP) is a common and distressing problem in patients with advanced chronic kidney disease (CKD) or end-stage kidney disease. The prevalence of UP varies widely among studies and seems to have declined over the last 30 years (from 85% in the 1970s and 50%–60% in the 1980s to 22% in the 2000s).[1]

It has become increasingly evident that central transmission and sensitization processes similar to those observed in chronic pain are important mechanisms in the pathogenesis of chronic pruritus.[2] Pruritus may arise from

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a diminished threshold of perception and abnormalities of nerve terminals and fibers that are commonly found in hemodialysis patients.[3] Therefore, we hypothesized that a drug designed as a potent therapy for neuropathic pain also might have a favorable effect on UP.

Pregabalin is an anticonvulsant drug used for neuropathic pain and as an adjunct therapy for partial seizures with or without secondary generalization in adults. It binds to the α2δ subunit of the voltage-dependent calcium channel in the central nervous system and reduces calcium influx into nerve terminals. Pregabalin also decreases the release of neurotransmitters such as glutamate, noradrenaline, and substance P and inhibits the release of calcitonin gene-related peptide, a mediator of itching.[4]

We routinely use pregabalin for the treatment of neuropathic pain in patients on hemodialysis. In addition to neuropathic pain, several of our patients have complained of severe chronic pruritus, and after pregabalin treatment, significant improvement in the intensity of pruritus was observed. This study presents the prospectively collected data on these patients.

Methods

Patient Population

We prospectively collected data on adult hemodialysis patients and on patients from the nephrology outpatient clinic, with CKD Stage III or IV. All hemodialysis patients received outpatient treatment using B. Braun CE0123 machines (B. Braun Melsungen AG, Melsungen, Germany). The dialysis sessions were for four hours each three times per week. Polysulfone hollow fiber dialyzers (polysulfone membranes; B. Braun Melsungen AG) and bicarbonate-based dialysate were used throughout the study. The blood flow rate varied between 200 and 300 mL/minute but was kept constant for a given patient.

Study Protocol

Patients with severe pruritus unresponsive to antihistamines and local moisturizers were eligible to receive pregabalin (Lyrica®; Pfizer, Berlin, Germany). These patients were asked to record the severity of their pruritus on a visual analogue scale (VAS) before the initiation of pregabalin therapy and weekly thereafter. The VAS was a 10 cm horizontal line marked from 0 (denoting no itch) to 10 (denoting the severest itch). Patients were excluded if they suffered from allergy to pregabalin, any acute illness, liver cirrhosis, decompensated heart failure, inability to give informed consent, or poor compliance. The initial dose was 25 mg administered orally thrice weekly at the end of the hemodialysis session. If no improvement in symptoms was observed by the end of the first week of therapy, the dose was increased to 25 mg/day and, subsequently, to 50 mg/day. Study participants were followed for 24 weeks. Adverse effects classified by severity and possible relation to the study medicine were recorded.

The following demographic and clinical characteristics were recorded prospectively: age, gender, history of heart failure, coronary artery disease, cause of end-stage renal disease, diabetes, hypertension, hyperlipidemia, peripheral vascular disease, cerebral vascular accident, time and duration of dialysis, predialysis and postdialysis weights, interdialytic weight gain, and pre- and postdialysis systolic and diastolic blood pressures. Medications, including antihypertensive agents, lipid-lowering agents, antihistamines, and local moisturizers, and values of the most recent monthly laboratory studies (hemoglobin, divalent ions, parathyroid hormone [PTH], creatinine, blood urea nitrogen, sodium, potassium, lipid profile, total protein, albumin, liver enzymes, adequacy of dialysis expressed as Kt/V, C-reactive protein, thyroid-stimulating hormone, iron, transferrin, and ferritin) also were recorded.

The study was approved by the Institutional Review Board of Shaare Zedek Medical Center, and all participants gave informed consent.

Study End Points and Statistical Analyses

The primary end point was a reduction in the VAS of ≥50% during the first two weeks of pregabalin administration. VAS scores were expressed as mean ± SD, and post-treatment values were compared with baseline scores using one-way analysis of variance, with differences reported as significant if $P < 0.05$. All analyses were conducted using SPSS software version 17 (SPSS, Inc., Chicago, IL).