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Review

Alejandro Marfil,¹ Ana Teresa Garza Martínez,¹ Jesús Anastacio Cantú,¹ María Fernanda Siller Reyes,¹ Juan Gilberto González de la Cruz,¹ Silvia Barrera Barrera.¹

¹Headache and Non-Oncological Chronic Pain Clinic
Neurology Service
University Hospital "Dr. J.E. González"
Autonomous University of Nuevo León.

Keywords

Neurogenic pruritus, treatment, levetiracetam.

Neurogenic Pruritus: Response to low-dose levetiracetam. Report of four cases

Prurito Neurogénico: Respuesta a dosis bajas de Levetiracetam.
Report of four cases

Abstract

Introduction: There is no satisfactory treatment for neurogenic pruritus. We present a series of four patients treated successfully with low dose levetiracetam.

Objective: To present the first series of patients with neurogenic pruritus treated successfully with levetiracetam.

Methods: Four case reports

Results: The average interval for clinical response was 3.7 days, and remained while treatment lasted. Only one case had a non-intentional, positive, treatment and retreatment test. There were no side effects attributable to the medication.

Conclusion: At least until this report elaboration, treatment was not suspended, so we cannot speculate about treatment duration.

Resumen

Introducción: El prurito neurogénico no tiene un tratamiento satisfactorio. Presentamos una serie de pacientes tratados exitosamente con dosis bajas de levetiracetam.

Objetivo: Presentar la primera serie de casos de pacientes con prurito neurogénico tratado exitosamente con levetiracetam.

Métodos: Reporte de cuatro casos

Resultados: El promedio del intervalo para la respuesta clínica fue de 3.7 días, y se mantuvo mientras duró el tratamiento. Sólo en el caso 1 hubo una prueba, no intencional, de tratamiento y retratamiento positiva.

Conclusiones: Al menos hasta la elaboración del reporte, no se suspendió el tratamiento, así que no podemos especular sobre la duración del mismo.

Palabras clave

*Prurito neurogénico,
tratamiento, levetiracetam.*

Corresponding author:

Dr. Med Alejandro Marfil.

Clínica de Cefaleas y Dolor Crónico No Oncológico, Servicio de Neurología, Hospital Universitario, "Dr. J.E. González", Universidad Autónoma de Nuevo León.

Madero y Gonzalitos s/n Col Mitras Centro, Monterrey, NL, México. CO: 64060.

Tel. +52-81-83471059.

Correo-e: alejandro.marfilrv@uanl.edu.mx

Introduction

Pruritus is a universal symptom. The etiology can vary between dermatological, systemic, neurological, and psychogenic diseases.¹ Neurogenic pruritus has been described accompanying lesions in the central and peripheral nervous system, including neuropathies, tumors, cerebral vascular disease, multiple sclerosis, spinal cord, and encephalon. (Table 1)²

In recent years there has been considerable progress understanding its pathophysiological complexity. To our knowledge, neurogenic pruritus has two neural pathways: receptor-specific (histaminergic), and polymodal-C fibers—from *Mucuna pruriens* (velvet bean, pica-pica, cowhage). At the medullary level (dorsal column) there is an afferent modulation of both pathways by means of a process that involves GABA.^{1,3} (Figure 1) It shares some similarities with pain in terms of the anatomical pathways and the brain areas that are activated by stimulation. (Figure 2)

Several GABAergic agents have been used to treat this condition, such as gabapentin and pregabalin, both with variable results.^{4,5}

Levetiracetam (LEV) is an antiepileptic drug with a mechanism of presynaptic action, coupling with the 2-a protein of the presynaptic neuronal vesicles, decreasing the release of Ca from the intracellular deposits, thus antagonizing the GABA negative feedback. In the end, it is a GABAergic drug. We found no publications in PubMed after cross-searching the terms pruritus, neurogenic pruritus, and levetiracetam.

In 2014, at the annual meeting of the American Academy of Neurology, a poster was presented of a case report on the success of therapy with LEV and tiagabine (TGB) in post-mastectomy neurogenic pruritus. The author explained its effect through the GABAergic effect of both.⁶

We will report here our experience with four patients suffering from neurogenic pruritus treated with low doses of LEV.

Table 1. Causas de prurito neurogénico (modificado de¹)

Localization	Representative diseases
Peripherals (receptors, nerves, roots)	Polyneuropathies Post-herpetic Brachioradial pruritus Notalgia paresthetica Trigeminal trophic syndrome Associated with post-burn keloid
Spinal cord	Transverse myelitis Neoplasia Cavernous hemangioma, AVM Post-traumatic Brown-Séquard
Encephalon	Brainstem or subcortical cerebrovascular disease Demyelinating disorders Neoplasia Paraneoplastic syndromes Creutzfeldt-Jakob disease

Figure 1. The peripheral pathways of pruritus in blue and red, pain is in green. Histamine and pica-pica stimulate the epidermis and dermis, respectively. The histaminergic impulses travel by mechanically insensitive C fibers. The others by polymodal C fibers—both to the dorsal horn where there is modulation by inhibitory interneurons. (Figure by author.)

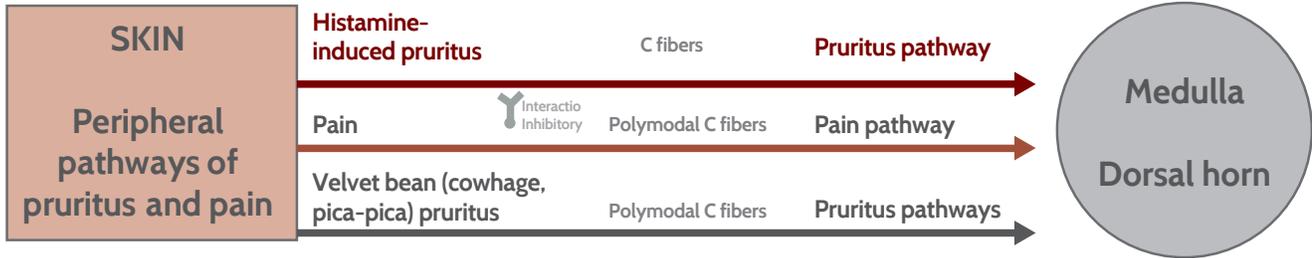
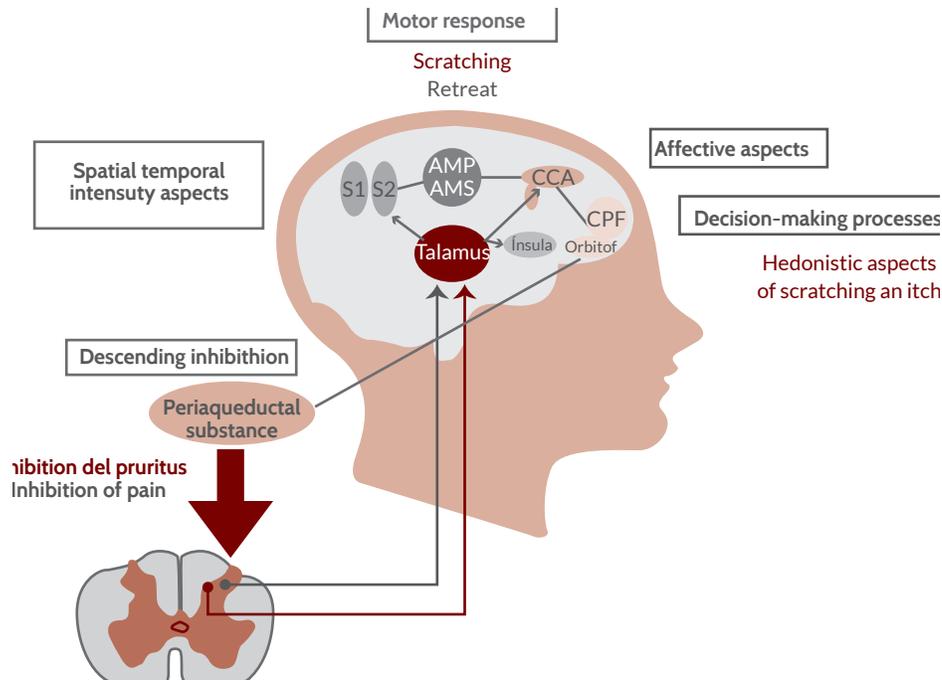


Figure 2. Brain areas activated by pain or pruritus. The thalamus, anterior cingulate, prefrontal and orbitofrontal cortex, primary and secondary sensory cortices, as well as the cerebellum, are activated by both. Functions of the different brain areas in black squares. Adapted from: Ständer S, Raap U, Weisshaar E, Schmelz M, Mettang T, Handwerker H, Luger TA. Pathogenesis of pruritus. JDDG; 2011 • 9:456–463.



Objective

Presentar la primera serie de casos de pacientes con prurito neurogénico tratado exitosamente con LEV.

Case report

Case 1. Female patient, age 70, evaluated for herpes zoster (HZ) in T5, successfully treated with acyclovir; however, the patient developed post-herpetic neuralgia with intense pruritus along the upper edge of the painful area. Treatment with pregabalin ameliorated only the pain. Topical treatments relieved the pruritus temporarily. Treatment with LEV, 250 mg in a single night dose, eliminated the pruritus after two days. The effect lasted while she received LEV. On one occasion the treatment was suspended and the pruritus recurred. When treatment was reinitiated, the same result when first starting this treatment was obtained. At the last follow-up visit, four months later, the patient remained sans pruritus.

Case 2. Female patient, age 75, with a diagnosis of generalized anxiety disorder developed pruritic skin lesions. No dermatological diagnosis. After the remission of the dermatological lesions, the patient complained of pruritus with sock distribution. Local treatments with hydroxyzine were ineffective. A dose of 250 mg LEV at night decreased the itching by 70% in six days. The benefit was maintained for six months, then the patient died due to an unrelated illness.

Case 3. Female patient, age 25, with T10 intercostal neuralgia, probably compressive, treated in another center with a rhizotomy, which failed, managed with polypharmacy, including opioids. In addition to the great neuralgic pain, she developed intense, continuous pruritus along the upper and lower edges of the painful area. With a 250 mg dose of LEV at night, the pruritus disappeared in three days but there was no effect on the pain.

Case 4. Male patient, age 80, with early Alzheimer's disease, who developed HZ in right V1. After successful treatment with acyclovir, he complained of post-herpetic pain and itching along the edge of the painful area. The 250 mg night dose of LEV eliminated the pruritus in four days, with no effect on pain or cognitive performance.

Discussion

Pruritus can be a serious clinical problem with a great impact on quality of life. The cases presented are mostly of peripheral origin; however, considering the continuous clinical presentation of pruritus in the absence of skin lesions, the proposed pathophysiology of a central mechanism of neurogenic pruritus (Figure 2) and the central gabaergic mechanism in LEV, we can assume that the therapeutic effect is central, probably at the level of the dorsal horn, modulating the peripheral afferents.

The average interval for clinical response was 3.7 days, and it was maintained while the treatment lasted. Only one case had an unintentional trial of treatment and retreatment, and it was positive. In the other cases, at least until the writing of this report, the treatments were not suspended, so we cannot speculate on their duration.

Although the series is short, considering the excellent and rapid response to treatment, and the inconsistent response to previously published treatments, we think that this work could be seen as a "proof of concept" to perform prospective studies of greater magnitude.

Conclusion

The LEV seems to be a possibility of treatment for neurogenic pruritus, although we do not know the time in which the management must be maintained.

Conflicts of interest

The authors state that there are no relevant conflicts of interest in this study.

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