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# LETTER TO THE EDITOR

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## Topical Gabapentin as Add-on Therapy for Trigeminal Neuralgia. A Case Report

Dear Editor,

Trigeminal neuralgia is a painful process especially affecting the elderly, a population prone to suffering adverse effects following systemic administration of drugs. The use of topical medications can be envisaged in these situations where standard treatment is not possible.

We report here the efficacy of 6% topical gabapentin in a female patient suffering idiopathic trigeminal neuralgia. The patient (age 81 years) was referred by her family physician to the Pain Unit of the hospital in December 2015 following the acute exacerbation of her trigeminal neuralgia, previously diagnosed by the Neurology Department. The affected area corresponded to the maxillary division of the nerve; no structural abnormalities had been detected by computerized axial tomography, and she was unresponsive to carbamazepine treatment as doses higher than 400 mg per 12 hours could not be prescribed due to the presence of adverse effects, the same trend being described after pregabalin (25 mg/12 hours). In this first consultation, she described suffering from paroxysmal attacks of pain of 10 to 15 minutes' duration from five years previously and every six months approximately, triggered by light touch or mouth movement such that sleeping, talking, or eating were impeded. Her social functions were completely nullified and, in addition, this paroxysmal pain was accompanied by concomitant persistent pain. She had been treated with transdermal fentanyl patches (150 μg/hour) and oxycodone/naloxone (30/15 mg/12 hours) that were ineffective in counteracting these painful symptoms. In addition, due to pain and medication, she was depressed, exhausted, and drowsy. Apart from recommending a future evaluation at the Neurosurgery Department in order to attempt an interventional procedure [1], drug treatment was readjusted: Oxycodone/naloxone was withdrawn and low doses of carbamazepine (50 mg/12 hours), together with clonazepam (0.5 mg/at night, just in case carbamazepine was ineffective), were prescribed while maintaining fentanyl patches. Five weeks later, in a second consultation, she referred to only a slight amelioration, especially at night, but painful manifestations persisted during the day. Because we aimed to progressively decrease fentanyl but kept in mind that an increase of carbamazepine would probably be impossible due to the production of adverse effects, we considered the use of an analgesic topically administered an add-on therapy. Although carbamazepine constitutes the firstline therapy in the medical treatment of trigeminal neuralgia [2], its topical administration has not been previously reported in this pathological setting. Other topical treatments shown to be useful, mainly lidocaine [3,4], were discarded due to the large surface area affected, which would make it difficult to maintain the patch. Thus, we envisaged using gabapentin, based on the reported efficacy of the

**Table 1** Pain scores before (basal) and after local treatment with 6% gabapentin

| | Basal, prior to cream (retrospective evaluation) | 10 weeks with 6% gabapentin cream treatment | 20 weeks with 6% gabapentin cream treatment |
|---|---|---|---|
| NRS (/10) | 9–10 | 0 | 3–4 |
| BPI-SF total (/110) | 94 | 2 | 22 |
| Pain intensity subscale (/40) | 34 | 2 | 14 |
| Pain impact subscale (/70) | 60 | 0 | 8 |
| DN4 (/10) | 4 | 0 | 1 |

BPI-SF = Brief Pain Inventory-Short Form; DN4 = neuropathic pain diagnostic questionnaire; NRS = numerical rating scale.

topical administration of this anticonvulsant in some limited cases of neuropathic pain [5,6].

Following compassionate use approval by the Hospital Ethical Committee, a cream containing 6% gabapentin was prepared by the hospital's Pharmacy Service; 45 g of Pentravan o/w emulsion (Fagron, Spain) were added to a mixture of gabapentin 3 g (Fagron, Spain) in 2 mL of purified water (Grifols), based on the previous description [5]. The patient signed the informed consent and was taught to apply the cream three times per day to the painful area. One month later, she (and her relatives) came to consultation very happy as she had experienced considerable amelioration of her pain and was able to cope with usual daily activities including speaking and social relationships; she also indicated that paroxysmal pain only appeared when chewing. She noted relief of persistent pain five to 10 minutes after applying the gabapentin cream and lasting for about three hours. During the follow up visits, the reported analgesic effect of the cream persisted and the doses of fentanyl were tapered until she was maintained with only a low dose of carbamazepine and clonazepam as well as tramadol/paracetamol (37.5/325 mg as needed). No skin alterations or other problems arose during treatment.

The patient was so severely affected in her initial visits, such as being unable to speak and drowsy, that we could only evaluate her level of pain with questionnaires during the subsequent consultations. Thus, we evaluated her pain values using a 0 to 10 numerical rating scale, the Spanish versions of the Douleur Neuropathique en 4 questions and the Short Form of the Brief Pain Inventory questionnaires, at the visit 10 weeks after applying the cream. At that time, she was asked to fill in, retrospectively, the questionnaires related to her previous level of pain (Table 1). The values obtained 20 weeks after applying the cream showed that her pain was not so well controlled as initially (Table 1). As she continued to experience considerable relief after applying the gabapentin cream and no tolerance or episodes of augmentation have been reported following the use of gabapentin [7,8], the reason might be the natural course of the process. Six months after starting topical gabapentin treatment, her pain was controlled with carbamazepine (100 mg/12 hours), clonazepam, and the gabapentin cream, with no drowsiness or evident adverse effects and being able to cope with social activities.

The analgesic effect of topical gabapentin is probably locally produced as the reported peak plasma concentration of a preparation of 10% gabapentin across human skin after topical application could be 0.01 μg/mL, a much lower quantity than that reported for orally administered gabapentin (2–20 μg/mL) [5]. Also, the pharmacological mechanism of the antiallodynic effect of gabapentin is derived from the blockade of the accessory $\alpha_2\delta$-1 subunit of voltage-dependent calcium $Ca_v2.2$ channels [9] that is expressed, among other sites, in medium-sized and small (peptidergic) dorsal root ganglia neurons [7]. In experimental models of neuropathic pain, the upregulation of $\alpha_2\delta$-1 subunits in trigeminal ganglia and their increased trafficking to presynaptic terminals has been demonstrated [9]. Thus, it could be thought that, in this setting, gabapentin might induce its local analgesic effects by blocking the $\alpha_2\delta$-1 subunits present in nociceptive neurons.

Considering, on the one hand, the analgesic efficacy of local gabapentin previously reported in neuropathic pain syndromes [5,6] and, on the other hand, the "in vitro" demonstration that the concentrations of gabapentin achieved in a similar pharmaceutical preparation are not cytotoxic to keratinocytes [10], the use of topical gabapentin could represent an attractive analgesic strategy, especially in painful pathologies affecting the elderly, who are less tolerant to systemic drugs. It must be remarked, however, that we describe here the temporal alleviation of pain in a case of idiopathic trigeminal neuralgia of unknown origin and that other types of trigeminal neuralgia (classical due to vascular compression of the nerve root or secondary to a neurologic disease) may not necessarily benefit from this particular analgesic strategy as the underlying pathogenic mechanisms are different [11]. Future studies are needed to evaluate the efficacy of topical gabapentin in the treatment of trigeminal neuralgia or related types of pain.

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# LETTER TO THE EDITOR

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## High-Frequency Spinal Cord Stimulation at 10 kHz for the Treatment of Chronic Neuropathic Pain After a II–III Degree Burn

Dear Editor,

High-frequency spinal cord stimulation at 10 kHz (HF10 therapy) has proven effective for the treatment of chronic pain of different etiologies [1,2]. We would like to present an interesting case describing the use of HF10 therapy for the treatment of a patient with chronic neuropathic pain after grade II–III burns in the lower legs. In addition to significant pain relief, HF10 therapy also demonstrated positive effects on the wound healing process.

A 54-year-old healthy man who suffered a burn accident in March 2008 with grade II–III burns in the lower legs was hospitalized in a primary care unit. Skin transplants were not done, and the wounds were instead left to heal by secondary intention. The wounds covered 80% of the