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# Eslicarbazepine acetate for trigeminal neuralgia

## Acetato de eslicarbazepina en neuralgia del trigémino

*Dear Editor:*

It was with great interest that we read the article by Alcántara Montero and Sánchez Carnerero on the usefulness of eslicarbazepine acetate (ESL) for neuropathic pain, headache, and cranial neuralgias.[1] The authors conducted a systematic review of the literature on the treatment of craniofacial pain with ESL, concluding that insufficient evidence is available to recommend ESL for these disorders. We concur that the lack of published studies analysing ESL in different models of neuropathic pain is striking, considering that several studies on the topic have been presented in previous congresses. As the authors rightly point out, this may be due to a publication bias: those studies may not have been published due to negative findings. However, after the study by Alcántara Montero and Sánchez Carnerero was accepted for publication in *Neurología*, our study group published the first study into the usefulness of ESL for the treatment of trigeminal neuralgia in humans.[2]

We conducted an open-label, multi-centre, retrospective intention-to-treat analysis of 18 patients, 15 of whom were women.[2] Mean age in our sample was 65.2 years (range, 28-92) and mean follow-up time was 21.1 months (range, 7 days to 78 months). Four patients met criteria for classical trigeminal neuralgia, 3 had secondary trigeminal neuralgia, and 11 had idiopathic trigeminal neuralgia. The main study variables were pain intensity and frequency. Both variables improved significantly after treatment: pain intensity improved from a median of 9.5 points (visual analogue scale, 0-10) to 2.5 points after treatment ($P < .001$), and pain frequency decreased from 70 episodes per week before treatment to 0.37 episodes after treatment ($P < .001$). Sixteen patients (88.9%) responded to treatment with ESL, with all symptoms resolving in 8 (44.4%). These results are noteworthy, since most patients in our series were refractory to several other treatments (mean of 2.1 previous treatments). Eleven patients (61%) presented adverse reactions, which led to treatment discontinuation in 4 cases. Two patients (11%) presented hyponatraemia, which in one case was severe (124 mmol/L). This rate is higher than those reported in previous studies[3]; in our experience, this is not a rare complication of ESL. Therefore, we recommend close monitoring of sodium levels in patients treated with ESL, as occurs with those receiving carbamazepine and oxcar-

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bazepine. Despite the aforementioned adverse reactions, 88.9% of our patients reported good tolerance to ESL.

Multi-centre phase 2 and 3 clinical trials of ESL for painful diabetic neuropathy and postherpetic neuralgia did not show greater efficacy than placebo.[1] These findings stand in contrast with our own. The reason for these differences is unclear, but they may at least partly be explained by the different pathophysiological mechanisms of these neuropathies. Trigeminal neuralgia is characterised by demyelination of A-δ fibres; it has been hypothesised that paroxysmal attacks result from ectopic afterdischarges in damaged axons, triggered and amplified by ephaptic conduction and crossexcitation transmitted by afferent A-β fibres after trivial sensory stimuli.[4] ESL inhibits voltage-dependent sodium channels in the slow inactivation phase, stabilising the neural membrane and suppressing ectopic discharges from hyperexcitable fibres. However, the drug may not be as effective in suppressing continuous hyperactivity secondary to lesions to unmyelinated C fibres, which cause sustained depolarisation of these fibres as well as central sensitisation, particularly in the case of persistent neuropathies, such as diabetic neuropathy.[5]

Carbamazepine and oxcarbazepine currently constitute the first line of treatment for trigeminal neuralgia.[6–8] ESL has a similar action mechanism to that of other dibenzazepines, but it presents several advantages over these: linear pharmacokinetics, reduced enzyme induction, fewer drug-drug interactions, and simpler dosage. In the light of these considerations, ESL may also be useful for trigeminal neuralgia. ESL had been shown to be efficacious in animal models of trigeminal neuralgia,[9] but had not previously been studied in humans for this indication.

Future studies should aim to corroborate our findings and address the limitations of our study. In any case, our results suggest that ESL may be an efficacious, well tolerated treatment for trigeminal neuralgia, even in refractory cases.

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## Conflicts of interest

The authors have no conflicts of interest to declare.

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