Lacosamide in the Treatment of Trigeminal Neuralgia Refractory to Conventional Treatment Due to Severe Leukopenia Induced by Anticonvulsants †

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1. Background

Trigeminal Neuralgia (TN) is one of the most frequent and severe types of neuropathic facial pain encountered by clinicians [1]. The first line medical approach generally involves treatment with first and second generation anticonvulsants [2]. However, unfavorable adverse events impair compliance with the treatment, especially in relation to elderly patients. Lacosamide (LCM) is a third-generation anticonvulsant drug; it is a functionalized amino acid, with a multimodal mechanism of action which is not completely clear (Table 1 and Figure 1) [3,4]. It has also come into consideration as a treatment for neuropathic pain.

We have aimed to investigate the efficacy and safety of LCM as a monotherapy in a case of TN who had not responded positively to previous treatments on account of severe leukopenia induced by several of the anticonvulsants previously used.

Table 1. Mechanism of action and advantages of treatment with Lacosamide.

| Mechanism of Action of Lacosamide                 | Advantages of Treatment with Lacosamide                       |
|--------------------------------------------------|----------------------------------------------------------------|
| Enhancing slow inactivation of VGSC peripheral   | Excellent oral bioavailability                                 |
| (Na-1.7 and Na-1.3) and central (Na-1.7)         | Minimal serum protein binding                                  |
| Stabilization of hyperexcitable neuronal membranes| Excreted unchanged by the kidney                               |
| Inhibition of neuronal firing                     | Drug-drug interaction are minimal                               |
| Binds CRMP-2 changes in axonal outgrowth          | No regular blood tests are recommended                        |

VGSC: Voltage-Gate Sodium Channels; CRMP-2: Collapsing Response Mediator Protein 2.
2. Presentation of the Case

A 60-year-old female patient was referred to the Oral Medicine Unit of the University Hospital of Federico II of Naples due to an acute exacerbation of TN, previously diagnosed by the Neurology Unit of our University.

The severe and unilateral pain was in the right side of her face, characterized by paroxysms of a strong stabbing nature extending in the sensory distribution of the maxillary and mandibular trigeminal right area and described as like an electric shock. The pain lasted only for seconds, occurring over intervals of a few minutes, and was triggered by swallowing or touching the affected area, without any autonomic or other neurological symptoms.

The patient was refractory to previous treatments (gabapentin, carbamazepine, lamotrigine and pregabalin) in terms of both the absence of any pain relief and the appearance of adverse events of leukopenia. We requested a routine blood test including a Complete Blood Count (CBC), glucose, electrolyte, blood urea nitrogen and creatinine levels, the erythrocyte sedimentation rate and an ECG evaluation. All results proved to be within normal limits. A Magnetic Resonance Imaging (MRI) of the brain and brainstem with and without intravenous paramagnetic contrast was required and proved to be normal except for a few subcortical white matter hyperintensities. An oro-facial evaluation and battery scales for an assessment of pain intensity and an evaluation of psychological profile were performed.

We started the treatment with a low dosage of oxcarbazepine (300 mg/daily) and re-evaluated the patient with a request for a blood examination after one month. We discovered that the WBC count had decreased from 5500 to 1900 cells/µL. We waited until the WBC had returned to a normal level and we started the treatment with 100 mg twice/daily of LCM. Pain relief was obtained in three weeks of treatment without any variations in the white blood cell count. The value of white blood cells was evaluated every month for the first six months of treatment and no changes have been detected. Currently, the patient takes a maintenance dosage of 100 mg/daily without any adverse
events, remaining in a state of complete well-being without pain and with an improvement of psychological profile.

3. Conclusions

LCM has shown efficacy and a good safety profile. It may be useful for patients who are either subject to refractory TN which is not responsive to conventional therapy or are affected by significant adverse side effects.

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