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Review Article

Use of Carbamazepine in the Treatment of Trigeminal Neuralgia: Clinical Experience at the "Manuel Velasco Suárez" National Institute of Neurology and Neurosurgery

De La Fuente Sosa Jorge Alfonso, Revuelta Gutiérrez Rogelio*

"Manuel Velasco Suárez" National Institute of Neurology and Neurosurgery (INNN), Mexico City, Mexico

***Corresponding Author:** Revuelta Gutiérrez Rogelio, Manuel Velasco Suárez" National Institute of Neurology and Neurosurgery (INNN), Mexico City, Mexico

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Abstract

Trigeminal Neuralgia (TN) is a debilitating cranial neuropathy characterized by paroxysmal, stabbing, unilateral pain that severely affects patients' quality of life; it is also known as "suicide pain" due to the significant impact it has on mental health.Carbamazepine (CBZ) has established itself as the first-line pharmacological treatment worldwide and in the clinical practice of the INNN, a national referral center in Mexico.This research expands the literature review on the mechanism of action, efficacy, safety, limitations, and institutional experience of the INNN in more than 800 patients treated over 20 years.Key publications from the INNN (Santos-Franco et al., 2005; Revuelta-Gutiérrez et al., 2003) and complementary Mexican studies are analyzed, along with international guidelines (AAN-EFNS 2008).CBZ offers a favorable initial response in >70–80% of cases (significant reduction in paroxysms), acting as a voltage-dependent sodium channel blocker and even serving as a diagnostic therapeutic test.However, it causes tachyphylaxis (progressive loss of efficacy), requires dose escalation (600–1,600 mg/day), and causes frequent adverse effects (somnolence, ataxia, hyponatremia, hematologic and hepatic toxicity), which limits its long-term use and justifies the transition to surgical treatment (primarily Microvascular Decompression [MVD]) in refractory or intolerant patients.In a Mexican hospital study involving referrals to the INNN, CBZ was used in 86.8% of in-hospital cases, achieving pain control in most patients at discharge, although many patients presented with poor prior pain control.It is concluded that, in the context of INNN, CBZ remains the cornerstone of comprehensive management (pharmacological + selective surgical), but its safety profile and the natural course of the disease favor early non-destructive interventions such as MVD to achieve lasting relief and functional preservation. Practical recommendations are proposed, and areas for future institutional prospective research are identified.

Keywords: Carbamazepine; Drug Therapy; INNN; Microvascular Decompression: Trigeminal Neuralgia

Introduction

Trigeminal Neuralgia (TN), historically known as "**tic douloureux"**, is one of the most intense facial pain syndromes described in medicine. It is characterized by paroxysmal episodes of stabbing, "electric shock"-like pain that are brief (lasting from seconds to 2 minutes), unilateral, and triggered by innocuous stimuli such as touching the face, chewing, speaking, or even the wind. It predominantly affects women in their sixties, with a higher incidence on the right side and in the maxillary (V2) and mandibular (V3) branches of the trigeminal nerve. Its annual prevalence ranges from 4 to 13 per 100,000 inhabitants, although in Mexico and Latin America, epidemiological data are limited and based on institutional series [1-3]. The primary cause is neurovascular compression at the Trigeminal Nerve's Entry Zone (TEZ) by the superior cerebellar artery (in ~80% of cases), which

leads to focal demyelination, neuronal hyperexcitability, and ectopic discharges. There are secondary forms (10-15%) associated with multiple sclerosis, tumors (epidermoid cysts, meningiomas), cysticercosis, trauma, or post-herpetic infections. The diagnosis is primarily clinical (ICHD-3 criteria of the International Headache Society), supplemented by high-resolution Magnetic Resonance Imaging (MRI) (3D-FIESTA or FIESTA-C sequences) to confirm vascular compression or rule out secondary causes, especially in young patients with bilateral or atypical pain [2]. In Mexico, the "Manuel Velasco Suárez" National Institute of Neurology and Neurosurgery (INNN) is the tertiary referral center for the management of complex neurosurgical conditions, including TN. Institutional publications from the past 20 years emphasize that the initial approach should always be pharmacological, reserving surgery for refractory cases, and that carbamazepine has historically been the drug of choice due to its proven efficacy, low cost, and availability in the public health system. [1,2]. This study expands upon the previous review, incorporating updated evidence from INNN publications, complementary Mexican studies, and international guidelines, with the aim of providing a comprehensive analysis and a bibliographic and clinical update; rigorously citing the role of CBZ in this institutional context, since, as the leading neurosurgery center in Mexico, the number of patients with TN seen on a daily basis helps make the experience with this drug more definitive.

Objectives

- To provide a detailed description of the mechanism of action, pharmacokinetics, efficacy, and safety profile of carbamazepine in the treatment of TN.
- To analyze the INNN's accumulated experience with CBZ based on institutional case series (>800 patients) and key publications.
- Evaluate clinical limitations (tachyphylaxis, adverse effects) and criteria for transition to surgical treatment in INNN practice.
- Compare CBZ with pharmacological and surgical alternatives, and propose recommendations based on institutional evidence and international guidelines.
- Identify knowledge gaps and suggest avenues for future research in the Mexican context.

Theoretical Framework

Pathophysiology and Diagnosis

Pain in classic trigeminal neuralgia arises from chronic vascular compression in the trigeminal nerve root, leading to demyelination and the generation of ectopic impulses. In secondary forms, inflammatory or demyelinating mechanisms (such as in multiple sclerosis) predominate. The differential diagnosis includes postherpetic neuralgia, dental pain, temporomandibular dysfunction, and migraine. MRI is essential for identifying neurovascular compression (high sensitivity on high-resolution sequences) and ruling out structural lesions [2].

Pharmacological Treatment: The Central Role of Carbamazepine

Carbamazepine is an iminostilbene anticonvulsant that acts primarily by blocking voltage-gated sodium channels (Nav1.7 and Nav1.8 subunits), stabilizing the neuronal membrane, inhibiting ectopic discharges, and reducing nociceptive transmission. According to the AAN-EFNS guidelines (2008), it has level A evidence (strong recommendation) for pain control in classic trigeminal neuralgia, superior to other options [4].

Pharmacokinetics and Dosage (based on INNN practice and guidelines):

●**Absorption:** Oral, slow and irregular (improved with food).

●**Metabolism:** Hepatic (CYP3A4), auto inducer (reduces its own levels over time).

●**Initial Dose:** 100–200 mg every 12 hours, gradual titration every 3–7 days.

●**Therapeutic dose:** 600–1200 mg/day (maximum 1600 mg/day divided into 3–4 doses).

●**Serum levels:** Monitoring recommended (4–12 µg/mL).

●**Used as a "therapeutic trial":** a rapid response confirms the clinical diagnosis [1,2].

Efficacy: Initial response >70–80% in the first few weeks (more than 50% reduction in the frequency and intensity of paroxysms). However, tachyphylaxis develops over months to years due to enzyme induction and disease progression, requiring a dose increase or combination therapy [1].

Adverse effects and monitoring: Drowsiness, dizziness, nausea, ataxia, hyponatremia (due to SIADH), skin rash (risk of Stevens-Johnson syndrome in HLA-B*1502 carriers, common in Asians), leukopenia, thrombocytopenia, elevated liver enzymes, and teratogenicity. Requires blood counts, liver function tests, and electrolyte levels every 1–3 months initially [2].

Pharmacological alternatives: Oxcarbazepine (lower toxicity, dose 600–1,800 mg/day, level B evidence); gabapentin or pregabalin (as adjunctive therapies); baclofen or lamotrigine in refractory cases. In Mexican studies, CBZ is frequently combined with gabapentinoids (60.6% in hospital series [3].

Surgical Treatment at the INNN

When medical therapy fails (due to ineffectiveness or intolerance), surgery is indicated: MVD (non-destructive, >90–98% long-term relief, ~15% recurrence) is the preferred option in young patients with confirmed vascular compression. Ablative techniques (radiofrequency rhizotomy, radiosurgery) are reserved for cases with high surgical risk [2].

Methodology

A narrative and systematic literature review of primary sources from the INNN and international evidence (2003–2023).Databases consulted PubMed, SciELO, Medigraphic, ResearchGate, and official Mexican websites. Inclusion criteria: publications that explicitly mention pharmacological management with CBZ in NT or INNN experience. Institutional articles (Santos-Franco 2005; Revuelta-Gutiérrez 2003) and complementary Mexican studies were prioritized. Isolated case reports without institutional data were excluded. The Vancouver style was used for citations.

Results

Overall Evidence of Carbamazepine Efficacy

According to the AAN-EFNS guidelines, carbamazepine is the only drug with Class I evidence for classic trigeminal neuralgia. It provides rapid pain relief, but its effectiveness diminishes over time [4].

Specific Experience at the INNN

The most representative series comes from Revuelta-Gutiérrez et al. (2003), based on more than 800 patients treated over a 20-year period at the INNN and the Hospital Español de México:

●"Initial treatment should be pharmacological, and carbamazepine is the medication that offers the best results; it is even sometimes used as a therapeutic trial."

●over time, "the dose required for pain control becomes higher, and this is sometimes associated with side effects that are not always well tolerated."

●**Indications for Surgery:** Secondary NT or poor response/ intolerance to medication.

●**Institutional Conclusion:** Microvascular decompression is the ideal procedure (non-destructive, minimally invasive, and with better long-term outcomes) [1].

Santos-Franco et al. (2005, INNN) emphasize CBZ as the drug of choice (600–1,600 mg/day), with significant toxicity (nausea, drowsiness, ataxia, hematological/hepatic abnormalities). They recommend an early transition to surgery if medical therapy fails due to loss of efficacy or adverse effects. MVD achieves relief in up to 98% of cases with preservation of function [2].

In a Mexican descriptive study (Bardales et al., 2022) conducted at a referral hospital with patients referred to the INNN:

●CBZ was prescribed for 86.8% (53/61) of patients as an inpatient treatment (alone or in combination).

●At discharge: **82% were pain-free or had mild pain.**

●13.1% (8 patients) with vascular compression were referred to the INNN for surgical decompression.

●It is emphasized that many patients arrive having previously been under dosed and that treatment follows guidelines for neuropathic pain [3].

Study/Source	Year	Population/Context	Use of carbamazepine	Main results	Limitations /Conclusions
Revuelta-Gutié rrez et al. (INNN)	2003	>800 patients (20 years)	First-line, therapeutic trial	Better initial results; dose escalation and adverse effects	MVD preferred because it is non-destructive
Santos-Franco et al. (INNN)	2005	Institutional review	600–1,600 mg/day, Na+ blockade	Initially effective, but toxicity and loss of effect	Early surgery recommended
Bardales et al. (MX hospital with referral to INNN)	2022	61 inpatients	86.8% in-hospital	Pain control in >80% at hospital discharge	Referral to INNN in 13.1% due to vascular compression
AAN-EFNS Guidelines	2008	International evidence	Level A (first-line)	Strong recommendation for classic TN	Oxcarbazepine better tolerated

Comparative Table of Key Evidence

Discussion

Carbamazepine remains the initial gold standard for INNN due to its proven efficacy, cost-effectiveness, and availability, in line with international guidelines. However, institutional series (>800 patients) consistently reveal its limitations: tachyphylaxis, the need for dose escalation, and adverse effects that reduce long-term adherence and quality of life. This explains the development of robust surgical expertise at the institute, where MVD surgery is positioned as the definitive treatment in selected patients (young, good life expectancy, confirmed compression)[2].Compared to oxcarbazepine (which causes less enzyme induction and has lower toxicity), CBZ is still the drug of choice for initial treatment in Mexico due to its lower cost. The study by Bardales (2022) illustrates the reality of referrals to the INNN: patients with severe pain (96.7% at admission) respond well to in-hospital CBZ treatment, but a significant proportion require surgery [3]. Limitations of this review: Predominance of retrospective and descriptive studies of the INNN (lack of specific prospective randomized trials on CBZ alone). No updated data from after 2023 are available on exact CBZ failure rates or time to surgery at the institute. Future research should include prospective cohorts evaluating adherence, quality of life, and cost-effectiveness of the INNN algorithm (CBZ →MVD).

Practical recommendations based on INNN:

●Initiate CBZ at a low dose, titrating slowly and monitoring closely.

●Perform an early MRI in all suspected cases.

●Assess for intolerance or medical failure (after 3–6 months) to determine the need for surgical referral.

●Educate the patient about adverse effects and warning signs.

Conclusions

Carbamazepine is the first-line medical treatment for patients with trigeminal neuralgia treated at the INNN, offering an excellent initial response and serving a diagnostic role as a therapeutic trial.

Its efficacy is limited in the medium to long term by tachyphylaxis and adverse effects, according to institutional experience with more than 800 patients (Revuelta-Gutiérrez 2003; Santos-Franco 2005).

The integral management approach of the INNN (initial pharmacological treatment + selective surgery with DMV) offers the best results in a national referral center.

We recommend continuing prospective institutional research to optimize titration protocols, monitoring, and criteria for referral to surgery, contributing to local guidelines adapted to the Mexican context, while also taking into account the emotional impact this condition has on patients.

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