ORIGINAL ARTICLE

Evaluating Drug Treatments for Trigeminal Neuralgia in Malaysian Patients

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ABSTRACT

Introduction: Trigeminal neuralgia (TN) is a debilitating neuropathic pain condition affecting the craniofacial region. Patients often experience pain of such intensity that it can be physically and mentally incapacitating. We aim to evaluate the effectiveness and tolerability of various prescribed medications for trigeminal neuralgia. While most earlier research has focused solely on carbamazepine, documentation on the use of other antiepileptic drugs (AEDs) remains limited. **Materials and Methods:** This retrospective study examines medications prescribed to TN patients from seven hospitals across Malaysia. We analyzed drug types, effectiveness, adverse reactions, patients' clinicodemographic characteristics, and comorbidities. **Results:** A total of 219 patients were included, with significantly more females (n = 141) than males (n = 78) ($p < 0.0001$). Ages ranged from 30 to 97 years, with a median age of 62.8 (SD ±1.231). Malays were the largest ethnic group (n = 135) ($p < 0.0001$). AEDs prescribed included carbamazepine, gabapentin, lamotrigine, and pregabalin, either alone or in combination. Carbamazepine was the most prescribed (86.3%, $p = 0.004$), showed significant pain relief (80.8%, $p = 0.004$), and had the highest rate of adverse reactions (23.7%, $p = 0.050$), from mild (e.g., drowsiness, headaches) to severe (e.g., Stevens-Johnson syndrome). **Conclusion:** Carbamazepine remains the most effective medication for TN pain control despite potential serious side effects. We recommend using low-dose carbamazepine in combination with other AEDs and suggest that clinicians consider newer medications offering comparable efficacy with better tolerability.

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Keywords: Trigeminal neuralgia; Facial pain; Tegretol; Carbamazepine; Drug adverse reaction

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INTRODUCTION

Trigeminal neuralgia (TN), also known as tic douloureux, is the most common form of craniofacial neuropathic pain and is widely regarded as one of the most debilitating pain conditions an individual can experience. Table I presents the classification and diagnostic criteria for TN as defined by the International Association for the Study of Pain (IASP) and the International Classification of Headache Disorders (ICHD) (1–5).

The classical form of TN is characterized by sudden, extreme, intermittent episodes of burning or shock-like facial pain lasting from a few seconds to two minutes. These paroxysmal attacks may occur in quick succession

Table I: Classifications and criteria for the diagnosis of TN

IASP criteria	
Definition	TN is orofacial pain restricted to one or more divisions of the trigeminal nerve. With exception of TN caused by MS, the pain affects one side of the face. It is abrupt in onset and typically lasts only a few seconds (2 min at maximum). Patients may report their pain as arising spontaneously, but these pain paroxysms can always be triggered by innocuous mechanical stimuli or movements. Patients usually do not experience pain between paroxysms. If they do report additional continuous pain, in the same distribution and in the same periods as the paroxysmal pain, they are considered to have TN with continuous pain
Classification	Classical TN: caused by vascular compression of the trigeminal nerve root resulting in morphological changes of the root. Secondary TN: caused by major neurological disease, eg. a tumour of the cerebellopontine angle or MS Idiopathic TN: no apparent cause.
ICHD criteria	
Definition	A. At least three attacks of unilateral facial pain full filling criteria B and C B. Occurring in one or more divisions of the trigeminal nerve, with no radiation beyond the trigeminal distribution C. Pain has at least three of the following four characteristics: i. recurring in paroxysmal attacks lasting from a fraction of a second to 2 min ii. severe intensity iii. electric shock-like, shooting, stabbing or sharp in quality iv. precipitated by innocuous stimuli to the affected side of the face D. No clinically evident neurological deficit E. Not better accounted for by another ICHD-3 diagnosis
Classification	1. Classical TN (classical TN, purely paroxysmal; classical TN with concomitant continuous pain) 2. Secondary TN (TN attributed to MS; TN attributed to space-occupying lesion; TN attributed to other cause 3. Idiopathic TN (idiopathic TN, purely paroxysmal; idiopathic TN with concomitant continuous pain

IASP International Association for the Study of Pain, ICHD International Classification of Headache Disorders, MS multiple sclerosis, TN trigeminal neuralgia

and persist for up to two hours. Triggers such as eating, speaking, or even light facial contact commonly provoke the pain. In contrast, the non-paroxysmal form of TN presents as a continuous, milder pain—described as throbbing, burning, or stabbing. Some patients may experience both pain types concurrently. Due to its severity, TN can be profoundly disabling, both physically and psychologically (3, 4).

In the mid-20th century, the annual incidence of TN was reported at 4 per 100,000 people (1). More recent estimates range from 4 to 13 per 100,000 per year. The condition predominantly affects females and individuals over the age of 40 (4–7).

Most TN cases are idiopathic, though some are secondary to underlying conditions such as multiple sclerosis, vascular malformations, or tumours. In elderly patients, TN is often attributed to atherosclerotic elongation of arteries that compress the trigeminal nerve root as it exits the pons (3–5, 8–10). This vascular compression typically leads to demyelination of nerve fibers, disrupting axonal function (Fig. 1).

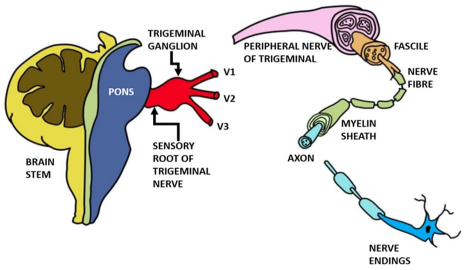

Figure 1: Illustration of the sensory root of a trigeminal nerve which supplies the face and muscle of mastication. There are three divisions of this nerve: V1: ophthalmic branch; V2: maxillary branch; V3: mandibular branch. The peripheral sensory nerves converge at the trigeminal ganglia that relay touch, pain, and temperature information from the ipsilateral face to the contralateral thalamus via the trigeminothalamic tract of the central nervous system. The pain in trigeminal neuralgia is brought about by focal demyelination of primary trigeminal afferents near the entry of the trigeminal root into the pons. This demyelinated nerve or disintegration of myelin sheath disrupts axon function which makes the axons hyper-impulsive and increases the susceptibility to ectopic excitation, ephaptic transmission, and high-frequency discharges.

Diagnosis of TN is based primarily on clinical history and symptomatology, supported by physical and neurological examinations. Differential diagnoses should be considered and ruled out. A trial of antiepileptic drugs (AEDs), particularly carbamazepine, often supports the diagnosis of classical TN, given its high efficacy in relieving symptoms. Despite the absence of a universally definitive treatment, AEDs are widely considered the first-line pharmacologic approach, with carbamazepine being the most studied and preferred option for both initial and long-term management (11–15). While evidence for the effectiveness of other AEDs remains limited, medications such as lamotrigine, topiramate, and baclofen have shown benefit—particularly as adjuncts to carbamazepine (16). Surgical intervention is typically reserved for patients who are refractory to medical treatment or who experience intolerable side effects. Fig. 2 illustrates the mechanisms of action of common AEDs.

Unlike earlier studies focused solely on carbamazepine (17, 18), the present study evaluates the comparative efficacy and tolerability of a broader range of medications, including newer AEDs like pregabalin and lamotrigine. This study responds to the need for alternative therapies in patient intolerant to carbamazepine. It also incorporates patient-reported outcomes using a pain scale comparison. Notably, we present the first evidence suggesting that combining gabapentin with carbamazepine offers improved pain management in TN patients.

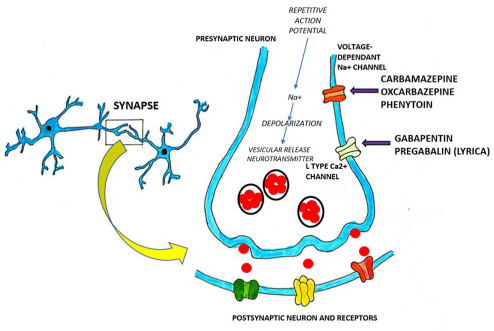

Figure 2: Illustration of the synapse region of neurons or nerve cells. The synapse is located between the pre-synaptic "sending" cell and the post-synaptic "receiving' cell. It shows the mechanism of action of common medications prescribed by the seven hospitals in this study namely carbamazepine, phenytoin, lamotrigine, gabapentin and pregabalin (Lyrica). Voltage-gated sodium channels on the pre-synaptic neuron are bonded by carbamazepine, phenytoin and lamotrigine, which prevent further entry of sodium into the neurons thus inhibiting repetitive action potentials and reducing the trigeminal pain. While for gabapentin and pregabalin, binding to the calcium channels will reduce the calcium influx into the neurons.

MATERIALS AND METHODS

Study Design and Population

This was a retrospective, multicenter study involving patients diagnosed with trigeminal neuralgia (TN) from seven healthcare facilities: the Oral Medicine Clinic, Faculty of Dentistry, Universiti Kebangsaan Malaysia (UKM); UKM Medical Center; Sultan Ismail Hospital, Johor Bahru; Kajang Hospital; Kuala Lumpur General Hospital; Raja Perempuan Zainab II Hospital, Kota Bharu; and Sarawak General Hospital. The study covered the period from 2000 to 2016.

Data was collected using convenience sampling, which is appropriate for research conducted with limited time or resources. Three research students at each center gathered the data by accessing patients' medical records, which were only available on-site during regular working hours. All patient information was kept confidential.

Inclusion criteria included patients with a definitive clinical diagnosis of typical TN, a minimum follow-up duration of six months, and treatment received between 2000 and 2016. Exclusion criteria included patients with facial pain not diagnosed as TN, incomplete pain score and/or medication data, and patients who had undergone surgical treatment for TN.

Data Collection

Co-researchers from the five Ministry of Health hospitals and two UKM centers prepared a list of TN patient registration numbers. Based on these numbers, patient folders were retrieved. Collected data included demographic information (age, gender, medical history, symptom duration) and clinical data such as pain severity (measured by Visual Analogue Scale [VAS]), attack frequency, pain characteristics, and known triggers.

Treatment parameters included type of medication, dosage, duration, and patient adherence, with the aim of evaluating therapeutic effectiveness. Side effects were documented by incidence and type. Effectiveness was defined by reductions in pain frequency and intensity as reported by patients. Pain was evaluated using the VAS and the Barrow Neurological Institute (BNI) Pain Intensity Score (16) (Table II). Effective pain relief was defined as a reduction in pain score of ≥1 point (pre-medication score minus post-medication score), assessed at least one month after the initiation of medication.

Table II. Barrow Neurological Institute Pain Intensity Score

SCORE	PAIN DESCRIPTION
I	No pain, no medications
II	Occasional pain, no medications required
III	Some pain, adequately controlled with medications
IV	Some pain, not adequately controlled with medications
V	Severe pain or no pain relief

Ethics

This study was registered with the National Medical Research Registry (NMRR-16-1995-33036). Ethical approval was obtained from the UKM Research Ethics Committee (UKM PPI/111/8/JEP-2017-009), and permissions were granted by all seven participating institutions.

Statistical Analysis

Descriptive statistical analysis was performed on data from 219 patients diagnosed with TN. Frequencies, percentages, means, and standard deviations were used to summarize demographic and clinical data. To minimize data entry errors, 5% of the entries were randomly validated by researchers at each center. Data analysis was performed using SAS JMP software, and comparisons were made where appropriate. Statistical significance was set at $p < 0.05$. All results were discussed and validated by the research team.

RESULTS

Clinicodemographic Results

The demographic data was obtained from a total of 219 patients diagnosed with trigeminal neuralgia (TN) and currently undergoing follow-up at each respective center (Fig. 3). Females (n = 141) significantly outnumbered male patients (n = 78) ($p < 0.0001$). Patients' ages ranged from 30 to 97 years, with a median age of 62.8 years (SD

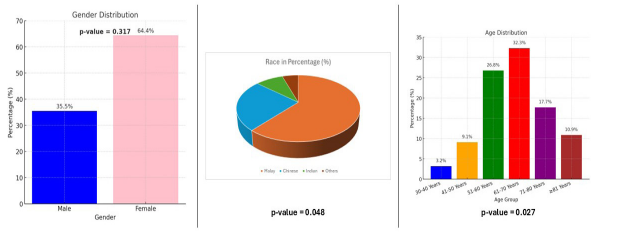

Figure 3: Demographic distribution of trigeminal neuralgia patients. An analysis of the demographic distribution of gender, age, and race among trigeminal neuralgia patients at all participating centres providing insights into the prevalence and diversity of trigeminal neuralgia among different groups.

± 1.231). Malays represented the largest ethnic group with TN (n = 135), followed by Chinese (n = 55), Indian (n = 19), Iban (n = 7), Bidayuh (n = 2), Sikh (n = 1), and non-Malaysians (n = 1) ($p < 0.0001$).

Regarding the involvement of the trigeminal nerve branches, the maxillary branch (V2) was the most commonly affected, with 83 patients reporting localized pain in this area. The mandibular branch (V3) was the second most commonly involved (n = 65), followed by combined involvement of two branches (maxillary and mandibular) in 30 patients, and three branches (ophthalmic, maxillary, and mandibular) in 31 patients. The least affected branch was the ophthalmic division (V1), with only 2 patients experiencing pain. However, no significant difference was noted across the trigeminal nerve divisions.

Medical History

103 patients (47.2%) had no prior comorbidities. The most common comorbidities were cardiovascular-related, affecting 42 patients (18.3%), including conditions like ischemic heart disease and hypertension. Endocrine-related comorbidities (such as diabetes mellitus and hyperlipidemia) were present in 8 patients (3.7%). Other comorbidities included conditions such as gout, asthma, or hepatitis B. A total of 54 patients (24.8%) had a combination of comorbidities.

Prescribed TN Medications

Table III presents the various common antiepileptic drugs (AEDs) used in TN patients, along with their adverse reactions, safe dosages, and modes of action. The typical pharmacological treatments and their effectiveness are shown in Fig. 4. However, less frequently used combinations have been excluded due to the overwhelming number of variations, making statistical grouping impractical and yielding insignificant findings. Carbamazepine was the first-line treatment for more than half of the patients (n = 189). Other AEDs prescribed included gabapentin, lamotrigine, and pregabalin. A variety of medication combinations were employed to achieve adequate pain control, including combinations with other AEDs, vitamins, antidepressants, analgesics, antifungals, antihistamines, and antispasmodics.

Table III: An overview of commonly used antiepileptic drugs (AEDs) for treating trigeminal neuralgia (TN) across the seven centres.

Medication	Mode of action	Safe dosage	Adverse reactions
Carbamazepine	1. Acts by inhibiting voltage-gated sodium channels, thereby reducing the excitability of neural membranes. 2. Potentiate gamma aminobutyric acid (GABA) receptors made up of alpha1, beta2, and gamma2 subunits. GABA is an inhibitory amino acid neurotransmitter that decreases neural membrane action potentials and therefore decreases nerve excitability. Glutamate has been implicated in the mechanisms contributing towards phenomenon of chronic pain.	1.100 to 200 mg twice daily. The daily dose should be increased by 100 mg every other day. 2. Typical total maintenance dose is 300-800 mg/d, given in 2-3 divided doses. 3. Max dose 1200 mg/d	1. Common - sedation, dizziness, nausea, vomiting, diplopia, memory problems, ataxia, elevation of hepatic enzymes, and hyponatremia. 2. More serious - leucopenia, aplastic anemia, allergic rash, systemic lupus erythematosus, hepatotoxicity, and Stevens-Johnson syndrome (SJS)
Oxcarbazepine	Oxcarbazepine is a 10-keto derivative of carbamazepine. 1. It binds to sodium channels and inhibits high-frequency repetitive neuronal firing. 2.Oxcarbazepine also inhibits the release of glutamate.	1. Starts at 150 mg twice daily. 2.The dose can be increased as tolerated in 300 mg increments every third day until pain relief occurs. 3. Maintenance doses range between 300-600 mg twice daily.26 4.The maximum suggested total dose is 1800 mg/d.	Improves side effect profile and fewer drug interactions than with carbamazepine
Phenytoin	Blockade of voltage-dependent membrane sodium channels responsible for increasing the action potential.	300–600 mg/day	1. Dizziness, nausea, hypotension, infusion pain, cutaneous rash, paraesthesia and itchiness. 2. Some patients may present more than one symptom.
Pregabalin	structurally related to gabapentin. It acts by interacting with the alpha-2-delta (α2-δ) subunit of voltage-gated calcium channels.	150-600 mg/d	1. Side effects less marked than other AEDs 2. most common are dizziness and sleepiness

CONTINUE

Table III: An overview of commonly used antiepileptic drugs (AEDs) for treating trigeminal neuralgia (TN) across the seven centres (CONT.)

Medication	Mode of action	Safe dosage	Adverse reactions
Lamo-trigine	1. Inhibits the release of glutamate and aspartate by blocking voltage-sensitive sodium channels. 2. Also acts at and inhibits calcium channels to enhance GABA synthesis.	1. initial dose of lamotrigine is 25 mg twice daily and can be increased gradually to a maintenance dose of 200-400 mg/d in 2 divided doses.15 2. The dosage required for adequate pain relief varied widely from 100-400 mg/d	1. Common - sleepiness, dizziness, headache, vertigo, and ataxia 2. Less common – skin rashes 3. Serious - SJS
Gaba-pentin	GABA receptor agonist, acts primarily on presynaptic calcium channels of neurons to inhibit the release of excitatory neurotransmitters.	1. 300 mg/d initially 2. gradually increased by 300 mg every 2-3 days as tolerated. 3. maximum efficacy, the dose can be increased to 1800 mg/d.1	No known drug interactions nor idiosyncratic skin reactions. Favorable side-effect profile are mild somnolence, dizziness, headache, confusion, nausea, and ankle edema. Hyperlipidemia is an important side effect to watch for with gabapentin therapy.

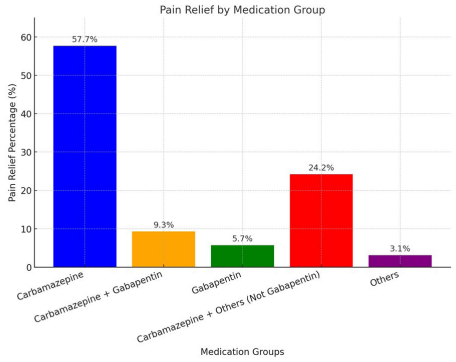

Figure 4: Frequency of commonly prescribed drugs in trigeminal neuralgia management. Analysis of commonly prescribed medications and their effectiveness reveals that carbamazepine is the most frequently used drug, either as a standalone treatment or in combination with other medications. Carbamazepine is notably the most common choice for trigeminal neuralgia patients, providing significant pain relief. However, less common combinations of carbamazepine with other drugs are not detailed in this analysis.

Approximately 52% of patients did not report any adverse reactions or side effects, while 27.9% experienced neurogenic symptoms such as dizziness, nausea, and giddiness. The medication most commonly associated with adverse reactions was carbamazepine, with 52 patients (23.7%) reporting side effects (p = 0.050). Skin lesions were the second most frequent adverse reaction, particularly among those taking carbamazepine (n = 30, 13.7%).

DISCUSSION

This study focuses on the commonly prescribed TN medications for Malaysian patients. We include all types of medications prescribed at the seven hospitals. Previous global studies have largely focused on the efficacy of carbamazepine as the first-line treatment for trigeminal neuralgia, with limited comparative data on newer medications like pregabalin or lamotrigine. This study also examines not only the effectiveness of these alternative medications but also their effectiveness, and adverse effects in patients resistant to first-line therapies (carbamazepine). The involved medication efficacy is explored in a more diverse patient population, including elderly patients and those with multiple comorbidities, which enhances the findings and makes them more generalizable to real-world clinical practice. In contrast to earlier research (17, 18), we explore the potential benefits of combining carbamazepine with newer medications like gabapentin to reduce breakthrough pain, an approach previously underexplored. By addressing critical gaps in comparative efficacy and safety profiles, this study contributes valuable insights toward developing more personalized and effective therapeutic strategies for trigeminal neuralgia.

Drugs adverse reactions of carbamazepine

Given its established efficacy, carbamazepine remains the first choice and most prescribed drug for paroxysmal pain in patients with TN in many health centres including ours. The more frequent and common side effects of carbamazepine include drowsiness, nausea, dizziness, diplopia, ataxia and elevation of transaminases and hyponatraemia. While the more serious but uncommon side effects apart from Steven-Johnson syndrome/ toxic epidermal necrolysis (SJS/TEN) include allergic rash, hepatotoxicity, lymphadenopathy, systemic lupus erythematosus, and aplastic anaemia. Specific contraindications are cardiac conduction problems or severe arrhythmias (12-28). Although it was found to be very effective in relieving the pain, adverse reactions can be life threatening. Previous studies have shown that individuals using carbamazepine were most likely to develop SJS and/or TEN if they are of Asian ethnicity. In Taiwan and Hong Kong Han Chinese (29), it has been demonstrated that the human leukocyte antigen HLA-B*1502 allele is substantially related with carbamazepine-induced hypersensitivity reactions, including SJS and TEN. A second study conducted in the Thai population (24) revealed a significant correlation between HLA-B*1502 and carbamazepine-induced SJS in all subjects. They showed a high rate of carbamazepine–induced hypersensitivity reactions and high incidence of SJS/TEN-related-carbamazepine (as supported by data from the WHO Uppsala Monitoring

Centre (WHO-UMC) and Novartis from 2000–2006) (20). These findings underscore the importance of considering genetic predispositions and potential side effects when prescribing carbamazepine, reinforcing the need for alternative or adjunctive treatment strategies as investigated in our study.

A Malaysian study investigating the relationship between the HLA-B*1502 allele and 27 epilepsy patients—comprising 19 Malays and eight Chinese—found that six patients developed SJS and 11 had skin rashes. Similarly, another Malaysian study reported that HLA-B*1502 was present in 75% of Malay patients who developed carbamazepine-induced SJS or TEN (20, 25). These findings align with broader regional data suggesting a significant genetic predisposition to severe cutaneous adverse reactions among certain Asian populations. However, in contrast to these findings, such severe hypersensitivity reactions were not prominently observed in our patient cohort. In addition, it's noteworthy to note that some Malay patients in Malaysia who experienced a skin rash after receiving the medication did not have the HLA-B*1502 allele. Even the Caucasian patients also lack this special DNA sequence. These observations suggest that other genetic factors may be involved. One candidate is the allele Cw0801, which may have a stronger association with carbamazepine-induced hypersensitivity, particularly in non-Han Chinese populations. This highlights the need for further genetic studies focusing on non-Han Chinese groups to better understand alternative risk alleles and their role in adverse drug reactions (20, 25).

In light of the risks associated with HLA-B*1502, the US Food and Drug Administration (FDA) has issued guidelines recommending that individuals with ancestry from regions where this allele is prevalent undergo genetic screening prior to initiating carbamazepine therapy (20, 25-26). This precaution aims to mitigate the risk of life-threatening hypersensitivity reactions. Understanding the scientific rationale behind such recommendations requires insight into the immunological function of HLA-B molecules and how genetic variation can influence immune responses to medications like carbamazepine.

The class I human major histocompatibility complexes, including HLA-B, are responsible for presenting antigenic peptides—both self and foreign—to the immune system's cytotoxic CD8+ T-lymphocytes. The T-cell receptors on circulating CD8+ T-lymphocytes engage with the HLA-B proteins to "read" the antigen being presented when these cells are proximate to nucleated cells containing antigen linked to HLA-B. The CD8+ T-cells will become activated and eventually die if they "see" or "read" the antigen being presented as alien or "non-self." In individuals with certain HLA-B variants, such as HLA-B*1502, this immune recognition may be dysregulated, triggering an inappropriate immune response to drug-antigen complexes. This mechanism offers a plausible immunogenetic basis for carbamazepine-induced hypersensitivity syndromes (20, 25, 26).

Other medications used

Together with carbamazepine, its structural analog - oxcarbazepine is also the first line therapy in TN (27). However, it was found that HLA-B*1502 was also significantly associated with SJS/TEN in Chinese and Thai populations for oxcarbazepine (12). Despite resulting in an improved side effect report and fewer drug interactions than with carbamazepine, oxcarbazepine is best avoided when carbamazepine allergy is evident. Oxcarbazepine, pregabalin and lamotrigine are not common medications used to treat TN in the seven hospitals, even though we observed pain reduction in the use of lamotrigine and pregabalin (28-34).

A 100-mg tablet of carbamazepine may produce significant and complete relief within two hours, although the effective dose ranges from 600-1200 mg/d, with serum concentrations between 40-100 mcg/ml. Indeed, serum levels of carbamazepine in ranges may be necessary at least to control initial symptoms, although a much smaller maintenance dosage may be adequate thereafter. From our observation as in Fig. 4, comparison of carbamazepine dosage when used alone vs in combination with other drugs showed inconsistent finding. The dosage of carbamazepine may not necessarily lower when combination of drugs is used. A further study on this dosage issue is needed and it probably may give a guideline on prescription dosage and help in reduction of carbamazepine adverse reaction. In addition, thus far, baclofen has the strongest evidence for efficacy in the treatment of TN after carbamazepine. While gabapentin showed adequate efficacy in only one RCT, where it was used in combination with ropivacaine, and this combination was found to be safe and effective (30-34).

We recommend using a low dosage of carbamazepine for the treatment of trigeminal neuralgia to minimize potential adverse effects and combining it with newer medications may help reduce pain more effectively. However, it is challenging to present this observation in the results section due to the limited number of specialists who prescribed the newer medications, and the variety of medication combinations used. As a result, the sample size is too small to produce statistically significant findings. For example, in Fig. 4, under the category 'carbamazepine and others (not gabapentin) (n=54),' carbamazepine can be combined in two, three, or even four different ways with phenytoin and/or neurobion, and/or analgesics such as tramal, mefenamic acid, arcoxia,or paracetamol, and/or muscle relaxants like baclofen, and/or antidepressants like amitriptyline. Thus, it was impossible to categorize them into distinct

groups for statistical purposes. Another group 'Others' (n=7), consisted of medications that were combinations excluding carbamazepine or gabapentin. This category included newer medications such as lamotrigine and pregabalin, which provided pain relief in six out of seven patients.

Clinicodemographic comparison

There are little epidemiological studies on TN, and it is regarded as a rare condition with a low incidence of four to 13 cases per 100,000/year. However, the incidence was high in a few western countries like the United States and United Kingdom with 15 and 27 new cases each year respectively (19). Asian countries like Korea, the incidence was very high with 100 new cases per 100,000/year (28-29, 35-36).

Like the other populations of the world, our findings revealed that TN was mostly identified in females with a very wide age range and commonly involved older adults of sixth and seventh decade of life. Female patients were almost twice the males with ratio 1.8: 1 in our study. In view of the Malay ethnicity which was the main race affected by TN as compared to other race in Malaysia, this could be due to the Malays are the largest ethnic group and contributing for more than half of the population (29, 36). On contrary with regards of the finding of location of TN, we found that the maxillary division was the most affected trigeminal nerve branch and not the mandibular branch as seen in other Malaysian and Asian studies (24, 29, 30, 37-38).

The presence of comorbidities among the TN patients in our cohort may influence pharmacological management. Certain comorbidities, such as cardiovascular diseases or psychiatric conditions, could impact the choice and dosing of medications. For example, AEDs can impact heart and blood vessel health in various ways, affecting both traditional and emerging risk factors such as weight, blood sugar control, cholesterol, inflammation, and blood clotting markers. Some AEDs may also cause or worsen abnormal heart rhythms (39). Since these drugs can interact with medications commonly used to manage cardiovascular risk like statins more research is needed to understand these interactions and ensure safe, effective treatment. Similarly, patients with depression or anxiety may have different tolerability profiles for medications like gabapentin or antidepressants used for neuropathic pain. For instance, the use of tricyclic antidepressants, especially amitriptyline, is discouraged due to their significant potential to lower the seizure threshold and induce seizures (40). It is therefore important to customize treatment approaches according to patients' comorbidities to ensure the best therapeutic results.

Limitation of our study is that it was only conducted in seven hospitals in Malaysia with exclusion of several TN subjects in which some of information on medications were incomplete, thus, making our findings may not be representable to all the populations with TN in Malaysia. Nevertheless, a thorough overview of the many drug types and combinations utilised at the seven hospitals might spark interest about the usage of newer medications for TN.

In addition, only descriptive statistical analysis could be conducted due to the extensive variety of drug combinations used in treatment. Patients were prescribed multiple medications in different combinations, including anticonvulsants, analgesics, muscle relaxants, and antidepressants, often tailored to individual needs. The overlapping and intersecting nature of these combinations made it nearly impossible to categorize them into distinct, statistically comparable groups. Any attempt at rigid classification would oversimplify the complexity of the actual prescribing patterns prescribing patterns, potentially leading to misleading conclusions. Therefore, descriptive approach was the most appropriate method to capture the true variability in treatment strategies and their outcomes.

CONCLUSION

The selection of medication for trigeminal neuralgia (TN) is typically individualized to meet the patient's specific needs, focusing on effective pain management while minimizing adverse drug reactions. Carbamazepine is often the first-line treatment due to its proven effectiveness in pain reduction. However, its side effects can be significant for some patients. To mitigate these adverse effects, a combination of low-dose carbamazepine with other antiepileptic drugs (AEDs) is recommended for treating TN. Additionally, clinicians may consider exploring newer medications that also provide effective pain control with an improved side effect profile.

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