Efficacy Of Gabapentin In Trigeminal Neuralgia: A Non-randomized Trial

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ABSTRACT:

Objective: To compare the efficacy of Gabapentin with carbamazepine in Trigeminal Neuralgia.

Material/Method: The study was conducted in Agha Khan University Hospital and Abbasi Shaheed Hospital for four months. 19 patients of TN were collected through purposive convenience sampling. DN4 questionnaire was used to differentiate between Somatic and Neuropathic pain. Numeric Pain Rating Scale was used to assess the severity of pain.

Results: Nine patients of Trigeminal Neuralgia refractory to carbamazepine were put on Gabapentin with male to female ratio of 4:5. All showed favorable response on 800-1600 mg Gabapentin on Numeric Pain Rating Scale. All patients were pain free in three weeks with no side effects. There was significant difference between pain response to carbamazepine and Gabapentin at P< .05. Four patients (44%) had pain relief on 900 mg Gabapentin, three (33%) on 1200 mg, one responded on 800 mg and one on 1600 mg.

Conclusion: Gabapentin is effective as first line treatment in Trigeminal Neuralgia

Key words: Gabapentin, Trigeminal Neuralgia, carbamazepine

INTRODUCTION:

Trigeminal Neuralgia (TN) is a potentially disabling condition resulting in facial pain. It is also known as “TicDouloureux” and is a neuropathic pain syndrome. According to International Classification of Headache Disorders, TN consists of the standardized set of salient features; paroxysmal episodes of stabbing pain accompanied by brief periods of facial spasm, a duration that lasts from a variable range of few seconds to couple of minutes and caused by stimulation with involvement of one or more divisions of the trigeminal nerve. It is a rare disorder with an estimated prevalence of 155 cases per million persons. The male to female ratio is 2:3. In United States, the prevalence is around four to five cases per 10,000 of the population. TN is primarily classified into two types. Classic TN is idiopathic in origin and most common in the age of 5th decade onwards. The compression or demyelination of the trigeminal ganglion causes the other type known as the symptomatic TN. This one is common in relatively young age group of 30-40 years. Pain follows the sensory distribution of Trigeminal nerve typically radiating to mandibular or maxillary area and rarely both. The diagnostic criteria for idiopathic TN by International Headache Society is follows.

• Paroxysmal attacks of facial or frontal pain lasting a few seconds to less than two minutes.
• Pain has at least four of the following characteristics
  I. Distributions along one or more divisions of trigeminal nerve
  II. Sudden, intense, sharp, superficial pain; burning or stabbing in nature
  III. Severe pain intensity
  IV. Precipitated from trigger areas or by certain daily activities eg. Eating, talking, washing face, cleaning teeth
• No symptoms between paroxysms
• No neurological deficit is present
• Attacks are stereotyped in individual patients
• Other causes of facial pain are excluded by history, physical examination and investigations when necessary.

Mechanism of pain in TN remains highly debated. The involvement of thalamic relay neurons result in perception of pain in the nucleus of trigeminal ganglion. The condition may further aggravate by the presence of tumors, aneurysms
and meningeal inflammation that result in chronic irritation along the pathway of trigeminal nerve root near the pons.\(^3\) An abnormal vascular course of superior cerebellar artery is often cited as the cause. It may be a symptom of multiple sclerosis or dental irritation. However in 90-95% of cases, no lesion is identified\(^6\). Management depends on the cause and as majority are idiopathic pharmacologic treatment is the mainstay\(^11\).

By most, carbamazepine is the medical treatment of choice\(^12,13,14\). Some advocate a trial of baclofen since it has fewer adverse effects\(^15\). While, gabapentin has shown promising results in some forms of neuropathic pain\(^16\).

The effects and response to these medications have not been studied before in Pakistan. The effectiveness of gabapentin in TN is gaining popularity through anecdotal reports and retrospective studies\(^17,18\).

The rationale of the study was to assess the effectiveness of gabapentin in patients that were not responding to carbamazepine at high doses or were unable to tolerate increment in dosage so that patients, refractory to carbamazepine in TN could be benefited with substitute of gabapentin.

**PATIENTS AND METHODOLOGY:**

A non-probability purposive sample type was selected for the study and sample size was determined by World Health Organization (WHO) sample size software keeping alpha at 0.05, 1-beta=90%. A study design of non-randomized trial was performed on patients having TN, refractory to carbamazepine (400-800 mg daily) who visited Aga Khan University Hospital (AKUH) and Abbasi Shaheed Hospital (ASH) for four months.

Those patients whose pain response was refractory to carbamazepine were selected consecutively. All new patients were initially started on carbamazepine 200mg titrating to 800 mg over a period of three weeks and patients already on carbamazepine were either dose titrated if on a low dose or switched to gabapentin if already on adequate doses for more than four weeks. Gabapentin was started from 300-400 mg with weekly increments titrating to pain control and its maximum dose used was of 1600 mg.

The patients with secondary TN or abnormal neurological examination were excluded from the study. Informed consent was taken from the patients and their autonomy, anonymity and confidentiality were strictly maintained according to ethical guidelines of Pakistan Medical and Dental Council (PMDC).

In order to differentiate between neuropathic and somatic pain, Douleur Neuropathy 4 question (DN-4) questionnaire was used. Numerical Pain Rating Scale (NPRS) was used to measure the subjective intensity of pain. NPRS is an 11 point scale from 0 (no pain) to 10 (the most intense pain imaginable). Patients verbally selected a value that was most in line with the intensity of pain that they had experienced in last 24 hours.

Categorical variable like gender was exhibited through charts. For age, mean and standard deviation were calculated. To find out significant difference between two drugs efficacy T-test was applied. P value was kept significant <.05.

**RESULTS:**

Total number of patients of TN was 19. A total of 9 patients were refractory to the 1\(^{st}\) line drug carbamazepine. 5 of these were unresponsive (800mg) and 4 failed to tolerate the dose (400 mg) and showed effects of fatigue and drowsiness. The flow chart demonstrating the entire process is given below. (Figure: 1)

The 9 patients (comprising of 4 males and 5 females) refractory to the monotherapy of carbamazepine were treated with various doses of gabapentin. The mean age of patients was 51 years. The initial dose was set to be 300-400 mg which was increased the following weeks with same increments every week till the patient was pain free. With regular follow up, all nine patients had pain relief from the dose ranging from 300-400 mg to 1200-1600mg. The response was overwhelmingly favorable and there were no drop-outs due to side effects.

![Flow-chart](image)

**DISCUSSION:**

Trigeminal Neuralgia is often referred as “tic douloureux” because of the characteristic muscle spasm coupled with pain.\(^1\) Some experts argue that this syndrome is caused as by neural trauma to the nerve that passes through the foramen in the skull to facial tissues and muscles\(^19\).

Certain evidence suggests that carbamazepine is still
considered to be the first line drug for medical management\(^2\). The mechanism of action of carbamazepine involves the inhibition of voltage-gated sodium channels that ultimately reduces the excitability of neural membranes. This reduction subsequently causes relief in neuropathic pain\(^2\).

On the contrary, Keppel Hesselink et al in their extensive review article claim that no convincing randomized controlled trials (RCTs) have been found in the medical literature that comprehensively substantiate the role of carbamazepine in TN\(^2\).

One report of 143 people with TN followed for 16 years found that carbamazepine was initially successful in 69% of cases, however after 5-10 years only 22% were still gaining benefit from carbamazepine monotherapy. Therefore patients require other drugs to control pain\(^2\).

A synergistic combination of carbamazepine with lamotrigine or baclofen is the second line treatment when monotherapy fails; however the evidence is weak\(^2\). The long term effects of carbamazepine have been assessed only in open trials. Common side effects include sedation, drowsiness, nausea, double vision, lack of muscle coordination and hyponatremia. This makes it contraindicated to old-age debilitated patients\(^3,4\).

Gabapentin is a GABA (gamma-aminobutyric acid) receptor agonist that, unlike carbamazepine, acts on calcium channels and inhibit the release of neurotransmitters in excitatory state\(^5\). The evidence shows that gabapentin has been tested in randomized control trials of neuropathic pain with proven efficacy\(^6\). Its use and effectiveness were also validated in numerous studies\(^7,8\).

The mere fact that gabapentin is well tolerated without serious side effects is an advantage when prescribing it for elderly patients\(^9\). Gabapentin has many advantages, including faster titration, no adverse drug reactions and a favorable side-effect profile. Studies have shown its efficacy particularly in patients with TN in multiple sclerosis and refractory cases\(^10,11\).

**CONCLUSION:**

The results of our study suggest that gabapentin can be as effective as first line treatment in TN, even in those cases that are resistant to traditional treatment modalities. Gabapentin shows good efficacy and is well tolerated in all patient groups. Further prospective double blind comparative studies would show a better efficacy profile and need to be done.

**REFERENCES:**

