ORIGINAL ARTICLE

GABAPENTIN FOR THE TREATMENT OF TRIGEMINAL NEURALGIA

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Abstract

The aim of this study was to investigate the efficacy and safety of Gabapentin in the treatment of trigeminal neuralgia. Anticonvulsant drugs are regarded as useful treatment for neuropathic pain. In this study the efficacy and side effects of Gabapentin in comparison with Carbamazepine for the treatment of trigeminal neuralgia were evaluated. The study was interventional and cross over comparison.

Fifty six patients with Trigeminal neuralgia were administered Gabapentin in comparison to fifty seven control group with Carbamazepine. The clinical trial comprised of two phases of 4 weeks each with three days of washout period . The final titration dose for Gabapentin was 900mg and Carbamazepine 1200mg. The efficacy of these medications was determined by visual analogue scale (VAS) and side effects were recorded through marking of profiles encountered on initiation as well as termination of each of two phase of clinical trial.

The Gabapentin benefited 55%(31/56) of the patients with pain relief ($p<0.05$) in contrast to 50% (29/57) who obtained relief of pain from Carbamazepine as control on visual analogue scale assessment. It was concluded that Gabapentin is more effective and safer drug for the treatment of Trigeminal Neuralgia.

Key words: *Trigeminal Neuralgia, Gabapentin, Carbamazepine, Side effects*

INTRODUCTION

Trigeminal Neuralgia is a severe neuropathic pain characterized by lancinating (Electric Shock like) attacks of severe unilateral facial pain usually affecting the second and third division of the trigeminal nerve. It is defined by the international headache society as "unilateral disorder characterized by brief electric shock like pain, abrupt in onset and termination and limited to the distribution of one or more division of the trigeminal nerve.[1] Trigeminal neuralgia was first described John Fothergill in 1773 it is also known as Prosopalgia, the suicide disease or Fothergilll's disease and Nicolas Andrew invented the term "Tic Doulourex" in 1756 in his book because of the distinctive facial spasm that often accompanies the face.[2]

Typically brief attacks are triggered by talking, chewing, teeth brushing, shaving or light touch. The paroxysmal shocks like pain is restricted to the innervation area of one or more trigeminal branches often set off by light stimuli in trigger zones. The Ophthalmic division of trigeminal nerve alone is involved in less than 5% case.[3, 4]

The pain lasts less than for a second or up to 2 minutes duration .Between paroxysms the patient is pain free.

The etiology of trigeminal neuralgia is idiopathic but the causes are compromised oral hygiene, habitual flushes and quality of life and patient often get depressed and desperate

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The mean age is around 60 years being more often in female gender. The right side maxillary and or mandibular trigeminal branches are more commonly involved than ophthalmic branch.

The treatment of trigeminal neuralgia should be initially pharmacological and several sodium channel blockers are used in the treatment of this neuropathic pain like carbamazepine, Ox carbamazepine, Lamotrigine, Valproate and the Carbamazepine present first line therapy for trigeminal neuralgia.

If pain relief is incomplete with carbamazepine or it produces adverse effects the drug suggested to be considered as second line agents for the treatment of trigeminal neuralgia include Lamotrigine Phenytoin, ox carbamazepine and Gabapentin.

Gabapentin is a new, water soluble antiepileptic agent with properties of an amino acid and is used for the treatment of epilepsy and currently to relieve neuropathic pain. Gabapentin is structural analogue of Gama amino butyric acid (GABA) but its receptor and biochemical function remains undiscovered. It is lipophilic and penetrates the blood brain barrier. Its mechanism of action remain has not yet been fully elucidated but appears not to involve binding to GABA receptors and is used as anticonvulsants. It is effective and widely used in neuropathic pain though lacks evidence in trigeminal neuralgia.[5]

METHODOLOGY

This interventional research study was conducted in the Department of Oral Medicine, Khyber College of Dentistry, Peshawar between Jan 2011 to June 2012 on 56 patients of already diagnosed as suffering from trigeminal neuralgia and 57 newly diagnose Control patients of ages 32-80 years.

The study got approval from the ethic review committee of the institution. The study was having experimental design of comparative, crossover clinical study in which carbamazepine was used as control for comparative purpose in order to check and evaluate the efficacy of gabapentin for the relief of pain in trigeminal neuralgia and occurrence of side effects.

The inclusion criteria was patients aged 18 years or older who have experienced pain for at least 6 months and intensity score of at least 4 out of 10 on visual analogue scale.

The exclusion criteria was patients who have previously taken gabapentin, nursing mother patients hypersensitive to gabapentin or Patients who had neurosurgical treatment and immune compromised State. Patients suffering from chronic hepatitis B or C during the past three months and HIV patients.

Each patient was asked to fill the written consent and detailed history and clinical examination was done. Complete blood examination and Liver function test was performed before and after the treatment for each patient.

The clinical trial was carried out in two phases:

Clinical Trial 1

The already diagnosed 56 patients of trigeminal neuralgia who were taking Carbamazepine were asked to stop taking the drug and were prescribed Gabapentin tablets 300mg as starting dose up to 900mg daily divided doses for 4 weeks and 57 newly diagnosed cases of trigeminal neuralgia patients were prescribed Carbamazepine in doses of 100mg to 1200mg in daily divided dose for a period of 4 weeks.

Clinical Trial 2

At the end of 4 weeks, fifty six patients who were taking Gabapentin in phase 1 were put on Carbamazepine 100 mg -1200mg in daily divide doses for further 4 weeks after 3 day of washing out period.

Similarly at the end of 4 week of Carbamazepine in newly diagnosed 57 patients in phase 1 were given Gabapentin for next 4 weeks. A three days washing out period was observed between phase 1 and phase 2.The Gabapentin was prescribed 300 mg starting dose up to 900 mg in daily divided .

Visual analogue Scale (VAS) were used as diagnostic criteria to determine the efficacy of these drugs .At the time of weekly follow up side effects were also recorded. At each subsequent visit inquiries were made about the pain(mild ,moderate and severe), the number of paroxysms daily and their duration, the presence / absence of triggering pain by talking ,eating contact, draughts and other factors. Finally they were asked about the side effects of drugs.

This was descriptive assessment of pain by VAS. Clinical difference between Gabapentine and Carbamazepine were assessed by performing Chi Square tests. The statistical significance was define as $P< 0.5$.

TABLE 1: EFFICIENCY STATUS IN RELATION TO NUMBER OF PATIENTS

	Pain relief with Gabapentin	Pain relief with control	Total
Yes (n)	31	25	56
No (n)	29	28	57
	60	53	113

TABLE 2: SHOWING TOTAL PAIN REDUCTION

	Gabapentin 31 (55%)	Control (CBZ)
Complete Relief	12 (21%)	11 (19%)
Nearly	9 (16%)	8 (14%)
Moderately	8 (14%)	7 (12%)
Partially	2 (3%)	3 (5%)

RESULTS

Fifty six patients of ages 32-80 years mean 63.5 years, 24 males(42.8%) and 32(57.2%) females were included in this study with 57 patients in control group. The mean duration of neuralgias was 7 years .The right side of face was involved in 12 cases (21%) while the left sided was in 10 cases (17%) and both sides were diagnosed in 3.5%. The Inferior dental nerve was involved in 49% while Infra orbital nerve was diagnosed in 10.7%. There was no case of Ophthalmic division of Trigeminal neuralgia seen in this study.

Both the groups were compared for age ,sex ,number of previous bouts, duration of present bouts and division of nerve involved but no striking difference was noticed in both groups. The severity of pain was recorded as Nil =0, mild =1, moderate -2 and severe =3 score. If patient started at +3 pain and moved to 0,the improvement was 100%.,While he moves from 2 to 1,the scores was+1 of possible +2 i.e. 50% improvement. The efficacy status in relation to number of patients pain and total pain reduction is shown in Table 1 and 2. The calculation showed the patients on Gabapentin achieved 55 %(31/56) while in control 50% patients (29/57) got relief with Carbamazepine.

DISCUSSION

The patho physiological mechanism for the genesis and continuing production of pain of Trigeminal neuralgia have not yet been defined. Therefore, the treatment for this type of neuropathic pain is not simple. Neuropathic pain related to chemotherapeutic agents is often resistant to standards analgesics. Anticonvulsants have been utilized as adjuvant analgesic from 1960. They act by potention of gamma-amino butyric acid (GABA) transmission, reduction of glutamate mediated excitatory transmission and blockade of voltage activated ion channels.

Carbamazepine was the first drug used for the treatment of TN as anticonvulsant in 1962-63 by Blom. The majority of patients tolerated Carbamazepine however; other medications may be tried if Carbamazepine is unsuccessful or provides only partial relief. New anticonvulsant have marked a new era in the treatment of neuropathic pain with clinical trial of higher quality standards .Comparison of guidelines from the International Association for the study of pain neuropathic pain special interest group ,European Federation for Neurological Societies and Canadian Pain society found a consensus for use of TCAs Gabapentin and pregabalin as first line treatment for neuropathic pain.[6,10]

Trigeminal neuralgia in contrast to more sustained forms of neuropathic pain is notoriously unresponsive to placebo [7, 21, 22, 23] in a number of clinical trials and the control is lack in comparison to these studies.

Gabapentin is multimodal peri operative drug has efficacy in the treatment of neuropathic pain [12,13,14] and syndromes like Diabetes neuropathy[17] Post herpetic neuralgia[18] multiple Sclerosis[15] erythromelalgia[19] Glossopharyngeal neuralgia.[7,16] Trigeminal neuralgia and GBS[20]

The result of study clearly shows that Gabapentin is effective in the treatment of Trigeminal neuralgia and quality of life improves with Gabapentin therapy. The clinical drug trial investigated the efficacy and safety of Gabapentin in direct comparison to an active control (Carbamazepine). Significant improvement was evident during the titration phase and continue to occur over the course of 8 weeks of treatment. Adverse effects of Gabapentin are minor and well tolerated. Despite doses of Gabapentin 900mg daily in population with an average age of 63.5 years, no serious drug related side effects were reported. The final titration

dose of Gabapentin was 900mg and 1200 mg was for Carbamazepine. The efficacy was determined by VAS while side effects were recorded through marking of profiles of side effects encountered on administration of Gabapentin and Carbamazepine.

On VAS, the Gabapentin benefitted 55% (31/56) of patients with pain relief ($p<0.05$) in contrast to for control. Fifty percent of patients experience at least one side effects on Gabapentin against 24% in placebo the most important sides effects seen is occurrence of rash. Dizziness, fatigue and somnolence were significantly more frequent among patients on Carbamazepine than Gabapentin. Adverse effects among patients on Carbamazepine was 24%; while in Gabapentin 13%

This study support the earlier studies [10,11] conducted on Gabapentin that it relieve the neuropathic pain in idiopathic Trigeminal neuralgia [9] and patients with MS experiencing Trigeminal neuralgia.[8] In this study Gabapentin reduces the pain of Trigeminal Neuralgia with very few side effects and thus concluded that Gabapentin is a safe drug in the treatment of Trigeminal neuralgia as second line of therapy if other anticonvulsants fail.

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