

Carbamazepine allergy: Gabapentin as a safer and effective alternative in the management of Trigeminal Neuralgia

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ABSTRACT

Trigeminal neuralgia is one of the classic neurological conditions which is described by the International Association for the Study of Pain as a sudden, usually unilateral, severe, brief, stabbing recurrent pain in the distribution of one or more branches of the fifth cranial nerve. Management of the neuralgic pain can be quite complicated since there is risk of relapse; the pain may be refractory to the medications prescribed or the occurrence of adverse reactions. Here we present a case wherein a female patient in the fifth decade of life has trigeminal neuralgia of the left mandibular division; she was prescribed carbamazepine for which she developed allergic reactions after which she discontinued the drug. Currently she is being effectively managed with gabapentin. The patient has not had any relapse and is on regular follow up since six years.

Key-words: Adverse reactions, carbamazepine, gabapentin, trigeminal neuralgia

Introduction

Trigeminal neuralgia is one of the classical neurological condition that is been known for centuries. Trigeminal neuralgia was defined by the International Association for the Study of Pain as a sudden, usually unilateral, severe, brief, stabbing recurrent pain in the distribution of one or more branches of the fifth cranial nerve.^[1] The paroxysms of electric shock like pain that are often triggered by light mechanical stimulation of a trigger point are extremely painful. Trigeminal neuralgia is known to occur in the fourth to seventh decade of life and frequently women are more prone to neuralgia. 85 % of the cases are the classical or idiopathic trigeminal neuralgia where the underlying aetiology usually is not known and the rest 15% is secondary trigeminal neuralgia where there is a definite cause for the neuralgic pain. There are two main treatment modalities which includes pharmacological and non-pharmacological. Routinely anti-epileptic drugs are used in the medical management of trigeminal neuralgia, of which carbamazepine, oxcarbazepine and phenytoin sodium are widely used.^[2] Various drugs have been tried in numerous case control studies but there is lack of evidence pertaining to the efficacy and adverse outcomes of these drugs. There is scarcity of randomized controlled trials for the drugs used in the management of trigeminal neuralgia. Under unusual circumstances patients may develop allergic reactions to carbamazepine. In the present case, the patient in her fifth decade of life has trigeminal neuralgia of the left mandibular division and was prescribed carbamazepine and she developed allergic reaction and she discontinued the drug. She was then prescribed gabapentin along with methylcobalamin after which she had no episodes of pain and no evidence of allergic reaction.

A 52 year old female patient reported to us with a complaint of sharp shock like pain for a brief time

period of 3-5 seconds on the left side of the mid and lower third of the face since 4-5 months. She had consulted a neurologist in her hometown and she was diagnosed with trigeminal neuralgia and was prescribed Carbamazepine 200mg thrice a day. Following intake of the medication she developed rashes associated with severe itching and had to discontinue the drug. She had taken the medication for two days and had complete relief from pain. After cessation of the drug due to adverse outcome there was relapse and she had multiple episodes of unbearable pain after which she had reported to us after the resolution of rashes. Her systemic health was remarkably good with no medical history. On thorough clinical examination there was no obvious odontogenic cause for pain. However pain was elicited on palpation over the left lower residual alveolar ridge in the pre-molar and first molar region (trigger point) which the patient described as electric shock like that lasted for 3-5 seconds. There was absence of extra-oral trigger points. Her complete hemogram was within normal limits.

Orthopantomograph revealed no significant findings. [Figure 1] Previous drug history showed that she is allergic to carbamazepine and hence she was prescribed gabapentin 300mg and mecobalamin 500mcg thrice daily after which she had complete relief from pain and absence of any allergic reaction to the drug. The patient was on 900mg/day of gabapentin for four months and she has not had any neuralgic episodes. After the fifth month the dose was reduced to 600mg/day. The patient is on regular follow up once in three months since 6 years and she has no relapse.

Discussion:

Review of literature on the medical management of Trigeminal neuralgia provides a multitude of drugs being administered providing varied outcomes. Providing adequate symptomatic relief is quite challenging in many of these patients. Over

the past few decades anti-convulsant drugs, anti-depressants and centrally acting muscle relaxants have been used to manage the pain in trigeminal neuralgia.^[3]

However there is availability of very few randomized controlled trials using these aforementioned drugs in the medical literature as to conclude their efficacy in the management of trigeminal neuralgia, mainly due to the reasons that the cause of trigeminal neuralgia is not known in majority of the cases and in severe cases it remains unethical and unjustifiable in giving a placebo. The degree of pain and episodes of pain is highly variable in early and late stages of the disorders and it also varies in different individuals thus it is difficult to design comparative studies hence there is deficiency of randomized controlled trials.^[4] Hence providing symptomatic relief remains the mainstay in the management of trigeminal neuralgia. Initially medical management of trigeminal neuralgia is attempted and if no relief is obtained surgical therapy may be considered. As per literature among the anti-convulsant drugs carbamazepine is reported to be very effective in causing pain alleviation.^[5, 6, 7] Carbamazepine is a tricyclic imipramine first synthesized in 1961 and introduced for treatment of trigeminal neuralgia by Blom.^[8] Since then it has been used in few randomized controlled trials and double blind placebo trials by authors, Sturman et al.^[9] Campbell et al.^[10] Killian et al.^[11] and the results were conclusive that the drug being beneficial in the management of trigeminal neuralgia. In majority of the cases administration of carbamazepine in doses as low as 100mg thrice daily relieves the neuralgic pain and also serves as the confirmatory diagnosis. Under few circumstances carbamazepine monotherapy may not provide complete pain relief, hence baclofen or clonazepam may be added to achieve pain free episodes.^[12] In late 1980's JM Zakrzewska and Patsalos PN reported in their study on managing six patients suffering from trigeminal

neuralgia refractory to carbamazepine with Oxcarbazepine, a keto derivative of Carbamazepine. The average doses ranged between 600-2400mg per day to achieve pain relief.^[13] Oxcarbazepine is generally not considered as the first line drug in management of trigeminal neuralgia since it is expensive and not widely available in the suburban and rural areas in India.

Under rare circumstances patients may develop allergic reactions to carbamazepine. Approximately 5-20% patients on carbamazepine for anti convulsant therapy exhibit adverse reactions, often to the extent of discontinuation of carbamazepine and switching over to another anti-epileptic drug.^[14] In the present case the patient gave a history of developing several maculopapular eruptions associated with severe pruritis after which the patient discontinued carbamazepine leading to relapse of the electric shock like pain.

Second line treatment includes various other anti-epileptic and centrally acting muscle relaxants like lamotrigine, gabapentin, clonazepam, topiramate, baclofen which have been tried in various trials and have provided symptomatic relief in trigeminal neuralgia. These are more often used as add-on drug to the primary drug or may be used as monotherapy. Lamotrigine acts by blocking voltage gated sodium channels thereby enhancing the action of the inhibitory neurotransmitter gamma amino butyric acid and prevents serotonin reuptake thereby reducing pain.^[15] Zakrzewska et al reported in their double blind placebo study on 13 patients with refractory trigeminal neuralgia were treated with lamotrigine 400mg and they concluded that lamotrigine was effective in providing relief from neuralgic pain compared to the placebo.^[16]

Centrally acting muscle relaxant Baclofen is also effective in alleviating pain in trigeminal neuralgia and is considered as the second line drug and also as add-on drug along with carbamazepine. Fromm GH et al reported in their double blind cross over study

in 10 patients with trigeminal neuralgia that Baclofen significantly reduced the painful paroxysms in 7 out of 10 patients. Baclofen acts by reducing the excitatory neurotransmission thereby reducing the pain.^[17] Till date Baclofen is considered the second best drug next only to carbamazepine.^[18]

Topiramate belongs to the newer group of anti-epileptic drug which has also been used in trigeminal neuralgia and very few studies and case reports have shown promising results. Topiramate doses ranged from 50mg/day to 400mg/day. Six randomized controlled trials involving 354 patients with trigeminal neuralgia were managed with topiramate and carbamazepine and the authors reported that there was no significant difference and they concluded that topiramate was equally efficacious in comparison to carbamazepine in relieving neuralgic pain.^[19,20]

The mechanism of action of Gabapentin is not known. However it has been hypothesized that gabapentin may predominantly act on the voltage dependent calcium channels in the spinal cord and thereby blocks the transmission of excitatory neurotransmitters from demyelinated nerve endings thereby decreasing pain. Gabapentin has plasma half-life of 6-8 hours; hence 300mg has to be given thrice daily to achieve complete pain relief.^[21]

Other Drugs

Pimozide a dopamine antagonist has been traditionally used in the treatment of Tourette syndrome.^[22] Lechin reported in his crossover blinded study of 48 patients with trigeminal neuralgia wherein pimozide was compared with carbamazepine and it was concluded that pimozide was far more superior to carbamazepine as it caused complete pain relief whereas carbamazepine caused pain relief in only 56% of the patients in the study.^[23]

Ziconotide is a non-opioid analgesic administered intrathecally which causes significant

pain relief in patients with chronic pain and in patients refractory to systemic analgesics, intrathecal opioids. Ziconotide targets the N-type sensitive calcium channels inhibiting the depolarization and calcium influx thereby causing inhibition of neurotransmitter thus causing pain relief.^[24]

Pregabalin: Obermann and co-authors reported in their prospective open label study in 53 patients suffering from trigeminal neuralgia who were administered pregabalin 150-600mg daily and the patients were reviewed for one year. They reported that Thirty-nine patients (74%) improved after 8 weeks with a mean dose of 269.8 mg/day and 13 (25%) experienced complete pain relief and 26 (49%) reported pain reduction greater than 50%, whereas 14 (26%) did not improve. Hence they concluded that pregabalin is effective in the management of trigeminal neuralgia.^[25,26]

Conclusion

Management of Classic Trigeminal neuralgia poses a challenging situation for both the patient and clinician as in many cases there may be a relapse of episodes even after adequate prolonged treatment with the standard first line drug of choice carbamazepine. This can cause significant impact on the quality of life. This may warrant routine semi-annual to quarter annual blood investigation in patients with or without systemic diseases since it can cause significant blood dyscrasias when taken for a longer duration. Provision of pain relief for longer duration of time with no or minimal side effects from drugs remains the mainstay in the management of trigeminal neuralgia. Hence the choice of drug should be based on patient's symptoms, medical history that best suits the clinical condition thereby achieving complete pain relief and also to avoid adverse drug reactions. The necessity of routine and timely review in these patients is also essential. In patients allergic to

carbamazepine, gabapentin can be considered as a safer alternative in the management of trigeminal neuralgia.

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