Original Research Article

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Therapeutic Benefit of Palmitoylethanolamide in the Management of Trigeminal Neuralgia

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Abstract

Background: "A Trigeminal neuralgia is a frequent and painful condition which in mostly Idiopathic and is rated by the patients as worst of all pains that afflict the mankind, affecting the all age group people". TGN in characterized by paroxystic episodes of lancing, or burning pain or pain felt as electric discharges, that present spontaneously or may be caused by the action of auditory or cutaneous stimuli , the basic pathogenesis is still mysterious. The safe and effective treatment for TGN and chronic pain is a large public health concern. Palmitoylethanolamide (PEA) is a endogenously produced amide cannabimimetic compound with tissue protection and anti inflammatory activity which is a new class of drug. "Neuropathic pain is defined by international Association for the Study of Pain (IASP), Pain caused by a lesion or disease of the somato sensory nervous system".

Objectives: The aim and objective of this study is to evaluate the effectiveness and safety of Palmitoylethanolamide (PEA) in the management of patient, suffering from TGN.

Materials and Methods: The Study was conducted in the Neurosurgery unit of Surgery Department in Gandhi Medical College and Associated Hamidia Hospital Bhopal India. A total no. of 40 patients aged 20-78 years were included in the study from Nov 1917 to May 1919 and divided into two groups group I (study group) and the group II (Controlled group) PEA was given to group I to evaluated the effect of PEA in TGN.

Result: We have studied 40 patients with PEA for 60 days and Palmitoylethanolamide 354 mg orally given Three times (TDS) a day for first2 weeks than Two times (bid) a day for 6 week. All patients refused surgery. It is available in India in the Name of Palmiges. PEA was associated with greater pain reduction in Study Group compare to the controlled group. The primary outcome measure was the mean pain reduction evaluated by VAS scale.

Conclusion: PEA seems to be useful in the treatment of TGN and it is well tolerated in patients with Study Group. Palmitoylethanolamide (PEA), reduces the inflammation which results in lowering/ reduction of TGN pain and PEA used successfully in the prophylaxis treatment of neuropathic pain. We used PEA in a series of patients surfing from TGN in addition to pharmacological therapy already used. The controlled trials are further needed to prove be efficacy and reliability and also to find out the adverse reaction associated with the drug. Thus, what is needed at this critical juncture is a Solution which corroborates to the care of TGN Pain with No side Effects.

Keywords: PEA; Palmitoylethanolamide; Trigeminal Neuralgia; Analgesics; VAS (Visual Analogue Score); Tic douloureux.

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Introduction

"A Trigeminal neuralgia is a frequent and painful condition which in mostly Idiopathic and is rated by the patients as worst of all pains that afflict the mankind, affecting the all age group people". TNG is also known as Tic douloureux

and is solely diagnosed on the patient's history. TGN in characterized by paroxystic episodes of lancing, or burning pain or pain felt as electric discharges, burning, stabbing and lightening type of pain on the face.[1] Generally pain is unilateral.[2,3] Each paroxysm of severe pain is followed by pain interval while stand for few minutes.[4] Women have been reported to be more affected in most series from western countries while in Indian series men are most affected.[5,6] The maxillary (V2) division is the most common single division to be involved and nearly a third of patients have the pain in the maxillary (V2) and Mandibular (V3) divisions. The pain can occur spontaneously or may be caused by the action of auditory or cutaneous stimuli or may be triggered by the light touch on the trigger zones i.e nasolabial fold, upper lip or tooth, talking, smiling, chewing, brushing the teeth or shaving are common daily activities which can precipitate pain. The basic pathogenesis is still mysterious. The incidence of TGN pain is 4 to 5 per 10000 who are experiencing this characteristic pain. The safe and effective treatment for TGN pain is a large public health concern. Palmitoylethanolamide (PEA) is an endogenously produced amide cannabimimetic compound with tissue protection and anti inflammatory activity which is a new class of drug. "Neuropathic pain is defined by international Association for the Study of Pain (IASP), Pain caused by a lesion or disease of the somato sensory nervous system". Now a day's many drugs are used especially Carbamazepine, Gabapentin, Topiramate and Pregabalin. The present study includes 40 patients of Trigaminal neuralagia who were treated with PEA and in combination with other drugs which are already used.

Objective

The aim and objective of this study is to evaluate the effectiveness and safety of Palmitoylethanolamide (PEA) in the management of patient, suffering from TGN. All patients were treated conservatively and most cases were idiopathic in nature.

Diagnostic Criteria: This is according to the international classification of Head ache and Disorders.

- Paroxysmal attacks of pain, lasting a second to two minutes and affecting one or more divisions of trigeminal nerve (typically maxillary or Mandibular branches).
- Pain has at least one of the following characteristics intense, sharp, superficial, stabbing, and precipitated by trigger areas.
- Attacks are similar in individual patients.
- There is no neurological deficit on examination. It is not caused by another disorder i.e. secondary Causes.

Causes of Secondary Trigeminal Neuralgia

Lesions causing secondary trigeminal neuralgia:

- Vestibular schwannoma
- Epidermoid tumor
- Meningioma
- Petrous Osteoma
- Abscess
- Tuberculoma
- Cysticercosis
- Chiari malformation
- Cavernoma of V nerve
- Aneurysm
- Arteriovenous malformation

Materials and Methods

This Study was conducted in the Neurosurgery unit of Surgery Department in Gandhi Medical College and Associated Hamidia Hospital Bhopal India. A total no. of 40 patients 24 were male and 16 were females. Aged 20-78 years were included in the study from Nov 1917 to May 1919 and divided into two groups group I (study group) and the group II (Controlled group) PEA was given to group I to evaluated the effect of PEA in TGN and in Group II patients already used drugs i.e. Carbamazepine, Gabapentin, Topiramate and pregabalin were given. 16 patients were taking Carbamazepine orally daily 600 to 800 mg. 10 patients were taking Gabapentin orally daily 1200 mg in divided closer. 4 patients were taking Carbamazepine with Topiramate oraly 600 and 100 mg in divided doses and 10 patients were taking Pregabalin orally 150mg in divided doses.

Palmiges: Contains the following components: -

A. Palmitoylethanolamide (PEA)

- PEA is considered an endogenous Peroxisome

Proliferator Activated Receptors (PPAR) agonist or activator, interacting with this receptor to inhibit inflammatory pathways and oxidative stress.

- During neuropathic pain, PEA can modulate the PPAR pathway that is able to attenuate Nuclear Factor Kappa B cells (NFKB) induced inflammatory factors or tumor necrosis factor (IL-1 or TNF), inhibit infiltration and activation of MC, reduce mesangial matrix proliferation induced by reactive oxidative stress (ROS) which then resulted in albuminuria.[8]

B. Genistein

- Genistein is a FAAH inhibitor that not only prevents the degradation of PEA from FAAH enzyme in the body but also exerts synergistic effect with PEA to reduce oxidative stress in the over- inflamed neuronal cells.

C. Daidzein

- Daidzein belongs to the class of isoflavones and serves as a potent FAAH inhibitor in conjunction with Genistein. It works as a competitive binder to FAAH disallowing it to degrade the externally supplemented PEA.

D. Mpfaitech

- A technology to ensure the proprietary blend is presented in a form that could be easily absorbed in the human body.

Palmitoylethanolamide(PEA)isacannabimimetic compound which reduces neuropathic pain. It is a special food for medical purpose in the treatment of chronic pain.

Current treatment drugs such as gabapentin, pregabalin and duloxetine etc. have annoying side effects such as drowsiness, dizziness, blurred vision, somnolence, peripheral edema etc. Moreover, using these drugs in the long term causes desensitization of neuron receptors. Therefore, the dose of these drugs has to be increased to elicit the desired response and that leads to more number of side effects. In addition, some drugs require dose adjustment in renal impairment. Hence, the current treatment paradigms have some gaps and require some new arsenal to fight against Trigeminal neuralgia. Thus, what is needed at this critical juncture is a solution which corroborates to the core of neuropathic pain with no side effects.

Result

Table 1: Age Distribution.

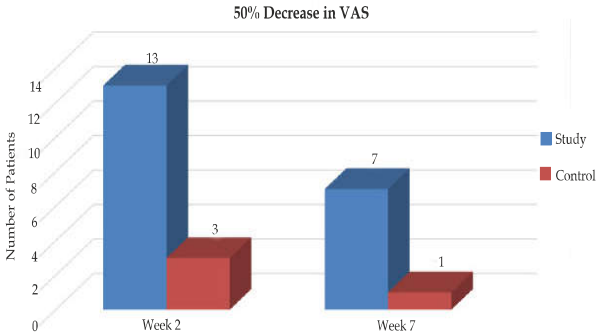
S. No.	Age Group	No.	Percentage
1	18-30	07	17.5
2	31-45	22	55
3	46-60	11	27.5

In our study, we found maximum patients in age group of 31-45 (55%), followed by 46-60 (27.5%). (Table 1)

Table 2: Gender Distribution.

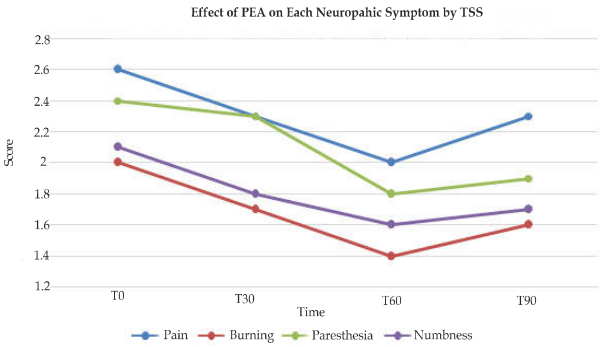
S. No.	Gender	No.	Percentage
1	Male	26	65
2	Female	14	35

In our study, we found male patients in (65%) whereas females (35%). (Table 2)



Graph 1: VAS Score 3.

Vas Score in Week 2 was 13 & 03 in cases & control respectively, whereas in Week 7 was 07 & 01 in cases & control respectively.(Graph 1)



Graph 2: Effect of Pea on Each Neuropahic Symptom by Tss the Observations Support the Recommendation to Use Pea for at Least 2 Month before Evaluating the Result of Pain Reductio.

Max. PEA score value found 2.6 in pain, 2.4 in Patesthesia, 2.1 in Numbness and 2.0 in Burning. (Graph 2)

We have studied 40 patients with PEA for 60 days and The PEA was started to Group I patients in the following doses. 354 mg orally given Three times (TDS) a day for first 2 weeks than two times (bid) a day for 6 week. All patients refused surgery. It is available in India in the Name of Palmiges. PEA was associated with greater pain reduction in Study Group compare to the controlled group. The primary outcome measure was the mean pain reduction evaluated by VAS scale. The mean decrease on the VAS was largest in the study group: a reduction from 7.1 to 2.4 which is more than 50% pain reduction. In controlled group the pain VAS score decreased from 6.8 to 5.0 PEA resulted in significant reduction in TGN pain symptom after 2-3 weeks. After completion of treatment after 8 weeks the same significant reduction ($P<0.001$) was continued in relation to the frequency and intensity of TGN pain symptoms.

Discussion

Trigeminal neuralgia is considered a painful disorder often severe and disabling Anticonvulsants are considered the efficient and effective drugs for the management of TGN pain carbamazepine is the sheet anchor drug in the treatment of trigeminal neurolagia.[7]

Gabapentin and pregablin have been used alone or in combination with trigger point with a local anaesthtic.[8] Toperamide was found ineffective.[9] Since the mostly used drugs revealing ineffective used even the surgery does not always show good results (yao et. al., 2016). The draw backs of current drugs in TGN pain need a new solution. Current treatment option for TGN mainly for used on neuronal symptom suppressing GABA or other inhibitory receptors. Most drugs used for TGN causes drowsiness, blurred vision, somnolence, peripheral oedema and parasthesia. Using these drugs for long time causes desensitization of receptors. Therefore there is increase in the dose of these drugs to elicit desired response that leads to more number of side effects. In conclusion the current treatment paradigms have some gaps and require some new arsenal to fight against TNG pain. PEA studies on trigeminal neuralgia have not been performed and the aim of this study was to test the effectiveness of PEA on TGN pain.

It seems that PEA reduces pain via the natural modulation pathway and besides modulation of the central nervous system, through the release of endorphins, serotonin, norepinephrine and dopamine. Pain reducing effects of acupuncture can also be explained by suppression of activated glial cell.[10] PEA may have a synergistic effect in modulating glial cells, mast cells and neurons.[11] We often observe pain reduction when we add PEA to our treatment. PEA also enhances the analgesic effect of compounds such as pregabalin and amitriptyline. PEA studies on trigeminal neuralgia have not been performed and the aim of this study was to test the effectiveness on trigeminal neuralgia pain. It should be noted that the response to the drug is individual, as in those patients showing pain improvement. It induces to continue using PEA to test the effects on trigeminal pain. In the future provide more comprehensive data, serving to widen the field of action of the mechanisms of the neuroinflammation.

Conclusion

Management of Trigeminal neuralgia remains a challenge for the clinician. It is sobering that till date no randomized controlled trial is available to compare the results of the various procedures used to treat trigeminal neuralgia. Anticonvulsants are sometimes effective in the treatment of trigeminal neuralgia. Carbamazepine and oxcarbamazepine are considered as the first chance of drugs. Use of PEA in painful syndromes is gradually widening, ranging from neuropathic pain to various chronic pains, neuropathies, migraine, stroke, peripheral nerve injuries and Post TBI headache, strengthening the hypothesis of its action on neuroinflamation mechanism. Use of PEA in trigeminal neuralgia seems to be another filed of action which should be encouraged and new trials to be done to see the effect of PEA. In our experience PEA is safe and well tolerated treatment for control/reduction of trigeminal pain. PEA also lacks acute and chronic toxicity and is not associated with gastric mucosal lesions. That is why it has become possible to include PEA in new class of therapeutic agents.

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