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Original Research Article

Oxcarbazepine: A usable alternative to carbamazepine in the treatment of trigeminal neuralgia- A pilot study and drug review

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ABSTRACT

Background: Trigeminal neuralgia (TN) is an extremely debilitating neuropathic pain in which Carbamazepine (CBZ) is the preferred drug of choice in pharmacological management and surgical intervention to be considered only when drug therapy proves ineffective. However, it's long-term use leads to refraction along with severe side effects has made to search for a suitable alternative to CBZ.
Aim & Objective : Present study was conducted to evaluate the effectiveness of Oxcarbazepine (OXC) in those patients, who failed to get adequate relief despite taking CBZ for longer span.
Materials and Methods: 15 patients including 12 males and 3 females (age group 30-65 years) mean age 53.3 years were prescribed OXC in subsequent doses of 300mg, 600mg, 900mg, maximum up to 2400mg and the pain relief was analysed using grading as No response, Moderate and Excellent response.
Result and Observations: Significant pain relief was observed as the dose was increased in the range of 1200-2400mg. Likert scale (5 points scale) for treatment satisfaction was used in which 2 patients marked as very satisfied, 11 patients were found to be satisfied, whereas only 2 marked as neither satisfied nor dissatisfied.
Conclusion: OXC, proves to be a useable alternative to CBZ in terms of being cost effective, better pain control and less side effects. A brief review of the drug OXC is also added.

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1. Introduction

Trigeminal neuralgia (TN) is a chronic painful condition involving any of the three branches of trigeminal nerve. It was described at the end of first century and is known by various names tic- doulourex, epileptiform neuralgia and Fothergill's disease.[1]

International association for the study of headache (IASH) has defined TN as painful unilateral affliction of face characterized by brief electric shock like (lancinating) pain limited to one or more divisions of trigeminal, the 5^{th} cranial nerve.[2]

The common cause of TN results from demyelination due to microvascular compression of trigeminal nerve root by the blood vessels as it enters the brain stem.[3] The recent most classification for simplicity of treatment options divides TN into following types.[4]

1.1. Possible TN, Classical TN, Idiopathic TN

Possible TN- Pain may be paroxysmal or may have a component of continuous pain. It is not triggered by any stimuli.

Classical TN- Paroxysmal attacks triggered by mechanical stimuli. Presence of neurovascular compressions on MRI can be present.

Idiopathic TN- Extraneous stimuli may trigger pain. No definitive cerebrovascular compression will be seen, but may be associated with multiple sclerosis.

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Pain may be of sudden onset, or starts with touching of "trigger zone" shaving, chewing, smiling, brushing, washing of face and contact with cold air making it impossible to do daily activities. One or more branches may be involved. Right side is more commonly affected as compared to left one, possibly due to narrow foramen rotundum and ovale on right side.[5]

More commonly found in advanced age group of 5^{ths} to 8^{th} decade of life with female to male ratio of 5.9-3.4%. Higher number of cases are seen in those from rural background than urban population.[6–8]

Patient may experience moderate to severe sharp, shooting, electric shock like pain. Any number of episodes of pain per day, provided each one lasts no more than 2 minutes. There may be absolutely no pain for weeks to months or pain free periods between two attacks. Pain usually do not occur at night and gets relieved after taking anticonvulsants.[9]

Treatment options varies from medical management to different nerve blocks and surgical interventions. CBZ is the first choice of drug in immediate pharmacological management of TN. Other drugs include OXC, gabapentin, lamotrigine, phenytoin, baclofen and topiramate.[10] Surgical intervention is only reserved for those, who failed to get adequate relief from drugs or where serious side effects prevails. Botulinum toxin injections, pulsed radiofrequency, neuromodulation, cryotherapy, microvascular decompression and gamma knife surgery are some of the few surgical options.[11]

2. Materials and Methods

This pilot study was conducted to estimate the effectiveness of OXC in chronic pain cases of TN in the department of oral medicine and radiology on 15 patients. Ethical clearance and patient's consent was obtained.

2.1. Inclusion criteria

1. Clinically proven cases of TN.
2. Refractory cases, who have tried other drugs except OXC.

2.2. Exclusion criteria

1. Person below 18 years of age.
2. Pregnant and lactating females.
3. Medically compromised patients.

Total 15 patients between the age group (30-65 years) were included in the study, out of which 12 were males and 3 were females. All of them were previously diagnosed with TN with the duration varying from 1.5- 2years. Involvement of any of the three branches of Trigeminal nerve was considered. 8 persons had involvement of right side and left side was painful in 7 cases.

Each patient was prescribed OXC (Tab Oxcarb, Cipla) 300mg on day 1 and pain response was noted as No Response, Moderate and Excellent. Dose was increased in step ladder manner from 300mg to 600mg, 900mg, 1200mg, maximum up-to 2400mg. Follow up was done after 3 days, 1 week, 2 weeks, 3 weeks, 4 weeks and then every month for total of 6 months. After completing 6 months, they were observed for 4 more weeks of a pain free period and the dose was tapered for those, who had complete relief and reiterate in those who still had pain.

3. Observation and Result

Drug compliances as well as pain recordance measurement of all patients was good. Dose response rate was assessed as No response (no relief from pain at all), Moderate response (patient experienced less pain) and excellent response (complete relief from pain). Dose response measurement is shown in tabulated form below. No response was seen in 11 patients at the beginning dose of 300mg, whereas 4 showed moderate response. As the dose was increased number of patients with moderate response also increased. Excellent response was observed when the dose has increased from 1200mg onwards reaching maximum up-to 2400mg. The patients found substantial relief from the pain at different doses (Table 1).

Table 1: Therapeutic dose response to Oxcarbazepine (OXC)

Dose	No response	Moderate response	Excellent response
300mg	11	4	0
600mg	2	10	3
900mg	1	9	5
1200mg	1	7	7
1500mg	0	5	10
1800mg	0	5	10
2100mg	0	3	12
2400mg	0	2	13

Likert scale (5 points scale) for treatment satisfaction was used in which 6 patients marked to be totally satisfied, 7 patients were found to be satisfied, whereas only 2 marked as neither satisfied nor dissatisfied (Table 2).

Table 2: Gender distribution of treatment satisfaction using Likert scale.

Likert's level	Meaning	Males	Females
1	Totally unsatisfied		
2	Unsatisfied		
3	Neither satisfied nor dissatisfied	2	
4	Satisfied	5	2
5	Totally satisfied	5	1

4. Discussion

CBZ is the drug of choice in management of TN. However, it's long-term usage causes ataxia, dizziness, raised hepatic enzymes, hyponatremia in adults with rare and uncommon side effects of leukopenia, aplastic anaemia and Steven Johnson syndrome. OXC was used in the present study, which has better tolerability and fewer side effects than other anti-convulsant drugs prescribed for TN.

Zakrzewska, J et al did a study on 6 patients (2 males and 4 females), (mean age 61 years), and found that OXC (dose range 1200-2400mg) was well tolerated with fewer side effects, except for mild hyponatremia in intractable cases of TN.[12] These findings are in accordance with the present study, where maximum number of patients found relief from pain at doses beginning from 900mg onwards.

Debta Mohan L et al in a clinical trial on 54 patients found OXC to be therapeutic more efficacious, cost effective and well tolerable than Gabapentin in both new as well as refractive cases of TN.[13]

Higher percentage of cases were reported in older age groups in present study (above 50 years). Katusic et al in their study also stated that the annual incidence rate for TN cases rises significantly as the age advances in both male and females.[14] No sensory deficit was reported in present study.

4.1. Drug review

Oxcarbazepine (10,11-dihydro-10-oxo-5H-dibenzazepine-5-carboxamide) is a keto-analogue of carbamazepine with a different metabolic profile. It has better tolerability and lesser side effects than Carbamazepine. It gets rapidly absorbed after oral ingestion and gets metabolized into10,11-dihydro-10hydroxycarbamazepine (10-OH Carbamazepine) and trans10,11-dihydro 10,11 dihydroxycarbamazepine in the liver. (10-OH Carbamazepine) is the chief metabolite and the active ingredient as anticonvulsant therapy.[15]

Carbamazepine- epoxide, (the compound that may be responsible for adverse effects in those taking carbamazepine) is not formed when oxcarbazepine is metabolized.

OXC gets completely absorbed when taken with or without food and the peak concentration rises within 2-4 hours following dose intake. No hepatic enzyme induction is seen. It is excreted via urine following hydroxylation. Dizziness, headache, nausea, vomiting, diplopia are some of its side effects.[16]

American academy of neurology and European federation of neurological societies advocates CBZ and OXC to be first line of choice in pharmacological management of TN.[17,18] Tolerability and side effects due to prolonged intake of CBZ has made OXC a suitable alternative in resistant cases of TN. Although both have comparable efficacy, OXC shows less drug interactions than CBZ.[19] One third of patients showing hypersensitive reaction to CBZ may possess sensitivity to OXC.[20] Rash is the most common idiosyncrasy reaction seen with OXC but less frequently than CBZ. None of our cases reported idiosyncrasy. Most of them tolerated the treatment significantly well except two, who felt nausea and dizziness and they were relieved following tapering of dose.

Poor quality of life due to prolonged periods of paroxysmal attacks and significant side effects on patient taking CBZ since many years can rely on OXC as far as medical management of TN is concerned due to its safe profile.

5. Conclusion

OXC may provide adequate pain relief from chronic pain sufferings in patients who showed unresponsiveness to CBZ. The drug is well tolerated, gives better patient satisfaction and less drug interactions. However, wider database and long-term clinical trials are still required to effectively use OXC as a substitute for CBZ in intractable and refractory cases of TN.

6. Conflict of Interest

None.

7. Source of Funding

None.

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