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Duloxetine: An Effective Drug for the Treatment of Trigeminal Neuralgia.

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ABSTRACT

To compare the efficacy of duloxetine vs carbamazepine in the treatment of trigeminal neuralgia and to assess any adverse effects. Forty patients of trigeminal neuralgia diagnosed using IHS diagnostic criteria 2004 were divided equally into two groups. In Group 1, patients were administered duloxetine 20mg, a selective nor epinephrine reuptake inhibitor twice daily for 2 months while in group2, patients were administered carbamazepine 200mgthrice daily for 2months.Pain assessment was done using Likert's numerical scale and Wong Baker's faces rating scale. Group 1 patients demonstrated statistically significant improvement in pain scores(pre-treatment and post treatment means on faces rating and numerical scale was 7.75± 1.06; 1.25 ±1.01 and 7.65± 0.87; 0.57± 0.76).Mild side effects like nausea, constipation and dizziness were noticed in six patients that subsided on prolonged use of drug. Due to minimal side effects and well tolerability, duloxetine is not only as effective as carbamazepine but seems to be a better drug for the treatment of trigeminal neuralgia.

Keywords: trigeminal neuralgia, selective norepinephrine reuptake inhibitor, duloxetine

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INTRODUCTION

Trigeminal neuralgia is an extremely painful condition that has a significant negative impact on the life of the patients. Symptoms may vary among patients but majority of patients describe it as an 'electric shock 'like pain lasting for few seconds. As it is evoked by stimuli, patients usually escape washing, shaving or combing, hence attaining a shabby appearance. Due to inadvertent diagnosis, often teeth are extracted thus adding to the suffering of the patients. Treatment of trigeminal neuralgia has been a challenging and frustrating task for the dentists. An example of early interventional treatment is that by Locke in 1677, who applied sulphuric acid to the face of the Duchess of Northumberland in an attempt to treat her trigeminal neuralgia. Since decades, carbamazepine has served as a first line drug for this ailment. But due to its side effects, there has always been a need for the advent of new drugs. Hereby, in this article, we compare the efficacy of duloxetine, a selective norepinephrine reuptake inhibitior with carbamazepine in the treatment of idiopathic trigeminal neuralgia.

MATERIALS AND METHODS

At total of 40 patients diagnosed with trigeminal neuralgia according to IHS diagnostic criteria for trigeminal neuralgia were included in this study. All the patients were aged between 41-78years.Before proceeding with the study, ethical clearance was obtained from the Institutional ethical committee and written informed consent was obtained from each patient.

Inclusion criteria

Patients (above 35 years of age) diagnosed with trigeminal neuralgia according to IHS diagnostic criteria 2004.

Exclusion criteria

- Patient who had earlier been treated for trigeminal neuralgia.
- Pregnant females and children.
- Patients suffering from atypical facial pain, postherpetic neuralgia or unstable medical condition.
- Patients allergic to drugs.

Patients were equally divided into two groups. In Group 1 or the study group, patients were administered duloxetine 20mg[Duzela 20, Sun Pharma,Sikkim] twice daily for 2 months while in group 2, patients were administered carbamazepine 200mg [Tegrital, Novartis, Mumbai] thrice daily for 2months.

Written informed consent was obtained from the patients. Blood investigations including complete hemogram and liver function tests were done prior to treatment and at each subsequent visit. All the recordings were noted in specially designed form. Trigger points were palpated and pain assessment was done using 0-10 numeric intensity scale and face scale. In numeric scale, markings are present from 0-10, indicative of minimum to worst

possible pain while Wong Baker's faces scale had faces demonstrating minimum to worst pain. Patients were assessed at an interval of 15days for 2months.

RESULTS

Group 1 comprised of 20 patients (11 males and 9 females) of trigeminal neuralgia with mean age of 59.85± 10.63 years while group B contained 20 patients (12 males and 8 females) with mean age of 62.5± 9.66 years. The youngest patient was 41 years old and the oldest was 78 years old. On comparing the data statistically, it was found that both the groups were matched for age and gender.

Routine haemogram, biochemical investigations and liver function test were all within normal limits. At each visit, pain assessment was done using Likert's numerical scale and Wong Baker's faces rating scale. Group 1 patients demonstrated statistically significant improvement in pain scores (pre-treatment and post treatment mean value on faces rating and numerical scale was 7.75± 1.06; 1.25 ±1.01 and 7.65 ±0.87; 0.57± 0.76). The improvement in pain relief was almost equal when compared with group 2 patients (pre-treatment and post treatment mean value on faces rating and numerical scale was 7.55± 1.01; 1.45 ±0.82 and 7.75 ±1.01; 0.95± 0.94) [as shown in table 1].On comparing the data statistically, no significant difference was noted in the efficacy of both these drugs. No significant changes were observed in blood pressure, pulse and respiratory rate. There was no drop out case.

Six patients in the study group complained of side effects like nausea, dizziness and dry mouth in the first week of treatment while majority of patients reported side effects in group 2.

DISCUSSION

Trigeminal neuralgia is 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]. Trigeminal neuralgia, or "Tic Doloureux", is a painful condition of the face often triggered by certain specific areas in head and neck region which are clinically known as trigger zones. Trigger zones are commonly located on the cheek, nose, lip and buccal mucosa. This pain has been known since ancient times. There are descriptions of facial pain by Ibn Sina (980–1073) in an Arabic text. Various researches and reviews have proved that trigeminal neuralgia significantly impacted the quality of life and the socioeconomic functioning of the affected patients. Trigeminal neuralgia is the most common form of facial pain in people older than 50 years of age and is more prevalent in women than men with a ratio of 1.5:1.3 [2]. The International Headache Society (HIS) proposed diagnostic criteria for trigeminal neuralgia in 2004, which states that:

- Paroxysmal attacks of pain (fraction of a second to two minutes)
- Pain has at least one of the following characteristics:
- Intense, sharp, superficial or stabbing
- Precipitated from trigger areas or by trigger factors

- Attacks are stereotyped
- No clinically evident neurological deficit
- Not attributed to any other disorder

Treatment is challenging and includes antiepileptics and anti-depressants. Carbamazepine is a tricyclic imipramine first synthesized in 1961 which was introduced for treatment of trigeminal neuralgia by Blom [3]. Various clinical studies have shown that carbamazepine resulted in almost 50% reduction of pain.[4] Not only are the intensity of attacks reduced, but the frequency is also lowered [4,5]. However, trial and observational data show that the efficacy of carbamazepine is compromised by its adverse effects. The reviewers found significantly more adverse effects (drowsiness, dizziness, constipation and ataxia) with carbamazepine than with placebo [4, 6]. The adverse effects of carbamazepine described in observational studies include leucopenia and abnormal liver function tests, dermatological rashes, Aplastic anaemia, somnolence/dizziness/nausea/nystagmus/,hepatic dysfunction/ hyponatremia. The pharmacokinetics of the drug also result in numerous drug interactions and one of special note is that with warfarin [6].

Back in 2011, K.S Anand et al conducted a study on 15 patients of trigeminal neuralgia. In their study, they assessed the efficacy, safety and tolerability of duloxetine in idiopathic trigeminal neuralgia and reported significant pain relief in the majority of patients. They also noticed minor adverse effects in nine patients [7].

Extrapolating the findings of their study, we tried to compare the efficacy of duloxetine and carbamazepine in trigeminal neuralgia.

Duloxetine has earlier been used to treat cases of major depression and anxiety, relieve nerve pain as in diabetic peripheral neuropathy, to improve mood, sleep, appetite, energy levels and to decrease nervousness. It belongs to the class of serotonin and norepinephrine reuptake inhibitors. It has low affinity for most 5-HT subtypes and for muscarinic, histamine H1, alpha-1adrenergic, alpha-2 adrenergic and dopamine D2 receptors. Absorption of duloxetine begins two hours after oral administration, reaching a maximum plasma concentration in six hours. It has bioavailability of 32-80% and 95% protein binding. It gets metabolised in liver by P450 isozymes CYPZD6 and CYP1Az. Half- life is 12 hours and 70% of drug is excreted via urine, 10% along with faeces. The recommended dosage is 40-80mg daily in two doses. Side effects reported in literature are nausea, dry mouth, constipation, tiredness, dizziness, increased sweating and blurred vision. Severe adverse effects may be fainting, unusual mental or mood changes, tremor or alteration of blood sugar in diabetic patients [7].

But in our study, only mild side effects like nausea, dizziness and constipation were noticed in the first week of treatment which subsided on prolonged use. Thus, the drug was well tolerated by all study patients. Significant pain relief was noticed within first week of treatment and appreciable pain relief was seen in majority of patients at the end of 2 months [table1].

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Table 1: Comparison of baseline and post treatment pain scores in group 1 and group 2 patients

GROUP1 (n=20)					GROUP 2 (n=20)				
Age in years/ sex	PAIN SCORES				Age in years/ sex	PAIN SCORES			
	Before treatment		After treatment			Before treatment		After treatment	
	Face scale	Numeric scale	Face scale	Numeric scale		Face scale	Numeric scale	Face scale	Numeric scale
41/F	8	8	3	2	45/M	8	9	3	2
72/M	7	8	2	0	70/M	8	7	2	3
49/M	9	8	2	1	48/M	8	9	2	2
55/F	6	8	2	0	50/F	7	8	3	2
63/F	10	9	2	1	64/F	7	7	2	2
70/M	9	9	3	2	55/M	7	8	2	2
62/M	8	7	2	1	73/F	10	9	1	1
56/F	7	6	0	0	59/F	9	9	1	1
65/M	7	7	0	0	62/M	8	9	1	1
76/M	9	8	1	2	65/M	8	8	2	0
74/F	7	6	1	0	67/M	9	8	2	0
71/M	8	7	0	0	72/F	9	7	0	0
45/F	8	7	0	0	75/M	8	6	0	0
47/M	8	7	0	0	78/M	6	7	1	0
65/M	6	8	1	0	70/M	6	8	1	1
48/F	8	8	1	1	56/F	7	7	2	1
52/M	8	8	0	0	59/F	6	6	2	1
69/F	8	9	1	0	63/M	7	9	1	0
64/M	8	7	2	1	70/M	6	6	1	0
53/F	6	8	2	1	49/F	7	8	1	0
TOTAL						TOTAL			
59.85 ±10.63	7.75 ±1.06	7.65 ±0.87	1.25±1.01	0.57 ±0.76	62.5 ±9.66	7.55± 1.14	7.75 ±1.01	1.45± 0.82	0.95 ±0.94
				P<0.05					P<0.05

Table: Comparison of baseline and post treatment pain scores in group 1 and group 2 patients

M: Male; F: Female
All quantitative data are expressed as mean ± SD . A p-value less than 0.05 was considered statistically significant

CONCLUSION

Duloxetine is as effective as carbamazepine in the treatment of trigeminal neuralgia, but owing to adverse effects, low tolerability and frequent dosage of carbamazepine, duloxetine proves itself to be a better drug. More controlled trials at large scale are needed to establish duloxetine as a treatment modality in cases of trigeminal neuralgia.

Take Home Messages

- Pain is mediated through descending serotonin and norepinephrine pathways in brain. Duloxetine increases the pain threshold as it blocks the reuptake of both serotonin and norepinephrine.

- Duloxetine, by virtue of its well tolerability, less number of side effects and optimal dosage, promises to be a better and efficient drug for the treatment of trigeminal neuralgia.

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