Original Article

Topiramate and Pregabalin in Lumbar Radicular Pain. Is Topiramate a better option?

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[2] *Conception of study*
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Abstract

Objective: To compare the efficacy of two anticonvulsant drugs topiramate and pregabalin on lumbar radicular pain and to find out whether topiramate is a better option or not.

Study design: Experimental study.

Place and Duration: This study was conducted at the Department of Neurosurgery, Combined Military Hospital, Lahore. The study duration was from January to March 2020.

Material and Methods: 60 patients of both gender divided into two groups of 30 each were included. Patients were assessed based on the subjective impairment scale of the Oswestry Disability Index. The maximum score was calculated in percentage with a higher score pointing to greater disability. Both drugs were given in low starting once-daily dose, 75 mg for pregabalin, and 25 mg for topiramate for two weeks followed by twice-daily dose for two more weeks in patients not getting pain relief.

Results: Male to female ratio of 4:1 in both groups. The age range of 27-77 years (41.5 $\pm$ 12.45) for pregabalin and 22-74 years (41.6 $\pm$ 14.6) for the topiramate group. Baseline demographics and pre-drug pain measurement index were identified amongst the two groups. Oswestry disability index was 49.2 $\pm$ 18.3 pre-drug and post-drug 41 $\pm$ 16.4 for pregabalin ($p<0.01$). For topiramate, it was 43.6 $\pm$ 37.9 pre-drug and 37.9 $\pm$ 17.3 post drug ($p<0.01$).

Conclusion: Both pregabalin and topiramate are effective in radicular pain management, and topiramate is not better but still a viable option as an alternative to pregabalin.

Keywords: Pain, Topiramate, Pregabalin.

Introduction

Lumbar radicular pain is defined as the pain radiation along with specific nerve roots in the dermatome distribution of the lower limb. Amongst the pain management drugs, pregabalin is one of the commonly used first-line medications.[1,2,3] Response to pain management is different for every individual hence treatment has to be tailored accordingly. Pregabalin is also widely used as a treatment for epilepsy, neuropathic pain, fibromyalgia, restless leg syndrome, and generalized anxiety disorder.[4] It was developed as a successor to gabapentin. Common side effects include headache, dizziness, confusion, memory lapse, poor coordination, peripheral edema, dry mouth, blurring of vision, and weight gain. Serious side effects include angioedema, drug misuse, associate degreed a multiplied suicide risk.

Topiramate is an anticonvulsant and is used to manage painful neuropathies including diabetic neuropathy and trigeminal neuralgia.[5,6] It has also been used in chronic lumbar radicular pain.[7] Its mechanism of action is by augmenting the γ aminobutyric acid activity and modulation of voltage-dependent sodium channels to block repetitive action potentials. There is a suggested mechanism of blocking kinate evoked currents through antagonist effect on α-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid (AMPA) pathway but not NDMA pathway which is the mechanism of action in other antiepileptic drugs. Its common side effects are giddiness, somnolence, paresthesia, and alter in style, anorexia, weight loss, itching, and nervousness.

Materials and Methods

The study was conducted at the Department of Neurosurgery, Combined Military Hospital, Lahore from January to March 2020. Patients who presented with lumbar radiculopathy with degenerative disc disease/ nerve root compression on magnetic resonance imaging of lumbosacral spine were included after getting hospital ethical board review approval to vide 143/2019. The sample size was calculated using the online "sampsize" calculator sample size calculation with a confidence interval of 95%, a margin of error of 5%, and a reference prevalence of 4% for radicular pain due to disc degenerative spine disease.[8] Patient's age range from 20 to 70 years of both gender. There were 60 patients, with 30 patients who received topiramate and 30 patients who were given pregabalin. The sampling technique used was non-probability convenience sampling Patients who were pregnant, undergone lumbar discectomy, received epidural steroids in the last 1 month and those with a history of diabetes mellitus/psychiatric illness/ narrow-angle glaucoma were excluded from the study. Topiramate was given at 25 mg every 12 hours for the first 2 weeks, followed by 50 mg 12 hourly for further two weeks as per pain relief. A control group was given Pregabalin 75 mg bed-time titrated to 75 mg 12 hourly after 2 weeks if required for pain management. The effects of both drugs were noticed at the end of their trial period of four weeks. A questionnaire was filled to score patients based on the Oswestry Disability Index. There were 10 questions about the effect or limitation on various routine activities and employment. Each question had items marked 0 to 5 (maximum total marks=50). Marks were divided by 50 and then multiplied with 100 to get a score in percentage. The higher the percentage, the more is the disability. The patient's response was again scored on the same questionnaire after 1 month. Some of the patients who did not report for follow-up were contacted on the telephone and the questionnaire was filled by the investigator. Data was entered and analyzed in SPSS version 20. Frequency, mean and standard deviation were calculated for quantitative variables. An Independent t-test to check the significance with a p-value ≤ 0.05 is regarded as significant.

Results

The patient's age range was 27-77 years (41.5 $\pm$ 12.45) for pregabalin and 22-74 years (41.6 $\pm$ 14.6) for the topiramate group of patients with a male to female ratio of 4:1 in both groups. Baseline demographics were the same for both groups of patients, as given in Table 1. Left-sided sciatica was most common in both groups i.e. 28 (46.7%) patients, backache was associated with sciatica in 13 (21.7%) patients. Pre-drug Oswestry Disability Index was 49.2 $\pm$ 18.3 for the pregabalin group and 43.6 $\pm$ 17.6 in the topiramate group. Patients who had a duration of pain for a year and more were 19 (63.3%) in the pregabalin group and 23 (76.6%) in the topiramate group. The transient blurring of vision of 2 (6.6%) patients was recorded in the topiramate group and the dose was 50 mg/day. Visual acuity was gradually restored two days after the drug was discontinued. Other adverse effects of the two drugs are as given in Table 2. Oswestry disability index was 49.2 $\pm$ 18.3 pre-drug and post-

drug 41 ± 16.4 for pregabalin (p<0.01), while it was 43.6 ± 37.9 pre-drug and 37.9 ± 17.3 post drug (p <0.01) for topiramate group as given in Figure 1.

Table 1: Baseline Demographics of two groups

Variable	Pregabalin Group n(%)	Topiramate Group n(%)
Age	41.1 ± 12.4	41.6 ± 14.6
Gender		
Male	24 (80%)	24 (80%)
Female	6 (20%)	6 (20%)
Marital Status		
Married	2 (6.7%)	3 (10%)
Single	28 (93.3%)	27 (90%)
Work Status		
Strenuous	15 (50%)	12 (40%)
Non Strenuous	15 (50%)	18 (60%)
Oswestry Disability Index		
Pre Drug	49.2 ± 18.31	43.6 ± 17.6

Table 2: Adverse effects of both drugs

Adverse effects	Topiramate n(%)	Pregabalin n(%)
Numbness	0 (0%)	3 (10%)
Peripheral Edema	0 (0%)	7 (23.3%)
Dizziness	4 (13.3%)	6 (20%)
Palpitations	2 (6.7%)	0 (0%)
Headache	0 (0 %)	1 (3.3%)
Blurring of vision	2 (6.7%)	0 (0%)
Flushing	0 (0%)	3 (10%)
Memory lapse	0 (0%)	2 (6.7%)
Vomiting	0 (0%)	1 (3.3%)
Weight loss	0 (0%)	1 (3.3%)
None	22 (73%)	14 (46.7%)

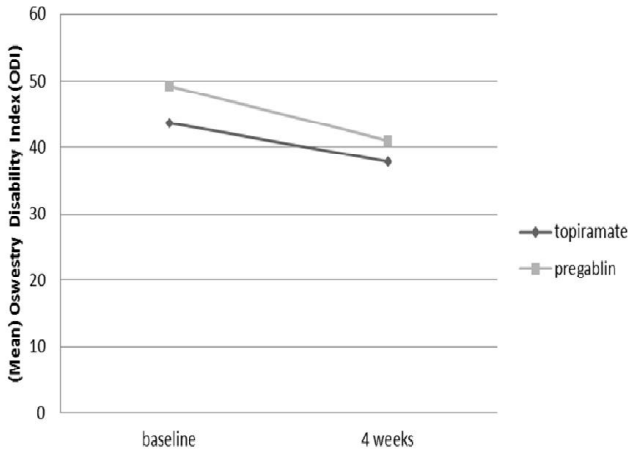

Figure 1: Change in Oswestry Disability Index over four weeks

Discussion

Radicular pain secondary to lumbar disc degenerative disease is one of the most common ailments with which patients present to the out-patient Department of Neurosurgery.[9] There are options of conservative vs surgical management of radicular pain due to sciatica.[10] Surgical intervention does give early pain relief in selected patients but over the long-term, both have a similar outcome in terms of pain relief.[11] National guidelines are made based on local population data.[12] All baseline demographic parameters were similar in both groups. The mean age of our patients of both groups was 41.1 years which is in accordance with the mean age of 42-47 years as found by Tubach.[13] In our study males were more common in both groups, 48 out of 60 patients (80%) whereas Konstantinou found females to be more common (62.6%) in their study.[14] When we studied the effect of gender it was not related to disability due to radicular pain is sciatica (p= 0.54). Hofstee and others did not find gender to be related to radicular pain but later research by Peul found that females did have more chronic pain and slower recovery as compared to males and he attributed that this is related to emotional lability and pain coping mechanism.[15,16] Similarly marital status and nature of work were statistically unrelated to the Oswestry Disability Index. Oswestry Disability Index was the pain assessment tool we used in our study. It is a reliable gauge applied to evaluate the baseline and response of treatment in patients of radicular pain such as sciatica.[17,18] Pregabalin is a commonly used drug for radicular pain and in our study, it statistically better pain outcome in Oswestry Disability Index improvement i.e. 49.2 ± 18.3 before drug improved to 41 ± 16.4 for pregabalin (p<0.01). Topiramate when given to patients had a similar response as 43.6 ± 17.6 pre-drug vs 37.9 ± 17.3 post drug (p <0.01). Khoromi compared topiramate to placebo for chronic lumbar radicular pain and found a significant pain-relieving effect of the drug (p< 0.005).[19] Topiramate had less number of patients without side effects as compared to pregabalin, 22 (73%) vs 14 (46.7%). Visual blurring in two patients of the topiramate group was a worrisome finding as patients had to discontinue the drug for reversal of its effect. Except for visual problem topiramate was well tolerated. Mathieson et al in their study found out that pregabalin when compared with placebo its side effects to be significantly high.[20] Thus the topiramate though as effective as pregabalin in relieving pain is a

better drug as patients would be more compliant due to fewer side effects.

The limitation of the study is that a longer follow-up will give information about compliance and the late side effects of the drugs if any. Efficacy on quality of life and return to work requires different parameter assessment. Future studies can focus on the relationship of response to higher doses of two drugs and whether a specific drug is more effective with any specific radiological abnormalities of disc degeneration on Magnetic Resonance Imaging.

Conclusion

Both pregabalin and topiramate are effective for pain relief in patients with radicular pain secondary to disc degenerative disease. Topiramate is a viable alternative for pain management with fewer side effects of the drug.

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