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STUDY TO KNOW THE EFFICACY OF PREGABALIN VERSUS AMITRIPTYLINE FOR THE TREATMENT OF PAINFUL DIABETIC NEUROPATHY

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Abstract:
Objective: *To associate the efficacy of amitriptyline, pregabalin and placebo in relieving pain linked with diabetic peripheral neuropathy.*
Study Design: *A Randomised Placebo-Based Study.*
Place and Duration: *In the Medicine Unit I of Jinnah Hospital Lahore for one year duration from February 2017 to February 2018.*
Methodology: *150 patients were randomly assigned to the study. Pain relief was assessed on an 11-point Likert scale [NRS]; 0 = no pain during a reference period of 7 days "10 = worst possible pain"). After a 1 week wash period without study drug, participants were divided into 3 groups of 70 patients each receiving placebo, amitriptyline or pregabalin for six weeks. The first dose of amitriptyline and pregabalin was 75 mg twice daily and 10 mg before bedtime. Doses were increased as required during the 1st and 3rd weeks of treatment. The maximum dose of pregabalin and amitriptyline was 300 mg twice daily and 75 mg before bedtime. Responders were those who experienced a 50% or more reduction in the initial pain score in NRS.*
Results: *210 patients were included in the study. 126 (60%) were male and 84 (40%) were female. The age ranged from 22 to 76 years. 112 (53.3%) had diabetes for <15 years and the remaining 98 (46.7%) had DM for 15 years. 105 (50%) experienced diabetic neuropathy for more than 6 months, while the remaining 50% had painful DN for more than 6 months. A significant improvement was observed in PNG pain in patients receiving pregabalin (48.1%) and amitriptyline (41.4%) than those receiving placebo (10.5%).*
Conclusion: *Pregabalin and amitriptyline treatment of patients with PND provides better pain relief than placebo. Of the two drugs, pregabalin showed a greater response.*
Key Words: *poly diabetic neuropathy (DPN), numerical rating scale (NRS).*

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INTRODUCTION:

The diabetic neuropathy prevalence is as high as 50% in diabetic patients for 25 years, and in 26% of all diabetics, painful diabetic peripheral neuropathy (DPN) occurs. Symptoms range from mild dysesthesia to intense and persistent pain[1]. Since patients often suffer from symptoms on a everyday basis, painful PND has a major undesirable effects on life quality[2]. A variety of various medications are used to treat painful PND at various degrees of tolerability, safety and efficacy. Clinical studies confirm the anticonvulsants and antidepressants efficacy in the painful diabetic neuropathy treatment[3]. Several randomized controlled trials have demonstrated the tricyclic antidepressants efficacy such as amitriptyline in painful PND[4]. Antiepileptic agents, pregabalin and gabapentin have been widely used in the painful PND treatment. These substances bind to the auxiliary α2-helper subunit of the stress-sensitive calcium channel, which reduces Ca2 + flow at the nerve terminals and modulates the release of neurotransmitters[5]. The aim of this study was to compare the amitriptyline, pregabalin and placebo efficacy in relieving pain associated with linked peripheral neuropathy.

MATERIALS AND METHODS:

This comparative Study was held in the Medicine Unit I of Jinnah Hospital Lahore for one-year duration from February 2017 to February 2018. 150 patients were randomly assigned to the study. Patients with the following criteria were included in the study: age ≥ 18 years, DPN for at least 6 months, mean pain score ≥4 (on a Likert numerical scoring scale of 11 points [NRS]; 0 = "No pain" 10 = "worst possible pain ") 7-day reference period. Exclusion criteria: pain not associated with PND, mononeuropathies or proximal neuropathies, previous therapeutic failure with any antidepressant or anticonvulsant therapy. Informed consent was obtained from all patients before participation. All participants received a 1-week washout period without study medication. Participants were divided into three groups of 70 patients receiving placebo, amitriptyline or pregabalin for 6 weeks. Active therapies were evaluated upward as required in the 1st and 3rd weeks of treatment. The first dose of pregabalin and amitriptyline was 75 mg B.I.D and 10 mg before bedtime. The amitriptyline and pregabalin maximum dose were 300 mg B.I.D and before bedtime 75 mg was given. The primary outcome of the study was pain reduction; Responders were those who experienced a 50% or more reduction in the initial pain score in NRS. Data were analysed using SPSS 19 for Windows through the application of descriptive statistics and cross-tabulation. Frequencies and percentages were calculated. Chi-square test was used for qualitative variables and t-test was used to compare the means. Significance was kept less than 0.05 at the p-value.

RESULTS:

A total of 210 patients were selected for the study. 126 (60%) were male and 84 (40%) were female. The age ranged from 22 to 76 years. It was found that 112 (53.3%) diabetes lasted <15 years and the remaining 98 (46.7%) had DM for> 15 years. 105 (50%) experienced diabetic neuropathy for more than 6 months, while the remaining 50% had painful DN for more than 6 months. Response to treatment was measured by decreasing NRS points after 6 weeks. Patients receiving pregabalin (48.1%) and amitriptyline (41.4%) had a significant improvement in PND pain compared to those receiving placebo (10.5%) (Table 1). Nine patients (12.8%) received better response compared to pregabalin and amitriptyline (Table 1).

Table 1: Comparison of response to therapy in various groups

Therapy	Response		Total
	<50%	>50%	
Placebo	56	14	70
Amitriptyline	15	55	70
Pregabalin	6	64	70
Total	77	133	210

Response to any drug was significantly better in those with a shorter DPN duration (80), ie, when the DPN duration was longer (6) than <6 months (Table 2).

Table 2: Effect of duration of neuropathy on the response to therapy

Therapy	Duration of neuropathy	Response		Total
		<50%	>50%	
Placebo	<6mns	21	7	28
	>6mns	35	7	42
	Total	56	14	70
Amitriptyline	<6mns	1	34	35
	>6mns	14	21	35
	Total	15	55	70
Pregabalin	<6mns	3	39	42
	>6mns	3	25	28
	Total	6	64	70
Total	<6mns	25	80	105
	>6mns	52	53	105
	Total	77	133	210

DISCUSSION:

Main findings of this study:

1. Painful PND patients receiving pregabalin or amitriptyline showed a statistically significant improvement over 6 weeks compared to placebo.
2. A greater improvement was observed in patients receiving pregabalin than in amitriptyline.

The results of the present trial reflect the results of some previous randomized trials comparing antidepressants and anticonvulsants with placebo and with each other in the treatment of painful diabetic neuropathy in which both drugs are effective in relieving at least one pain[6]. Bansal et al., in a study comparing amitriptyline and pregabalin, showed little difference in efficacy between the two treatments, but pregabalin may be an alternative option because it is associated with less adverse effects in our population[7-9]. In our study, pregabalin showed some advantages over amitriptyline in the treatment of DPN pain. Another observation in the study was the presence of factors impeding the clinical recovery of patients in the study groups, including longer and poorly controlled diabetes and a longer duration of PND[10-11]. The results of this study may leave the doctor in a riddle: what exactly is the best treatment for painful diabetic neuropathy? Given that multiple therapies are effective for the treatment of diabetic peripheral neuropathy, it can be concluded that the individual factors and preferences of the patient are essential in deciding which treatment to choose[12-13]. An important factor in this decision for many patients is the profound difference in price between drugs such as pregabalin and amitriptyline[14]. Given the average doses used in this study, pregabalin treatment may be more expensive than amitriptyline treatment. However, the low cost of amitriptyline should be compared with the more important profile of adverse events, especially in elderly patients. Such events include the risk of falls and life-threatening arrhythmias[15].

CONCLUSION:

Antidepressants and Anticonvulsants are the most frequently used for painful diabetic neuropathy, although rise in number of trials to control neuropathic pain have investigated different drug types. Long-term analysis on the side effects and efficacy of antidepressants and anticonvulsants are required because these drugs are widely used in clinical settings. Further revisions are required on non-pharmacological strategies as well as N-methyl-D-aspartate antagonists, opioids and ion channel blockers.

REFERENCES:

1. Azmi, S., ElHadd, K.T., Nelson, A., Chapman, A., Bowling, F.L., Perumbalath, A., Lim, J., Marshall, A., Malik, R.A. and Alam, U., 2019. Pregabalin in the Management of Painful Diabetic Neuropathy: A Narrative Review. Diabetes Therapy, 10(1), pp.35-56.
2. Borgfeld, Nathan, Gaurav Mehta, Kia Ousley, Hayden Head, and James Ryan Menard. "Does topical lidocaine provide comparable relief to oral neuropathic agents in the treatment of neuropathic pain?." Evidence-Based Practice 22, no. 5 (2019): 10-11.
3. Derry, Sheena, Rae Frances Bell, Sebastian Straube, Philip J. Wiffen, Dominic Aldington, and R. Andrew Moore. "Pregabalin for neuropathic pain in adults." Cochrane Database of Systematic Reviews 1 (2019).
4. Ciaramitaro, P., Cruccu, G., de Tommaso, M., Devigili, G., Fornasari, D., Geppetti, P., Lacerenza, M., Lauria, G., Mameli, S., Marchettini, P. and Nolano, M., 2019. A Delphi consensus statement of the Neuropathic Pain Special Interest Group of the Italian Neurological Society on pharmacoresistant neuropathic pain. Neurological Sciences, pp.1-7.
5. Onakpoya, Igho J., Elizabeth T. Thomas, Joseph J. Lee, Ben Goldacre, and Carl J. Heneghan. "Benefits and harms of pregabalin in the management of neuropathic pain: a rapid review and meta-analysis of randomised clinical trials." BMJ open 9, no. 1 (2019): e023600.
6. Jordan, Berit, Franziska Jahn, Sandra Sauer, and Karin Jordan. "Prevention and Management of Chemotherapy-Induced Polyneuropathy." Breast Care 14, no. 2 (2019): 79-84.
7. Matsuoka, Hiromichi, Keita Tagami, Keisuke Ariyoshi, Shunsuke Oyamada, Yoshiyuki Kizawa, Akira Inoue, and Atsuko Koyama. "Attitude of Japanese palliative care specialists towards adjuvant analgesics cancer-related neuropathic pain refractory to opioid therapy: a nationwide cross-sectional survey." Japanese journal of clinical oncology(2019).
8. Azmi, Shazli, Maryam Ferdousi, Alise Kalteniece, Hamad Al-Muhannadi, Abdulrahman Al-Mohamedi, Nebras H. Hadid, Salah Mahmoud et al. "Diagnosing and managing diabetic somatic and autonomic neuropathy." Therapeutic advances in endocrinology and metabolism 10 (2019): 2042018819826890.
9. Narayanan, Varsha. "Combined Psychophysical Approach to Pharmaco-therapeutic Management of Chronic Pain: A Review." The Indian Practitioner 72, no. 5 (2019): 33-38.
10. Azmi, S., Petropoulos, I.N., Ferdousi, M., Ponirakis, G., Alam, U. and Malik, R.A., 2019. An update on the diagnosis and treatment of diabetic somatic and autonomic neuropathy. F1000Research, 8.

11. Baba, Masayuki, Norimitsu Matsui, Masanori Kuroha, Yosuke Wasaki, and Shoichi Ohwada. "Mirogabalin for the treatment of diabetic peripheral neuropathic pain: A randomized, double-blind, placebo-controlled phase III study in Asian patients." Journal of diabetes investigation (2019).
12. Michaelides, Athena, Robert DM Hadden, Ptolemaios G. Sarrigiannis, Marios Hadjivassiliou, and Panagiotis Zis. "Pain in Chronic Inflammatory Demyelinating Polyradiculoneuropathy: A Systematic Review and Meta-Analysis." Pain and therapy (2019): 1-9.
13. Finnerup, Nanna B. "Nonnarcotic Methods of Pain Management." New England Journal of Medicine 380, no. 25 (2019): 2440-2448.
14. Breen, J., Schrubbe, H. and Smallwood, S., 2019. Does topical capsaicin provide pain relief for patients suffering from chronic neuropathic pain?. Evidence-Based Practice, 22(5), p.1.
15. Callaghan, Brian C., Evan Reynolds, Mousumi Banerjee, Kevin A. Kerber, Lesli E. Skolarus, and James F. Burke. "Longitudinal pattern of pain medication utilization in peripheral neuropathy patients." Pain 160, no. 3 (2019): 592-599.