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COMPARISON OF EFFICACY AND SAFETY BETWEEN GABAPENTIN AND AMITRIPTYLINE IN PATIENTS WITH DIABETIC PERIPHERAL NEUROPATHY PAIN

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ABSTRACT:

INTRODUCTION: The most disturbing sign of diabetic peripheral neuropathy is pain. Of patients with diabetes mellitus, almost thirty to fifty percent develop peripheral neuropathies. Most often occurring kind is distal symmetric sensorimotor polyneuropathy (DSPN). Two most often used medications in pain related with this disorder are amitriptyline and gabapentin. This study was conducted to compare the effectiveness and safety between Gabapentin and Amitriptyline in patients with painful diabetic peripheral neuropathy**.**

MATERIALS AND METHODS: This study was a randomized, open-label, comparative study done over a duration of six months. Sixty patients with diabetic polyneuropathic pain were randomly assigned to two groups. Group A was administered oral Amitriptyline, whereas Group B was given oral Gabapentin for a period of 12 weeks. The patients had examination four times during the study duration. Following the baseline appointment, patients were instructed to return for following sessions at four-week intervals up to twelve weeks. Efficacy was assessed with an 11-point numeric pain rating scale and the MNSI score and adverse consequences were documented.

RESULTS: The study comprised a total of 60 patients, with 30 individuals assigned to each group (Amitriptyline group and gabapentin group). The mean age of patients was 62.11 ± 3.47 in Group A and 63.46 ± 4.90 in Group B. Group A included 21 males and 9 females, whereas Group B consisted of 20 males and 10 females. The mean decrease in NPRS scores was significant between the two groups, with a greater reduction in pain seen in the Gabapentin group compared to the Amitriptyline group. The reduction in the mean MNSI (H/O) score was significant across the two groups, with a greater decrease seen in the Gabapentin group compared to the Amitriptyline group. A greater incidence of adverse events was found in the amitriptyline group compared to the gabapentin group.

CONCLUSION: Both therapy groups offered clinically significant pain reduction with manageable side effects. However, gabapentin produced much more pain alleviation than amitriptyline, and gabapentin has a lower rate of side effects. Hence It may be established that gabapentin is safer and more effective than amitriptyline in individuals with painful diabetic peripheral neuropathy.

KEYWORDS: Efficacy, Gabapentin, Amitriptyline, Diabetic Peripheral Neuropathy (DPN).

INTRODUCTION: The prevalence of diabetes mellitus (DM) is rising and poses a significant threat to public health [1]. Diabetes mellitus management must be conducted continuously to regulate blood glucose levels and prevent problems [2]. of the most prevalent consequences is neuropathic pain, namely painful diabetic peripheral neuropathy (DPN), affecting around 25% to 30% of individuals with diabetes mellitus.3 Symptoms of diabetic peripheral neuropathy (DPN) include numbness, tingling, stabbing pain, burning sensations, electric shock sensations, and discomfort in the lower limbs and/or hands, sometimes referred to as "glove-stocking" distribution [4]. Pain from diabetic neuropathy might disrupt work or everyday activities, necessitating treatment [5].

DPN pain is common in diabetic patients; however, existing therapy options such as antidepressants, anticonvulsants, antiarrhythmics, and topical capsaicin are constrained by inconsistent effectiveness and side effects [6]. Amitriptyline hydrochloride demonstrates efficacy in around 60% to 75% of individuals undergoing treatment for diabetic peripheral neuropathy (DPN), regularly surpassing the effectiveness recorded with other medications [7]. The considerable adverse effects of all existing pharmacological therapy, especially the anticholinergic effects of tricyclic antidepressants, are concerning.

In 1993, gabapentin, a γ-aminobutyric acid derivative, obtained Food and Drug Administration clearance for supplementary therapy of partial seizures, both with and without subsequent generalization in people with epilepsy [8]. Despite comprehensive studies [9,10], the mechanism of action of gabapentin remains unidentified. Despite the incomplete understanding of its mechanism of action, there has been a growing body of case reports regarding gabapentin's application in neuropathic pain syndromes, including reflex sympathetic dystrophy, post-herpetic neuralgia, migraine, trigeminal neuralgia, erythromelalgia, Guillain-Barré syndrome, and other intractable pain conditions, with dosages varying from 900 to 2400 mg per day [11,12]. A recent placebo-controlled clinical study in individuals with diabetic peripheral neuropathy pain has shown the effectiveness of gabapentin in alleviating pain. Gabapentin, characterized by a minimal side effect and medication interaction profile, may be an efficacious therapy for diabetic peripheral neuropathy pain.

This study was conducted to compare the effectiveness and safety between Gabapentin and Amitriptyline in patients with painful diabetic peripheral neuropathy**.**

MATERIALS AND METHODS:

The current prospective, open-label, and randomized comparative study was conducted at Bhaskar Medical College & General Hospital. A total of 60 patients with diabetic peripheral neuropathic pain were represented. After obtaining written informed consent, patients who met the inclusion criteria and did not meet any of the exclusion criteria were included in the study. The criteria for inclusion and exclusion were as follows:

INCLUSION CRITERIA: A total of 60 consenting patients aged 60 years and above of either sex with the diagnosis of Diabetic Peripheral Neuropathy based on Michigan Neuropathy Scoring Instrument (MNSI)

EXCLUSION CRITERIA: Patients taking medication for PDN prior to enrolment, patients with other causes of neuropathy, patients taking anticonvulsants, antidepressants or opioids, Pregnant and lactating women, patients with clinically significant medical or psychiatric illnesses, known cases of renal dysfunction, chronic liver diseases, known cases of epilepsy, malignancy, uncontrolled hypertension.

STUDY DESIGN*:* This study was conducted after obtaining ethical clearance was obtained from the Institutional Ethics Committee. A simple randomization was carried out in this study using a computer-generated list of random numbers. 60 patients were randomly allocated to two groups. Patients in group A (n=30) were administered oral amitriptyline 50mg/day in daily divided doses and patients of group B received Gabapentin 1800mg/day in daily divided doses [14]. Following selection and recruitment, the individual patient's therapy lasted 12 weeks. The patients were examined four

times during the study. Following the baseline visit, patients were requested to report at four-week intervals for up to twelve weeks. Participants in the study were individually advised not to consume nonsteroidal anti-inflammatory drugs, vitamin B12, antidepressants, sedative-hypnotic or psychotropic drugs, local anesthetics, opioids, or alcohol concurrently during the study period, and to report any such use immediately if there was an emergency. At monthly intervals, a blood sample was submitted to the laboratory for fasting blood glucose testing.

EFFICACY AND SAFETY ASSESSMENTS:

NPRS SCORE: The primary end point of the study was the reduction in mean pain score from baseline as assessed by the numeric pain rating scale (11- point scale from 0-10) at the end of 4, 8 and 12 weeks. NPRS is a standard instrument in chronic pain. studies. It is an 11-point Numerical pain rating scale (NPRS), where 0 = no pain and 10 = worse pain [15].

MNSI SCORE: The MNSI score consists of two parts, history and physical assessment were assessed at baseline, 4, 8 and 12 weeks. History contains 15 "yes or no" questions (>4 correlates DPN). Physical assessment includes foot inspection, ulceration, vibration, muscle stretch reflexes and monofilament testing. It consist of total score of 10 (>2 correlates DPN) [16].

ADVERSE EVENTS: Safety was assessed by recording adverse drug reactions

STATISTICAL ANALYSIS*:* The data were presented as mean ± S.D for quantitative data and number and percentages for qualitative data. Data were analyzed using the unpaired t-test for comparing the mean difference between the two groups. p value <0.05 was considered to be statistically significant.

RESULTS: A total of 60 patients, 30 patients in each group (Amitriptyline group A and Gabapentin group B) were included in the study. The average age of the patients was 62.11 ± 3.47in Group A and 63.46 ± 4.90 in group B. There were 21 males and 9 females in group A and 20 males and 10 females in group B. The average BMI was 26.73 ± 3.71in group A & 26.15 ± 2.96 in group B. The average FBS level was 152.46±31.78 and 10.23±3.65 in Group B. The average Duration of diabetes was 10.57±3.65 in group A and 10.23±3.65 in group B. The average NPRS score was 7.5±1.32 in group A and 7.3±1.28 in group B. The average MNSI (H/O) score was 6.32 ± 1.44 in group A & 6.26 ± 1.29 in Group B. The average MNSI (PS) score was 6.12± 1.54 in Group A & 6.11 ± 1.45 in Group B as shown in Table 1

Table 1: Baseline demographic and clinical characteristics

Characteristics	Group A (n=30)	Group B (n=30)
Age (Years)	62.11 ± 3.47	63.46 ± 4.90
Sex		
Male	21 (70%)	20 (67%)
Female	9 (30%)	10 (33%)
BMI ($Kg/m^{2)}$	26.73 ± 3.71	26.15 ± 2.96
FBS levels (mg/dl)	152.46±31.78	154.35± 33.86
Duration of diabetes (years)	10.57±3.65	10.23±3.65
NPRS score	7.5±1.32	7.3±1.28
MNSI (H/0) score	6.32 ± 1.44	6.26 ± 1.29
MNSI (PS) score	6.12± 1.54	6.11 ± 1.45

Mean NPRS score reduction was significant when compared between the 2 groups and Pain reduction was more in Gabapentin group when compared with Amitriptyline group as shown in Table 2

Table 2: comparison of Mean NPRS score in both groups

Mean NPRS scosre	Group A	Group B	p value
Base line	7.5±1.32	7.3±1.28	0.2
4 weeks	4.8±0.95	3.6±0.92	0.03*
8 weeks	2.3±0.54	1.6±0.48	0.02*
12 weeks	1.3±0.38	1.1±0.39	0.003*

*** significance**

Mean MNSI (H/O) score reduction was significant when compared between the 2 groups and reduction was more in Gabapentin group when compared with Amitriptyline group as shown in Table 3

Table 3: comparison of Mean MNSI (H/O) score in both groups

Mean MNSI (H/O) score	Group A	Group B	p value
Base line	6.32 ± 1.44	6.26 ± 1.29	0.08
4 weeks	5.9 ± 1.32	5.4 ± 1.28	0.03*
8 weeks	4.6± 1.12	4.4 ± 1.16	0.004*
12 weeks	3.8 ± 1.01	3.2 ± 1.03	0.01*

*** significance**

Side effects were mild and there were no serious adverse effects reported in either of the treatment groups. higher number of adverse events reported in the amitriptyline group when compared with Gabapentin group as shown in Table 4.

Table 4: Adverse effects reported in both groups

Adverse effects	Group A	Group B
Dry mouth	11 (36.6%)	4 (13.3%)
sedation	9 (30%)	8 (26.6%)
fatigue	8 (26.6%)	4 (13.3)
dizziness	8 (26.6%)	3 (10%)
constipation	2 (6.6%)	0 (0.0%)

DISCUSSION:

In order to assess distal symmetrical peripheral neuropathy in 28 distinct clinical sites, W.H. Herman et al. examined the Michigan Neuropathy Screening Instrument (MNSI) in 1184 diabetic subjects. They came to the conclusion that the MNSI is an easy, non-invasive, and reliable indicator of distal symmetrical peripheral neuropathy [17]. Improvement in the patients' neuropathic signs and symptoms as measured by the NPRS score and MNSI score at baseline, 4, 8, and 12 weeks served as the basis for evaluating the trial medications' effectiveness. The baseline mean pain score according to the MNSI and NPRS measures was comparable to that of another research that assessed the effectiveness using both scales [18,19].

This study shows statistically significant difference in reduction in mean pain score between the two groups. At the end of the study it was seen that gabapentin reduces pain more significantly than amitriptyline at 4, 8 and 12 weeks ($p<0.05$) as per NPRS scale. Another study by Dallocchio et al conducted on 25 patients for 12 weeks had showed similar significant difference in pain reduction in Gabapentin and Amitriptyline groups [20].

In this study, the well-established MNSI score was used to assess the neuropathy status at baseline, 4, 8, and 12 weeks. The two groups' MNSI ratings significantly decreased, according to our research. This demonstrates that gabapentin is more effective than amitriptyline in reducing the symptoms of neuropathy. These findings are comparable to those of a 12-week research that examined paraesthesia scores [21].

CONCLUSION: Both gabapentin & amitriptyline therapy groups offered clinically significant pain reduction with manageable side effects. However, gabapentin produced much more pain alleviation than amitriptyline, and gabapentin has a lower rate of side effects. Hence It may be concluded that gabapentin is safer and more effective than amitriptyline in individuals with painful diabetic peripheral neuropathy.

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