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Comparing the effectiveness of pregabalin and duloxetine in the management of neuropathic pain

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Abstract

Background and objective: Neuropathic pain is a type of pain that originates from damage or dysfunction of the somatosensory nervous system. Managing neuropathic pain is a challenging task as it is chronic and has limited treatment options. Pregabalin and duloxetine aim to alleviate neuropathic pain symptoms and enhance quality of life for patients. The comparative effectiveness of these drugs, particularly at lower doses that are typically provided in the Kurdistan Region of Iraq, is still a topic of inquiry that is presently being carried out. The objective of the study is to evaluate and compare the effectiveness of pregabalin and duloxetine on pain management and sleep quality in patients with neuropathic pain. Such insights are crucial for optimizing neuropathic pain management strategies and improving patient outcomes.

Methods: in this prospective study, 80 patients displaying signs and symptoms of neuropathic pain such as sharp, stabbing, numbness, and/or burning pain as well as tingling, loss of balance and coordination, and/or muscle weakness, especially in the feet were prescribed either pregabalin (n=40) or duloxetine (n=40) with mean doses of 82.5± 5.16 mg/day and 34.5± 2.46 mg/day, respectively, administered once or twice daily for 4 weeks. The results were based on the effectiveness of the drugs in reducing visual analogue scale and pain related sleep interference scale scores.

Results: Both pregabalin and duloxetine reduced the signs and symptoms of neuropathic pain, demonstrating similar efficacy within the first 3 weeks of the treatment. However, by the 4th week, duloxetine exhibited superior effectiveness in managing neuropathic pain (P = 0.001). On the other hand, findings showed no significant difference in the reduction of sleep scores (P = 0.978).

Conclusion: Both pregabalin and duloxetine are similarly effective in managing neuropathic pain during the first 3 weeks of treatment. However, when the treatment duration extends beyond 3 weeks, duloxetine demonstrates superior effectiveness in reducing neuropathic symptoms.

Keywords: Pregabalin; Duloxetine; Neuropathic pain; Effectiveness; Sleep.

Introduction

Neuropathic pain (NeP) is linked with an increased frequency of prescriptions and healthcare provider visit. Chronic NeP affects millions worldwide and presents significant challenges in management and treatment. NeP may occur as either peripheral, due to nerve lesion or disease impacting the somatosensory system (such as postherpetic neuralgia, lumbar radiculopathy, neuropathy related to diabetes or HIV, or pain following surgery), or as central, following events like a stroke or spinal cord injury. The somatosensory system plays a crucial role in detecting sensations like touch, pressure, pain, temperature, body position, movement, and vibration.[1-3] However, not everyone

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experiencing peripheral neuropathy, central nervous system injury, or a nerve lesion or disease of the somatosensory system develops NeP. For instance, only about 26% of people with type 2 DM and 21% of those who get shingle send up having NeP.[4]

NeP is both prevalent and profoundly impactful, often perceived as more severe than non-NeP conditions. People experiencing NeP rate various aspects of health and QoL as poorer compared to those with non-NeP, even when the severity of pain is taken into account.[5,6] Therefore, selecting a treatment that is both effective and safe is important for enhancing the quality of life of the patients. Epidemiological studies showed that a considerable number of individuals experiencing NeP are not receiving suitable treatment. The causes could include inaccurate diagnosis, ineffective medications, and potentially inadequate awareness regarding effective medications and their proper utilization in clinical settings.[7,8] Therefore, it is essential to have guidelines based on evidence for the pharmacological treatment of NeP. Many approaches for the treatment of NeP have been taken over the years, and the drugs that have the strongest recommendations in terms of effectiveness and safety so far are gabapentin, pregabalin, selective serotonin reuptake inhibitors like duloxetine (DLX), venlafaxine, and tricyclic antidepressants[9] Pregabalin (PGB) and duloxetine are both approved by the U.S. Food and Drug Administration (FDA) in 2004 for the management of diabetic NeP. In addition, these two drugs are the only ones approved by the FDA specifically for this indication.[10,11]

Pregabalin was the most used anti-neuropathic drug in Iraq in 2021.[12] However, since duloxetine has only recently been used for the treatment of NeP in Iraq, it is not as widely prescribed for NePas pregabalin in Iraq. Despite the availability of these drugs, there is still a need for comparative studies to assess their effectiveness, especially in Iraq, as studies have shown that the effectiveness and safety of a medication can differ across regions due to variations in genetics and environmental factors.[13] Currently, there has been no study conducted in Iraq to directly compare the effectiveness of pregabalin and duloxetine. This study aims to fill this gap by conducting a comparison of pregabalin and duloxetine, assessing their effectiveness in reducing pain and enhancing sleep quality disrupted by pain in the management of chronic NeP to guide physicians in making tailored treatment plans for their patients to improve patient outcome.

Methods

Patients

4-week prospective observational cohort study conducted at Mihrabani, Arzheen, Rizgary, and Paky Hospitals in Erbil, Kurdistan Region of Iraq. A total of 80 patients were diagnosed with NeP between November 2023 and January 2024. Forty of them were prescribed DLX with a mean daily dose of 34.5± 2.46 mg (34 of them were prescribed 30mg once daily and 6 of them were prescribed 30mg twice daily), and forty of them were prescribed PGB with a mean daily dose of 82.5± 5.16 mg (36 of them were prescribed 75mg/d, and 4 of them were prescribed 150mg/d). We originally enrolled 92 patients; however, twelve of them were excluded because they were either lost to follow-up or started taking other pain relief medications that relieve NeP. Patients who visited these sites and met the study criteria during these 3 months were continuously enrolled to minimize selection bias. Patients were followed up with every week for 4 weeks.

Inclusion Criteria

People diagnosed with NeP of all ages and genders, patients enrolled onto either PGB or DLX right after diagnosis, patients who were willing to comply with questions and follow-ups, and whose who were able to provide informed consent and capable of understanding and completing pain

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assessment tools were included in this study.

Exclusion Criteria

Patients who were in concurrent use of other neuropathic pain relief medications that alleviate NeP, and who were planning surgical intervention during the study period that could impact pain assessment or treatment outcomes, and patients who were unable to comply with study requirements or expected to be unavailable for follow-ups were excluded from this study.

Ethical Considerations

All patients provided verbal consent before answering the questionnaire and for the follow-ups. Approval number HMU-EC-PH 04062024-32 was granted to this work by the Committee of the Ethics in the Hawler Medical University/College of Pharmacy.

Visual Analogue Scale

The visual analogue scale (VAS) is a regularly employed and straight forward tool for evaluating changes in pain intensity. In clinical settings, the degree of pain relief, as determined by VAS, is frequently regarded as an indicator of treatment effectiveness. The pain score spans from 0 to 10 (Figure 1) where 0 signifies “no pain” and 10 signifies “worst pain possible”.[14]

Pain-Related Sleep Interference Scale

The Pain-Related Sleep Interference Scale (PRSIS) is used to measure the extent of sleep disruption caused by pain. This scale also has scores ranging from 0 to 10, where 0 means ‘does not interfere with sleep’ and 10 ‘completely interferes with sleep – unable to sleep due to pain’ (Figure 2). Patients are requested to

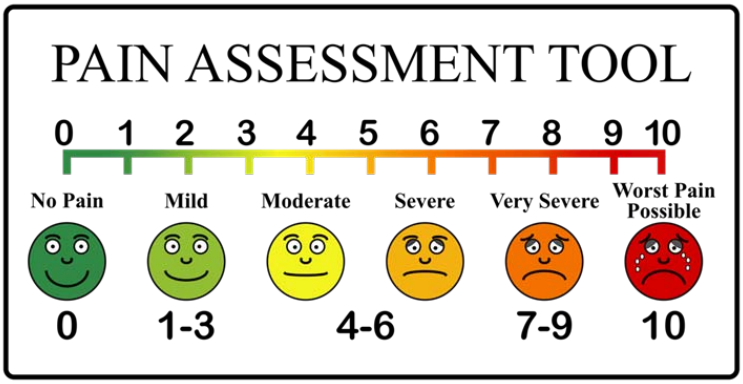

Figure 1 Visual Analogue Scale (VAS) used for measuring pain intensity[14]

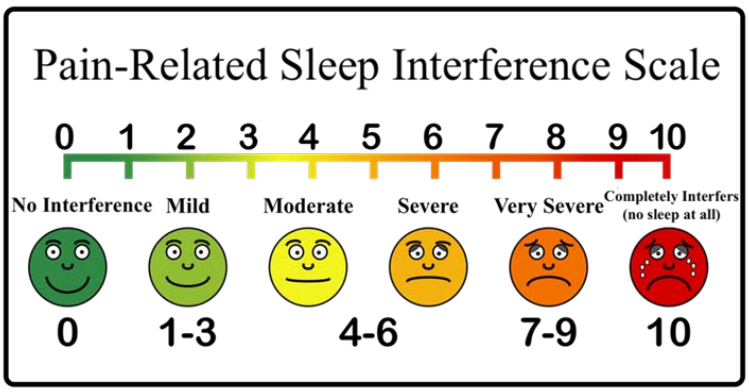

Figure 2 Pain-Related Sleep Interference Scale (PRSIS) used for measuring the effect of pain on sleep.[15]

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choose the number that most accurately represents the degree to which their pain disrupts their sleep within 24 hours.[15]

Statistical Analysis

The data were represented as the mean ± standard error (M ± SE). Results were calculated by using Statistical Package for Social Sciences software (version 27). The student's t-test was employed to compare the means of the two groups. The difference is presumed to be significant when the *P* value is less than 0.05.

Results

Patients diagnosed with NeP from medical centers: Rizgary, Arzheen, Mihrabai, and Paky Hospitals, were included in the study. A total of 80 patients who met the inclusion criteria were followed up with for 4 weeks and recruited for the final analysis. Among these patients, the majority were females (60 females versus 20 males). The demographic and clinical representation of patients are represented in Table 1.

Table 1 Patients Demographic and Clinical Representation

Variables		PGB (n=40)	DLX (n=40)
Age (years)	30 – 49	22 (55%)	34 (84%)
	50 - 69	14 (35%)	6 (16%)
	70 - 90	4 (10%)	0 (0%)
Gender	Female	28 (36%)	32 (40%)
	Male	12 (15%)	8 (10%)
Duration of NeP	0 – 6 months	22 (55%)	14 (35%)
	> 6 months	18 (45%)	26 (65%)
Type of Pain	Numbness	26 (65%)	18 (45%)
	Stabbing	12 (30%)	26 (65%)
	Shooting	16 (40%)	14 (35%)
	Electric shock-like	16 (40%)	14 (35%)
	Burning	12 (30%)	14 (35%)
	Pins and needles	8 (20%)	8 (20%)
	Tingling	4 (10%)	10 (25%)
Comorbidities	DM	14 (35%)	8 (20%)
	HTN	16 (40%)	4 (10%)
	CVD	4 (10%)	4 (10%)
On pain relief medications		14 (35%)	14 (35%)
Timing of Pain	Continuous	28 (70%)	18 (45%)
	Comes and goes	8 (20%)	10 (25%)
	Intermittent	4 (10%)	8 (20%)
	Brief constant	0 (0%)	4 (10%)
Side Effects	Drowsiness	14 (35%)	10 (25%)
	Dizziness	10 (25%)	6 (15%)
	Stomach upset	6 (15%)	2 (5%)
	Nausea	2 (5%)	0 (0%)
	Vomiting	2 (5%)	0 (0%)
	Dry mouth	4 (10%)	4 (10%)
	Tinnitus	2 (5%)	0 (0%)
	Headache	0 (0%)	4 (10%)
	Fatigue	0 (0%)	2 (5%)
	Nightmare	0 (0%)	2 (5%)
	Tachycardia	0 (0%)	2 (5%)
	No side effect	22 (55%)	24 (60%)
Stopped Treatment Due To Side Effects		8 (20%)	6 (15%)

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Based on the pain VAS score (Table 2), the intensity of NeP was reduced within 4 weeks, with DLX found to be slightly more effective at week 4, a statistically significant finding (P = 0.001). However, with the PRSIS score (Table 3), the results were not found to have a statistically significant difference (P >0.05).

As for adverse effects, drowsiness (35%), dizziness (25%), stomach upset (15%), nausea (5%), vomiting (5%), and tinnitus (5%) were more frequent in PGB, while DLX was associated more with tachycardia (5%), headache (10%), fatigue (5%), and nightmares (5%). Dry mouth was reported equally for both drugs (10%).

Table 2 Effects of PGB and DLX on pain VAS score

	PGB	***DLX***	***P-Value***
Week 0	7.00±0.562	8.58±0.332	0.009
Week 1	5.05±0.764	5.35±0.54	0.37
Week 2	4.05±0.63	3.70±0.45	0.74
Week 3	3.00±0.55	2.94±0.39	0.15
Week 4	3.07±0.78	1.85±0.34*	0.001

The star indicates significant differences at P <0.05
The values are expressed as mean±SE

Table 3 Effects of PGB and DLX on PRSIS score

	PGB	***DLX***	***P-Value***
Week 0	4.52±0.95	7.58±0.56	0.05
Week 1	3.41±0.75	5.42±0.72	0.65
Week 2	2.11±0.56	3.23±0.53	0.89
Week 3	2.0±0.57	2.53±0.55	0.972
Week 4	1.57±0.51	1.92±0.47	0.978

The values are expressed as mean±SE

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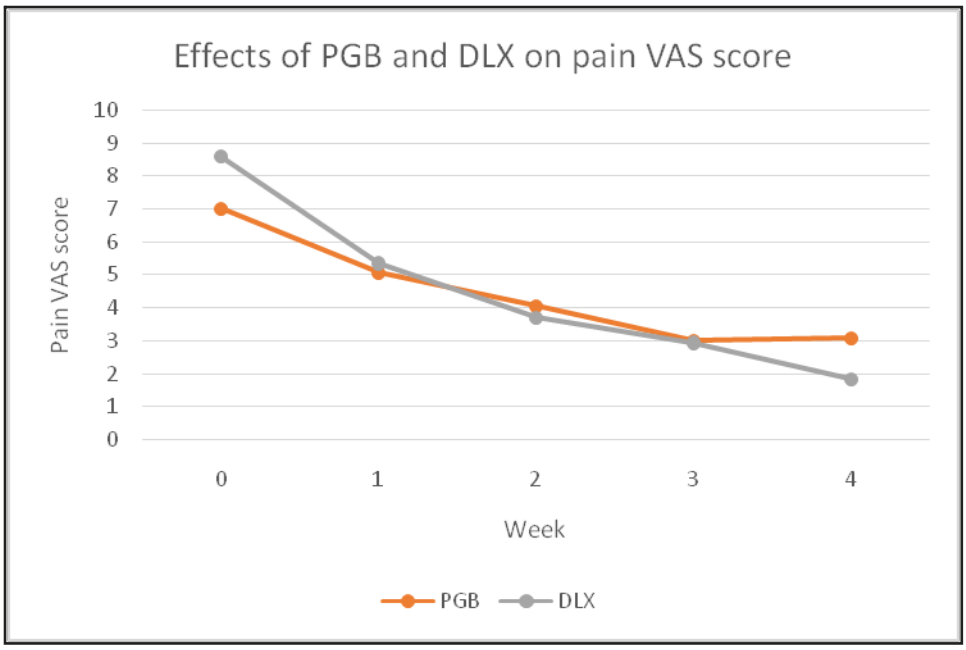

Figure 3 Line graph showing the effects of PGB and DLX on pain VAS score over 4 weeks

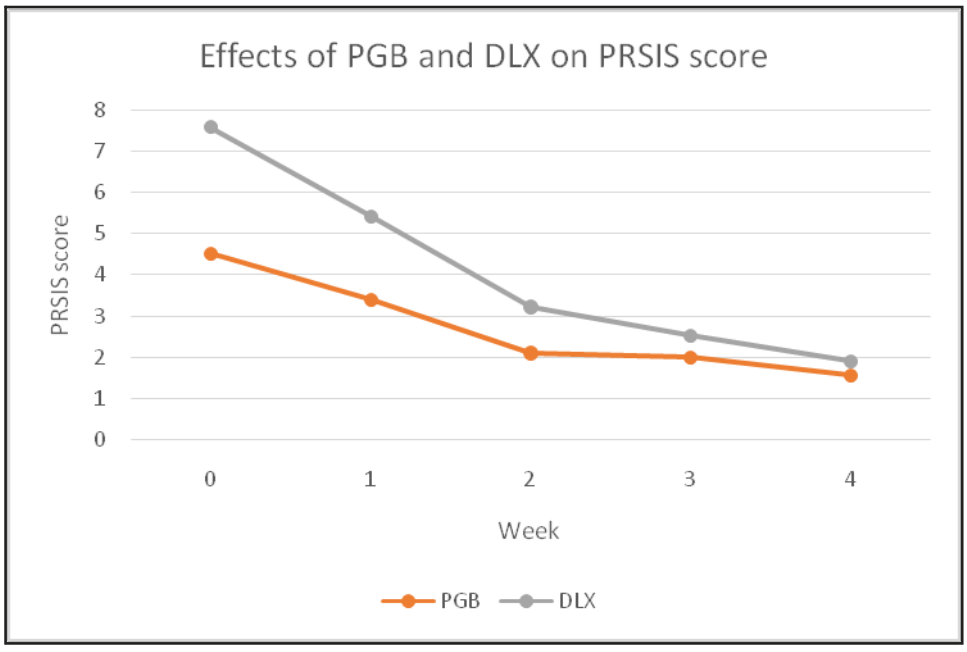

Figure 4 Line graph showing the effects of PGB and DLX on PRSIS score over 4 weeks

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Discussion

The overall outcome obtained from the 80 patients in Rizgary, Arzheen, Mihrabani, and Paky Hospitals indicates that both PGB and DLX significantly reduced the intensity of NePat week 4, being DLX slightly more effective. PGB was shown to be as effective as DLX. There wasn't a statistically significant difference in pain scores during the follow-ups at weeks 1 and 2. Improvement started becoming noticeable by week 3, with a statistically significant difference observed by week 4, favoring DLX which correlates with a meta-analysis conducted by Quilici and her colleagues.[16] However, after discontinuing treatment at 4 weeks, some patients experienced a return of their pain with both drugs. Many other studies found no significant difference between PGB and DLX in reducing NeP.[17,18] Most of these studies were done on higher doses of PGB and DLX (150 mg and 60 mg, respectively) whereas in our study, we mostly studied lower doses of PGB and DLX (75 mg and 30 mg, respectively). These are the doses most prescribed in the Kurdistan Region of Iraq, and our study showed they are effective. This can also help reduce the events of adverse effects. The doses of the drugs were flexible depending on the patient's responsiveness and tolerability.

Both drugs improved sleep quality however they were not found to have a statistically significant difference. Some patients reported improved sleep quality despite no reduction in their pain scores. Both drugs showed a quicker improvement in sleep quality compared to pain scores. Many studies have shown that PGB and DLX improve sleep quality[19-21]

PGB was deemed safer than DLX based on its side effects, as it primarily had mild to moderate effects. In contrast, DLX caused more severe side effects, including tachycardia, leading some patients to discontinue treatment. The majority of patients experienced drowsiness only during the first week of treatment with both drugs. However, the treatment of DLX was discontinued by 15% of patients midway due to severe adverse effects, including fatigue and tachycardia. The frequently observed side effects of PGB in the majority of previous studies involved cognition/coordination and vestibulo-cerebellar/brainstem structures such as dizziness, drowsiness, incoordination, balance disorder, ataxia, and tremors.[22] As for DLX, nausea, drowsiness, dizziness, sexual dysfunction, dry mouth, headache, insomnia, constipation, and decreased appetite were the most frequent adverse effects.[23,24] One of the infrequently observed side effects was nightmare which was reported with DLX (5%) that has also been reported in previous studies, however, it is uncommon.[22]

We excluded 12 out of 92 patients (13%). Among them, 7 started using other pain relief medications that could potentially aid in reducing NeP, including flurazepam, fluoxetine, escitalopram, etoricoxib, and ketoprofen. Additionally, 5 patients (10%) were lost to follow-ups.

Conclusion

Both PGB and DLX were capable at reducing NeP. The physician may prescribe either PGB or DLX if the treatment period is intended to last up to three weeks, based on effectiveness. However, DLX is more effective if the treatment period is four weeks, as indicated by this study. Furthermore, PGB reported low to moderate side effects in comparison to DLX, which exhibited more severe but less frequent side effects, including cardiovascular-related adverse effects such as tachycardia and central nervous system adverse effects such as nightmares, as indicated by the safety profile.

Both drugs, PGB and DLX, equally and rapidly improved the quality of sleep disrupted by pain regardless of pain reduction.

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Competing interests

The authors declare that they have no competing interests.

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