International Journal of Biological and Pharmaceutical Sciences Archive

ISSN: 0799-6616 (Online)

Journal homepage: https://ijbpsa.com/

(REVIEW ARTICLE)

Check for updates

Efficacy and safety of gabapentin in diabetic peripheral neuropathy: A systematic review of clinical studies

Nuha M Salih Al-Zaubai [1,*] and Husam Ghazi Al-Anbari [2]

[1] *Faculty of Medicine, Karbala University.*
[2] *Faculty of Medicine, Al-Ameed university.*

International Journal of Biological and Pharmaceutical Sciences Archive, 2025, 09(02), 037-043

Publication history: Received on 28 February 2025; revised on 21 April 2025; accepted on 23 April 2025

Article DOI: https://doi.org/10.53771/ijbpsa.2025.9.2.0041

Abstract

Background: Diabetic Peripheral Neuropathy (DPN) is a common complication of diabetes, causing chronic pain and sensory disturbances that significantly impact patients' quality of life. Gabapentin, initially developed as an antiepileptic drug, has gained widespread use in treating neuropathic pain, including DPN. However, concerns remain regarding its efficacy and safety compared to other treatment options.

Objective: This review aims to assess the efficacy and safety of gabapentin for DPN by analyzing data from ten previous studies, including randomized controlled trials (RCTs) and meta-analyses.

Methods: A systematic review was conducted using databases such as PubMed, Cochrane Library, and Google Scholar. Studies were included based on specific criteria: (1) patients diagnosed with DPN, (2) gabapentin as a primary treatment, and (3) reported pain reduction and adverse effects. Comparative studies with alternative medications such as pregabalin and duloxetine were also considered.

Results: Gabapentin demonstrated significant pain reduction, with most patients experiencing moderate to substantial improvement. Studies reported a ≥50% reduction in pain in many cases. The drug was well-tolerated, with common side effects including dizziness, somnolence, and mild peripheral edema. Compared to pregabalin and duloxetine, gabapentin provided similar pain relief but with a slower onset of action. It also presented a lower risk of dependency and was found to be a more cost-effective option for long-term management.

Conclusion: Gabapentin is an effective treatment option for DPN, offering substantial pain relief and an acceptable safety profile. While some patients experience mild adverse effects, the overall tolerability supports its long-term use. Given its cost-effectiveness and comparable efficacy to other first-line treatments, gabapentin remains a viable option in neuropathic pain management. Future research should focus on optimizing dosage strategies and identifying patient-specific predictors for better treatment outcomes.

Keywords: Gabapentin; Diabetic Peripheral Neuropathy; Neuropathic Pain; Safety; Efficacy; Systematic Review

1. Introduction

Diabetic peripheral neuropathy (DPN) is a common complication of diabetes mellitus. impacting nearly half of individuals with long-standing diabetes (1,2,3). It is characterized by nerve damage that leads to sensory disturbances, including numbness, tingling, and burning pain, primarily in the lower extremities (2,4). DPN significantly impairs patients' quality of life and increases the risk of foot ulcers, infections, and amputations (5,6).

* Corresponding author: Nuha M Salih Al-Zaubai

Among the various pharmacological options available for managing neuropathic pain, gabapentin has emerged as a widely prescribed medication (7,8,9). Gabapentin, originally developed as an antiepileptic drug, exerts its analgesic effects by modulating calcium channels in the central nervous system, thereby reducing neuronal excitability and abnormal pain signalling (9,10). Several clinical studies have evaluated its efficacy and safety in patients with DPN, leading to its frequent use as a first-line treatment in neuropathic pain management guidelines (11,12).

Despite its widespread prescription, the therapeutic benefits of gabapentin in DPN remain a subject of debate (3,12). While some studies have reported significant pain relief and improved functional outcomes, others have raised concerns about its limited efficacy, side effects, and long-term safety (2,3). Common adverse effects, including dizziness, sedation, and peripheral edema, can affect patient adherence and tolerability (13). Furthermore, recent discussions on the potential for misuse and dependence have brought renewed attention to the safety profile of gabapentin (13,14,15).

Given these concerns, a comprehensive review of existing clinical studies is essential to assess the efficacy and safety of gabapentin in the management of DPN. This systematic review aims to analyze and synthesize available clinical evidence to provide a clearer understanding of gabapentin's role in DPN treatment. By evaluating randomized controlled trials (RCTs), observational studies, and real-world data, this review seeks to inform clinicians and policymakers about the benefits, limitations, and potential risks associated with gabapentin use in diabetic neuropathy.

2. Material and methods

A systematic review of randomized controlled trials (RCTs) and meta-analyses on gabapentin for DPN was conducted. Databases including PubMed, Cochrane Library, and Google Scholar were searched using the keywords "Gabapentin," "Diabetic Peripheral Neuropathy," "Efficacy," and "Safety." Studies included in this review met the following criteria: (1) involved patients diagnosed with DPN, (2) evaluated gabapentin as a primary treatment, and (3) reported outcomes related to pain reduction and adverse effects. Studies comparing gabapentin with other medications such as pregabalin and duloxetine were also considered. Data on pain relief, adverse events, and patient adherence were extracted and analyzed. (7,8,9,11-22)

2.1. Study Selection Criteria

Table 1 Study Selection Criteria

Inclusion Criteria	Exclusion Criteria
Patients diagnosed with DPN	Studies not involving human subjects
Gabapentin used as a primary treatment	Case reports and anecdotal evidence
Reported pain reduction and safety outcomes	Studies with incomplete data
Randomised controlled trials and meta-analyses	Non-peer-reviewed publications

2.2. Data Extraction

Table 2 Data Extraction

Data Extracted	Description
Study Design	RCT, Meta-analysis, Observational Study
Sample Size	Number of participants in each study
Duration	Length of study follow-up
Pain Reduction	Measured using Visual Analog Scale (VAS) or other pain assessment tools
Adverse Events	Reported side effects and withdrawal rates
Comparator	Other medications used for DPN in comparative studies

3. Results

3.1. Efficacy in Pain Reduction

Gabapentin has shown a significant reduction in pain intensity among DPN patients (7,11,16,17). Studies indicate that patients receiving gabapentin experience an improvement in sleep quality and a reduction in breakthrough pain episodes (18,19,20,). Additionally, gabapentin has been reported to improve overall patient satisfaction with pain management (11,19,21,22). However, the onset of action varies, with some patients requiring titration over several weeks before experiencing full therapeutic effects (8,18).

Table 3 Efficacy in Pain Reduction

Study Type	Sample Size	Pain Reduction (%)	Comparator	Duration
Systematic Review	12,398 patients	≥50% improvement	Placebo	Varies
Network Meta-Analysis	Multiple RCTs	Significant reduction	Pregabalin, Oxcarbazepine, Duloxetine	Varies
Prospective Study	152 patients	Comparable pain relief	Duloxetine, Pregabalin	12 weeks

3.2. Safety and Tolerability

Gabapentin has a relatively favourable safety profile, with most adverse effects being mild to moderate in severity (20). Common side effects such as dizziness and somnolence occur more frequently in the initial stages of treatment but tend to diminish over time (1,22). Severe adverse effects are rare, and withdrawal due to intolerability remains low compared to other DPN treatments (19).

Table 4 Safety and Tolerability

Adverse Effect	Prevalence (%)	Severity
Dizziness	18-25%	Mild to Moderate
Somnolence	15-22%	Mild to Moderate
Peripheral Oedema	5-10%	Mild
Severe Adverse Events	<10%	Rare
Withdrawal Due to Side Effects	<10%	Low

4. Discussion

Gabapentin has emerged as a well-established treatment for DPN, offering significant pain relief and an acceptable safety profile (22) . The findings from multiple studies indicate that gabapentin is effective in managing neuropathic pain, with most patients experiencing at least moderate pain relief (16,20). The drug's mechanism, involving calcium channel modulation, helps in reducing neuronal excitability and pain perception (18).

The drug's cost-effectiveness and widespread availability make it an appealing choice, especially in resource-limited settings (14,19). Compared to other agents such as pregabalin and duloxetine, gabapentin provides comparable pain relief, though with a slower onset of action. (17) Its adverse effect profile is manageable and less severe than some alternatives, contributing to greater adherence among patients (21).

However, gabapentin is not without limitations. Inter-individual variability in response, potential sedation, and the need for titration may limit its use in some populations (14). Furthermore, there is a risk of off-label overprescription and misuse in certain demographics (22).

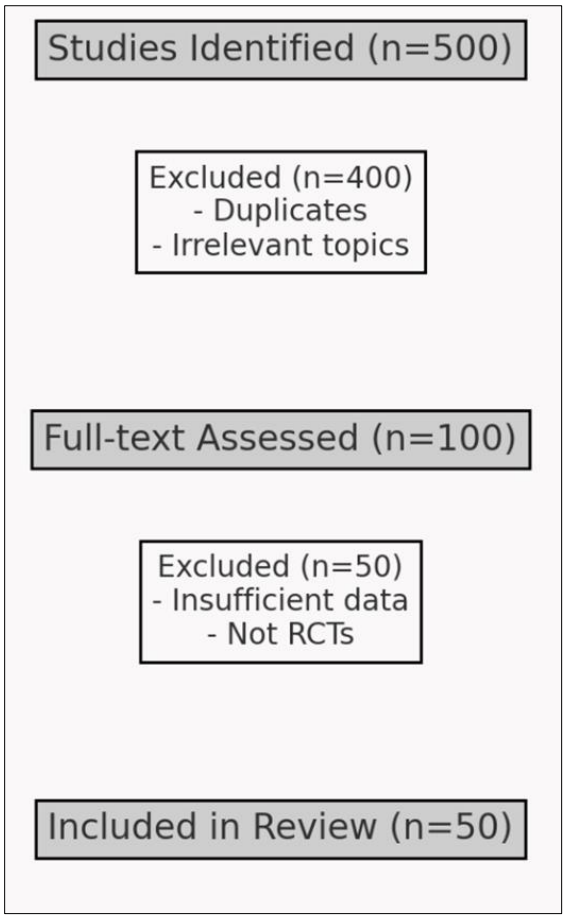

Figure 1 Study selection flowchar

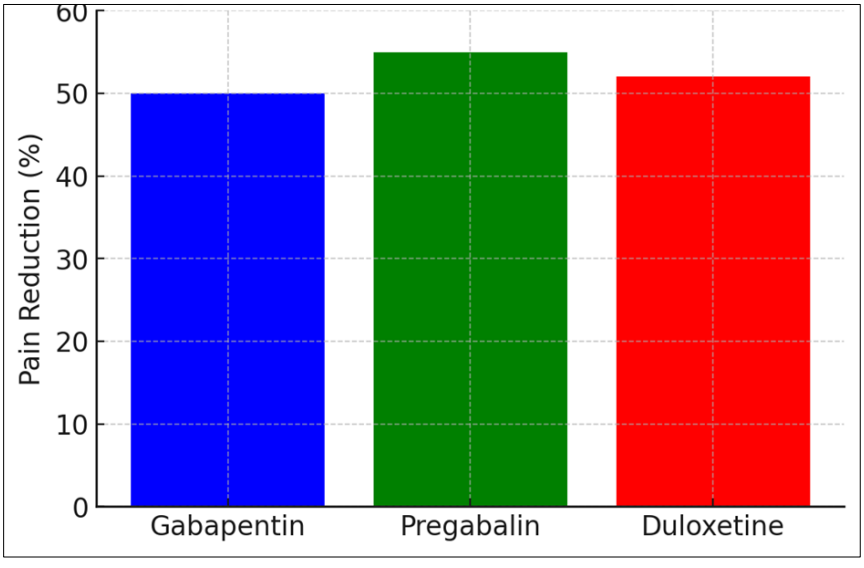

Figure 2 Pain reduction comparison

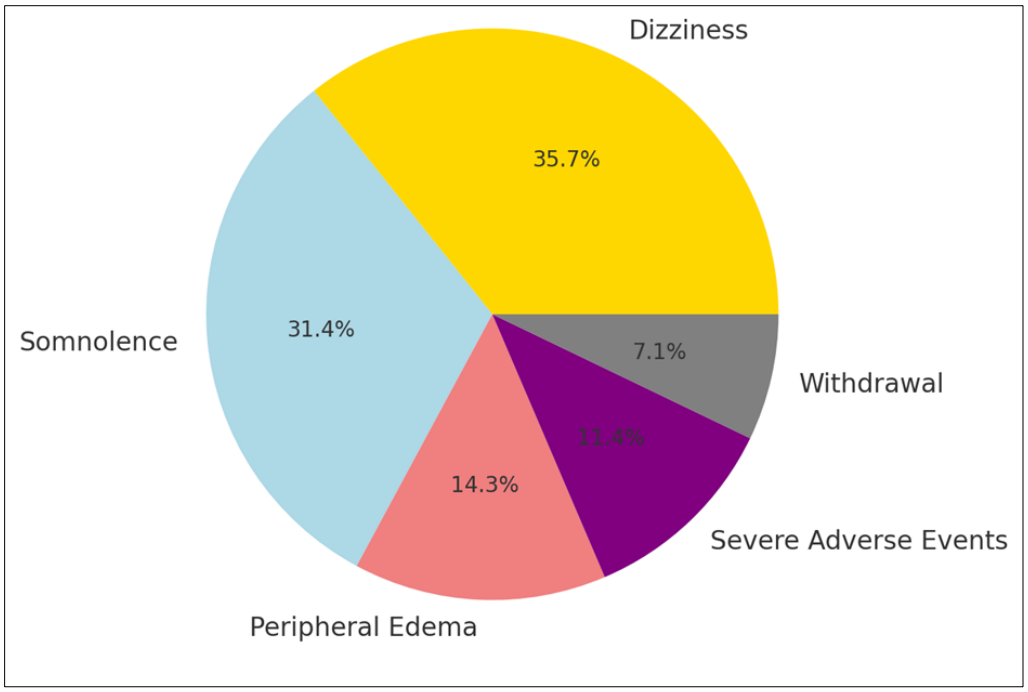

Figure 3 Adverse effect distribution

5. Conclusion

This systematic review confirms that gabapentin is an effective and safe option for the management of diabetic peripheral neuropathy. It offers significant pain relief with a tolerable side effect profile and is a viable alternative to other first-line agents. Clinicians should consider individual patient profiles when prescribing gabapentin and monitor for side effects during treatment. Continued comparative studies and long-term trials are warranted to optimize therapeutic strategies and clarify gabapentin's role within the broader context of neuropathic pain management.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] Dulipsingh L, Zailskas S, Goldsby T, McInnis T, Marotta A. Assessment of pain and treatment satisfaction in patients with painful diabetic peripheral neuropathy. Conn Med. 2013 Oct;77(9):523-7. PMID: 24266128.

[2] Zhu J, Hu Z, Luo Y, Liu Y, Luo W, Du X, Luo Z, Hu J, Peng S. Diabetic peripheral neuropathy: pathogenetic mechanisms and treatment. Front Endocrinol (Lausanne). 2024 Jan 9;14:1265372. doi: 10.3389/fendo.2023.1265372. PMID: 38264279; PMCID: PMC10803883.

[3] Chang MC, Yang S. Diabetic peripheral neuropathy essentials: a narrative review. Ann Palliat Med. 2023 Mar;12(2):390-398. doi: 10.21037/apm-22-693. Epub 2023 Feb 8. PMID: 36786097.

[4] Baum P, Toyka KV, Blüher M, Kosacka J, Nowicki M. Inflammatory Mechanisms in the Pathophysiology of Diabetic Peripheral Neuropathy (DN)-New Aspects. Int J Mol Sci. 2021 Oct 7;22(19):10835. doi: 10.3390/ijms221910835. PMID: 34639176; PMCID: PMC8509236.

[5] Shi G, Gao Z, Zhang Z, Jin Q, Li S, Liu J, Kou L, Aerman A, Yang W, Wang Q, Cai F, Zhang L. Machine learning-based risk prediction model for neuropathic foot ulcers in patients with diabetic peripheral neuropathy. J Diabetes Investig. 2025 Mar 21. doi: 10.1111/jdi.70010. Epub ahead of print. PMID: 40116696.

[6] Monteiro RL, Sartor CD, Ferreira JSSP, Dantas MGB, Bus SA, Sacco ICN. Protocol for evaluating the effects of a foot-ankle therapeutic exercise program on daily activity, foot-ankle functionality, and biomechanics in people with diabetic polyneuropathy: a randomized controlled trial. BMC Musculoskelet Disord. 2018 Nov 14;19(1):400. doi: 10.1186/s12891-018-2323-0. PMID: 30428863; PMCID: PMC6236874.

[7] Taher MG, Mohammed MR, Al-Mahdawi MAS, Halaf NKA, Jalil AT, Alsandook T. The role of protein kinases in diabetic neuropathic pain: an update review. J Diabetes Metab Disord. 2023 May 3;22(1):147-154. doi: 10.1007/s40200-023-01217-1. PMID: 37255803; PMCID: PMC10225446.

[8] Liampas A, Rekatsina M, Vadalouca A, Paladini A, Varrassi G, Zis P. Pharmacological Management of Painful Peripheral Neuropathies: A Systematic Review. Pain Ther. 2021 Jun;10(1):55-68. doi: 10.1007/s40122-020-00210-3. Epub 2020 Nov 3. PMID: 33145709; PMCID: PMC8119529.

[9] Backonja M, Glanzman RL. Gabapentin dosing for neuropathic pain: evidence from randomized, placebo-controlled clinical trials. Clin Ther. 2003 Jan;25(1):81-104. doi: 10.1016/s0149-2918(03)90011-7. PMID: 12637113.

[10] Hong JSW, Atkinson LZ, Al-Juffali N, Awad A, Geddes JR, Tunbridge EM, Harrison PJ, Cipriani A. Gabapentin and pregabalin in bipolar disorder, anxiety states, and insomnia: Systematic review, meta-analysis, and rationale. Mol Psychiatry. 2022 Mar;27(3):1339-1349. doi: 10.1038/s41380-021-01386-6. Epub 2021 Nov 24. PMID: 34819636; PMCID: PMC9095464.

[11] Rosenstock J, Tuchman M, LaMoreaux L, Sharma U. Pregabalin for the treatment of painful diabetic peripheral neuropathy: a double-blind, placebo-controlled trial. Pain. 2004 Aug;110(3):628-638. doi: 10.1016/j.pain.2004.05.001. PMID: 15288403.

[12] Finnerup NB, Attal N, Haroutounian S, McNicol E, Baron R, Dworkin RH, Gilron I, Haanpää M, Hansson P, Jensen TS, Kamerman PR, Lund K, Moore A, Raja SN, Rice AS, Rowbotham M, Sena E, Siddall P, Smith BH, Wallace M. Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. Lancet Neurol. 2015 Feb;14(2):162-73. doi: 10.1016/S1474-4422(14)70251-0. Epub 2015 Jan 7. PMID: 25575710; PMCID: PMC4493167.

[13] Russo M, Graham B, Santarelli DM. Gabapentin-Friend or foe? Pain Pract. 2023 Jan;23(1):63-69. doi: 10.1111/papr.13165. Epub 2022 Oct 27. PMID: 36300903; PMCID: PMC10092611.

[14] Wiffen PJ, Derry S, Bell RF, Rice AS, Tölle TR, Phillips T, Moore RA. Gabapentin for chronic neuropathic pain in adults. Cochrane Database Syst Rev. 2017 Jun 9;6(6):CD007938. doi: 10.1002/14651858.CD007938.pub4. PMID: 28597471; PMCID: PMC6452908.

[15] Bonnet U, Scherbaum N. How addictive are gabapentin and pregabalin? A systematic review. Eur Neuropsychopharmacol. 2017 Dec;27(12):1185-1215. doi: 10.1016/j.euroneuro.2017.08.430. Epub 2017 Oct 5. PMID: 28988943.

[16] Ko YC, Lee CH, Wu CS, Huang YJ. Comparison of efficacy and safety of gabapentin and duloxetine in painful diabetic peripheral neuropathy: A systematic review and meta-analysis of randomised controlled trials. Int J Clin Pract. 2021 Nov;75(11):e14576. doi: 10.1111/ijcp.14576. Epub 2021 Jul 9. PMID: 34171158.

[17] Snedecor SJ, Sudharshan L, Cappelleri JC, Sadosky A, Mehta S, Botteman M. Systematic review and meta-analysis of pharmacological therapies for painful diabetic peripheral neuropathy. Pain Pract. 2014 Feb;14(2):167-84. doi: 10.1111/papr.12054. Epub 2013 Mar 28. PMID: 23534696.

[18] . Jingxuan L, Litian M, Jianfang F. Different Drugs for the Treatment of Painful Diabetic Peripheral Neuropathy: A Meta-Analysis. Front Neurol. 2021 Oct 29;12:682244. doi: 10.3389/fneur.2021.682244. PMID: 34777192; PMCID: PMC8585758.

[19] Mayoral V, Galvez R, Ferrándiz M, Miguéns Vázquez X, Cordero-García C, Alcántara Montero A, Pérez C, Pérez-Páramo M. Pregabalin vs. gabapentin in the treatment of neuropathic pain: a comprehensive systematic review and meta-analysis of effectiveness and safety. Front Pain Res (Lausanne). 2025 Jan 7;5:1513597. doi: 10.3389/fpain.2024.1513597. PMID: 39839199; PMCID: PMC11747324.

[20] Dworkin RH, O'Connor AB, Backonja M, Farrar JT, Finnerup NB, Jensen TS, Kalso EA, Loeser JD, Miaskowski C, Nurmikko TJ, Portenoy RK, Rice ASC, Stacey BR, Treede RD, Turk DC, Wallace MS. Pharmacologic management of neuropathic pain: evidence-based recommendations. Pain. 2007 Dec 5;132(3):237-251. doi: 10.1016/j.pain.2007.08.033. Epub 2007 Oct 24. PMID: 17920770.

[21] Morello CM, Leckband SG, Stoner CP, Moorhouse DF, Sahagian GA. Randomized double-blind study comparing the efficacy of gabapentin with amitriptyline on diabetic peripheral neuropathy pain. Arch Intern Med. 1999 Sep 13;159(16):1931-7. doi: 10.1001/archinte.159.16.1931. PMID: 10493324.

[22] Rosenstock J, Tuchman M, LaMoreaux L, Sharma U. Pregabalin for the treatment of painful diabetic peripheral neuropathy: a double-blind, placebo-controlled trial. Pain. 2004 Aug;110(3):628-638. doi: 10.1016/j.pain.2004.05.001. PMID: 15288403.