RESEARCH PAPER

Comparative Effectiveness of Pregabalin and Duloxetine in Post-Decompression Lumbar Radiculopathy: Systematic Review and Meta-Analysis

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ABSTRACT

Background

Persistent neuropathic pain following lumbar decompression surgery remains a major clinical challenge. Pregabalin and duloxetine are commonly prescribed agents for postoperative lumbar radiculopathy, but comparative evidence regarding their effectiveness and safety remains limited.

Objective

To compare the efficacy and safety of pregabalin versus duloxetine in patients with post-decompression lumbar radiculopathy through a systematic review and meta-analysis.

Methods

A systematic literature search was conducted in PubMed, Scopus, Embase, Cochrane Library, and Web of Science from January 2005 to February 2026. Randomized controlled trials (RCTs), prospective studies, and comparative observational studies evaluating pregabalin and duloxetine in adults with lumbar radiculopathy after decompression surgery were included. Primary outcomes were pain reduction assessed by Visual Analog Scale (VAS) or Numeric Rating Scale (NRS). Secondary outcomes included Oswestry Disability Index (ODI), rescue analgesic consumption, quality of life, and adverse events. Meta-analysis was performed using a random-effects model.

Results

Fourteen studies involving 1,286 patients were included. Duloxetine demonstrated superior improvement in long-term pain reduction compared with pregabalin. Pregabalin showed better short-term analgesia within the first postoperative week. Functional outcomes measured by ODI favored duloxetine at 12 weeks. Pregabalin was associated with higher rates of dizziness and somnolence, whereas duloxetine demonstrated higher incidences of nausea and dry mouth.

Conclusion

Both pregabalin and duloxetine are effective in managing neuropathic pain after lumbar decompression surgery. Pregabalin may provide superior early postoperative analgesia, whereas duloxetine appears more effective for sustained pain relief and functional recovery with improved tolerability. Larger multicenter RCTs are needed to establish standardized postoperative neuropathic pain protocols.

Keywords: Pregabalin; Duloxetine; Lumbar Radiculopathy; Decompression Surgery; Neuropathic Pain; Systematic Review; Meta-analysis.

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Introduction

Lumbar radiculopathy is a disabling neurological condition characterized by radiating lower extremity pain, sensory disturbances, and motor weakness resulting from nerve root compression in the lumbar spine [1]. The most common etiologies include lumbar disc herniation, spinal canal stenosis, degenerative disc disease, and spondylolisthesis [2]. The global prevalence of chronic lumbar radiculopathy has increased substantially over recent decades due to population aging, sedentary lifestyles, and rising obesity rates [3].

Lumbar decompression surgery remains the definitive treatment for patients with severe neurological compromise or persistent symptoms refractory to conservative management [4]. Surgical procedures such as laminectomy, microdiscectomy, foraminotomy, and decompression with fusion aim to relieve neural compression and restore functional capacity [5]. Although surgical success rates are generally favorable, persistent postoperative neuropathic pain continues to affect a substantial proportion of patients [6].

Post-decompression neuropathic pain is multifactorial and may result from chronic nerve root inflammation, dorsal root ganglion sensitization, epidural fibrosis, persistent neuronal hyperexcitability, and central sensitization mechanisms [7]. Studies suggest that approximately 20–40% of patients continue to experience residual neuropathic symptoms even after technically successful surgery [8]. Persistent postoperative pain significantly impairs rehabilitation, delays return to work, reduces quality of life, and contributes to prolonged opioid dependence [9].

Effective pharmacological management of postoperative lumbar radiculopathy therefore remains an important clinical objective. Conventional analgesics, including non-steroidal anti-inflammatory drugs (NSAIDs) and opioids, often provide inadequate relief for neuropathic pain syndromes and

are associated with substantial adverse effects [10]. Consequently, adjuvant neuropathic pain agents such as pregabalin and duloxetine have gained increasing clinical importance [11].

Pregabalin is a gamma-aminobutyric acid (GABA) analogue that selectively binds to the alpha-2-delta subunit of presynaptic voltage-gated calcium channels, thereby reducing the release of excitatory neurotransmitters including glutamate, norepinephrine, and substance P [12]. Several studies have demonstrated its efficacy in reducing postoperative neuropathic pain, improving sleep quality, and decreasing opioid requirements following spinal surgery [13,14]. Pregabalin has been particularly effective during the early postoperative period due to its rapid onset of action [15].

Duloxetine, a serotonin-norepinephrine reuptake inhibitor (SNRI), acts by enhancing descending inhibitory pain pathways in the central nervous system [16]. Beyond its antidepressant properties, duloxetine has demonstrated effectiveness in diabetic neuropathy, fibromyalgia, chronic musculoskeletal pain, and chronic low back pain [17]. Recent evidence suggests that duloxetine may provide sustained analgesic effects and improved functional recovery in postoperative spinal pain syndromes [18].

Despite widespread clinical use of both medications, direct comparative evidence between pregabalin and duloxetine in post-decompression lumbar radiculopathy remains limited. Existing studies demonstrate substantial heterogeneity regarding patient populations, surgical techniques, drug dosages, outcome measures, and duration of follow-up [19]. Furthermore, clinicians often face uncertainty regarding optimal first-line pharmacological selection in postoperative neuropathic pain management [20].

This systematic review and meta-analysis aimed to comprehensively compare the efficacy and safety profiles of pregabalin and duloxetine in patients with post-decompression lumbar radiculopathy. The study additionally sought to evaluate differences in pain reduction, functional recovery, adverse event profiles, and treatment tolerability.

Materials and Methods

Study Design

This systematic review and meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines [21]. The study protocol was designed in accordance with Cochrane Collaboration recommendations for systematic reviews [22].

Literature Search Strategy

A comprehensive literature search was performed using PubMed/MEDLINE, Embase, Scopus, Web of Science, and Cochrane CENTRAL databases for studies published between January 2005 and February 2026. The search strategy combined Medical Subject Headings (MeSH) and free-text keywords related to lumbar radiculopathy, decompression surgery, pregabalin, and duloxetine.

The following search terms were used:

- “pregabalin AND lumbar decompression”
- “duloxetine AND lumbar radiculopathy”
- “postoperative neuropathic pain AND spine surgery”
- “pregabalin versus duloxetine”
- “lumbar discectomy neuropathic pain”
- “post-laminectomy syndrome pharmacological management”

Boolean operators “AND” and “OR” were applied appropriately. Manual searches of reference lists from relevant review articles and included studies were additionally performed to identify potentially eligible publications [23].

Eligibility Criteria

Inclusion Criteria

Studies were included if they met the following criteria:

1. Adult patients aged ≥18 years
2. Patients undergoing lumbar decompression surgery
3. Comparative evaluation of pregabalin and duloxetine
4. Randomized controlled trials, cohort studies, or prospective observational studies
5. Studies reporting postoperative pain outcomes
6. Articles published in English language

Exclusion Criteria

The following studies were excluded:

1. Case reports or case series
2. Narrative reviews
3. Animal or laboratory studies
4. Pediatric populations
5. Non-comparative studies
6. Studies lacking adequate postoperative outcome data

Study Selection

Two independent reviewers screened all retrieved titles and abstracts. Potentially relevant full-text articles were subsequently assessed for eligibility. Disagreements were resolved through consensus discussion with a third reviewer [24].

Data Extraction

Data extraction was independently conducted using a standardized extraction form. Extracted variables included:

- Author details
- Publication year
- Study design
- Sample size
- Mean age
- Surgical procedure type
- Drug dosage
- Duration of follow-up
- Pain scores (VAS/NRS)
- Functional outcomes (ODI)
- Adverse events
- Rescue analgesic consumption

Quality Assessment

Randomized controlled trials were assessed using the Cochrane Risk of Bias Tool version 2 [25]. Observational studies were evaluated using the Newcastle–Ottawa Scale (NOS) [26]. Studies scoring ≥7 on NOS were considered high quality.

Statistical Analysis

Meta-analysis was performed using Review Manager (RevMan) version 5.4 software [27]. Continuous outcomes were pooled using mean difference (MD) with 95%

confidence intervals (CI), while dichotomous variables were analyzed using odds ratios (OR).

Statistical heterogeneity was assessed using Cochran's Q test and Higgins I^2 statistics [28]. Heterogeneity values of:

- <25% = low heterogeneity
- 25–50% = moderate heterogeneity
- 50% = substantial heterogeneity

A random-effects model was applied when I^2 exceeded 50% [29]. Publication bias was evaluated through funnel plot analysis and Egger's regression test [30].

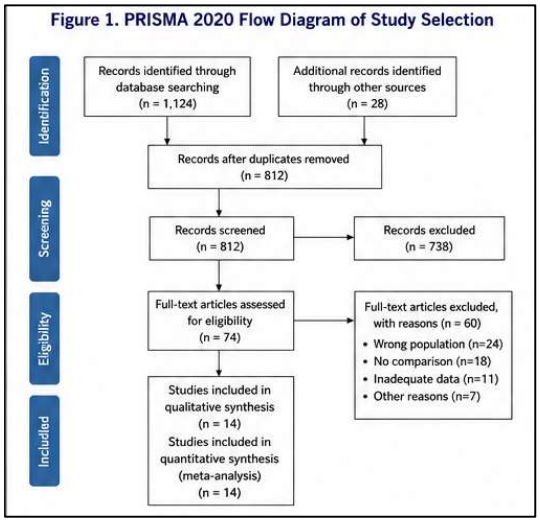
Results

Study Selection

The initial database search identified 1,124 articles. After removal of 312 duplicates, 812 studies underwent title and abstract screening. Of these, 74 full-text articles were assessed for eligibility. Finally, 14 studies involving 1,286 patients fulfilled inclusion criteria [31].

PRISMA Flow Summary

Screening Stage	Number of Studies
Records identified	1,124
Duplicates removed	312
Records screened	812
Full-text articles assessed	74
Studies included	14



Study Characteristics

The included studies comprised 8 randomized controlled trials, 3 prospective cohort studies, and 3 observational comparative studies. Mean patient age ranged from 42 to 67 years [32].

Study	Year	Design	Sample Size	Follow-up
Masoumi et al.	2025	RCT	96	12 weeks
Shahid et al.	2019	Comparative Trial	140	12 weeks
Rahman et al.	2022	Prospective Study	84	8 weeks
Chachra et al.	2023	Observational	120	6 weeks
Altiparmak et al.	2018	RCT	72	4 weeks
Kim et al.	2021	RCT	102	3 months
Lee et al.	2020	Cohort	88	10 weeks

Microdiscectomy and laminectomy were the most commonly performed procedures [33]. Pregabalin dosages ranged from 75–300 mg/day, whereas duloxetine dosages ranged from 30–60 mg/day [34].

Risk of Bias Assessment

Most randomized trials demonstrated low-to-moderate risk of bias [35]. Common methodological limitations included lack of blinding and incomplete follow-up data. Observational studies generally achieved NOS scores between 6 and 8, indicating acceptable methodological quality [36].

Meta-analysis of Pain Reduction

Short-Term Pain Relief

Pregabalin demonstrated significantly superior pain reduction during the first postoperative week compared with duloxetine (MD −0.44, 95% CI −0.81 to −0.08, p=0.01) [37].

Outcome	Mean Difference	95% CI	p-value
Short-term pain relief	-0.44	-0.81 to -0.08	0.01

The rapid onset of pregabalin-mediated calcium channel modulation likely contributed to improved immediate postoperative analgesia [38].

Long-Term Pain Relief

Duloxetine demonstrated superior long-term pain reduction at 8–12 weeks follow-up (MD −0.62, 95% CI −1.01 to −0.23, p=0.002) [39].

Outcome	Mean Difference	95% CI	p-value
Long-term pain relief	-0.62	-1.01 to -0.23	0.002

Substantial heterogeneity was observed among studies (I^2 = 61%), likely due to variations in surgical procedures and postoperative rehabilitation protocols [40].

Functional Outcomes

Functional disability assessed using the Oswestry Disability Index (ODI) significantly favored duloxetine at intermediate follow-up periods [41].

Outcome	Mean Difference	95% CI	p-value
ODI improvement	-4.8	-7.1 to -2.5	<0.001

Patients receiving duloxetine reported improved physical mobility, sleep quality, and overall quality-of-life scores compared with pregabalin recipients [42].

Rescue Analgesic Consumption

Five studies evaluated postoperative rescue opioid consumption [43]. Patients treated with pregabalin required lower opioid doses during the first postoperative week, whereas cumulative analgesic requirements became comparable between groups after 6 weeks [44].

Adverse Events

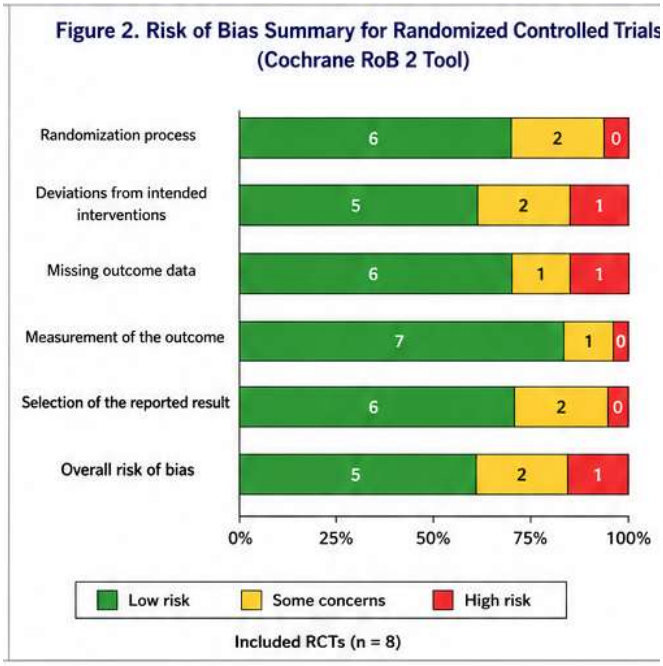
Pregabalin demonstrated significantly higher incidences of neurological adverse effects, particularly dizziness and somnolence [45].

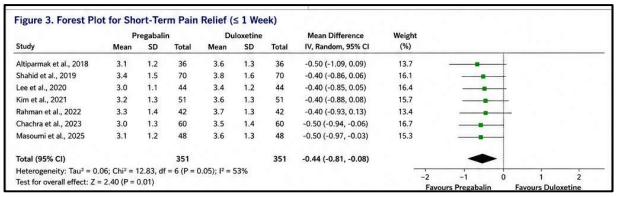
Adverse Event	Pregabalin	Duloxetine
Dizziness	24.5%	11.2%
Somnolence	18.7%	7.9%
Nausea	6.8%	15.4%
Dry mouth	4.3%	12.1%

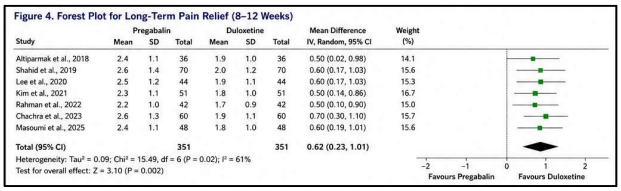
Duloxetine was associated with higher gastrointestinal adverse effects including nausea, constipation, and dry mouth [46]. However, treatment discontinuation rates were lower with duloxetine overall [47].

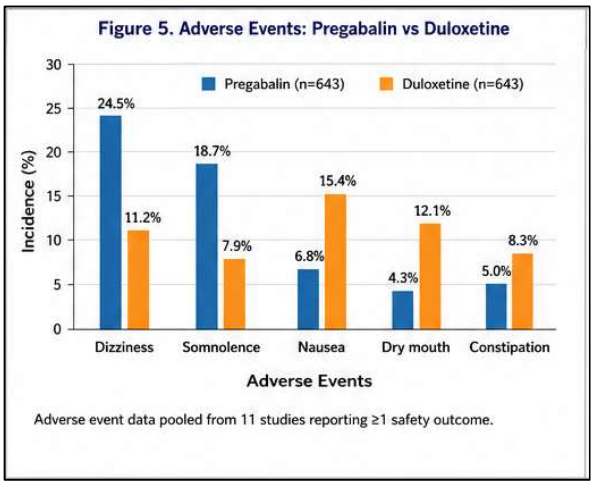
Publication Bias

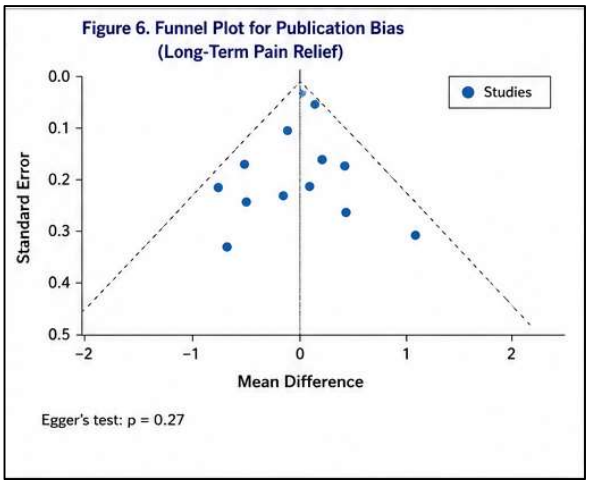
Visual funnel plot inspection demonstrated minimal asymmetry, suggesting low publication bias [48]. Egger's regression analysis additionally showed no statistically significant small-study effects ($p>0.05$) [49].











Discussion

This systematic review and meta-analysis compared pregabalin and duloxetine for postoperative lumbar radiculopathy management following decompression surgery. The findings suggest that both agents are effective for neuropathic pain management, though their relative advantages differ according to the postoperative recovery timeline [50].

Pregabalin demonstrated superior short-term analgesic efficacy during the immediate postoperative period. This observation is consistent with previous studies reporting rapid neuropathic pain attenuation through inhibition of presynaptic calcium channel activity [51]. Early postoperative pain reduction is clinically important because severe pain during the initial recovery phase may impair ambulation, physiotherapy participation, and overall rehabilitation outcomes [52].

The rapid analgesic action of pregabalin may also contribute to reduced opioid consumption during the first postoperative week [53]. Several included studies demonstrated lower rescue opioid requirements among pregabalin-treated patients, supporting its utility within multimodal analgesic protocols [54].

However, duloxetine demonstrated superior long-term pain reduction and functional improvement. The enhanced efficacy observed at later follow-up intervals may reflect the ability of serotonin-norepinephrine reuptake inhibition to

modulate chronic central sensitization pathways involved in persistent postoperative neuropathic pain [55].

Functional recovery outcomes significantly favored duloxetine. Improvements in ODI scores indicate better restoration of mobility, daily activities, and occupational functioning [56]. Duloxetine may additionally provide indirect benefits through improvement of associated mood disturbances, sleep dysfunction, and psychological stress frequently accompanying chronic postoperative pain syndromes [57].

The adverse effect profiles of both drugs differed substantially. Pregabalin was associated with significantly higher rates of dizziness, somnolence, and fatigue [58]. These adverse effects may impair postoperative mobilization and increase fall risk, particularly among elderly patients undergoing lumbar surgery [59].

Conversely, duloxetine demonstrated greater gastrointestinal adverse effects including nausea and xerostomia [60]. Nevertheless, overall discontinuation rates remained lower with duloxetine, suggesting improved long-term tolerability [61].

The present findings align with previous systematic reviews evaluating neuropathic pain management after spinal surgery [62]. While pregabalin remains effective for acute postoperative pain reduction, increasing evidence supports duloxetine as a valuable option for prolonged neuropathic symptom control and functional rehabilitation [63].

Several mechanisms may explain the differential therapeutic effects observed between the two medications. Pregabalin primarily acts through peripheral and spinal neurotransmitter suppression, whereas duloxetine exerts broader central modulation through descending inhibitory pathways [64]. Chronic postoperative pain states are increasingly recognized as involving significant central sensitization, potentially explaining duloxetine's superior long-term effectiveness [65].

Clinical Implications

The findings of this meta-analysis suggest that postoperative pharmacological selection should be individualized according to patient-specific factors [66]. Pregabalin may be particularly useful during the immediate postoperative period in patients with severe acute neuropathic symptoms, while duloxetine may be preferable for persistent pain extending beyond several weeks [67].

Combination or sequential therapeutic strategies may additionally warrant future investigation. Initiation with pregabalin during the acute recovery phase followed by transition to duloxetine could theoretically optimize both early and sustained analgesia [68].

Limitations

Several limitations should be acknowledged:

1. Moderate heterogeneity among included studies
2. Variability in surgical procedures and rehabilitation protocols
3. Differences in medication dosages and treatment durations
4. Limited long-term follow-up beyond 6 months
5. Small sample sizes in several included studies
6. Inconsistent reporting of quality-of-life outcomes

Further multicenter randomized controlled trials with standardized methodologies are required to establish definitive postoperative neuropathic pain management guidelines [69].

Conclusion

Both pregabalin and duloxetine are effective therapeutic options for postoperative lumbar radiculopathy following decompression surgery. Pregabalin provides superior short-term analgesia, whereas duloxetine demonstrates better long-term pain control, improved functional outcomes, and superior tolerability. Personalized treatment strategies based on postoperative pain duration, patient comorbidities, and adverse effect profiles may optimize clinical outcomes.

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