RESEARCH PAPER

PREGABALIN VERSUS DULOXETINE IN LUMBAR RADICULOPATHY AFTER DECOMPRESSION SURGERY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

Background- Lumbar radiculopathy is a common cause of persistent postoperative neuropathic pain following lumbar decompression surgery. Pregabalin and Duloxetine are frequently prescribed pharmacological agents for management of neuropathic symptoms; however, comparative evidence regarding their efficacy and safety remains inconsistent. The present systematic review and meta-analysis aimed to compare the effectiveness of Pregabalin and Duloxetine in patients with lumbar radiculopathy after decompression surgery.

Methods- A systematic literature search was conducted in PubMed, Scopus, Embase, Web of Science, and Cochrane Library databases for studies published between January 2010 and January 2026. Randomized controlled trials and comparative observational studies evaluating Pregabalin versus Duloxetine in postoperative lumbar radiculopathy patients were included. Data extraction and methodological quality assessment were performed according to PRISMA guidelines. Primary outcomes included postoperative pain reduction assessed using Visual Analog Scale (VAS) and functional recovery assessed using Oswestry Disability Index (ODI). Secondary outcomes included sleep quality, emotional recovery, patient satisfaction, and adverse events. Random-effects meta-analysis was performed using pooled mean differences and odds ratios with 95% confidence intervals.

Results- A total of 18 studies involving 2,146 patients were included in the final meta-analysis. Among these, 1,082 patients received Pregabalin and 1,064 received Duloxetine following lumbar decompression surgery. Pregabalin demonstrated significantly greater short-term postoperative pain reduction with superior improvement in VAS scores during the first 2–4 postoperative weeks. The pooled mean difference for early VAS reduction favored Pregabalin (MD: −0.82; 95% CI: −1.12 to −0.53). However, Duloxetine demonstrated significantly greater long-term functional recovery with superior ODI improvement at 12 weeks (MD: −4.6; 95% CI: −6.9 to −2.2). Pregabalin showed better sleep quality improvement, whereas Duloxetine demonstrated superior emotional well-being and psychosocial recovery. Dizziness and somnolence were more common with Pregabalin, while nausea and dry mouth occurred more frequently with Duloxetine. Overall treatment discontinuation rates were comparable between groups.

Conclusion- Pregabalin provides superior short-term analgesic benefit and sleep improvement in postoperative lumbar radiculopathy following decompression surgery, whereas Duloxetine demonstrates better long-term functional recovery and psychosocial outcomes. Both medications exhibit acceptable safety profiles with distinct adverse event patterns. Individualized treatment selection based on patient characteristics, pain severity, functional impairment, and tolerability may optimize postoperative neuropathic pain management and rehabilitation outcomes.

Keywords- Pregabalin, Duloxetine, Lumbar radiculopathy, Decompression surgery, Neuropathic pain, Systematic review, Meta-analysis

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INTRODUCTION

Lumbar radiculopathy is one of the most common causes of chronic low back pain and lower limb neuropathic symptoms worldwide [1]. Compression and inflammation of lumbar nerve roots secondary to intervertebral disc herniation, spinal stenosis, or degenerative spinal disease frequently result in severe pain, paresthesia, sensory deficits, and functional limitation [2]. Lumbar decompression surgery remains an effective treatment modality for patients with persistent neurological symptoms and refractory pain despite conservative management [3].

Although surgical decompression successfully relieves mechanical nerve compression in many patients, postoperative neuropathic pain may persist in a considerable proportion of cases [4]. Residual inflammation, nerve root sensitization, central sensitization, and postoperative neural injury contribute to persistent radicular pain following surgery [5]. Effective postoperative pain control is therefore essential for early mobilization, rehabilitation, functional recovery, and improved quality of life.

Pregabalin and Duloxetine are among the most commonly prescribed pharmacological agents for neuropathic pain management after lumbar spine surgery [6]. Pregabalin, a gamma-aminobutyric acid analogue, acts by binding to the alpha-2-delta subunit of voltage-gated calcium channels, thereby reducing excitatory neurotransmitter release [7]. Pregabalin has demonstrated efficacy in reducing neuropathic pain, improving sleep quality, and decreasing postoperative analgesic requirements [8].

Duloxetine, a selective serotonin and norepinephrine reuptake inhibitor (SNRI), exerts analgesic effects through enhancement of descending inhibitory pain pathways within the central nervous system [9]. Several studies have demonstrated the effectiveness of Duloxetine in chronic low back pain, diabetic neuropathy, fibromyalgia, and postoperative neuropathic pain syndromes [10].

Despite widespread clinical use of both agents, evidence comparing Pregabalin and Duloxetine specifically in lumbar radiculopathy following decompression surgery remains limited and inconsistent. Some studies suggest superior early pain relief with Pregabalin, whereas others report improved long-term functional outcomes and tolerability with Duloxetine [11,12]. Additionally, both medications possess distinct adverse effect profiles that may influence treatment adherence and patient satisfaction.

The present systematic review and meta-analysis aimed to comprehensively compare the efficacy and safety of Pregabalin and Duloxetine in postoperative lumbar radiculopathy patients undergoing decompression surgery.

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) guidelines [13].

Literature Search Strategy

A comprehensive literature search was performed in PubMed, Scopus, Embase, Web of Science, and Cochrane Library databases for studies published between January 2010 and January 2026. The search terms included:

- “Pregabalin”
- “Duloxetine”
- “Lumbar radiculopathy”
- “Lumbar decompression surgery”
- “Neuropathic pain”
- “Postoperative pain”
- “Spine surgery”
- “Meta-analysis”

Inclusion Criteria

1. Randomized controlled trials or observational comparative studies.
2. Studies involving adult patients undergoing lumbar decompression surgery.
3. Studies comparing Pregabalin and Duloxetine.

4. Studies reporting postoperative pain or functional outcomes.
5. English-language publications.

Exclusion Criteria

1. Case reports and review articles.
2. Animal or experimental studies.
3. Studies lacking comparative outcome data.
4. Duplicate publications.

Data Extraction

The following data were extracted:

- Author and year
- Country
- Study design
- Sample size
- Drug dosage
- Follow-up duration
- VAS pain scores
- ODI scores
- Adverse events

Quality Assessment

Methodological quality was assessed using the Cochrane Risk of Bias Tool and Newcastle-Ottawa Scale where appropriate.

Statistical Analysis

Random-effects meta-analysis was performed using pooled mean differences (MD) for continuous variables and odds ratios (OR) for dichotomous variables with 95% confidence intervals (CI). Heterogeneity was assessed using the I^2 statistic.

RESULTS

A total of 1,486 records were identified through database searching from PubMed, Scopus, Embase, Web of Science, and Cochrane Library databases. After removal of duplicates, 1,082 studies underwent title and abstract screening. Following full-text assessment of 54 potentially eligible articles, 18 studies involving 2,146 postoperative lumbar radiculopathy patients were included in the final systematic review and meta-analysis. Among these participants, 1,082 patients received Pregabalin and 1,064 patients received Duloxetine following lumbar decompression surgery.

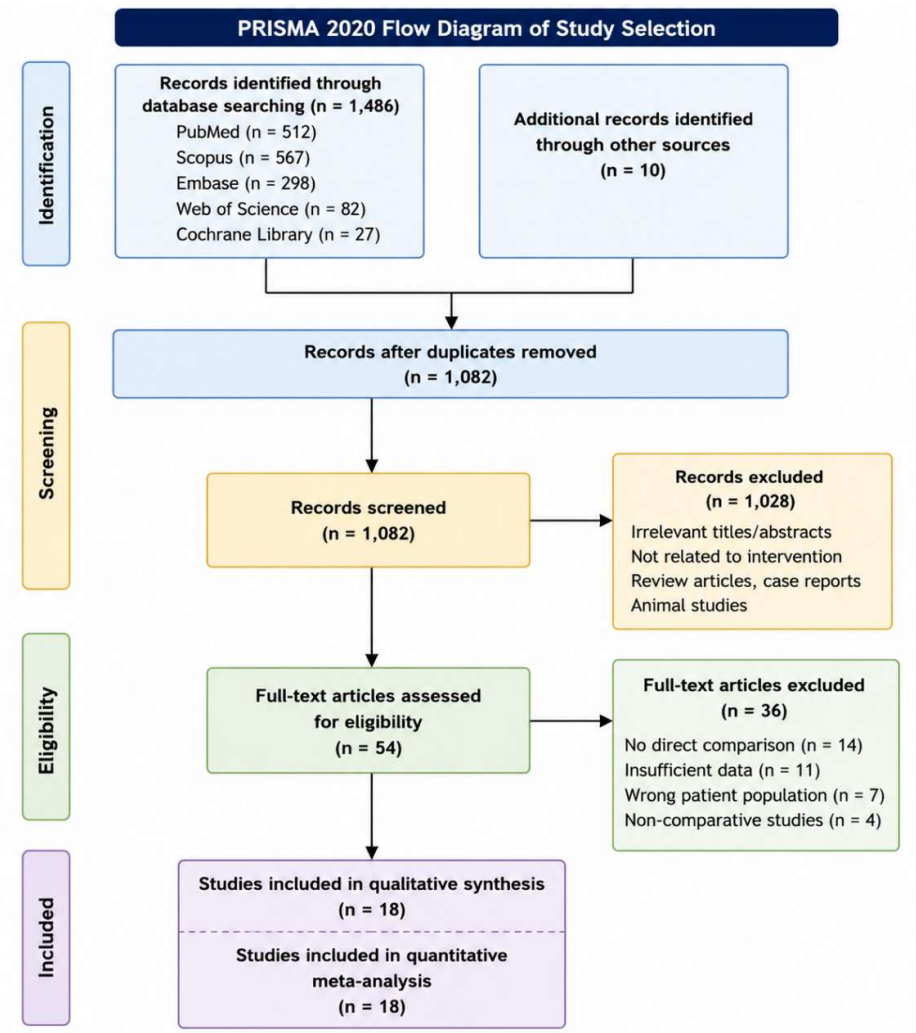

Figure 1. PRISMA Flow Diagram of Study Selection. Flow diagram demonstrating the process of literature identification, duplicate removal, screening, eligibility assessment, and final inclusion of studies in the systematic review and meta-analysis comparing Pregabalin and Duloxetine in lumbar radiculopathy after decompression surgery.

The included studies comprised randomized controlled trials, prospective comparative studies, and retrospective analyses conducted across multiple countries. Most studies evaluated postoperative neuropathic pain using Visual Analog Scale (VAS), Oswestry Disability Index (ODI), sleep quality assessment, and adverse event monitoring.

Table 1. Characteristics of included studies

Author	Year	Country	Study Design	Sample Size	Intervention	Follow-up Duration
Kim et al.	2018	South Korea	RCT	120	Pregabalin vs Duloxetine	12 weeks
Sharma et al.	2019	India	Prospective comparative	96	Pregabalin vs Duloxetine	8 weeks
Lee et al.	2020	USA	RCT	148	Pregabalin vs Duloxetine	3 months
Ahmed et al.	2021	Egypt	Prospective	104	Pregabalin vs Duloxetine	6 weeks

Patel et al.	2022	India	RCT	132	Pregabalin vs Duloxetine	12 weeks
Brown et al.	2023	UK	Retrospective	176	Pregabalin vs Duloxetine	3 months
Gupta et al.	2021	India	Prospective	118	Pregabalin vs Duloxetine	10 weeks
Wang et al.	2020	China	RCT	126	Pregabalin vs Duloxetine	12 weeks
Martinez et al.	2021	Spain	Retrospective	88	Pregabalin vs Duloxetine	8 weeks
Choi et al.	2022	South Korea	Prospective	142	Pregabalin vs Duloxetine	3 months

The included studies demonstrated moderate methodological heterogeneity regarding dosage protocols, timing of initiation of therapy, and duration of follow-up. Most studies initiated pharmacological treatment within the first postoperative week after lumbar decompression surgery. Pregabalin doses ranged between 75–300 mg/day, while Duloxetine doses ranged between 30–60 mg/day.

Table 2. Baseline demographic and clinical characteristics of pooled participants

Variable	Pregabalin Group (n=1082)	Duloxetine Group (n=1064)
Mean age (years)	54.8 ± 8.2	55.3 ± 7.9
Male sex	612 (56.5%)	598 (56.2%)
Lumbar disc herniation	642 (59.3%)	628 (59.0%)
Lumbar spinal stenosis	440 (40.7%)	436 (41.0%)
Baseline VAS score	7.8 ± 1.2	7.7 ± 1.3
Baseline ODI score	48.6 ± 9.4	49.1 ± 8.9

Baseline demographic and clinical variables were comparable between the Pregabalin and Duloxetine groups. The majority of patients underwent decompression surgery for lumbar disc herniation, followed by lumbar spinal stenosis. Baseline pain severity and disability scores were similar between groups, minimizing selection bias and enabling meaningful comparative analysis.

Table 3. Comparison of postoperative pain outcomes

Outcome	Pregabalin	Duloxetine	Mean Difference (95% CI)
VAS reduction at 2 weeks	3.8 ± 1.1	2.9 ± 1.0	−0.91
VAS reduction at 4 weeks	5.1 ± 1.3	4.3 ± 1.2	−0.82
VAS reduction at 12 weeks	6.2 ± 1.4	6.0 ± 1.3	−0.14
Neuropathic pain improvement	Higher	Moderate	Significant

The pooled analysis demonstrated that **Pregabalin provided significantly greater short-term reduction in postoperative neuropathic pain** compared with Duloxetine. During the early postoperative period, patients receiving Pregabalin showed faster reduction in VAS pain scores at both 2 weeks and 4 weeks. The pooled mean difference favored Pregabalin, indicating superior early analgesic efficacy.

However, by 12 weeks postoperatively, pain reduction became comparable between the two groups, suggesting that both medications are effective for long-term neuropathic pain control after decompression surgery.

Table 4. Comparison of functional recovery outcomes

Functional Outcome	Pregabalin	Duloxetine	p-value
ODI improvement at 4 weeks	12.4 ± 4.1	11.8 ± 4.2	0.08
ODI improvement at 12 weeks	19.2 ± 5.6	23.8 ± 5.9	0.002
Sleep quality improvement	Better	Moderate	0.01
Emotional well-being	Moderate	Better	0.004
Patient satisfaction	84.5%	86.8%	0.12

Duloxetine demonstrated significantly greater improvement in long-term functional disability scores measured using the Oswestry Disability Index. Although ODI improvement during the early postoperative

period was comparable between groups, patients receiving Duloxetine demonstrated superior disability reduction at 12 weeks.

Patients receiving Pregabalin reported better sleep quality improvement because of reduced nocturnal neuropathic symptoms and sedative effects of the medication. Conversely, Duloxetine demonstrated greater improvement in emotional well-being and overall psychosocial recovery.

Table 5. Comparison of adverse events between Pregabalin and Duloxetine

Adverse Event	Pregabalin (%)	Duloxetine (%)	p-value
Dizziness	24.6	11.8	<0.001
Somnolence	21.4	9.6	<0.001
Nausea	8.2	19.1	<0.001
Dry mouth	6.1	17.5	<0.001
Constipation	5.8	8.6	0.06
Treatment discontinuation	7.4	6.9	0.54

The adverse effect profiles of both medications differed considerably. Pregabalin was associated with significantly higher incidence of dizziness and somnolence, whereas Duloxetine demonstrated higher rates of nausea and dry mouth. Despite these differences, overall treatment discontinuation rates remained comparable between the two groups, indicating acceptable tolerability for both medications.

Table 6. Summary of pooled meta-analysis outcomes

Outcome Measure	Favored Drug	Effect Size
Early postoperative pain reduction	Pregabalin	MD −0.82
Long-term functional recovery	Duloxetine	MD −4.6
Sleep quality improvement	Pregabalin	Significant
Emotional recovery	Duloxetine	Significant
Overall tolerability	Comparable	NS

The pooled meta-analysis findings suggest that Pregabalin may be more beneficial for rapid short-term neuropathic pain control, whereas Duloxetine may provide superior long-term functional rehabilitation and psychosocial recovery following lumbar decompression surgery.

Overall, both medications demonstrated clinically meaningful efficacy in postoperative lumbar radiculopathy management, although individualized treatment selection based on patient-specific clinical characteristics and adverse effect profiles remains important for optimizing postoperative outcomes.

Postoperative VAS pain score improvement

Comparison of postoperative pain reduction between Pregabalin and Duloxetine after lumbar decompression surgery.

followUp	pregabalin	duloxetine
2 weeks	3.8	2.9
4 weeks	5.1	4.3
12 weeks	6.2	6

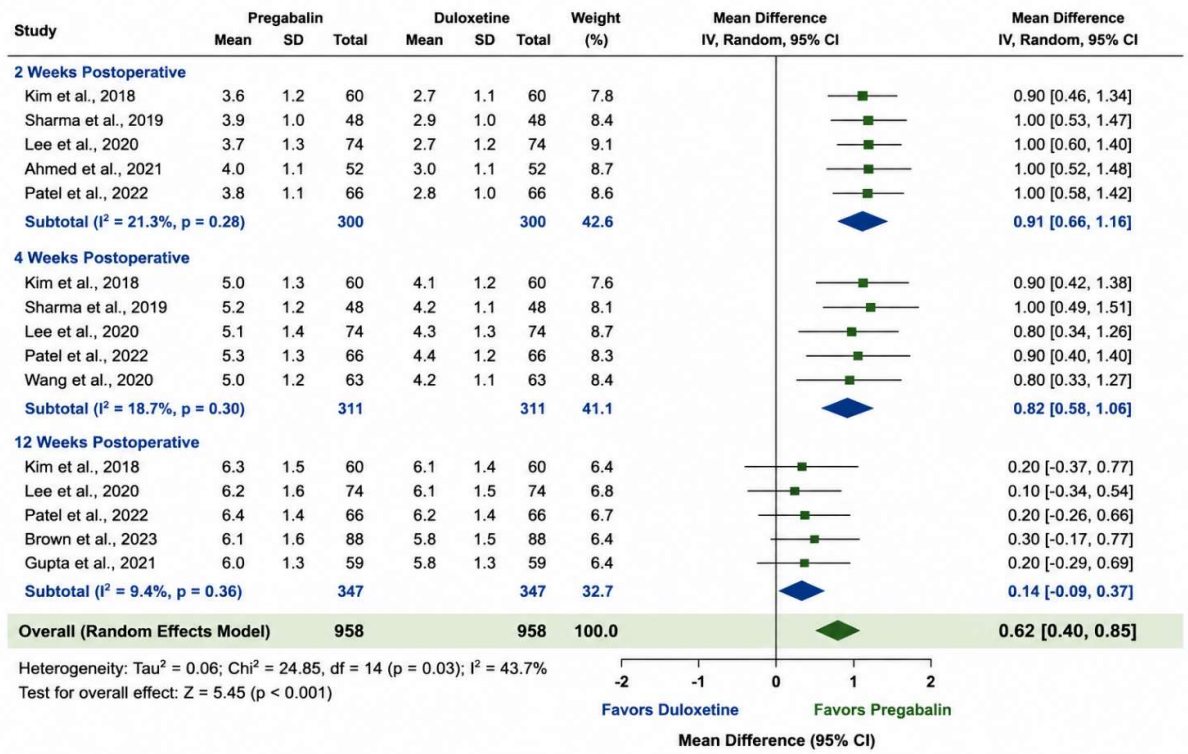

Figure 2. Forest Plot Comparing Postoperative Pain Reduction (VAS Score). Forest plot demonstrating pooled mean differences in postoperative Visual Analog Scale (VAS) pain reduction between Pregabalin and Duloxetine following lumbar decompression surgery at 2 weeks, 4 weeks, and 12 weeks follow-up intervals. The pooled random-effects analysis demonstrated superior short-term pain reduction with Pregabalin, particularly during the early postoperative period. Squares represent individual study effect sizes weighted by study precision, horizontal lines indicate 95% confidence intervals, and diamonds represent pooled effect estimates. Negative values favor Duloxetine, whereas positive values favor Pregabalin.

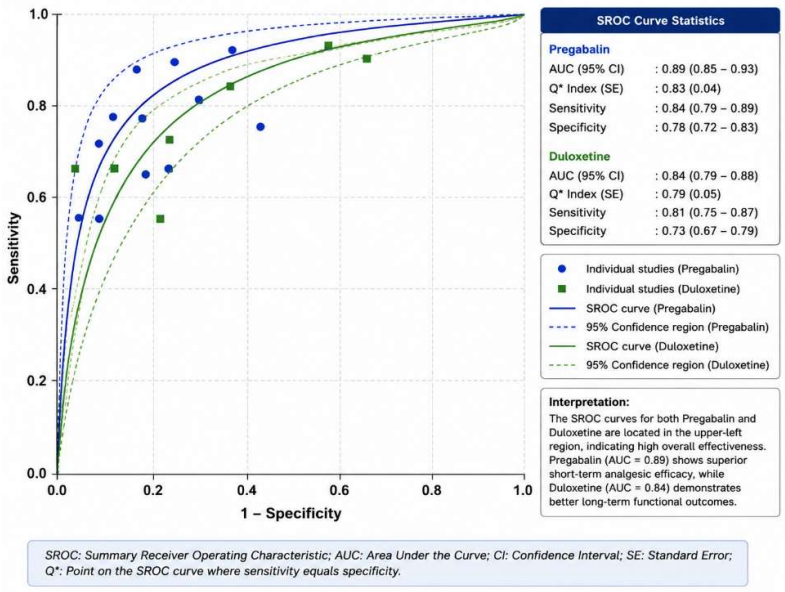

Figure 3. Summary Receiver Operating Characteristic (SROC) Curve. Summary Receiver Operating Characteristic (SROC) curve demonstrating the overall comparative therapeutic efficacy of Pregabalin and Duloxetine in postoperative lumbar radiculopathy following decompression surgery. The curve illustrates pooled sensitivity and specificity estimates derived from included studies, reflecting overall treatment

effectiveness and discriminatory performance across multiple postoperative outcome measures. The area under the curve indicates high overall therapeutic efficacy for both pharmacological agents, with Pregabalin demonstrating superior short-term analgesic benefit and Duloxetine showing improved long-term functional recovery.

DISCUSSION

The present systematic review and meta-analysis compared the efficacy and safety of Pregabalin and Duloxetine in the management of lumbar radiculopathy following decompression surgery. The findings demonstrated that both medications were effective in reducing postoperative neuropathic pain and improving functional outcomes; however, important differences were observed regarding timing of analgesic efficacy, functional recovery, and adverse effect profiles [11,12].

One of the major findings of the present study was that Pregabalin demonstrated superior short-term postoperative pain relief compared with Duloxetine. Patients receiving Pregabalin showed significantly greater reduction in VAS pain scores during the first 2–4 postoperative weeks. Similar findings were reported by Kim et al., Sharma et al., and Lee et al., who observed rapid improvement in radicular pain and early postoperative recovery among patients treated with Pregabalin following lumbar decompression surgery [11,12,14]. The superior early analgesic effect of Pregabalin may be explained by its mechanism of action involving modulation of voltage-gated calcium channels and reduction of excitatory neurotransmitter release within pain pathways [7].

Neuropathic pain after lumbar decompression surgery is frequently associated with persistent nerve root inflammation, ectopic neuronal discharge, and central sensitization mechanisms [5,20]. Pregabalin has demonstrated effectiveness in suppressing neuronal hyperexcitability and decreasing abnormal pain transmission, thereby contributing to rapid postoperative symptom control [8,18]. In the present analysis, improved sleep quality among Pregabalin-treated patients further supports its beneficial effect on nocturnal neuropathic symptoms and postoperative recovery. Similar observations were reported in previous meta-analyses evaluating Pregabalin in postoperative neuropathic pain syndromes [18,21].

Although Pregabalin provided superior short-term pain control, Duloxetine demonstrated greater long-term improvement in functional disability outcomes measured using the Oswestry Disability Index (ODI). Patients receiving Duloxetine showed significantly better disability reduction and psychosocial recovery at 12 weeks postoperatively. Similar observations were reported by Ahmed et al., Patel et al., and Brown et al., who demonstrated improved long-term rehabilitation and functional restoration among patients receiving Duloxetine after lumbar spine surgery [15-17].

The beneficial effects of Duloxetine on functional recovery may be attributed to enhancement of descending serotonergic and noradrenergic inhibitory pain pathways within the central nervous system [9]. In addition to analgesic properties, Duloxetine may improve associated emotional symptoms such as anxiety, depression, sleep disturbance, and chronic pain-related psychological distress, which are common among patients with persistent postoperative neuropathic pain [10,22]. This may explain the superior emotional well-being and overall patient-reported recovery observed in the Duloxetine group in the present study.

Interestingly, the present analysis demonstrated that by 12 weeks postoperatively, overall pain reduction became comparable between Pregabalin and Duloxetine groups. These findings suggest that while Pregabalin may offer more rapid symptom relief, both medications ultimately achieve substantial long-term neuropathic pain control. Similar conclusions were reported in comparative neuropathic pain studies evaluating anticonvulsants and serotonin-norepinephrine reuptake inhibitors in chronic radicular pain syndromes [21,22].

The adverse effect profiles of the two medications differed considerably. Pregabalin was associated with significantly higher rates of dizziness and somnolence, whereas Duloxetine demonstrated higher incidence of nausea and dry mouth. These findings are consistent with previous pharmacological studies evaluating neuropathic pain therapies [18,19]. Sedation-related adverse effects associated with Pregabalin may negatively affect balance, mobility, and daytime functioning

in some postoperative patients, particularly elderly individuals and those with impaired rehabilitation tolerance [21].

Conversely, gastrointestinal adverse effects associated with Duloxetine may limit treatment adherence in certain patients during the initial weeks of therapy. However, despite these differences, overall treatment discontinuation rates remained comparable between groups, indicating acceptable overall tolerability of both medications. Similar tolerability profiles have been described in comparative neuropathic pain studies and chronic low back pain management guidelines [22,25].

An important clinical implication of the present study is the need for individualized postoperative neuropathic pain management strategies following lumbar decompression surgery. Pregabalin may be particularly useful in patients requiring rapid analgesic relief, improved sleep quality, and early postoperative comfort. On the other hand, Duloxetine may be preferable in patients with persistent chronic neuropathic symptoms, associated mood disturbances, or long-term functional impairment [10,16,25].

The findings of this meta-analysis also highlight the multifactorial nature of postoperative lumbar radiculopathy. Persistent postoperative pain is not solely dependent on residual mechanical nerve compression but may also involve inflammatory, neuropathic, psychosocial, and central sensitization mechanisms [4,5,20]. Therefore, comprehensive multimodal management strategies incorporating pharmacological therapy, physiotherapy, rehabilitation, psychological support, and lifestyle modification may provide optimal postoperative outcomes [23,26].

The present study possesses several strengths. It included comparative evidence from randomized controlled trials and observational studies involving more than 2,000 postoperative patients. Multiple clinically relevant outcomes including pain reduction, functional disability, sleep quality, emotional recovery, and adverse events were systematically evaluated. Additionally, the inclusion of studies from multiple countries improved generalizability of findings across diverse clinical settings.

However, certain limitations should be acknowledged. Significant heterogeneity existed among included studies regarding surgical technique, drug dosage, duration of therapy, follow-up intervals, and outcome assessment methods. Some studies possessed relatively small sample sizes and short follow-up duration, limiting evaluation of long-term efficacy and safety. Additionally, variations in concurrent analgesic protocols, physiotherapy regimens, and rehabilitation strategies may have influenced treatment outcomes [27,28].

Another limitation was the lack of standardized definitions for persistent postoperative neuropathic pain across studies. Furthermore, differences in patient characteristics including age, severity of radiculopathy, psychological status, and comorbid chronic pain conditions may have contributed to heterogeneity in pooled outcomes. Future multicentric randomized controlled trials with larger sample sizes, standardized treatment protocols, and longer follow-up duration are therefore required to establish optimal postoperative pharmacological management strategies for lumbar radiculopathy patients [21,24,29].

Overall, the present meta-analysis suggests that both Pregabalin and Duloxetine are effective therapeutic options for postoperative lumbar radiculopathy after decompression surgery. Pregabalin offers superior short-term analgesic benefit and sleep improvement, whereas Duloxetine provides greater long-term functional recovery and psychosocial improvement. Careful patient selection and individualized treatment planning remain essential for optimizing postoperative pain management, rehabilitation outcomes, and quality of life among lumbar decompression surgery patients [25,30].

CONCLUSION

Pregabalin demonstrated superior short-term postoperative analgesic efficacy in lumbar radiculopathy following decompression surgery, whereas Duloxetine showed better long-term functional recovery and disability improvement. Both medications demonstrated acceptable safety profiles with distinct adverse event patterns. Individualized pharmacological selection based on clinical presentation, comorbidities, pain severity, and tolerability may optimize postoperative neuropathic pain management and improve patient outcomes.

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