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Systematic review

Effects of Intravenous Analgesic Infusions on Pain Intensity and Functional Outcomes in Adults with Fibromyalgia or Neuropathic Pain: A Systematic Review

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Abstract

Background: Intravenous analgesic infusions are used for persistent fibromyalgia and neuropathic pain. Their effects on pain intensity and everyday function require separate evaluation. This review examined analgesic benefit, functional outcomes, durability, and adverse effects. **Methods:** We included the original controlled studies published through 31 May 2026. Intravenous

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lidocaine, ketamine, and morphine were compared with placebo or active control. Findings were synthesized qualitatively according to diagnosis, infusion regimen, outcome domain, and follow-up duration. **Results:** Eleven original articles formed the data synthesis. Early fibromyalgia experiments reported immediate analgesia and selected improvements in endurance or disease impact. A short ketamine infusion produced no sustained advantage over midazolam during eight weeks of follow-up. Lidocaine added to amitriptyline generally produced no persistent additional benefit. A recent comparative fibromyalgia trial reported improvements in pain, function, and quality of life after repeated infusions. Neuropathic pain studies demonstrated variable immediate responses, including greater pain reduction with lidocaine than placebo in diabetic neuropathy. Trials assessing outcomes four to twelve weeks after treatment generally found no sustained superiority in pain or quality of life. **Conclusion:** Intravenous infusions provide short-term analgesia in selected populations. The data does not support treating immediate pain reduction as proof of sustained recovery, and treatment evaluation requires patient-centered functional outcomes with pain scores and safety.

Keywords: Fibromyalgia; neuropathic pain; intravenous infusion; lidocaine; ketamine; physical function.

Introduction

Fibromyalgia is a chronic syndrome characterized by widespread pain accompanied by fatigue, disturbed sleep, cognitive symptoms, and impaired daily functioning. Its clinical burden extends beyond pain intensity because several interacting symptoms influence participation, well-being, and treatment satisfaction (1). Contemporary terminology recognizes nociplastic pain as pain arising from altered nociception without sufficient evidence of tissue damage or a somatosensory lesion explaining the symptoms (2).

Neuropathic pain differs mechanistically because its definition requires a lesion or disease affecting the somatosensory nervous system. Diagnostic grading integrates a compatible clinical history, neuroanatomically plausible pain distribution, sensory findings, and appropriate confirmatory investigations (3). These distinctions support examining fibromyalgia and neuropathic pain separately, even when both conditions involve hypersensitivity and disturbances in pain processing (2,3).

Management differs between these populations, although both require attention to physical and psychological functioning (4,5). Revised European League Against Rheumatism recommendations emphasize education and non-pharmacological treatment for fibromyalgia, with exercise receiving the strongest recommendation (4). Recommendations for neuropathic pain identify tricyclic antidepressants, serotonin-noradrenaline reuptake inhibitors, pregabalin, and gabapentin as first-line pharmacotherapies, reflecting a larger evidence base than that available for infusion treatment (5).

Intravenous analgesic infusions have attracted interest for pain that persists despite conventional treatment, with ketamine and lidocaine representing distinct pharmacological approaches. Ketamine antagonizes N-methyl-D-aspartate receptors, whereas lidocaine acts through sodium-channel blockade, providing different rationales for modifying abnormal nociceptive activity. The ketamine consensus guideline documents differences in patient selection, dose, treatment duration, monitoring, and evidence strength between pain diagnoses. Conclusions derived from one diagnosis or infusion schedule require careful interpretation before application to another clinical setting (6). Pain reduction alone does not describe the full clinical value of an intervention because physical function, emotional function, and global improvement represent separate outcome domains. Interpretation also requires distinguishing change within an individual from differences between treatment groups and considering the duration and tolerability of benefit (7). The present

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review examined controlled data on intravenous analgesic infusions in adults with fibromyalgia or neuropathic pain, showing the relationship between pain relief, functional outcomes, and persistence of benefit after treatment.

Methods

The review was organized using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses framework (Fig 1). Eligibility include the original controlled studies published through 31 May 2026. The question followed a population, intervention, comparator, and outcome structure addressing adults with fibromyalgia or clinically diagnosed neuropathic pain receiving systemic intravenous analgesic infusions.

The proposed electronic sources were PubMed, Scopus, Web of Science Core Collection, and the Cochrane Central Register of Controlled Trials. The core strategy combined condition terms with administration and drug terms: (fibromyalgia OR neuropathic pain OR neuralgia OR diabetic neuropathy OR nerve injury) AND (intravenous OR infusion) AND (lidocaine OR lignocaine OR ketamine OR morphine). Database-specific subject headings and field restrictions complemented the free-text terms. Reference lists of eligible reports and relevant reviews were examined for additional studies.

Eligible designs included randomized parallel-group and crossover studies comparing an infusion with saline, an active placebo, or another analgesic intervention. Studies reporting pain intensity were eligible regardless of whether functional outcomes were measured, preventing exclusion based on selective outcome availability. Functional measures, disease impact, quality of life, medication use, and adverse effects were extracted whenever reported. Acute postoperative studies, healthy-volunteer experiments, isolated intravenous boluses, non-intravenous treatment, uncontrolled case reports, and cancer-related pain were excluded.

Two authors screened titles and abstracts and evaluated eligible reports. The same authors extracted study design, diagnostic criteria, sample denominators, intervention details, comparators, outcome measures, follow-up intervals, and adverse effects. Disagreements were resolved through discussion. Reports describing the same participant cohort were treated as linked publications to avoid duplicate counting.

Methodological appraisal addressed randomization, allocation concealment, treatment masking, incomplete outcomes, selective reporting, and crossover-specific concerns. Particular attention was given to washout intervals, potential carryover, active-placebo selection, and differences between enrolled and analyzed populations.

Synthesis was narrative because diagnoses, infusion schedules, outcome instruments, and observation periods differed substantially. Results were grouped by condition and drug, with immediate responses separated from outcomes measured after treatment completion. Between-group findings were prioritized over within-group improvement, and individual responder proportions were distinguished from average treatment effects. No pooled effect estimate, cross-trial ranking, or combined participant total was calculated. Functional outcomes were not inferred from pain scores, sensory thresholds, or reduced rescue medication use, since these represent different dimensions of treatment response. The analysis used published aggregate information without recruitment or access to identifiable patient data.

Results

In the 1995 fibromyalgia report, Sörensen and colleagues examined morphine, lidocaine, and ketamine in separate placebo-controlled

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experiments involving 31 patients; lidocaine and ketamine reduced pain during or shortly after administration, whereas morphine produced no significant changes. Ketamine also improved static endurance without increasing muscle strength (8). Their crossover study involving 18 patients reported improved Fibromyalgia Impact Questionnaire scores after ketamine and pain relief lasting one to five days in seven drug responders (9). Noppers et al. found no sustained treatment advantage during eight weeks after a single 30-minute S-ketamine infusion in 24 treated participants (10). Fifteen minutes post-infusion, eight ketamine recipients and three midazolam recipients achieved greater-than-50% pain reduction; at eight weeks, two participants in each group met that threshold (10). These findings supported a brief response without showing lasting superiority over the active comparator throughout follow-up or establishing durable functional recovery after infusion completion (10).

Vlainich et al. studied 30 women receiving amitriptyline and four weekly infusions of either lidocaine or saline, finding no additional benefit in pain intensity or associated manifestations (11). Albertoni Giraldes et al. reported lower pain intensity with lidocaine at week two, without consistent differences at other assessments or an overall meaningful treatment advantage (12). El Derh et al. compared repeated lidocaine, ketamine, and saline in 75 patients, reporting improved pain, physical disease-impact measures, and quality of life in the active-treatment groups (13). This newer report supplied a positive functional signal alongside the inconsistent findings from earlier fibromyalgia trials (9-13).

For peripheral neuropathic pain, Kvarnström et al. studied 12 patients with traumatic nerve injury and reported mean pain reductions of 55%, 34%, and 22% with ketamine, lidocaine, and placebo, respectively (14). The ketamine-placebo difference was significant, and somnolence and dizziness were frequent adverse effects (14). Kim et al. evaluated four weekly lidocaine infusions in postherpetic neuralgia or complex regional pain syndrome type II; 42 participants completed treatment. Pain reduction was greater after the final infusion, although the advantage was absent at four-week follow-up (15).

Moulin et al. enrolled 34 participants in a crossover trial comparing lidocaine with diphenhydramine, finding no significant benefit in pain, physical function, mood, or quality of life. The reported four-week between-treatment pain difference was 0.17 points, with a 95% confidence interval from −0.50 to 0.84 (16). Todorovic and colleagues enrolled 34 participants with painful diabetic neuropathy, with 31 completing both sessions; pain reduction at 60-120 minutes was 51% after lidocaine and 33.5% after placebo. The difference was 17.6 percentage points, and quantitative sensory testing did not predict treatment response (17).

Wangnamthip et al. randomized 50 participants with recent-onset peripheral neuropathic pain, with 29 completing the protocol. Four weekly lidocaine infusions produced no significant advantage in pain intensity, quality of life, or psychological outcomes through 12 weeks, despite lower tramadol use at selected assessments (18). These reports distinguished short-lived analgesic responses from inconsistent longer-term improvement, while functional findings remained dependent on the diagnosis, regimen, instrument, and follow-up interval examined.

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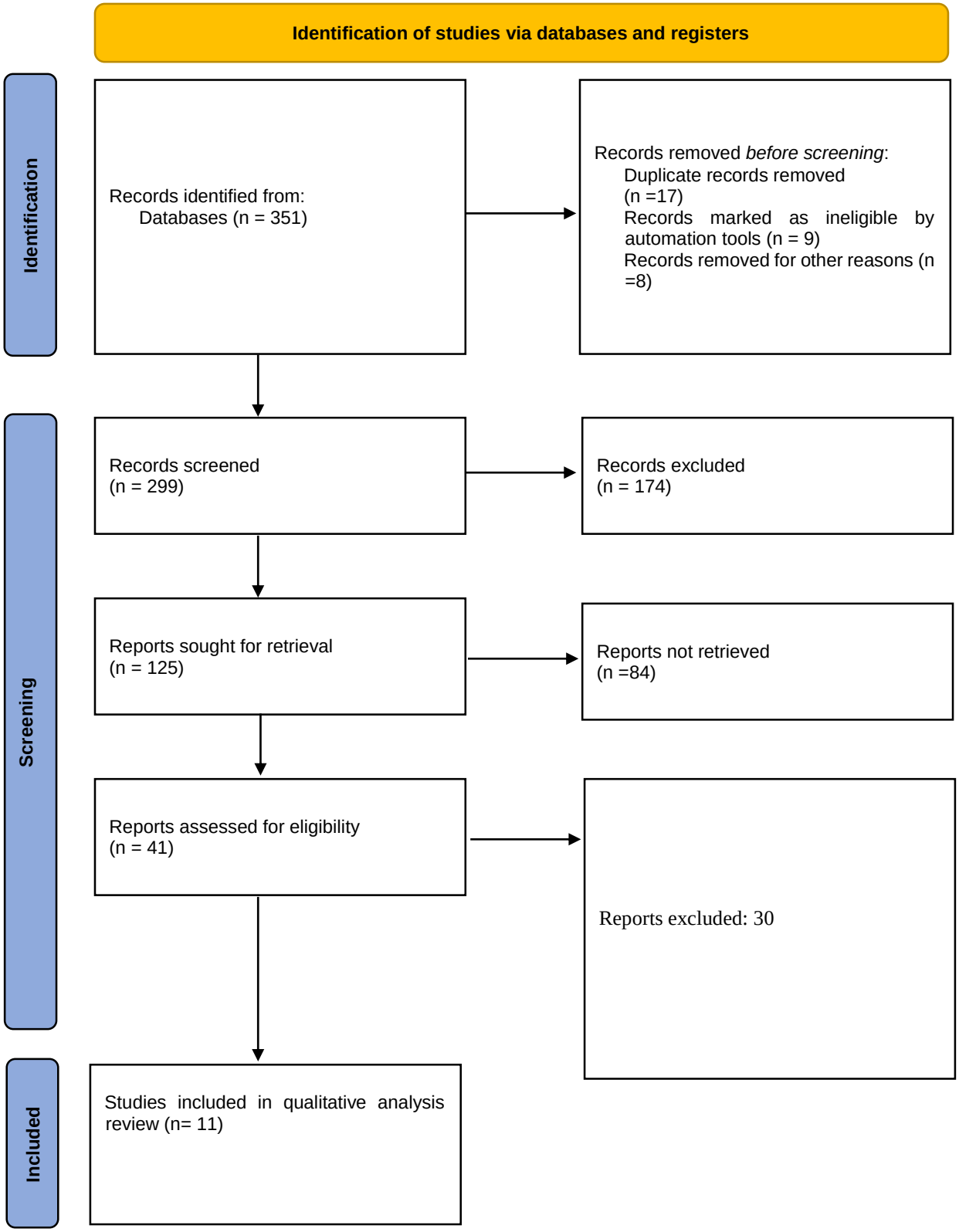


Figure 1: PRISMA flow chart

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Table 1. Controlled studies of intravenous analgesic infusions in fibromyalgia

Study	Participants	Infusion and comparator	Pain and functional findings
Sörensen, 1995 (8)	31 across three drug experiments	Morphine, lidocaine, or ketamine versus placebo	Lidocaine and ketamine reduced immediate pain; ketamine improved endurance, with unchanged muscle strength (8)
Sörensen, 1997 (9)	18	Crossover comparison of morphine, lidocaine, ketamine, and saline	FIQ improvement after ketamine; seven drug responders reported analgesia lasting 1-5 days; responder-specific results limit generalization (9)
Noppers, 2011 (10)	24 treated	S-ketamine 0.5 mg/kg over 30 minutes versus midazolam 5 mg	Early responder difference; no sustained VAS or FIQ advantage during eight-week follow-up (10)
Vlainich, 2010 (11)	30 women	Lidocaine 240 mg weekly for four weeks versus saline; both groups received amitriptyline	No additional benefit in pain or associated manifestations despite improvement in both groups (11)
Albertoni Giraldes, 2016 (12)	42	Lidocaine 240 mg weekly for four weeks versus saline; background amitriptyline	Lower pain at week two; no consistent later advantage or overall meaningful benefit through eight weeks (12)
El Derh, 2025 (13)	75	Lidocaine 5 mg/kg, ketamine 0.5 mg/kg, or saline; three weekly treatments	Active groups reported improvements in pain, physical disease impact, and SF-12 quality of life at four-week assessment (13)

Table 2. Controlled studies of intravenous analgesic infusions in peripheral neuropathic pain

Study	Participants and condition	Infusion and comparator	Pain, function, and durability
Kvarnström, 2003 (14)	12; traumatic peripheral neuropathic pain	Ketamine 0.4 mg/kg, lidocaine 2.5 mg/kg, or saline	Mean pain reduction: 55%, 34%, and 22%, respectively; significant ketamine-placebo difference; frequent somnolence and dizziness (14)
Kim, 2018 (15)	42 completed; postherpetic neuralgia or CRPS II	Lidocaine 3 mg/kg over one hour versus saline, weekly for four weeks	Greater pain reduction after the final infusion; benefit absent at four-week follow-up; no serious treatment complications reported (15)
Moulin, 2019 (16)	34 enrolled; peripheral neuropathic pain	Lidocaine 5 mg/kg versus diphenhydramine 50 mg	No significant pain, physical-function, mood, or quality-of-life advantage; four-week pain difference 0.17 points, 95% CI −0.50 to 0.84 (16)
Todorovic, 2022 (17)	34 enrolled; 31 analyzed; painful diabetic neuropathy	Lidocaine 5 mg/kg ideal body weight over 40 minutes versus saline	Pain reduction 51% versus 33.5% at 60-120 minutes; difference 17.6 percentage points; sensory testing did not predict response (17)
Wangnamthip, 2024 (18)	50 randomized; 29 completed; recent-onset peripheral neuropathic pain	Lidocaine 3 mg/kg over one hour versus saline, weekly for four weeks	No pain, quality-of-life, or psychological advantage through 12 weeks; lower tramadol use at selected assessments; no serious adverse events reported (18)

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Discussion

The principal finding was the separation between immediate analgesia and persistent clinical benefit, which is consistent with Zhu et al. lidocaine meta-analysis, their analysis favored lidocaine during the early post-infusion period, without establishing a persistent effect after repeated treatment over four weeks (19). Pastrak et al. identified predominantly short-term analgesic effects from low-dose ketamine in fibromyalgia, with limited controlled evidence supporting sustained benefit (20). These reviews support interpreting an infusion response within its measured time window, rather than assuming that an early change predicts recovery over subsequent weeks (19,20).

The 2025 Cochrane review strengthens this cautious interpretation because data concerning intravenous ketamine remained limited by low or very low certainty. Its findings did not establish clear reductions in pain intensity at the immediate, short-term, or medium-term assessments examined. We also identified increase in adverse events with intravenous ketamine, emphasizing that uncertain benefit and treatment burden require joint consideration. These findings explain why selected positive trials do not establish broad efficacy across diagnoses, doses, and treatment schedules, when trial populations and outcome definitions differ substantially. Uncertainty does not demonstrate absence of benefit for every patient (21). Reporting favorable and unfavorable outcomes is essential when explaining the balance between an individual observed response and continuing treatment burden (7,21).

For fibromyalgia, the lidocaine review by de Carvalho and Skare described short-term improvements and substantial variation in treatment schedules and follow-up (22). The controlled trials summarized here demonstrate an important distinction between improvement after treatment and improvement specifically attributable to the infusion. In trials with background amitriptyline, symptom reduction in both groups did not establish an additional sustained lidocaine effect (11,12). The positive El Derh report broadens the functional evidence, while its findings require interpretation with the negative longer-term ketamine study and the inconsistent adjunctive-lidocaine results (10-13).

Function remained a separate clinical outcome throughout the synthesis, consistent with the outcome framework proposed by IMMPACT (7). Improved experimental endurance, altered sensory thresholds, reduced medication use, and better questionnaire scores describe different phenomena and are not interchangeable measures of recovery (7-9,17,18). Moulin's negative physical-function and quality-of-life findings are relevant because they directly assessed outcomes beyond pain intensity (16). Reduced tramadol use without better pain or quality-of-life scores in the Wangnamthip trial represents a limited secondary finding rather than data of comprehensive functional improvement (18).

Interpretation is constrained by small samples, heterogeneous protocols, different placebo strategies, and incomplete follow-up, including completion by 29 of 50 randomized participants in the recent neuropathic-pain trial (14,16,18). Cross-trial comparisons therefore do not establish superiority of one infusion or identify an optimal maintenance schedule (19-22). Future trials require pre-specified pain-responder thresholds, validated functional measures, explicit handling of missing outcomes, and observation beyond treatment completion.

Conclusion

Intravenous lidocaine and ketamine produced short-term analgesia in several controlled studies of fibromyalgia and neuropathic pain. Sustained pain reduction and functional improvement were

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inconsistent, with several trials finding no advantage over control during follow-up. Recent positive fibromyalgia findings add clinically relevant evidence without establishing a universally effective regimen. Immediate analgesic response therefore requires separate interpretation from durable improvement in daily activities and quality of life. Treatment evaluation requires documented functional goals, reassessment after infusion completion, and attention to adverse effects. Larger controlled studies with standardized outcomes and longer follow-up are necessary to define the populations and schedules offering lasting benefit.

Abbreviations

CI: Confidence interval.

CRPS II: Complex regional pain syndrome type II.

FIQ: Fibromyalgia Impact Questionnaire.

IMMPACT: Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials.

NMDA: N-methyl-D-aspartate.

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

SF-12: 12-Item Short Form Health Survey.

VAS: Visual analogue scale.

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