

Efficacy of Cetirizine and Gabapentin in the management of Postburn Pruritus – A Systematic Review and Meta-analysis

Dr. K Eshwar Karthikeyan¹, Dr S Satish Kumar², Dr V M Arvindraj³, Dr R Santharam⁴, Dr S Arun Prasath⁵, Dr Sangamithra A⁶

¹Department of Plastic Surgery, SRM Medical College and Research Center, Kattankulathur, Chennai. E: mail: eshez@gmail.com Orcid id- 0000-0002-0403-9071

²MS, MCH, Assistant Professor, Department of Plastic Surgery, SRM Medical College and Research Center, Kattankulathur, Chennai. Email id: satishks1@srmist.edu.in

³MS, MCH, Assistant Professor, Department of Plastic Surgery, SRM Medical College and Research Center, Kattankulathur, Chennai. Email id: arvind.raj1991@gmail.com

⁴DNB, MCH, Professor, Department of Plastic Surgery, SRM Medical College and Research Center, Kattankulathur, Chennai. Email id: rsramplastic@gmail.com

⁵MS, MCH, Associate Professor, Department of Plastic Surgery, SRM Medical College and Research Center, Kattankulathur, Chennai. Email id: arunpras1@srmist.edu.in

⁶MS MCH, Assistant professor, Department of Plastic Surgery, SRM Medical College and Research Center, Kattankulathur, Chennai. Email id: drsangamithra.surgeon@gmail.com

Abstract

Background: Pruritus is a common and debilitating complication of burn wound healing and rehabilitation, and although it appears to be related to the release of histamine, is poorly responsive to conventional H1-antihistamines, likely because of underlying neuropathic mechanisms. Gabapentin may be a new possibility, and is less well documented.

Objective: To synthesize and evaluate the comparative effectiveness and safety of gabapentin versus cetirizine in the management of postburn pruritus.

Methods: The systematic review and meta-analysis (SRMA) will be carried out according to the guidelines of PRISMA 2020 and Cochrane Handbook. PubMed, Embase, Cochrane Library, Web of Science, Scopus, and Google Scholar were used to perform electronic database search for both language and date restrictions. Randomized controlled trials (RCTs) were selected that compared oral gabapentin with the antihistamine cetirizine for postburn use. The risk ratios (RR) for dichotomous itch remission outcomes and the mean difference (MD) for continuous post-treatment Visual Analogue Scale (VAS) scores were computed by pooling using the Review Manager (RevMan 5.4) software with random-effects models.

Results: Four RCTs with 287 participants were included. In pooled analysis, gabapentin was significantly more effective and more effective in improving itch remission rates than cetirizine (RR 0.46; 95% CI: 0.28–0.78; $p=0.004$). The post-treatment VAS scores for continuous pooling showed significant heterogeneity ($I^2=71\%$ to 92%) and were significantly lower for gabapentin (MD -1.56; 95% CI: -2.79 to -0.32; $p=0.01$). Gabapentin was more effective than placebo at reducing itch and at providing secondary sleep benefits, but was associated with an increased incidence of transient central nervous system side-effects like drowsiness, dizziness, and sedation.

Conclusion: Gabapentin is more effective than cetirizine in achieving postburn pruritus severity reduction and remission for postburn pruritus, and should be used with caution because of its sedative effects.

Keywords: Postburn pruritus; Gabapentin; Cetirizine; Systematic review; Meta-analysis; Visual Analogue Scale

1. Introduction

A burn injury is still a serious health issue throughout the world and is responsible for a high level of morbidity and disability in the long term [1]. Pruritus is one of the many complications and is the most frequent, troubling and experienced by most of the patients during wound healing and rehabilitation [2]. Post burn itching is seen in over 90% of patients shortly after the burn; although it tends to improve with time, a significant number of patients, especially those with a large T.B.S.A. burn, thick scarring or grafted areas may have itching for years after the burn [3]. These days, postburn pruritus is known to be a combination of both pruritoceptive and neuropathic mechanisms. After thermal injury, inflammatory mediators, neuropeptides secreted from keratinocytes, mast cells, and regenerating cutaneous nerve fibers sensitize peripheral itch receptors, and changes in central processing may maintain the itch feeling even after the wound has been healed [4]. This combination of mechanisms is thought to account for the poor response to conventional antihistamine therapy for postburn itch, which is thought to be mediated by histamine-dependent rather than neuropathic pathways [5].

Cetirizine is a second-generation H1-antihistamine and has long been recommended as 1st line treatment for postburn pruritus due to its safety profile, however this can sometimes be limited, particularly when the itching

becomes chronic [6]. This restriction has led to increased interest in use of the anticonvulsant, gabapentin, which regulates calcium-channel activity that plays a role in the transmission of neuropathic pain and itch. Gabapentin has been reported in several comparative trials to significantly reduce itch severity, and to provide secondary benefits in sleep quality [7-9]. But existing systematic reviews, such as a recent Cochrane review, suggest that there is low to moderate certainty of evidence for either agent, and this is mainly because of the size of the trials and the different outcome measures used across them [10-12]. In view of these discrepancies, a systematic review and meta-analysis are indicated to synthesize and provide clarity about the comparative effectiveness of cetirizine and gabapentin in postburn pruritus.

2. Materials and Method

Study Design and Registration

This study was a systematic review and meta-analysis (SRMA) of the effectiveness of cetirizine and gabapentin for the treatment of postburn itchy skin. The review was carried out according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations 2020 [13] and recommended method in the Cochrane Handbook for Systematic Reviews of Interventions [14]. To ensure transparency and reproducibility in evidence synthesis, the protocol was prospectively registered on the International Prospective Register of Systematic Reviews (PROSPERO) before screening was started [15].

Eligibility Criteria

Eligible studies were those that met the following criterion known as PICOS: Population — patients of any age with pruritus after a burn injury; Intervention — oral gabapentin alone or in combination; Comparator — cetirizine alone or in combination; Outcomes — change in itch severity measured by validated tools (Visual Analogue Scale, 5-D Itch Scale, or equivalent), sleep quality, and treatment-related adverse events; Study design — randomized controlled trials and comparative clinical studies reporting head-to-head or indirect comparisons between the two agents.

Inclusion Criteria

Studies were included when they were (1) randomized controlled trials or prospective comparative studies, (2) enrolled patients with a confirmed diagnosis of postburn pruritus, (3) compared cetirizine with gabapentin alone and/or in combination with other agents, (4) reported at least one quantifiable outcome related to itch severity or associated symptoms.

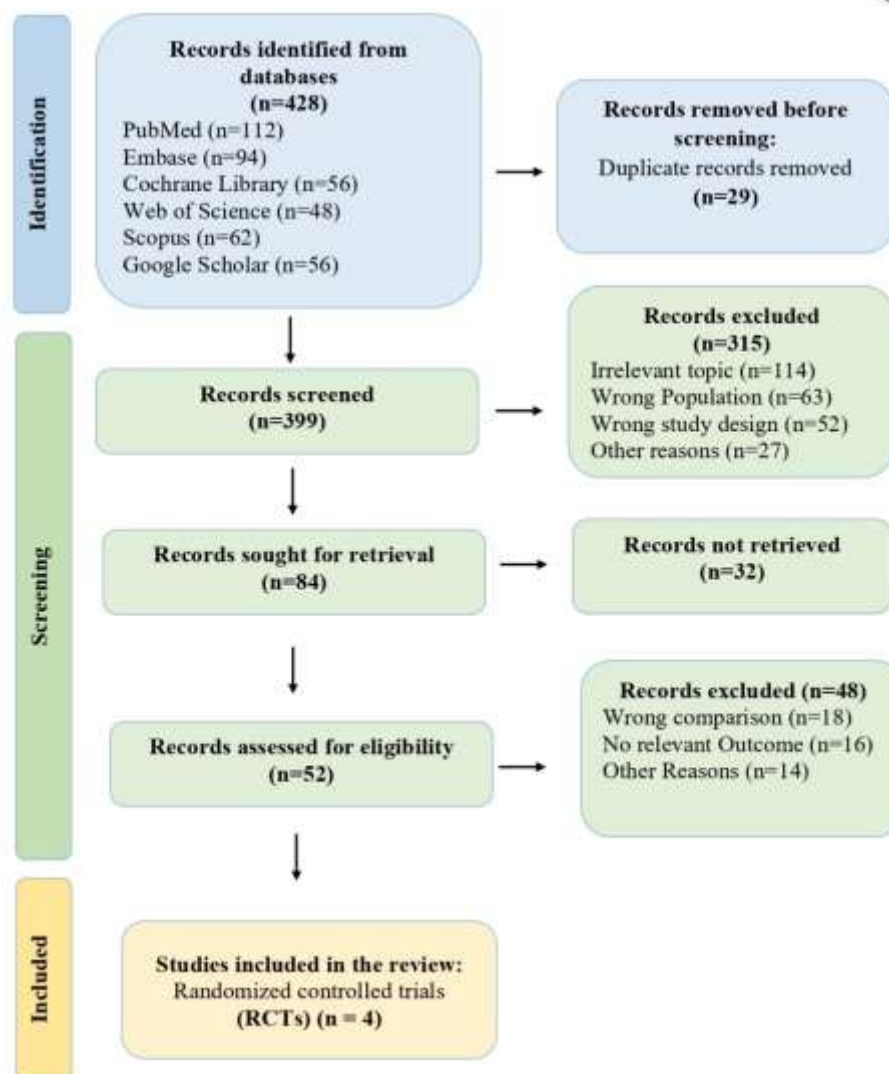
Exclusion Criteria

The studies that were excluded were (1) case reports, case series, editorials, conference abstracts or narrative reviews without original data; (2) studies performed on animal and in vitro models; (3) studies that evaluated pruritus caused by other etiologies (e.g., uremic, cholestatic or idiopathic pruritus); (4) studies without a comparator arm or data not separated for cetirizine and gabapentin; and (5) studies from which insufficient data could be extracted and which could not be obtained from the corresponding author.

Study Selection and Search Strategy

An extensive search of the following electronic databases was carried out from the dates of the inception of the databases through the search date without any language or publication date restrictions: PubMed, Embase, Cochrane Library, Web of Science, Scopus, and Google Scholar. To perform the search, controlled vocabulary (MeSH) and free-text terms that were related to the population, intervention and comparator (PIC) were used and combined with the boolean operators “AND” and “OR”, such as “postburn pruritus”, “burn itch”, “cetirizine”, and “gabapentin”. Hand searching of reference lists of eligible articles also was done. Records that were retrieved were moved to reference management software and de-duplicated. Titles/abstract and then full texts were screened independently by two reviewers and discrepancies were resolved by discussion or a third reviewer. The entire selection process is described in the flow chart – PRISMA 2020 (Figure 1).

Figure 1: PRISMA Flow chart



Data Extraction

Two reviewers independently extracted data from the included studies from a pre-piloted data extraction spreadsheet. The variables extracted were first author and year of publication, country of origin, study design, sample size, characteristics of participants, description of the intervention/ comparator regimens (drug, dose, frequency and duration), outcome measures and time points of assessment, main efficacy results, and reported adverse events. Extracted data were verified for accuracy, and between the two reviewers when discrepancies arose, they were resolved by consensus and/or by a third reviewer. Studies for which corresponding authors were unavailable for the incomplete or inconsistent outcome data were excluded; corresponding authors of studies with missing information were contacted to provide the missing data, as specified in the exclusion criteria.

Quality Assessment — Cochrane Risk of Bias Tool

Two reviewers independently used the revised Cochrane Risk of Bias tool for randomized trials (RoB 2) [16] to measure the methodological quality of the included randomized trials. Five aspects of bias were assessed in each study: bias from the randomization process, bias resulting from deviation from intended interventions, bias resulting from missing outcome data, bias with respect to the measurement of the outcome, and bias in reporting the result. All domains and the study as a whole were deemed to be 'low risk', 'some concerns' or 'high risk' of bias. Conflicting

opinions of reviewers were settled by discussion, or by arbitration by a third reviewer.

Outcome of the Study

The main outcome was the reduction in the intensity of pruritus from baseline after treatment with cetirizine versus gabapentin, which was assessed using pruritus severity scales, validated for this purpose. Secondary outcomes were improvements in sleep quality, time to symptom resolution and incidence of treatment related adverse effects (sedation or somnolence).

Statistical Analysis

Review Manager software (RevMan, version 5.4) [17] was used to perform the meta-analyses. Data were summarized to risk ratios (RR) with 95% CI for dichotomous outcomes (itch remission, clinical efficacy) and mean differences (MD) with 95% CI for continuous outcomes (post-treatment Visual Analogue Scale (VAS) scores) with the Mantel-Haenszel method and inverse-variance method respectively. Because of the suspected clinical and methodological heterogeneity in the trials included in any pooled analysis, random-effects (DerSimonian-Laird) analyses were used a priori. Cochran's Q (χ^2) test was used to evaluate the statistical heterogeneity and the I^2 statistic, which was interpreted as substantial heterogeneity at $I^2 > 50\%$, was used to quantify the heterogeneity. A two sided p value less than 0.05 was regarded as being statistically significant. Since there are very few studies, funnel plots were not conducted to assess publication bias.

3. Results

Study Selection and Characteristics

The systematic search identified 428 records: PubMed (n = 112), Embase (n = 94), Cochrane Library (n = 56), Web of Science (n = 48), Scopus (n = 62), and Google Scholar (n = 56). 315 were excluded due to irrelevant topic (n = 114), wrong population (n = 63), wrong study design (n = 52), or other reasons (n = 27) after the 29 duplicate records were removed. Of the 399 unique records, 315 were screened and excluded due to irrelevant topic (n = 114), wrong population (n = 63), wrong study design (n = 52), or other reasons (n = 27). Full texts of the remaining 84 records were sought, but 32 could not be retrieved. There were 52 full-text articles that were evaluated for eligibility; 18 of these were excluded due to the wrong comparison, 16 were excluded due to no relevant outcome and 14 were excluded due to other reasons. Four randomized controlled trials (RCTs) ultimately fulfilled all of the inclusion criteria and were included in the qualitative and quantitative synthesis (Figure 1).

A total of 287 patients with postburn pruritus were enrolled in the four trials randomized controlled trials conducted in India, Pakistan, Ghana, and China. Sample sizes ranged from 58 to 100 participants per trial (Table 1). The participants were mainly young-to-middle aged adults who had burns affecting 5% – 30% of their total body surface area, and in three of the four trials, itch intensity was measured on the 0-10 VAS. Doses of gabapentin ranged from 300 mg once to three times a daily dose, titrated to the level of itch at baseline, and cetirizine doses were 10 mg once or twice a day; treatment durations were all 28 days (4 weeks) and outcomes were measured at baseline and every 28 days (Table 2). Reported outcomes were itch-free status, remission rate, post-treatment VAS score, sleep quality and treatment-related side effects of sedation/drowsiness/dizziness.

Table 1: Characteristics of the included studies

Author, Year	Country	Study Design	Sample Size	Participant Characteristics	Intervention	Comparator	Treatment Duration/Follow-up
Ahuja et al., 2011	India (New Delhi)	Randomized, three-arm comparative trial (stratified randomization)	N=60 total; 20/arm (Group A: cetirizine; Group B: gabapentin; Group C: combination)	Adults 12–70 yrs; post-burn healing phase (>80% wounds epithelialized or healed <1 month prior); >5% TBSA, predominantly 2nd-degree burns. Mean age: A 26.75y, B 28.65y, C 29.1y; M:F — A 12:8, B 10:10, C 9:11; mean %TBSA burn — A 28%, B 26%, C 29%; mean baseline VAS — A 6.6, B 6.3, C 6.45	Gabapentin monotherapy (Group B); cetirizine + gabapentin combination (Group C)	Cetirizine monotherapy (Group A)	28 days treatment; assessed days 0, 3, 7, 14, 21, 28
Fayyaz & Fayyaz, 2025	Pakistan (Peshawar)	Comparative study; non-probability convenience sampling, randomized by lottery method into 2 arms	N=100 total; 50/arm (Group A: gabapentin; Group B: cetirizine)	Ages 18–70y; thermal/electrical/scalding burns >5% TBSA; pruritus duration >1 week. Mean age: A 38.26±12.84y, B 32.54±8.94y; gender — A 62% M/38% F, B 76% M/24% F; duration of complaint — A 2.74±0.94 wks, B 2.84±0.88 wks; baseline VAS — A 5.06±1.05, B 5.20±1.04; %TBSA — A 15.96±6.58, B 14.72±4.96; weight — A 74.04±11.87 kg, B 67.94±12.31 kg	Gabapentin monotherapy (Group A)	Cetirizine monotherapy (Group B)	28 days treatment; single follow-up assessment at day 28

Arko-Bohah et al., 2024	Ghana (Centre for Tropical Clinical Pharmacology and Therapeutics, University of Ghana Medical School)	Randomized, three-arm trial	N=69 total; 23/arm (Cetirizine; Gabapentin; Cetirizine + Gabapentin)	Burn patients; ~97% presented with moderate-to-severe itch, 69% with acute itch, 94.2% experienced pruritus onset between weeks 1–4 post-burn. (Age, sex, %TBSA not reported in available abstract)	Gabapentin (n=23); cetirizine + gabapentin combination (n=23)	Cetirizine (n=23)	Assessed at baseline (day 0), day 3, day 7, day 14 for sleep quality; itch also assessed at 14 days and beyond 6 weeks (protracted itch)
Li et al., 2015	China (Chengdu, Sichuan)	Randomized, three-arm, placebo-controlled trial (random number table method)	N=58 total; placebo n=18, cetirizine n=20, gabapentin n=20	Adults 18–60y with pruritus of scar after deep second-degree (deep partial-thickness) burn; TBSA ≥5%, wound epithelialization ≥80% or healed <3 months prior. Overall 47 M/11 F. Placebo: 13M/5F, age 18–56 (38±15)y, TBSA 8–30% (14±8%); Cetirizine: 18M/2F, age 20–60 (36±17)y, TBSA 8–27% (17±6%); Gabapentin: 16M/4F, age 22–58 (35±16)y, TBSA 10–30% (16±10)%. No significant baseline differences among groups ($\chi^2=3.85$; $F=1.77, 1.82$; $P>0.05$)	Gabapentin 300 mg BID	Cetirizine 10 mg BID; Placebo (vitamin C 100 mg BID)	4 weeks (28 days) treatment; VAS assessed pre-treatment, PTD 3, PTD 28

Table 2: Summary of Interventions, comparators, outcome measures, and reported findings of the included studies

Author, Year	Intervention and Dosage	Comparator and Dosage	Outcome Measures	Assessment Time Points	Reported Outcomes	Adverse Events
--------------	-------------------------	-----------------------	------------------	------------------------	-------------------	----------------

Ahuja et al., 2011	Gabapentin: 300 mg OD (VAS 2–5), 300 mg BD (VAS 6–8), 300 mg TID (VAS 9–10); Combination: cetirizine + gabapentin at matched doses per VAS subgroup	Cetirizine: 10 mg OD (VAS 2–5) or 10 mg BD (VAS ≥6)	VAS (0–10) for itch intensity; side effects (sedation, depression, blurred vision, fatigue, headache) recorded each visit	Days 0, 3, 7, 14, 21, 28	Gabapentin produced a 95% reduction in VAS versus 52–58% with cetirizine at day 28; 20/20 gabapentin patients were itch-free by day 28 versus 3/20 with cetirizine	No side effects with gabapentin monotherapy (Group B). All patients in Group A (cetirizine) and Group C (combination) reported increased somnolence/sedation
Fayyaz & Fayyaz, 2025	Gabapentin: 300 mg OD/BD/TID per VAS score (2–5/6–8/9–10), 28 days	Cetirizine: 10 mg OD (VAS 2–5) or 10 mg BD (VAS ≥6), 28 days	VAS (efficacy defined as VAS=0 at day 28); stratified analysis by age, gender, duration of complaint, burn type, TBSA%, baseline VAS, weight	Day 0 (baseline) and Day 28	90% (45/50) achieved VAS = 0 with gabapentin versus 50% (25/50) with cetirizine; mean post-treatment VAS 0.26 ± 0.80 vs 1.20 ± 1.27	Not studied in detail; authors note dose-dependent side effects were not assessed and flag this as a study limitation
Arko-Boham et al., 2024	Gabapentin, standard dose (n=23; regimen NR in abstract); cetirizine + gabapentin combination, standard doses (n=23)	Cetirizine, standard dose (n=23; regimen NR in abstract)	Itch severity/intensity (scale NR); sleep quality/insomnia assessment	Baseline (day 0), day 3, day 7, day 14; itch also assessed at >6 weeks (protracted itch)	Itch reduction at day 14: 92.9% with gabapentin versus 61.8% with cetirizine; gabapentin also showed greater reduction in protracted itch	Not reported in the available abstract

Li et al., 2015	Gabapentin 300 mg, oral, twice daily, 4 weeks (n=20)	Cetirizine 10 mg, oral, twice daily, 4 weeks (n=20); Placebo: vitamin C 100 mg, oral, twice daily, 4 weeks (n=18)	VAS (0–10) for itching degree (0–1 no itch; 2–5 mild; 6–8 moderate; 9–10 severe); pruritus remission rate = (pre-treatment mean VAS – post-treatment mean VAS)/pre-treatment mean VAS × 100%; adverse reactions (drowsiness, dizziness)	Baseline (pre-treatment), PTD 3, PTD 28	Baseline VAS similar across groups (placebo 5.7±1 Day-28 VAS: 0.6 ± 0.3 with gabapentin versus 2.8 ± 1.2 with cetirizine; remission 91 ± 17% versus 56 ± 14%	5/20 patients in gabapentin group had mild-to-moderate drowsiness and dizziness within 24–48h of dosing, untreated, resolved within 1 week; no adverse events in cetirizine or placebo groups
-----------------	--	---	---	---	--	---

Table 3: Quantitative data extracted for meta-analysis of gabapentin versus cetirizine

Study	Outcome	Gabapentin Events	Gabapentin Total	Cetirizine Events	Cetirizine Total	Gabapentin Mean VAS	Gabapentin SD	Cetirizine Mean VAS	Cetirizine SD
Ahuja et al., 2011	Itch-free (VAS 0–1) at day 28	20	20	3	20	NR	NR	NR	NR
Fayyaz & Fayyaz, 2025	Efficacy (VAS = 0) at day 28	45	50	25	50	0.26	0.80	1.20	1.27
Li et al., 2015	Remission at day 28	18	20	11	20	0.6	0.3	2.8	1.2

Quality Assessment and Risk of Bias

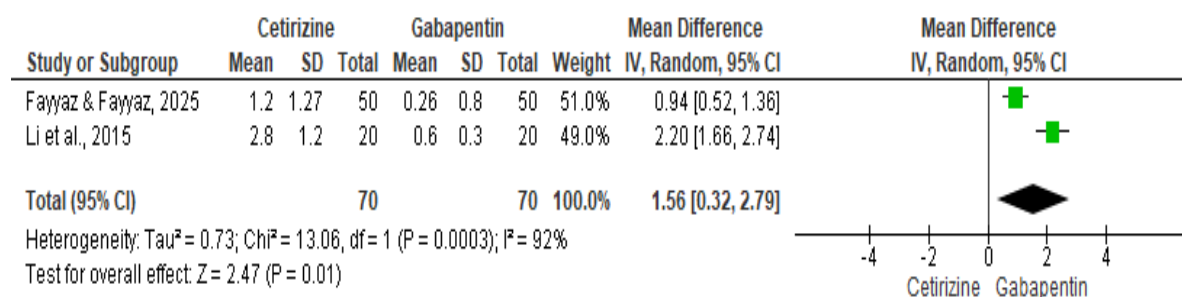
The Cochrane RoB 2 was used to evaluate the methodological quality of the studies, with five domains assessed (Figures 4 and 5). Three trials (6,8,18) were rated some concerns for the randomization process and one trial (19) was rated low risk. Two trials [6,8] had high risk for not following intended interventions (Domain 2), one had some concerns [18] and one was low risk [19]. Most missing outcome data (Domain 3) were handled adequately with a few rated low risk, one rated some concerns [18]. Ahuja et al. [6] was assessed as high risk for Measurement of the outcome (Domain 4), two trials were assessed as some concerns and Li et al. [19] was assessed as low risk for Measurement of the outcome (Domain 4). The outcome of the reported result (Domain 5) was not considered to be of high risk for any of the four trials. Overall, one trial [19] was rated low risk, one [18] some concerns, and two [6,8] high risk of bias, with most being unblinded and reporting variable outcome assessment reporting across the included evidence base.

Primary Outcomes

Three of the four trials (6,18,19) gave data on dichotomous rates of itch remission or clinical efficacy at Day 28, and were pooled for meta-analysis; one trial (8) was excluded in a non-quantitative fashion because standard-dose

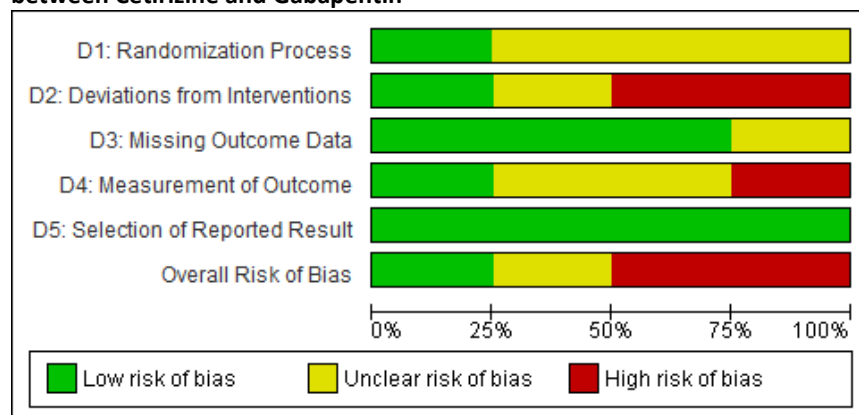
regimen and itch-severity data were not numerically reported in the abstract made available. The risk ratio for itch remission was 0.46 (95% CI: 0.28–0.78; $Z = 2.91$, $p = 0.004$) in favor of gabapentin (83 of 90 patients) compared with cetirizine (39 of 90 patients) (Figure 2). Heterogeneity across these three trials was substantial ($\tau^2 = 0.14$; $\chi^2 = 6.92$, $df = 2$, $p = 0.03$; $I^2 = 71\%$).

Figure 2: Forest plot comparing the risk ratio of pruritus remission (clinical efficacy) at day 28 between Cetirizine and Gabapentin



140 participants in two trials [18,19] were reported to have post-treatment VAS scores that were suitable for continuous pooling. Gabapentin was consistently more effective than cetirizine in reducing post-treatment itch severity, as reflected by lower mean VAS scores in both trials, both in inducing a decrease in itch and in reducing the residual itch, as measured by mean post-treatment VAS (0.26 ± 0.80 and 0.6 ± 0.3 vs 1.2 ± 1.27 and 2.8 ± 1.2 , respectively). The pooled mean difference was 1.56 (95% CI: 0.32–2.79; $Z = 2.47$, $p = 0.01$) in favor of gabapentin (Figure 3), although heterogeneity between the two trials was considerable ($\tau^2 = 0.73$; $\chi^2 = 13.06$, $df = 1$, $p = 0.0003$; $I^2 = 92\%$). In all individual trials (Table 2 and Table 3) gabapentin was significantly associated with more reductions in itch severity and more high rates of remission compared to cetirizine, and one trial found that gabapentin resulted in greater improvements in protracted itch and sleep quality compared to cetirizine [8]. The gabapentin group had a significant proportion of patients experiencing sedation or somnolence or dizziness, while the cetirizine and placebo groups had few such side effects, suggesting a balance between efficacy and severity of central nervous system side effects.

Figure 3: Forest plot comparing the mean difference in post-treatment Visual Analog Scale (VAS) scores at day 28 between Cetirizine and Gabapentin



Secondary Outcomes and Adverse Events

In addition to the main endpoint of relief from itching, secondary outcomes in the clinical trials were meaningful clinical advantages. Arko-Boham et al. [8] and literature cited in the preceding sections highlighted significant improvements in sleep quality and decrease in burn-induced insomnia among gabapentin-treated patients, with the majority of patients reporting that the medication had helped control neuropathic itch pathways. As for safety and

tolerability, adverse event reporting was inconsistent among studies. Systemic sedation and somnolence often occurred with cetirizine administration. On the other hand, gabapentin was well tolerated with generally mild drowsiness and dizziness side effects that rarely required treatment discontinuation and usually subside spontaneously during the first week of treatment as reported by Li et al.[19].

Figure 4: Risk of bias graph

	D1: Randomization Process	D2: Deviations from Interventions	D3: Missing Outcome Data	D4: Measurement of Outcome	D5: Selection of Reported Result	Overall Risk of Bias
Ahuja et al., 2011	?	-	+	-	+	-
Arko-Boham et al., 2024	?	-	+	?	+	-
Fayyaz & Fayyaz, 2025	?	?	?	?	+	?
Li et al., 2015	+	+	+	+	+	+

4. Discussion

A systematic review and meta-analysis of four randomized controlled trials with 287 patients showed gabapentin to consistently outperform cetirizine for the treatment of postburn pruritus. Gabapentin was significantly more likely to achieve itch remission by day 28 (RR 0.46; 95% CI 0.28–0.78), and had lower residual post-treatment VAS scores (MD 1.56; 95% CI 0.32–2.79) than cetirizine. These results support the pathophysiological explanation: postburn itch is a condition caused to a large extent by a neuropathic mechanism and thus not well controlled by H1-antihistamines, but is reduced by calcium-channel modulators like gabapentin [4,23]. Results of this study are generally similar to previous narrative and systematic reviews on the treatment of postburn pruritus. Nearly everyone who used gabapentin in the trials pooled here reported feeling relief from itchiness, particularly because it was used in combination with antihistamines, as did Zachariah et al. [20] in their study, which noted that gabapentin showed particular promise for itch relief in patients who did not respond to antihistamine therapy alone. Likewise, the GRADE-based review by Goutos et al. [21] was conducted before there was a lot of RCT evidence, and placed gabapentin next to cetirizine as a first-line pharmacological choice, an ordering that the present quantitative synthesis now bolstered by direct comparative effect estimates, rather than expert opinion alone, does. Larger syntheses have come up with similar results: With respect to the relief of itch associated with burns, both McGovern et al. [10] and Andrade et al. [11] reported that the neuropathic agents were more effective than antihistamines, and the 2024 Cochrane review by Sinha et al. [12] concluded that gabapentin, pregabalin, and doxepin were more effective than oral antihistamines, though the certainty of evidence remained low to moderate (with substantial heterogeneity, $I^2 = 71\text{--}92\%$, as we did). This pattern was further supported by the literature outside of burns: Xu et al. [22] found a significant decrease in pruritus with gabapentinoids over the controls for a meta-analysis of 27 trials from general pruritus literature, suggesting that the calcium channel mechanism to which gabapentin binds is also relevant to other patients who are not burns patients. However, it was not without price. Gabapentin was consistently linked with greater sedation, dizziness and drowsiness than cetirizine, similar to the safety signal suggested by Matsuda et al. [23] with gabapentinoid use in chronic pruritus in general. The framing is the efficacy/tolerability trade-off, not superiority; cetirizine is a good starting point with tolerable CNS side effects, especially in mild itch or when CNS side effects are not desired, while gabapentin is more suited to moderate-to-severe or antihistamine-refractory pruritus, with dose titration to limit CNS side effects.

Limitations

Four trials (with one of low or moderate risk of bias for randomization or blinding) were available for synthesis and one trial [8] could not be synthesized quantitatively due to incomplete reporting of outcomes. The evidence base is still not broad enough, confined to four locations, and dosing, itch-severity measurement tools, and assessment time points were different between studies, with considerable statistical heterogeneity found. Formal evaluation of publication bias was also not possible, due to the small number of studies.

5. Conclusion

Existing comparative data (in small numbers and inconsistent) show that gabapentin offers more and longer-lasting relief from postburn itching than cetirizine, but with a greater frequency of transient sedative effects. These findings are in line with previous systematic reviews and previous mechanistic studies that support a neuropathic component of postburn itch. In patients with persistent or severe symptoms, Gabapentin can be considered earlier in therapy, as a single agent or in combination with Cetirizine, in view of its greater tolerability and efficacy as an initial therapy. Further, larger, multicenter, blinded randomized trials with uniform outcome measurements and longer follow-up are required to enhance the evidence and to establish optimal dosing regimens.

References

1. World Health Organization. (2023, October). Burns [Fact sheet]. <https://www.who.int/news-room/fact-sheets/detail/burns>
2. Chung, B. Y., Kim, H. B., Jung, M. J., Kang, S. Y., Kwak, I. S., Park, C. W., & Kim, H. O. (2020). Post-burn pruritus. *International Journal of Molecular Sciences*, 21(11), 3880. <https://doi.org/10.3390/ijms21113880>
3. Carrougheer, G. J., Martinez, E. M., McMullen, K. S., Fauerbach, J. A., Holavanahalli, R. K., Herndon, D. N., Wiechman, S. A., Engrav, L. H., & Gibran, N. S. (2013). Pruritus in adult burn survivors: Postburn prevalence and risk factors associated with increased intensity. *Journal of Burn Care & Research*, 34(1), 94–101. <https://doi.org/10.1097/BCR.0b013e3182644c25>
4. Steinhoff, M., Schmelz, M., Szabó, I. L., & Oaklander, A. L. (2018). Clinical presentation, management, and pathophysiology of neuropathic itch. *The Lancet Neurology*, 17(8), 709–720.
5. Nedelec, B., & LaSalle, L. (2018). Postburn itch: A review of the literature. *Wounds*, 30(5), E118–E124.
6. Ahuja, R. B., Gupta, R., Gupta, G., & Shrivastava, P. (2011). A comparative analysis of cetirizine, gabapentin and their combination in the relief of post-burn pruritus. *Burns*, 37(2), 203–207. <https://doi.org/10.1016/j.burns.2010.06.004>
7. Kaul, I., Amin, A., Rosenberg, M., Rosenberg, L., & Meyer, W. J., III. (2018). Use of gabapentin and pregabalin for pruritus and neuropathic pain associated with major burn injury: A retrospective chart review. *Burns*, 44(2), 414–422. <https://doi.org/10.1016/j.burns.2017.08.011>
8. Arko-Boham, E., Paintsil, A. B., Arko-Boham, B., & Adjei, G. O. (2024). Effectiveness of postburn pruritus treatment and improvement of insomnia—A randomized trial. *Journal of Burn Care & Research*, 45(5), 1165–1174. <https://doi.org/10.1093/jbcr/irae083>
9. Kneib, C. J., Sibbett, S. H., Carrougheer, G. J., Muffley, L. A., Gibran, N. S., & Mandell, S. P. (2019). The effects of early neuropathic pain control with gabapentin on long-term chronic pain and itch in burn patients. *Journal of Burn Care & Research*, 40(4), 457–463. <https://doi.org/10.1093/jbcr/irz036>
10. McGovern, C., Quasim, T., Puxty, K., Shaw, M., Ng, W., Gilhooly, C., Arkoulis, N., Basler, M., Macfarlane, A., & Paton, L. (2021). Neuropathic agents in the management of pruritus in burn injuries: A systematic review and meta-analysis. *Trauma Surgery & Acute Care Open*, 6(1), Article e000810. <https://doi.org/10.1136/tsaco-2021-000810>
11. Andrade, L. F., Abdi, P., Kooner, A., Eldaboush, A. M., Dhimi, R. K., Ntarelli, N., & Yosipovitch, G. (2024). Treatment of post-burn pruritus – A systematic review and meta-analysis. *Burns*, 50(2), 293–301. <https://doi.org/10.1016/j.burns.2023.09.012>
12. Sinha, S., Gabriel, V. A., Arora, R. K., Shin, W., Scott, J., Bharadia, S. K., Verly, M., Rahmani, W. M., Nickerson, D. A., Fraulin, F. O. G., Chatterjee, P., Ahuja, R. B., & Biernaskie, J. A. (2024). Interventions for postburn pruritus. *Cochrane Database of Systematic Reviews*, 2024(6), Article CD013468. <https://doi.org/10.1002/14651858.CD013468.pub2>

13. Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., McDonald, S., ... Moher, D. (2021). The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ*, 372, Article n71. <https://doi.org/10.1136/bmj.n71>
14. Higgins, J. P. T., Thomas, J., Chandler, J., Cumpston, M., Li, T., Page, M. J., & Welch, V. A. (Eds.). (2024). *Cochrane handbook for systematic reviews of interventions* (Version 6.5). Cochrane. <https://training.cochrane.org/handbook>
15. Booth, A., Clarke, M., Dooley, G., Ghersi, D., Moher, D., Petticrew, M., & Stewart, L. (2012). The nuts and bolts of PROSPERO: An international prospective register of systematic reviews. *Systematic Reviews*, 1, Article 2. <https://doi.org/10.1186/2046-4053-1-2>
16. Sterne, J. A. C., Savović, J., Page, M. J., Elbers, R. G., Blencowe, N. S., Boutron, I., Cates, C. J., Cheng, H.-Y., Corbett, M. S., Eldridge, S. M., Emberson, J. R., Hernán, M. A., Hopewell, S., Hróbjartsson, A., Junqueira, D. R., Jüni, P., Kirkham, J. J., Lasserson, T., Li, T., ... Higgins, J. P. T. (2019). RoB 2: A revised tool for assessing risk of bias in randomised trials. *BMJ*, 366, Article l4898. <https://doi.org/10.1136/bmj.l4898>
17. Review Manager (RevMan) [Computer program]. (2020). Version 5.4. The Cochrane Collaboration.
18. Fayyaz, H., & Fayyaz, L. (2025). Comparison of efficacy of gabapentin versus cetirizine in patients with post-burn pruritus at Hayatabad Medical Complex, Peshawar. *Journal of Postgraduate Medical Institute*, 39(1), 63–69. <https://doi.org/10.54079/jpmi.39.1.3467>
19. Li, Z., Zhang, B., Li, W., & Wang, Q. (2015). Clinical effects of gabapentin on the treatment of pruritus of scar resulting from deep partial-thickness burn. *Zhonghua Shao Shang Za Zhi* [Chinese Journal of Burns], 31(3), 177–180. <https://doi.org/10.3760/cma.j.issn.1009-2587.2015.03.005>
20. Zachariah JR, Rao AL, Prabha R, Gupta AK, Paul MK, Lamba S. Post burn pruritus — a review of current treatment options. *Burns*. 2012;38(5):621-629.
21. Goutos I, Clarke M, Upson C, Richardson PM, Ghosh SJ. Review of therapeutic agents for burns pruritus and protocols for management in adult and paediatric patients using the GRADE classification. *Indian J Plast Surg*. 2010;43(Suppl):S51-S62.
22. Xu W, Dong H, Ran H, Liu H, Wang L, Li H, et al. Efficacy and safety of pregabalin and gabapentin for pruritus: a systematic review and meta-analysis. *J Pain Symptom Manage*. 2025;69(1):65-81.
23. Matsuda KM, Sharma D, Schonfeld AR, Kwatra SG. Gabapentin and pregabalin for the treatment of chronic pruritus. *J Am Acad Dermatol*. 2016;75(3):619-625.