REVIEW ARTICLE

Systematic Review of Topical Capsaicin 0.075% for the Treatment of Neuropathic Pain: Efficacy, Safety, and Tolerability

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Received: 09 February 2026; *Accepted:* 06 March 2026

Abstract

Background: Neuropathic pain, characterized by nerve damage, can significantly impact quality of life. Traditional treatments often fall short, prompting the exploration of topical therapies such as capsaicin. This systematic review aims to evaluate the efficacy, safety, and tolerability of topical capsaicin in treating neuropathic pain.

Methods: A systematic review of clinical studies assessing the topical use of capsaicin for neuropathic pain of different etiologies, including painful diabetic peripheral neuropathy (DPN) and postherpetic neuralgia (PHN), was conducted. Data were extracted regarding pain relief and adverse effects. A systematic review of literature identified through database searches, including PubMed and ScienceDirect, was conducted using the search term "topical capsaicin."

Results: A total of 22 studies were included (placebo-controlled: n = 13; active-controlled: n = 4; uncontrolled: n = 4; comparison of two capsaicin formulations: n = 1). Topical capsaicin demonstrated significant efficacy in reducing pain intensity and improving quality of life across various neuropathic pain conditions. Localized adverse effects were reported but were generally tolerable and occurred more often in the first week of treatment. Comparisons between 0.025% and 0.075% formulations indicated that the higher concentration is generally more effective. The development of a new roll-on formulation of capsaicin retains efficacy while reducing adverse effects.

Conclusion: Topical capsaicin 0.075% is a promising and effective option for neuropathic pain management, providing meaningful pain relief and improved quality of life with a manageable and favorable safety profile. Further research is needed to evaluate long-term efficacy and explore combination treatment approaches.

Journal of The Association of Physicians of India (2026): 10.59556/japi.74.1470

Introduction

Pain that arises as a result of a disease or a lesion of the somatosensory system has been defined as "neuropathic pain." The typical characteristics include allodynia and dysesthesia in the affected area, pain evoked by abnormal stimulus, or spontaneous pain. Specific symptoms reported by patients include electrical sensation, tingling, tightness, burning pain, shooting pain, and loss of thermal perception.[1] Neuropathic pain arises from lesions of the nervous system at the peripheral nerve, spinal cord, brain, or at the receptor, and affects up to 8% of the population globally.[2,3] India today has 101 million people with diabetes.[4] Diabetes in India affects people at a younger age.[5] The incidence of new-onset diabetes is also high,[6] and an unhealthy diet,[7] along with physical inactivity,[8] contribute to the diabetes epidemic. It has been established that uncontrolled diabetes can lead to complications.[9–11] Neuropathy is seen in 26.1% of patients with diabetes in India.[10] Studies from India have revealed a prevalence of painful neuropathy up to 2,400 per 10,000 population. Furthermore, 10–32% of diabetic patients develop peripheral neuropathy.[12–14] In fact, painful diabetic neuropathy (DPN) accounts for 72% of the cases of neuropathy.[15]

The broad classification of neuropathic pain is central neuropathic pain and peripheral neuropathic pain. Central neuropathic pain is a result of lesions in the central somatosensory nervous system, often due to spinal cord injury, stroke, and multiple sclerosis, with immediate or delayed onset. Peripheral neuropathic pain has a significant disease burden with several treatment challenges. Pathologies of peripheral neuropathic pain include postherpetic neuralgia (PHN), diabetic polyneuropathy, and peripheral nerve injury.[2,16] Neuropathic pain is localized in 60% of cases, and affects only a specific area of the body.[1] Individuals with neuropathic pain report impaired emotional functioning, decreased quality of life, and a higher risk of anxiety and depression.[17,18]

The management of neuropathic pain primarily involves symptomatic management, while the etiological causes may be addressed in case of pathological conditions. Pharmacotherapeutic options for neuropathic pain include first-line agents such as serotonin–norepinephrine reuptake inhibitors, gabapentinoids, and tricyclic antidepressants. Opioids are reserved as second-line options, while topical treatments are prescribed for patients who do not tolerate oral medication or patients with localized neuropathic pain. Current treatments, including systemic medications such as anticonvulsants and antidepressants, often provide insufficient relief or intolerable side effects. Therefore, there has been an interest in topical therapeutic agents for pain relief.[1,19,20]

The analgesic effect of capsaicin has been applied in therapeutics despite the known potent algogenic effects (inducing burning pain on topical application). It blocks mechanotransduction, nerve firing, and conduction by activating the transient receptor potential vanilloid 1 (TRPV1). High-dose capsaicin or repeated use of low-dose concentration leads to ablation of axonal terminals and long-lasting analgesia. Low-dose capsaicin application leads to

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How to cite this article: Mohan V, Tiwaskar M, Jayapaul M, *et al.* Systematic Review of Topical Capsaicin 0.075% for the Treatment of Neuropathic Pain: Efficacy, Safety, and Tolerability. J Assoc Physicians India 2026;74(4):e6–e12.

simultaneous defunctionalization and desensitization, which is reversible. On repeated application, capsaicin accumulates due to its slow metabolism, resulting in short- and long-term defunctionalization mediated by the ablation of afferent terminals. Topical formulations of capsaicin include gels, sprays, creams, and patches and have relatively few side effects, which are transient and occur only at the site of application. Additionally, there is a lack of drug interaction.[21,22]

The aim of this systematic review was to summarize the literature on the application of topical capsaicin for the management of neuropathic pain arising due to postherpetic neuralgia and diabetic peripheral neuropathy.

Methods

Search Strategy

This systematic review adhered to PRISMA guidelines.[23] An electronic search of published literature was conducted on PubMed and ScienceDirect. A search was conducted covering articles published until October 2025. Search terms included "topical capsaicin," "capsaicin cream," "capsaicin lotion," and "neuropathy." Duplicate references were excluded; the title and abstract were screened to assess eligibility for inclusion in this analysis. Inclusion criteria for full-text articles were: randomized controlled trials assessing the efficacy of topical capsaicin for neuropathic pain, studies involving adults (≥18 years) with diagnosed neuropathic pain, and trials comparing capsaicin to placebo or active comparators. Exclusion criteria were articles written in any language other than English, incomplete articles, and conference papers (Fig. 1).

Data Extraction

Data were extracted for efficacy measures [e.g., Visual Analog Scale (VAS) for pain intensity], safety outcomes, and study demographics.

Results

Study Characteristics and Summary of Key Findings

A total of 22 studies were included, comprising over 1,800 participants with various neuropathic pain conditions, primarily painful DPN and PHN. The studies varied in design, with many multicenter and double-blind. Table 1 describes the key findings of the efficacy of topical capsaicin. Table 2 summarizes the safety findings of the included studies.

Efficacy of Topical Capsaicin

Painful Diabetic Peripheral Neuropathy

A total of 12 studies reported the efficacy findings of topical capsaicin for patients with DPN, of which seven were placebo-controlled, four were comparisons with active molecules (amitriptyline, clonidine, turpentine oil), and one was a comparison of capsaicin cream and roll-on formulations. One study reported the efficacy findings in patients with PHN or DPN. All studies on DPN included in this systematic review reported the efficacy of topical capsaicin at a concentration of 0.075%. Seven studies were placebo-controlled, two compared capsaicin with amitriptyline, one compared capsaicin with clonidine, one compared capsaicin with turpentine oil, and one compared two formulations of capsaicin (cream and roll-on). One placebo-controlled study evaluated sensory function.

Placebo-controlled trials of capsaicin 0.075% in patients with DPN demonstrated its efficacy in three trials, with VAS pain intensity improvements ranging from 38.1% to 65% [one study reported a 16% improvement in VAS pain intensity (NS)]. A statistically significant difference compared with placebo was reported in three out of four trials. Three studies reported significant improvement in physicians' global evaluation (PGE) scores (60–71.3% of patients had improved PGE scores after capsaicin treatment). One study reported that 59% of patients had improved PGE scores, though this was not statistically significant compared with the placebo group (66.7%). The proportion of patients with significant VAS pain relief was significant in one 8-week study (58.4% vs 45.3%, p = 0.004). Two studies reported no significant difference compared with placebo for all outcomes evaluated.[24,26,27,31,34] An evaluation of the sensory effects of capsaicin cream by Tandan et al. reported that topical capsaicin significantly reduced the cold threshold compared with placebo. Additionally, the warm threshold and vibration threshold were not altered by topical capsaicin.[32]

Acknowledging the challenges of handling capsaicin creams, such as inadvertent contact with mucous membranes, a roll-on formulation has been developed. A comparison of the efficacy of capsaicin 0.075% roll-on and cream formulations among patients with DPN confirms the noninferiority of the new roll-on formulation, as evidenced by similar pain reduction, responder rates, and improvements in quality of life compared with the cream formulation. A trend toward fewer adverse effects was noted for the roll-on formulation, though this did not reach statistical significance.[33]

In studies comparing capsaicin 0.075% with oral amitriptyline, both groups effectively reduced neuropathic pain, as evaluated by VAS pain intensity, pain relief, and PGE scores, with no significant differences between groups. Quality of life, as assessed through activities of daily living, also improved significantly after 8 weeks of treatment in both groups. The advantage of capsaicin over oral amitriptyline is evidenced by the absence of systemic side effects. Local adverse effects such as burning did not persist

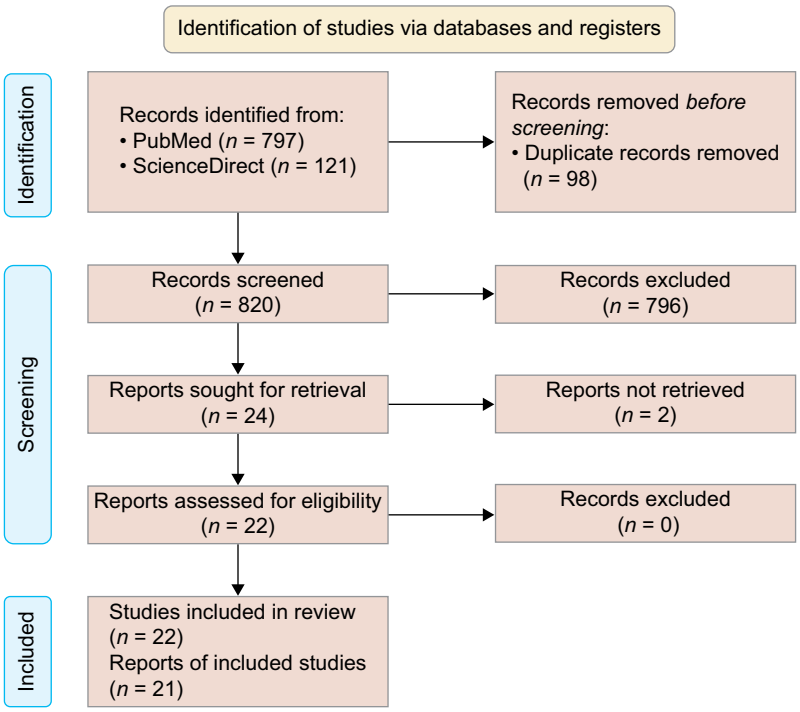

Fig. 1: PRISMA flow diagram

Table 1: Summary of clinical study characteristics and key findings for efficacy of topical capsaicin 0.075%

Study/reference	*Study design*	*Population*	*Sample size (N)*	*Baseline characteristic*	*Pain improvement measurement*	*Duration and frequency*	*Key findings*
Capsaicin Study Group (1991)[24]	Multi-center, double-blind, placebo-controlled, parallel-group	Painful DPN	277 (efficacy group: *n* = 252)	Pain severity: Moderate 10.8%, severe 58.1%, very severe 31%	VAS pain intensity (VAS-I), VAS pain relief (VAS-R), physician's global evaluation scale	8 weeks	Efficacy of capsaicin 0.075% vs placebo: VAS-R: 58.4% vs 45.3% ($p = 0.004$) Reduction in VAS-I: 38.1% vs 27.4% ($p = 0.037$) Patients with improved PGE: 69.5% vs 53.4% ($p = 0.012$)
Biesbroeck et al. (1995)[25]	Multi-center, parallel-group trial	Painful DPN	235	Mean duration of neuropathy: 3.76–5.02 years	VAS pain intensity (VAS-P), VAS pain relief (VAS-R), physician's global evaluation (PGE) scale	8 weeks	Efficacy of capsaicin 0.075% vs oral amitriptyline: At least a better PGE score: 73% in both groups Reduction in VAS-P: 42% vs. 43.8% (p = NS)
Capsaicin study group (1992)[26]	Double-blind vehicle-controlled, parallel-group, randomized trial	Painful DPN and/or radiculopathy	277	Pain severity: Moderate 7.9%, severe 41.8%, very severe 22.3%	Physicians' global evaluation of change in pain status, VAS-I, and functional capacity scales to rate the interference of pain with daily activities	8 weeks	Efficacy of capsaicin 0.075% vs placebo: Patients with improved PGE: 71.3% vs 51.3% ($p = 0.007$) Reduction of VAS-I: 40.1% vs 27.8% ($p = 0.014$)
Low et al. (1995)[27]	Double-blind, placebo-controlled randomized study	Bilateral symmetric chronic painful peripheral neuropathy	39	Duration of pain: Median 56 months (6–180 months)	Investigator global, patient global, VAS pain severity, VAS pain relief, activities of daily living, allodynia	12 weeks	Efficacy of capsaicin 0.075% vs placebo: Investigator global: 59% vs 66.7% VAS pain severity: 65 vs 68.9 VAS pain relief:37 vs 35 ADL: 67 vs. 67 Allodynia: 0 vs 0
Kiani et al. (2015a)[28]	Randomized, double-blind and parallel-group trial	Painful DPN	139	Pain duration: 18–21 months	VAS pain score (VAS-P)	12 weeks	Efficacy for capsaicin 0.075% vs topical clonidine: Responders with ≥50% reduction of VAS-P score: 40.6% vs 57.1% ($p = 0.051$)
Kiani et al. (2015b)[29]	Randomized, double-blind, parallel-group and noninferiority trial	Diabetic peripheral neuropathy	102	Pain duration: 18.9–19 months	VAS pain score	12 weeks	Efficacy for capsaicin 0.075% vs amitriptyline cream: ≥50% reduction of VAS from baseline 37.3% vs. 43.1% ($p = 0.545$)
Musharraf et al. (2017)[30]	Randomized controlled trial	Painful DPN	300	Pain duration: 6.99–7.21 months	VAS pain score	3 months	Efficacy of capsaicin 0.075% vs. turpentine oil: Change in VAS score: 2.81 ± 1.021 vs 0.496 ± 0.190 Efficacy (>3-point reduction in pain): 53% vs 47% ($p = 0.399$)
Tandan et al. (1992a)[31]	Randomized, placebo-controlled study	Chronic severe painful diabetic neuropathy	22	Pain duration: 4.2–5.7 months	Physician's global evaluation, VAS pain intensity, categorical pain severity	8 weeks	Efficacy of capsaicin 0.075% vs. placebo: Improvement in PGE: 60% vs 20% ($p = 0.038$) Reduction in pain severity (categorical): 70% vs 20% ($p = 0.057$) Reduction in VAS pain intensity 16% vs 4.1% ($p = 0.11$) VAS pain relief: 44.6% vs 23.2% ($p = 0.09$)
Tandan et al. (1992b)[32]	Double-blind, randomized, vehicle-controlled study	Painful diabetic neuropathy	22	Pain duration: 4.2–5.7 months	Quantitative sensory testing for determination of cold, warm, and vibration thresholds	8 weeks	No significant change in warm and vibration thresholds Both capsaicin 0.075% and placebo significantly reduced the cold threshold to an equal degree
Araya, et al. (2025)[33]	Randomized, open-label, multicenter, crossover, noninferiority clinical trial	Painful diabetic neuropathy	160	Pain severity: Moderate or severe	Numerical rating scale (NRS) for pain intensity	8 weeks	Efficacy of capsaicin roll-on 0.075% vs. cream 0.075%: Both groups showed significant reductions in pain, with no significant differences in absolute ($p = 0.115$) or relative ($p = 0.157$) pain reduction; noninferiority of roll-on formulation was confirmed

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Study/reference	*Study design*	*Population*	*Sample size (N)*	*Baseline characteristic*	*Pain improvement measurement*	*Duration and frequency*	*Key findings*
Agoons, et al. (2020)[34]	Prospective double-blind placebo-controlled randomized clinical trial	Painful diabetic neuropathy	22	Pain intensity: Median 5.8–6.8 units	VAS, physician's global evaluation	8 weeks	Efficacy of capsaicin 0.075% vs placebo: Median pain intensity 3.3 vs 4.8 at week 6, 6.6 vs 5.2 at week 8
Kulkantrakorn, et al. (2015)[35]	Randomized, double-blinded, crossover, placebo-controlled trial	Painful diabetic neuropathy	42	Pain duration: Mean 3.20 ± 2.66 years	VAS, short form McGill Pain Questionnaire (SF-MPQ), Neuropathic Pain Scale (NPS).	8 weeks of each treatment with 4-week washout period between treatment	No significant improvement in pain control with capsaicin lotion 0.075% compared with placebo for all pain measures and proportion of patients who had 30% or 50% pain relief, respectively
Moon et al. (2017)[36]	Early phase II, multi-center, randomized, semi-double-blind, and placebo-controlled clinical trial	Chronic PNP due to diabetic polyneuropathy and postherpetic neuralgia	60	Duration of pain: 33.5 ± 31.2 months	Numerical rating scale (NRS) pain score, Daily Sleep Interference Scale, Global Impression Change (GIC)	6 weeks	Capsaicin cream led to significantly improved pain, sleep disorder scores; capsaicin patch 0.625% led to significantly improved pain; GIC scores improved in capsaicin cream, capsaicin patch and placebo groups
Peikert et al. (1991)[37]	Uncontrolled study	Postherpetic neuralgia	21	Pain duration: Median 24 months	VAS and verbal outcome scale	8 weeks	Substantial improvement: 48.7%, no benefit: 38.5%, discontinued treatment: 12.8%
Teixeira et al. (2015)[38]	Double-blind, crossover randomized trial	Postherpetic neuralgia	13	Pain duration: mean 33.4 ± 21.0 months	VAS pain intensity, categorical verbal scale, intensity of evoked pain, allodynia, pain relief scale after treatment	6 weeks	Efficacy of capsaicin vs. placebo: Moderate-to-severe allodynia: 38.46% vs 61.54% of patients ($p = 0.434$) Symptom improvement: 55.63% vs. 48.85% of patients ($p = 0.260$) Significant change in VAS after treatment: −24% vs −6% ($p = 0.008$)
Watson et al. (1988)[39]	Open-label study	Postherpetic neuralgia	33	Pain duration: Median 2 years (3 months–14 years)	VAS pain intensity, verbal intensity scale (VIS)	4 weeks	Pain improved or better: 55% Good result: 39% Good or excellent pain relief: 56% At least some improvement in pain: 78%
Bernstein, et al. (1989)[40]	Double-blind, vehicle-controlled clinical trial	Severe intractable postherpetic neuralgia	32	Pain duration: 30–41.8 months	VAS, physician's global evaluation, categorical scale	6 weeks	Efficacy of capsaicin vs placebo: Physician's global rating: 77% vs 31% ($p < 0.05$) Change in VAS pain: −30% vs. +1% ($p < 0.05$) Patients with pain relief: 54% vs 6% ($p <0.02$) Response rate on categorical scale: 46% vs 6% ($p < 0.01$)
Paice et al. (2000)[41]	Multicenter, controlled, randomized, double-masked study	HIV-associated DSPN	26	Current pain: 4.7 ± 6 2 Worst pain: 6.6 ± 1.9	Brief pain inventory (BPI), Sickness impact profile (SIP)	4 weeks	No significant differences between the capsaicin and vehicle groups for current pain, worst pain, pain relief, sensory perception
Watson et al. (1989)[42]	Uncontrolled study	Postmastectomy pain syndrome	14	Pain duration: Median 4 years (7 months–20 years)	VAS pain intensity, verbal intensity scale	4 weeks	Improvement in pain: 85.7% Good or excellent response: 57% Good pain relief at 6 months after trial completion: 50%
Watson et al. (1992)[43]	Randomized, double-blind, placebo-controlled, parallel-group study	Postmastectomy pain syndrome	25	Pain severity: Moderate: 60% Severe: 40% Pain duration: Median 4 years (5 months–16 years)	VAS pain intensity, verbal intensity scale, pain relief, disability, degree of satisfaction with pain relief, percentage improvement	6 weeks	Efficacy of capsaicin: Significant change in VAS from baseline but no significant difference vs. placebo Good-to-excellence response to capsaicin: 62% Good response (placebo): 10%

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Study/reference	*Study design*	*Population*	*Sample size (N)*	*Baseline characteristic*	*Pain improvement measurement*	*Duration and frequency*	*Key findings*
Dini et al. (1993)[44]	Open-label trial	Postmastectomy pain syndrome	21	Pain duration: Median 17 months (3 months–12 years) Pain severity: Moderate to severe	VAS and verbal intensity scale (VIS)	8 weeks	Efficacy of capsaicin: Excellent result (complete disappearance of pain) 10.5%, good result (pain that was never worse than mild) 57.9%. Overall response rate 68.4%; at 3 months after the end of the trial, pain relief persisted unmodified in 84.6% of responding patients
Ellison et al. (1997)[45]	Randomized, placebo-controlled, double-blind study	Postsurgical neuropathic pain in cancer patients	99	Pain severity in the previous week: Mild 4%, moderate 63.5%, severe 27.5%, very severe 7%	VAS and verbal intensity scales	8 weeks of capsaicin followed by 8 weeks of placebo	Efficacy of capsaicin vs placebo: Reduction in pain: 53% vs 17% ($p = 0.001$)

Table 2: Key findings of the safety of topical capsaicin

Study/Reference	*Capsaicin concentration (%)*	*Local adverse reactions (capsaicin vs placebo/active control)*	*Discontinuation of treatment (capsaicin vs placebo/active control)*
Capsaicin Study Group (1991)[24]	0.075	78.3% vs 29.5%	10.14% vs 2.9%
Biesbroeck et al. (1995)[25]	0.075	44% vs 1.7% (amitriptyline)	NR
Capsaicin Study Group (1992)[26]	0.075	63% vs. 17%	10.1% vs NR
Low et al. (1995)[27]	0.075	86% vs 45%	NR
Kiani et al. (2015a)[28]	0.075	58% vs. 5.7% (clonidine group)	42.85% vs. 23.1% (clonidine group)
Kiani et al. (2015b)[29]	0.075	56.9% vs 25.5% (amitriptyline group)	43.1% vs 31.3% (amitriptyline group)
Musharraf et al. (2017)[30]	0.075	NR	NR
Tandan et al. (1992a)[31]	0.075	54.5% vs 18.1%	18.1% vs 0%
Tandan et al. (1992b)[32]	0.075	NR*	NR*
Araya et al. (2025)[33]	0.075	14.4% vs 17.5%	1.3% vs 1.9%
Agoons et al. (2020)[34]	0.075	72.7% vs 0%	None
Kulkantrakorn et al. (2015)[35]	0.075	50% vs 11.1%	11.1% in each group
Moon et al. (2017)[36]	0.075	15.4% vs 46.67% (capsaicin patch)	7.7% vs 0%
Peikert et al. (1991)[37]	0.025	66.7%	12.8%
Teixeira et al. (2015)[38]	0.025	87.5% vs 60%	None
Watson et al. (1988a)[39]	0.025	27.3%	27.3%
Bernstein et al. (1989)[40]	0.075	31.2% vs 12.5%	–
Paice JA et al. (2000)[41]	0.075	NR	67% vs 18%
Watson et al. (1989)[42]	0.025	7.14%	7.14%
Watson et al. (1992)[43]	0.075	92.3%	7.7%
Dini et al. (1993)[44]	0.025	28.6%	None
Ellison N et al. (1997)[45]	0.075	8% vs 8%	30% vs 33%

NR, not reported; *Tandan et al. (1992b) is a companion article to Tandan et al. (1992a) reporting on different outcomes of the same study

beyond the first week in most patients in the capsaicin group. Kiani et al. compared topical capsaicin with topical amitriptyline, reporting no significant difference in the proportion of treatment responders (37.3% vs 43.1%), with significantly fewer adverse effects for the amitriptyline group (56.9% vs 25.5%, $p = 0.001$).[28,29]

Comparison of 12 weeks of treatment with capsaicin cream or clonidine gel revealed that the capsaicin group had numerically fewer responders than the clonidine group (40.6% vs 57.1%, $p = 0.051$), and no significant difference for change in VAS score. However, local adverse effects and treatment discontinuations were more common in the capsaicin group.[28]

Postherpetic Neuralgia

Two placebo-controlled trials and two open-label uncontrolled studies reported the efficacy of topical capsaicin for the management of PHN, and one study included patients with PHN and DPN. Uncontrolled, open-label studies report improvement in pain of 48.7–56%,[37,39] and placebo-controlled studies report significant improvements in various outcome measures, including moderate-to-severe allodynia, VAS pain score, physician's global rating, and symptom improvement.[38,40] Notably, significant pain relief has been reported within the first 2 weeks of treatment.[37,39] Data on long-term follow-up indicate that 72.2% of patients continue to have moderate-to-excellent pain relief at 10–12 months poststudy completion.[39]

A comparison of 0.025% and 0.075% capsaicin shows that 0.075% capsaicin leads to 30% reduction in VAS pain, while 0.025% capsaicin leads to 24% reduction in VAS pain after 6 weeks of treatment. Pain relief or improvement of symptoms was reported in 55.63% of patients in the study evaluating 0.025% capsaicin. The study evaluating 0.075% capsaicin reported that 54% of patients had symptom improvement and 77% of patients had a reduction in pain based on the physician's global rating.[38,40]

Postmastectomy Pain Syndrome

Three studies evaluated the efficacy of capsaicin in patients with PMPS, including one placebo-controlled study and two uncontrolled studies. Good-to-excellent response to capsaicin was reported in 57%, 62%, and 68.4% of patients in these studies.[42–44] It is notable that pain relief persisted in 69–85% of patients at 3 months after trial completion and 50% of patients at 6 months after trial completion, indicating the long-lasting effect of topical capsaicin.[42,44]

Evaluation of the efficacy of capsaicin by concentration indicates efficacy of both formulations; however, it has been suggested that the occurrence of capsaicin-induced burning sensation may compromise the double-blind study design. Nonetheless, the use of 0.075% capsaicin cream reduced VAS scores for jabbing pain and produced significant pain relief compared with placebo, with only 1 patient (out of 13) discontinuing due to local adverse effects. Additionally, ~75% of patients of patients continuing capsaicin after trial completion reported good-to-excellent pain reduction. When accounting for efficacy, safety, and satisfaction, the global ratings revealed that 62% of patients achieved a response of ≥50%, indicating that 0.075% capsaicin provides satisfactory pain relief that persists for a prolonged period of time.[43]

Other Indications

Postsurgical neuropathic pain in cancer patients is effectively managed using capsaicin 0.075% cream, with 53% reduction in pain, and more patients preferring capsaicin over placebo or neither (60% vs 18% vs 22%, $p = 0.001$).[45] However, capsaicin cream was not beneficial in patients with HIV-associated DSPN.[41]

Safety and Tolerability

Local side effects were the most common, reported by 30–60% of patients, including sensation of stinging or burning at the application site, as well as erythema. However, these effects were generally mild and temporary. Most studies indicated that patients tolerated capsaicin well compared to systemic treatments. In patients with postsurgical neuropathic pain, capsaicin cream was preferred over placebo (60% vs 18%) despite the significantly higher incidence of adverse effects, including burning, redness, and coughing. It is notable that these adverse effects did not lead to a higher discontinuation rate compared with placebo (30% for capsaicin vs 33% for placebo, for a toxicity rate of 8% in each group).[45]

Discussion

The findings of this systematic review justify the utility of topical capsaicin as an effective treatment for neuropathic pain of diverse origin. Its efficacy is particularly pronounced in patients with DPN and PHN, where it outperforms placebo and is comparable to established systemic therapies like amitriptyline. The side effects, while common, are generally manageable, making capsaicin a viable option for patients who are intolerant of or unresponsive to oral medications.

Capsaicin, derived from plants of the capsicum family, has been used as a therapeutic for challenging pain control, such as that associated with nerve injury. The pain-relieving action of capsaicin has been attributed to desensitization, nociceptive dysfunction, and terminal destruction, as well as depletion of neuropeptides. Capsaicin application, though initially painful, leads to analgesia on repeated application.[46] This paradox is important in the early stages of treatment when patients are more likely to experience local adverse effects, as has been reported in clinical trials. It is reported that capsaicin reduces sensitivity to heat and mechanical stimulus, and a 74% reduction in nerve fibers in blister specimens has been reported at 3 days after capsaicin application.[47] Prolonged application of low-dose topical capsaicin leads to desensitization of heat-sensitive nociceptors, which diminishes heat pain sensation (heat threshold increases by 3.5°C after 6 weeks) and neurogenic vasodilatation.[48] Patient education regarding the nature of efficacy of capsaicin and the importance of repeated application to overcome the initial adverse effects could help reduce treatment discontinuation rates and improve treatment outcomes.

Topical capsaicin is the guideline-recommended option for neuropathic pain. The European Federation of the Neurological Sciences (EFNS) recommends topical capsaicin as second-line treatment for PHN, and National Institute for Health and Care Excellence (NICE) recommends capsaicin cream as first-line treatment for localized neuropathic pain where oral therapy is avoided or when oral medications are not tolerated.[49,50] American Academy of Neurology (AAN) guidelines for painful diabetic polyneuropathy recommend topical capsaicin 0.05% four times a day in patients who prefer topical treatment.[51]

Patients with DPN and PHN do experience improvement in VAS and PGE scores. Patients with PHN report improvement in VAS of 48.7–56%, and pain relief has been noted within the first 2 weeks.[37,39] Higher rates of symptom improvement have been reported for patients with DPN using capsaicin 0.075% vs capsaicin 0.025%.[24,26,28,37] The findings indicate that capsaicin 0.075% does provide treatment benefit in these patient groups. It may be particularly useful in patients who do not tolerate oral medication or those who prefer topical treatment or have localized neuropathic pain.

Although the occurrence of burning sensation compromises the double-blind nature of clinical trials, it has been debated that since burning sensation is reported even among patients receiving a placebo, the integrity of the study design is intact. Furthermore, the burning sensation is noted to diminish with repeated applications of capsaicin and is often absent after 3 days of regular application of capsaicin.[40] Discontinuation of treatment due to this adverse effect is also more common during the initial days of treatment.[26] Since the reactions reduce with repeated application, it is necessary to encourage patients to continue with treatment despite the occurrence of adverse local reactions. Healthcare practitioners must therefore prioritize patient education in the management of neuropathic pain.

Certain practices can increase the efficacy of topical capsaicin, such as frequent application (up to four times a day) and persistent use (for 4–6 weeks). Patients should be educated regarding safe handling of capsaicin preparations, including thorough handwashing after application and avoidance of contact of the medication with the eyes. Application of topical capsaicin on broken or irritated skin should be avoided. Patients with lesions of herpes zoster should be advised that topical capsaicin should be applied only after lesions heal completely, so as to reduce adverse effects. Postcapsaicin burning in the early period of treatment can be managed using pretreatment with topical lidocaine. Alternatively, it has been suggested that oral analgesia can be prescribed for a few days.[43,52] A roll-on formulation of capsaicin has been developed to avoid inadvertent contact with mucous membranes, and it has been demonstrated to have numerically fewer adverse effects than the cream formulation. The formulation has the potential to increase ease of application and patient satisfaction through a reduction in adverse effects that are common with the cream formulation.[33]

Conclusion

Topical capsaicin 0.075% represents a promising treatment for neuropathic pain, as it produces significant pain relief with acceptable tolerability and improved quality of life. The risk-benefit profile of capsaicin 0.075% indicates that it is an effective treatment option with a manageable safety profile. Patient understanding of the temporal effects of repeated topical capsaicin application could increase treatment continuation rates and lead to subsequent improvement in outcomes. Clinicians should consider therapy with topical capsaicin 0.075% for patients with neuropathic pain experiencing inadequate pain relief from conventional treatments. Future studies could be designed to assess the long-term efficacy of topical capsaicin, and its use along with oral/topical therapies would provide valuable evidence for neuropathic pain management.

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