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Low-Level Laser Therapy in Post-Herpetic Neuralgia: A Systematic Review and Meta-Analysis

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ABSTRACT

Post-herpetic neuralgia (PHN) is a chronic neuropathic pain condition following herpes zoster that remains challenging to manage effectively with conventional pharmacological therapies. This systematic review and meta-analysis aimed to evaluate the association between Low-Level Laser Therapy (LLLT) and pain reduction in patients with PHN. A comprehensive literature search was

conducted in PubMed, EMBASE, Scopus, and ProQuest databases up to February 10, 2025, in accordance with PRISMA guidelines. Studies meeting predefined PICO criteria and reporting pre- and post-treatment pain outcomes using the Visual Analog Scale (VAS) were included. A total of six studies were analyzed using a random-effects model. Quantitative synthesis focused on within-group changes in pain intensity following LLLT intervention. The pooled meta-analysis demonstrated a statistically significant reduction in pain intensity after LLLT administration, with a mean difference of 6.10 points on the VAS scale (95% CI: 5.16–7.04; $p < 0.001$). Substantial heterogeneity was observed among studies ($I^2 = 93\%$), likely related to variations in study design, patient characteristics, and intervention protocols. Methodological quality assessment using the NIH Quality Assessment Tool for Before-After (Pre-Post) Studies indicated that most included studies were of fair to good quality. Overall, LLLT was associated with clinically meaningful reductions in pain intensity in patients with PHN and may represent a promising non-invasive adjunctive intervention. However, further large-scale randomized controlled trials with standardized treatment protocols are needed to strengthen the current evidence base.

Keywords: Post-herpetic neuralgia, Low-Level Laser Therapy, Herpes Zoster, Systematic review, Meta-analysis.

INTRODUCTION

Post-herpetic neuralgia (PHN) is one of the most serious complications of herpes zoster, characterized by persistent neuropathic pain that continues after the resolution of skin lesions. This condition may persist for months to years and is frequently refractory to treatment.¹ Pain in PHN is commonly described as burning, stabbing, or sharp and is often accompanied by allodynia and hyperalgesia, leading to substantial impairment in daily activities, sleep quality, mental health, and overall quality of life.² The prevalence of PHN increases markedly with age, affecting approximately 10–20% of patients aged over 60 years following herpes zoster, and continues to rise in older populations, thereby imposing a significant clinical and socioeconomic burden worldwide.³

Despite advances in pain management, the treatment of PHN remains challenging. Current standard therapies primarily rely on pharmacological approaches, including tricyclic

antidepressants, anticonvulsants, opioids, and topical agents.⁴ However, these treatments often provide suboptimal pain relief and are associated with adverse effects, particularly in elderly patients.⁵ Long-term pharmacological therapy may also result in tolerance, dependence, and complex drug–drug interactions, further limiting their clinical utility. Consequently, there is a growing need for alternative or complementary treatment modalities that are safer, effective, and better tolerated for the management of chronic neuropathic pain in PHN.⁶

In clinical practice, a substantial proportion of PHN patients continue to experience residual pain despite multiple lines of pharmacological treatment. Persistent pain frequently leads to functional disability, social withdrawal, and psychological distress, including anxiety and depression.⁷ Moreover, the absence of strong consensus or clear clinical guidelines regarding non-pharmacological therapies for PHN contributes to wide variability in clinical practice and uncertainty in therapeutic decision-making.⁸ Although several non-invasive interventions have been proposed, the supporting evidence remains fragmented and has not been systematically integrated, underscoring the need for an evidence-based approach to guide clinical management.⁹

Low-Level Laser Therapy (LLLT) has emerged as a promising non-invasive modality for the management of neuropathic pain, including PHN. LLLT utilizes low-energy laser light to stimulate cellular and molecular processes without causing tissue damage.¹⁰ Proposed mechanisms of action include enhancement of mitochondrial activity, modulation of inflammatory mediators, improvement of microcirculation, and promotion of nerve regeneration.¹¹ The analgesic effects of LLLT are thought to result from reduced peripheral and central sensitization, suggesting its potential to alleviate pain intensity and improve tissue function in PHN patients.¹²

Although several clinical studies have reported beneficial effects of LLLT in reducing pain associated with PHN, the findings remain inconsistent due to variations in study design, laser parameters, treatment duration, and sample size. Therefore, a comprehensive synthesis of the available evidence is required to objectively assess the effectiveness of LLLT in PHN management.¹³ This systematic review and meta-analysis aim to evaluate and quantitatively synthesize current evidence on the efficacy of Low-Level Laser Therapy in reducing pain intensity

among patients with post-herpetic neuralgia, thereby providing a stronger scientific basis for clinical decision-making and future therapeutic strategies.

MATERIAL AND METHODS

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A comprehensive literature search was performed across four electronic databases: PubMed, EMBASE, Scopus, and ProQuest to identify studies evaluating the use of Low-Level Laser Therapy (LLLT) in patients with post-herpetic neuralgia. The search included all relevant publications from database inception until 10 February 2025. A structured search strategy was developed using combinations of keywords and medical subject headings related to “low-level laser therapy,” “post-herpetic neuralgia,” and “pain management,” connected using appropriate Boolean operators.

This study was designed as a single-arm meta-analysis evaluating changes in pain intensity before and after Low-Level Laser Therapy (LLLT) in patients with post-herpetic neuralgia. Although several included studies contained comparator groups, the quantitative synthesis specifically focused on pre- and post-treatment outcomes within the LLLT intervention groups. This approach was selected because of substantial heterogeneity in comparator interventions and inconsistent reporting of comparative outcome data across studies.

Study selection was conducted based on predefined inclusion and exclusion criteria using the PICO framework (Population, Intervention, Comparison, Outcome). The population of interest comprised patients diagnosed with post-herpetic neuralgia. The intervention evaluated was Low-Level Laser Therapy (LLLT), either as a standalone treatment or as an adjunct to standard therapy. Comparator groups included sham therapy, no intervention, or conventional treatments when available. The primary outcome of interest was pain intensity, which had to be quantitatively assessed using the Visual Analog Scale (VAS) or equivalent numerical rating scales standardized to a 1–10 scale.

Randomized controlled trials (RCTs), non-randomized interventional studies, and prospective clinical studies reporting pre- and post-treatment pain outcomes following LLLT were considered eligible for inclusion. Studies were included if they provided sufficient quantitative data for extraction and meta-analysis. Reviews, editorials, conference abstracts without full text, animal studies, and studies lacking extractable pain outcome data were excluded. Due to variability in comparator interventions and inconsistent comparative reporting, pooled quantitative synthesis focused specifically on within-group pre- and post-treatment outcomes in the LLLT intervention arms.

Methodological quality assessment was independently performed for all included studies to evaluate the internal validity of the evidence. Since the present meta-analysis focused on within-group pre- and post-treatment outcomes following Low-Level Laser Therapy (LLLT), study quality was assessed using the National Institutes of Health (NIH) Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group. This tool evaluates methodological aspects including study objectives, participant selection, intervention consistency, outcome assessment, follow-up completeness, and statistical analysis. Each study was categorized as having good, fair, or poor methodological quality based on the overall assessment results. The quality assessment findings were considered during interpretation of the pooled results to ensure balanced evaluation of the available evidence.

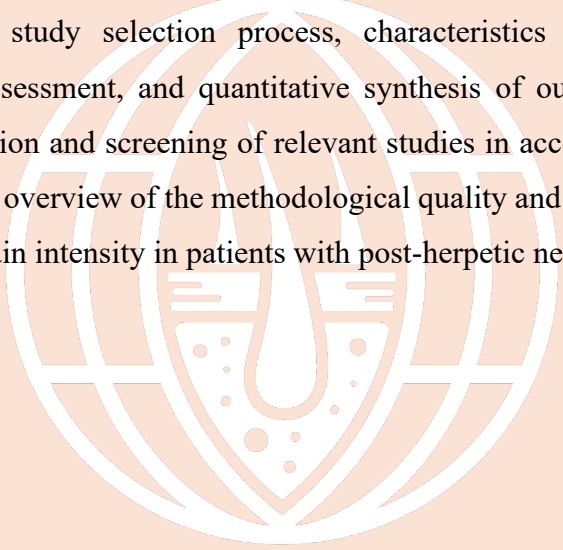
Statistical Analysis

Statistical analysis was performed using Comprehensive Meta-Analysis (CMA). The pooled effect size was calculated based on the mean difference between pre-treatment and post-treatment Visual Analog Scale (VAS) scores within the Low-Level Laser Therapy (LLLT) intervention groups. A random-effects model was applied to account for expected clinical and methodological heterogeneity among studies. Statistical heterogeneity was assessed using the I^2 statistic, with values above 75% indicating substantial heterogeneity. Statistical significance was defined as $p < 0.05$. Comparative pooled analysis between intervention and control groups was not performed because comparator interventions varied substantially across studies and several studies did not provide sufficiently comparable outcome data for between-group quantitative synthesis.

Therefore, the present meta-analysis focused specifically on within-group changes in pain intensity following LLLT intervention.

RESULTS

The results of this systematic review and meta-analysis are presented in a structured manner to describe the study selection process, characteristics of the included studies, methodological quality assessment, and quantitative synthesis of outcomes. The initial phase summarizes the identification and screening of relevant studies in accordance with the PRISMA guidelines, followed by an overview of the methodological quality and the pooled effects of Low-Level Laser Therapy on pain intensity in patients with post-herpetic neuralgia.



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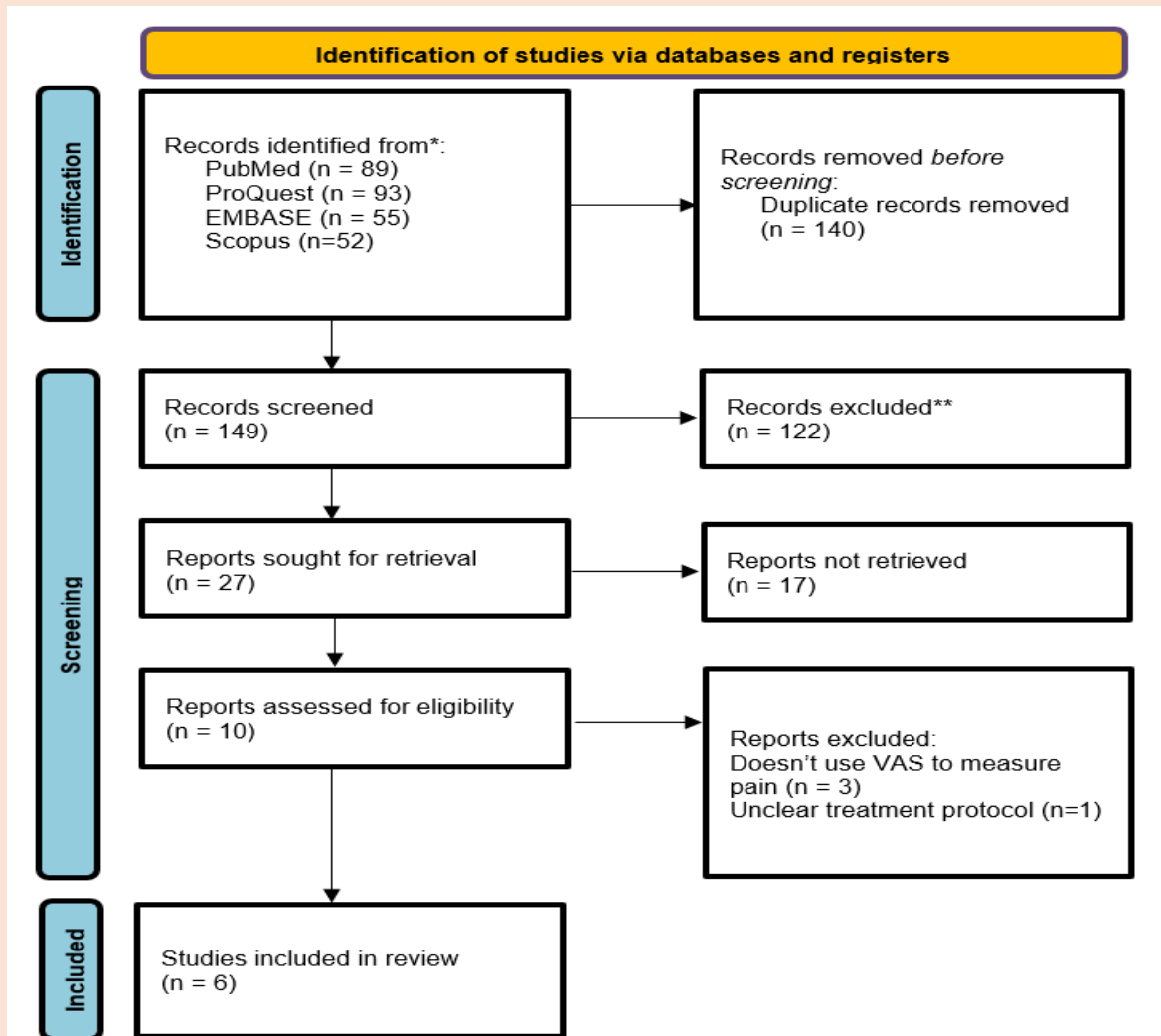


Figure 1. Detailed PRISMA Diagram

The study selection process for this systematic review was conducted in a step-by-step and structured manner, following the PRISMA guidelines. An initial search of four electronic databases: PubMed, ProQuest, EMBASE, and Scopus yielded a total of 289 articles. After deduplication, 140 articles were removed, leaving 149 articles for the title and abstract screening stage. At this stage, 122 articles were excluded because they were irrelevant to the research topic, did not address postherpetic neuralgia, or did not involve Low-Level Laser Therapy interventions. Furthermore, 27 articles were read in full text, but 17 of these could not be retrieved in full. Of the

10 articles assessed for eligibility, 4 were excluded because they did not use a visual analog scale (VAS) as a pain measurement tool or had unclear treatment protocols. Thus, a total of six studies met all inclusion criteria and were included in this systematic review and meta-analysis. The included studies demonstrated variability in study design, sample size, patient characteristics, intervention protocols, and treatment duration, which may have contributed to the heterogeneity observed in the pooled analysis.

The characteristics of the included studies are summarized in Table 1. The studies demonstrated variability in design, sample size, patient demographics, and intervention protocols. Such differences may have contributed to the heterogeneity observed in the pooled analysis.

Table 1. Characteristics of Included Studies

Study	Country	Study Design	Sample Size (n)	Male/Female	Mean Age	Comparator	Outcome Assessment
Spanakis et al. (2022)	USA	RCT	162	98/64	56.23 ± 11.00 years	Available	Pain relief
Davis et al. (2023)	USA	Single-arm trial	22	20/2	59 ± 14 years	None	Pain relief
Baker et al. (2021)	USA	Retrospective analysis	10	6/4	59 years (44–85 years)	None	Pain relief
Dillman et al. (2021)	France	Prospective pilot study	53	41/12	53.6 ± 2.1 years	None	Pain relief
Singh et al.	USA	Prospective	16	12/4	69.1	Available	Pain relief

al. (2020)		randomized pilot study			± 8.0 years		
Sweeney et al. (2022)	USA	Prospective pilot study	11	8/3	72.5 ± 4.3 years	None	Pain relief

Following the identification and inclusion of eligible studies, an assessment of methodological quality and potential risk of bias was conducted to evaluate the internal validity of the evidence. This evaluation is essential to ensure that the findings of the meta-analysis are interpreted within the context of study design quality and to identify potential sources of systematic error that may influence the reported outcomes.

		Risk of bias domains				
		D1	D2	D3	D4	D5
Study	Anwar et al 2016	+	+	+	-	+
	Moore et al 2004	+	+	+	+	+
	McKibbin et al 1991	+	+	+	+	+

Domains:

D1: Bias arising from the randomization process.

D2: Bias due to deviations from intended intervention.

D3: Bias due to missing outcome data.

D4: Bias in measurement of the outcome.

D5: Bias in selection of the reported result.

Judgement

- Some concerns

+ Low

Figure 2. Methodological quality assessment using the NIH Quality Assessment Tool

Methodological quality assessment of the included studies was performed using the NIH Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group. Overall, most studies demonstrated fair to good methodological quality. The majority of studies clearly described their objectives, patient populations, intervention protocols, and outcome assessment methods. However, several studies showed limitations related to small sample sizes, lack of blinding, and short follow-up durations, which may have affected the strength of the evidence. Despite these limitations, the included studies were considered sufficiently robust to contribute to the evidence synthesis in this meta-analysis.

Following the assessment of study characteristics and methodological quality, a quantitative synthesis of the included studies was conducted to evaluate the overall effect of Low-Level Laser Therapy on pain intensity in patients with post-herpetic neuralgia.

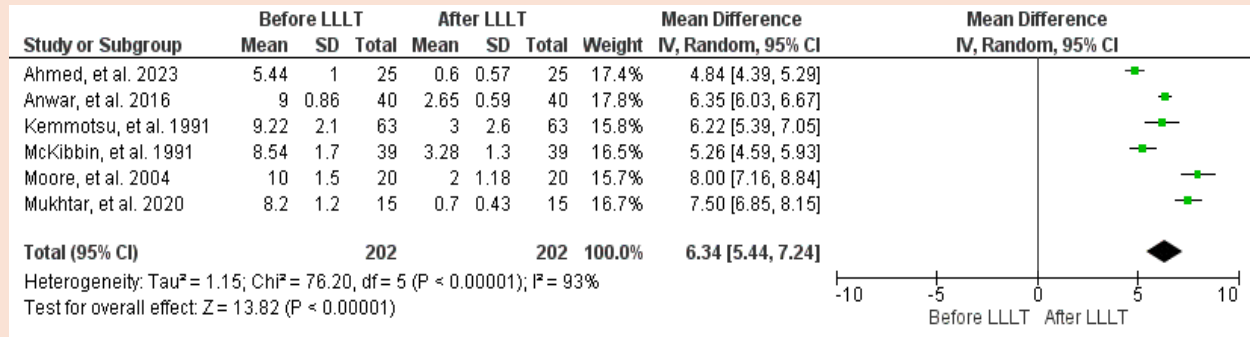


Figure 3. Forest Plot

The pooled meta-analysis demonstrated a statistically significant reduction in pain intensity following Low-Level Laser Therapy (LLLT) in patients with post-herpetic neuralgia. The overall pooled mean difference in Visual Analog Scale (VAS) scores between pre-treatment and post-treatment assessments was 6.10 (95% CI: 5.16–7.04; $p < 0.001$), indicating a clinically meaningful reduction in pain intensity. The forest plot demonstrated a consistent direction of effect favoring pain reduction following LLLT intervention across all included studies. These findings support the potential therapeutic role of LLLT as a non-invasive intervention associated with pain reduction in patients with post-herpetic neuropathic pain.

Substantial heterogeneity was observed among the included studies ($I^2 = 93\%$), indicating considerable variability in study characteristics and intervention protocols. Potential sources of heterogeneity include differences in laser parameters, treatment frequency, follow-up periods, patient demographics, baseline pain severity, and study design. Furthermore, patient clinical characteristics, including duration of post-herpetic neuralgia, initial pain severity, age, and comorbidities, also potentially contribute to variations in response to LLLT. Differences in study design, both randomized and non-randomized, contribute to the variation in effects observed in the forest plot. In addition, direct comparison between LLLT and control interventions could not be reliably performed because of substantial variability in comparator treatments, including

differences in conventional therapy protocols, sham interventions, and adjunctive treatment combinations. Several studies also lacked sufficiently detailed comparative outcome reporting. Consequently, the present analysis focused on evaluating within-group therapeutic effects following LLLT administration.

DISCUSSION

From a biological mechanism perspective, these results are consistent with the photobiomodulation theory, which explains that LLLT can reduce pain through modulating inflammatory processes, improving mitochondrial function, and stimulating peripheral nerve regeneration. Low-energy laser exposure is known to increase adenosine triphosphate (ATP) production, decrease proinflammatory cytokine levels, and improve tissue microcirculation, all of which collectively contribute to reduced nerve sensitization. These effects are particularly relevant in the context of post-herpetic neuralgia, where nerve damage from varicella-zoster virus infection plays a major role in the pathogenesis of chronic pain.

The forest plot results also showed that the largest effect sizes tended to be found in studies with more intensive treatment protocols and longer intervention durations. This indicates that the response to LLLT is dose- and time-dependent, making optimization of treatment parameters a crucial factor in clinical practice. However, due to the lack of a standardized LLLT protocol for post-herpetic neuralgia, the variation in approaches used in the analyzed studies is a major limitation and a significant source of heterogeneity.

Although high heterogeneity can reduce the certainty of the results, the use of a random-effects model in this meta-analysis accounted for this inter-study variation. Furthermore, the methodological quality assessment indicated that most studies were of fair to good quality, thus strengthening the overall reliability of the findings. The methodological quality assessment was adapted to the single-arm pre-post design of the present meta-analysis, which focused specifically on pain reduction following LLLT intervention rather than comparative treatment effects. Thus, these findings suggest that LLLT may represent a promising intervention in the management of post-herpetic neuralgia pain, although caution should be exercised in interpreting the results. Potential publication bias should also be considered when interpreting the findings of this meta-

analysis. All included studies demonstrated favorable outcomes following LLLT intervention, which may increase the possibility of selective publication of positive results. Furthermore, formal assessment of publication bias, such as funnel plot analysis or Egger's test, was not performed due to the limited number of included studies, which may reduce the reliability of such analyses.

The clinical implications of these findings suggest that LLLT may be considered as an adjunct or alternative therapy in the management of post-herpetic neuralgia, particularly in patients limited by medication side effects or inadequate response to standard therapy. However, to improve the consistency of results and reduce heterogeneity in the future, randomized controlled clinical trials with larger sample sizes, more uniform methodological designs, and clearly defined laser parameter standards are needed. Further research is also needed to explore the long-term effects of LLLT and its combination with pharmacological approaches to develop a more comprehensive and evidence-based pain management strategy.

Limitations

Several limitations should be acknowledged in this study. First, the present meta-analysis applied a single-arm pre-post design, limiting direct comparison between Low-Level Laser Therapy (LLLT) and control interventions. Comparative pooled analysis was not feasible because of substantial variability in comparator treatments and inconsistent reporting of comparative outcome data across studies. Second, considerable heterogeneity was observed among the included studies, likely related to differences in laser parameters, treatment duration, intervention frequency, patient characteristics, and study design. Third, several included studies had relatively small sample sizes and short follow-up periods, which may limit the generalizability of the findings. In addition, potential publication bias should be considered, as all included studies reported favorable therapeutic outcomes following LLLT intervention. Formal publication bias analysis was not performed due to the limited number of included studies. Therefore, the findings of this meta-analysis should be interpreted with caution despite the overall positive therapeutic effect observed.

CONCLUSION

Low-Level Laser Therapy (LLLT) was associated with significant reductions in pain intensity among patients with post-herpetic neuralgia based on the findings of this systematic review and meta-analysis. The consistent improvement in pain outcomes across included studies suggests that LLLT may provide clinically meaningful reductions in pain intensity in patients with post-herpetic neuropathic pain.

However, the high inter-study heterogeneity and variations in laser parameters and study designs suggest that the available evidence still requires further strengthening. Therefore, further studies with larger sample sizes, rigorous randomized controlled trial designs, and standardized LLLT protocols are needed to confirm these findings and improve the generalizability of the results. Such efforts will hopefully lead to stronger, evidence-based clinical recommendations and clarify the place of LLLT in future post-herpetic neuralgia treatment algorithms.

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COMPETING INTEREST

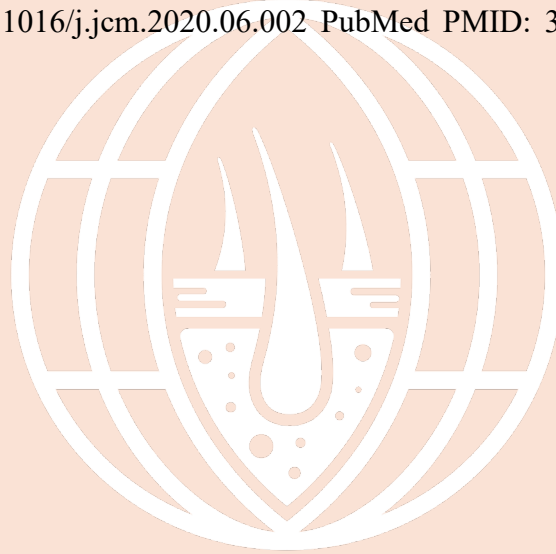
The authors declare that they have no competing interests.

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