http://dx.doi.org/10.18623/rvd.v23.5483

THERAPEUTIC EFFICACY OF DIFFERENT WAVELENGTHS OF LOW-LEVEL LASER THERAPY IN THE TREATMENT OF CERVICOGENIC HEADACHE: A DOUBLE-BLINDED RANDOMIZED CLINICAL TRIAL

EFICÁCIA TERAPÊUTICA DE DIFERENTES COMPRIMENTOS DE ONDA NA TERAPIA A LASER DE BAIXA INTENSIDADE NO TRATAMENTO DA CEFALEIA CERVICOGÊNICA: UM ENSAIO CLÍNICO RANDOMIZADO DUPLO-CEGO

Article received on: 11/20/2025
Article accepted on: 2/19/2026

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The authors declare that there is no conflict of interest

Abstract

Background: Cervicogenic headache is a disabling secondary headache disorder associated with cervical musculoskeletal dysfunction, reduced quality of life, and limited long-term comparative evidence for wavelength-specific photobiomodulation strategies. Objective: To compare the therapeutic efficacy of 820-nm near-infrared laser photobiomodulation, 675-nm red-spectrum laser photobiomodulation, and multiwavelength LED-based photobiomodulation, each combined with standardized physiotherapy, in adults with cervicogenic headache. Methods: This single-centre, three-arm, parallel-group randomized clinical trial enrolled 150 adults with ICHD-3-confirmed cervicogenic headache at a tertiary care hospital in Lahore, Pakistan. Participants were randomized equally to 675-nm laser photobiomodulation plus routine physiotherapy, 820-nm laser photobiomodulation plus routine physiotherapy, or multiwavelength LED-based photobiomodulation plus routine physiotherapy. Treatment was delivered three times weekly for

Resumo

Antecedentes: A cefaleia cervicogênica é um distúrbio de cefaleia secundária incapacitante associado à disfunção musculoesquelética cervical, à redução da qualidade de vida e à escassez de evidências comparativas de longo prazo sobre estratégias de fotobiomodulação com comprimentos de onda específicos. Objetivo: Comparar a eficácia terapêutica da fotobiomodulação a laser no infravermelho próximo de 820 nm, da fotobiomodulação a laser no espectro vermelho de 675 nm e da fotobiomodulação baseada em LED de múltiplos comprimentos de onda, cada uma combinada com fisioterapia padronizada, em adultos com cefaleia cervicogênica. Métodos: Este ensaio clínico randomizado, de centro único, com três braços e grupos paralelos, recrutou 150 adultos com cefaleia cervicogênica confirmada pela ICHD-3 em um hospital de atendimento terciário em Lahore, Paquistão. Os participantes foram randomizados igualmente para fotobiomodulação a laser de 675 nm mais fisioterapia de rotina, fotobiomodulação a laser

6 weeks. The prespecified co-primary outcomes were change in visual analogue scale pain intensity and headache frequency at 6 weeks. Secondary outcomes included neck disability, cervical mobility, craniovertebral angle, and health-related quality of life. Analyses were performed according to the intention-to-treat principle. Results: Of 198 individuals screened, 150 were randomized and 130 completed 6-month follow-up. At 6 weeks, mean VAS pain intensity was 37.8 mm in the 675-nm group, 21.6 mm in the 820-nm group, and 46.2 mm in the multiwavelength group. Adjusted analyses showed significantly greater pain reduction with 820 nm versus 675 nm (adjusted mean difference, -16.2 mm; 95% CI, -21.2 to -11.2) and versus multiwavelength therapy (-24.6 mm; 95% CI, -29.6 to -19.6), with a significant overall group effect ($F[2,146] = 48.3$; $p < 0.001$). Mean headache frequency at 6 weeks was 6.4, 3.8, and 8.6 days per 4 weeks, respectively, with significant adjusted differences favoring 820 nm ($F[2,146] = 42.1$; $p < 0.001$). Improvements in disability, cervical flexion, craniovertebral angle, and SF-36 physical health scores also favored 820 nm. No serious adverse events occurred. Conclusion: In adults with cervicogenic headache receiving standardized physiotherapy, 820-nm near-infrared photobiomodulation was associated with greater reductions in headache frequency and pain intensity than 675-nm laser photobiomodulation or multiwavelength LED-based photobiomodulation.

Keywords: Cervicogenic Headache. Photobiomodulation Therapy. Low-Level Laser Therapy. Neck Pain. Physiotherapy. Randomized Clinical Trial.

de 820 nm mais fisioterapia de rotina ou fotobiomodulação baseada em LED de múltiplos comprimentos de onda mais fisioterapia de rotina. O tratamento foi administrado três vezes por semana durante 6 semanas. Os desfechos coprimários pré-especificados foram a mudança na intensidade da dor na escala visual analógica e a frequência da cefaleia às 6 semanas. Os desfechos secundários incluíram incapacidade cervical, mobilidade cervical, ângulo craniocervical e qualidade de vida relacionada à saúde. As análises foram realizadas de acordo com o princípio da intenção de tratar. Resultados: Dos 198 indivíduos selecionados, 150 foram randomizados e 130 completaram o acompanhamento de 6 meses. Após 6 semanas, a intensidade média da dor na EVA foi de 37,8 mm no grupo de 675 nm, 21,6 mm no grupo de 820 nm e 46,2 mm no grupo de múltiplos comprimentos de onda. Análises ajustadas mostraram redução significativamente maior da dor com 820 nm em comparação com 675 nm (diferença média ajustada, -16,2 mm; IC 95%, -21,2 a -11,2) e em comparação com a terapia de múltiplos comprimentos de onda (-24,6 mm; IC 95%, -29,6 a -19,6), com um efeito global significativo entre os grupos ($F[2,146] = 48,3$; $p < 0,001$). A frequência média de cefaleia às 6 semanas foi de 6,4, 3,8 e 8,6 dias por 4 semanas, respectivamente, com diferenças ajustadas significativas a favor de 820 nm ($F[2,146] = 42,1$; $p < 0,001$). Melhorias na incapacidade, flexão cervical, ângulo craniocervical e pontuação de saúde física no SF-36 também favoreceram 820 nm. Não ocorreram eventos adversos graves. Conclusão: Em adultos com cefaleia cervicogênica submetidos a fisioterapia padronizada, a fotobiomodulação por infravermelho próximo de 820 nm foi associada a maiores reduções na frequência das cefaleias e na intensidade da dor do que a fotobiomodulação a laser de 675 nm ou a fotobiomodulação baseada em LED de múltiplos comprimentos de onda.

Palavras-chave: *Cefaleia Cervicogênica. Terapia de Fotobiomodulação. Terapia a Laser de Baixa Intensidade. Dor Cervical. Fisioterapia. Ensaio Clínico Randomizado.*

1 INTRODUCTION

Headache disorders remain among the leading causes of neurological disability worldwide, with migraine and tension-type headache accounting for most of this burden [1]. Within this spectrum, cervicogenic headache (CGH) is a distinct secondary headache disorder arising from nociceptive structures of the cervical spine and its associated soft tissues [2,3]. Although less prevalent than primary headache disorders, CGH is increasingly recognized in both specialist and rehabilitation settings because of its diagnostic complexity, chronicity, and functional impact. Recent epidemiological evidence suggests that CGH accounts for a pooled clinical frequency of approximately 3.1% among adults presenting for headache care, with women comprising the majority of affected patients [4,5]. This pattern highlights CGH as a clinically important but comparatively under-investigated headache subtype requiring more targeted therapeutic research [4,5].

Clinically, CGH is characterized by unilateral, often side-locked head pain that is typically provoked or aggravated by cervical movement, sustained neck postures, or mechanical pressure over upper cervical structures [6]. Beyond pain itself, the disorder is associated with substantial functional limitation, including impaired neck mobility, reduced work capacity, and diminished health-related quality of life [7]. Patients with CGH frequently report poorer physical functioning than individuals with other common headache disorders, reflecting the combined burden of pain, cervical dysfunction, and postural impairment [7]. Diagnostic assessment is further complicated by symptomatic overlap with migraine and tension-type headache, which can delay targeted management and contribute to persistent disability [6,8]. This challenge is increasingly relevant in contemporary clinical practice, where prolonged screen exposure and forward head posture have become more common and may amplify mechanical loading of the upper cervical region implicated in CGH pathophysiology [8,9].

Conservative management of CGH commonly relies on manual therapy, therapeutic exercise, and postural correction strategies. Although these interventions may reduce headache intensity and frequency, recent systematic reviews and meta-analyses suggest that their effects are often modest, heterogeneous, and insufficiently supported

by long-term high-quality comparative evidence [10-12]. This therapeutic uncertainty has encouraged interest in adjunctive, non-invasive modalities that may enhance clinical response when incorporated into rehabilitation programs. Low-level laser therapy (LLLT), more broadly described within the framework of photobiomodulation therapy, has emerged as one such candidate because of its analgesic, anti-inflammatory, and bioenergetic effects [13-15]. Proposed mechanisms include photon absorption by cytochrome c oxidase within the mitochondrial respiratory chain, leading to modulation of oxidative metabolism, increased adenosine triphosphate synthesis, altered nitric oxide signaling, and downstream reduction of inflammatory activity [13-15]. Although photobiomodulation has shown therapeutic value in general neck pain and related musculoskeletal conditions, its specific role in CGH remains uncertain because existing evidence is limited and treatment parameters have not been adequately standardized across studies [16-18].

One of the most important unresolved issues in photobiomodulation research is whether wavelength selection materially influences clinical efficacy in deep cervical pain syndromes. Red-spectrum light around 675 nm is generally thought to exert its effects more superficially, making it potentially suitable for cutaneous and myofascial targets but less optimal for deeper anatomical structures [19,20]. In contrast, near-infrared wavelengths such as 820 nm are believed to penetrate more deeply into soft tissues and may therefore more effectively reach the suboccipital musculature, upper cervical joint capsules, and periarticular nociceptive structures implicated in CGH [19]. Near-infrared wavelengths also overlap with an established absorption region of cytochrome c oxidase, providing a biologically plausible basis for enhanced photobiomodulatory activity, although this mechanistic advantage remains inferential rather than clinically proven in CGH-specific populations [13,20]. At the same time, multi-wavelength cluster LED devices have been promoted on the premise that broader spectral delivery may target tissues at varying depths simultaneously; however, whether such devices perform as well as or better than focused monochromatic laser probes has not yet been established in a rigorous head-to-head trial [20,21].

Despite growing interest in wavelength-specific photobiomodulation, the comparative evidence base in cervicogenic headache remains notably sparse. Prior studies have largely evaluated photobiomodulation in broader neck pain populations,

used heterogeneous protocols, or examined CGH without directly comparing mechanistically distinct wavelength strategies under controlled conditions [16-18]. As a result, clinicians lack robust trial-level evidence to determine whether red-spectrum laser, near-infrared laser, or multi-wavelength cluster therapy offers the greatest therapeutic value when added to a standardized physiotherapy program for patients with CGH. Addressing this gap is clinically important because wavelength selection is often treated as a technical device parameter rather than a potentially decisive treatment variable, even though tissue penetration, target specificity, and photobiological response may differ substantially across spectra [19-21].

Accordingly, the WELL trial was undertaken to compare the therapeutic efficacy of 675 nm red-spectrum LLLT, 820 nm near-infrared LLLT, and multi-wavelength cluster LED therapy, each administered in combination with standardized physiotherapy, in adults with ICHD-3-confirmed cervicogenic headache [3,22]. It was hypothesized that 820 nm near-infrared photobiomodulation would produce greater reductions in headache frequency and pain intensity than either 675 nm red-spectrum therapy or multi-wavelength cluster treatment because of its more favorable depth of tissue penetration and stronger mechanistic alignment with established photobiomodulation targets [13,19,20].

2 METHODS

The WELL trial was a single-centre, three-arm, parallel-group, participant- and assessor-blinded randomized clinical trial designed to compare wavelength-specific photobiomodulation therapy protocols when delivered in combination with a standardized physiotherapy program for adults with cervicogenic headache. The trial was prospectively registered at ClinicalTrials.gov (NCT07163208), and ethical approval was obtained from the Research Ethical Committee of The University of Lahore before enrolment of the first participant (Ref: REC-UOL-/520/08/24; approval dated September 05, 2024). Recruitment and treatment delivery were conducted between September 2024 and September 2025, and follow-up assessments were completed by January 2026. The study was conducted and reported in accordance with contemporary guidance for randomized trials and non-pharmacological interventions [22,23].

Participants were recruited from the Department of Physiotherapy, Sir Ganga Ram Hospital, Lahore, Pakistan, a tertiary-care teaching hospital with an established outpatient rehabilitation service. Consecutive adults presenting with headache complaints were screened for eligibility. Patients were eligible if they were 18 to 65 years of age, had a diagnosis of cervicogenic headache according to the International Classification of Headache Disorders, third edition (ICHD-3; code 11.2.1), had symptoms for at least 3 months, and had not previously received low-level laser or other photobiomodulation treatment [2]. Diagnostic confirmation was based on standardized ICHD-3 criteria, clinical examination, medical-record review, and the cervical flexion-rotation test performed by a physiotherapist not involved in outcome assessment. Patients were excluded if they had coexisting primary headache disorders, including migraine or tension-type headache, previous cervical spine surgery, pregnancy or lactation, known photosensitivity, active use of photosensitizing medications, or any other clinical condition that could interfere with safe participation or unbiased outcome assessment. Written informed consent was obtained from all participants before baseline procedures, and all study procedures adhered to the principles of the Declaration of Helsinki.

Participants were randomized in a 1:1:1 ratio to one of three intervention groups using a computer-generated permuted-block sequence with randomly varied block sizes of 6 and 9. Randomization was stratified by sex and baseline pain severity on the visual analogue scale (VAS; 50 mm or less vs greater than 50 mm) to preserve balance across groups for two clinically relevant prognostic variables. The sequence was generated by an independent biostatistician using R software (version 4.3.2; randomizeR package) and was concealed by sequentially numbered, opaque, sealed envelopes held by the trial coordinator. Envelopes were opened only after eligibility had been confirmed and written consent had been obtained. Allocation information was released to the treating therapist immediately before the first session, while outcome assessors remained unaware of treatment assignment throughout the study.

Because the interventions involved active devices with distinct probe configurations, the trial used participant blinding and assessor blinding, with operator masking to study hypotheses and coded treatment presets rather than full therapist blinding. Participants were informed that they would receive one of several active photobiomodulation protocols but were not told the wavelength or device category

assigned. During treatment, the device display was concealed and probes were applied in the same clinical manner to reduce the likelihood of participant identification of group allocation. All outcome measurements at baseline, week 3, week 6, month 3, and month 6 were obtained by a blinded assessor who had no role in treatment delivery. Treating physiotherapists delivered the assigned protocol using sealed preset configuration cards prepared by the trial coordinator and were instructed not to disclose device parameters to participants. Given the visible and operational differences between probes, therapist blinding was not considered complete; accordingly, the trial should be interpreted as assessor-blinded and participant-blinded with partial masking of treatment operators. Blinding success was evaluated at the end of the treatment phase using the James Blinding Index [23].

All participants received active photobiomodulation therapy using the Omega XP photobiomodulation device (Omega Laser Systems, United Kingdom), a CE-certified therapeutic system equipped with interchangeable single-contact laser probes and a 46-diode cluster LED probe. To maintain consistent terminology across groups, the two monochromatic arms are described as laser photobiomodulation therapy and the cluster arm as LED-based photobiomodulation therapy; collectively, all three are referred to as photobiomodulation therapy (PBMT). Device parameters were standardized a priori, verified before each session using the built-in calibration function, and recorded in treatment logs to support treatment fidelity. Group 1 received 675-nm red-spectrum laser PBMT through a single-contact pencil probe with output power 30 mW, irradiance 222 mW/cm², spot size 0.9 cm², and fluence 6.7 J/cm². Each point received 6 J over 30 seconds in continuous and pulsed mode at 2.5 Hz. Group 2 received 820-nm near-infrared laser PBMT using the same delivery format, target sites, and surface fluence, with output power 200 mW and identical irradiance and spot size. Group 3 received multiwavelength LED-based PBMT using a 46-diode cluster probe delivering wavelengths of 660, 820, 870, 880, 940, and 950 nm, with spot size 10 cm², irradiance 95 mW/cm², fluence 11.4 J/cm², and 114 J per treatment area over 120 seconds. In all groups, treatment targets were standardized and included the cervical lymphatic chain at the C2-C4 region, suboccipital musculature, upper cervical zygapophyseal joint region, nerve root exit zones, and clinically identified active trigger points. Probe placement was guided by predefined surface anatomical landmarks. All PBMT sessions were delivered by a trained

physiotherapist certified in photobiomodulation therapy using written protocols developed before study initiation.

In addition to PBMT, all participants received the same standardized routine physiotherapy program during each treatment visit. This co-intervention was deliberately kept constant across groups so that the trial would estimate the comparative effectiveness of wavelength- and device-specific PBMT strategies added to usual physiotherapy rather than the isolated efficacy of PBMT alone. The physiotherapy program included active cervical range-of-motion exercises within pain-free limits, stretching of the upper trapezius, levator scapulae, and sternocleidomastoid muscles, strengthening exercises for the deep cervical flexors and scapular stabilizers, superficial hot-pack application, and conventional transcutaneous electrical nerve stimulation. Stretching dosage was standardized to 15 to 30 seconds for 3 to 5 repetitions, while strengthening dosage was prescribed as 2 to 3 sets of 10 to 15 repetitions and progressed weekly according to tolerance using a target Borg rating of perceived exertion of 11 to 13. The hot pack was applied at 40 to 45°C for 15 minutes, and TENS was delivered at 80 to 100 Hz with pulse width 50 to 100 microseconds for 20 minutes. Sessions were supervised, scheduled three times weekly for 6 weeks, and separated by at least 24 hours, for a total of 18 treatment sessions. PBMT was always administered before physiotherapy to preserve a uniform sequence across all groups. Participants were instructed not to initiate new headache-related rehabilitation or procedural treatments during the intervention period, to maintain their usual analgesic regimen if required, and to record rescue medication use in the headache diary.

Outcome assessments were conducted at baseline (T0), week 3 (T1), week 6 at end of treatment (T2), month 3 (T3), and month 6 (T4). The two co-primary outcomes were headache frequency and pain intensity. Headache frequency was captured prospectively using a structured headache diary and expressed as headache days per 4-week period. To maintain comparability across assessment points, diary entries collected at the interim 3-week visit were prorated to a 4-week equivalent using a prespecified scaling rule. Pain intensity was measured on a 100-mm horizontal visual analogue scale ranging from 0 mm for no pain to 100 mm for worst imaginable pain; the minimal clinically important difference for headache pain was prespecified as 15 mm [24,25]. Secondary outcomes included cervical range of motion in six planes measured with a

calibrated universal goniometer, pain-related disability measured with the Urdu version of the Neck Disability Index, health-related quality of life measured with the Short Form-36 Health Survey, and forward head posture assessed by craniovertebral angle derived from standardized lateral digital photographs analyzed with ImageJ software [26,27]. For craniovertebral angle measurement, participants stood in a relaxed habitual posture while reflective markers were placed on the tragus of the ear and the spinous process of C7; the angle formed between the horizontal line through C7 and the line joining C7 to the tragus was measured from standardized photographs taken at a fixed camera height and distance. A smaller craniovertebral angle indicated greater forward head posture. Adverse events were actively solicited at every treatment session and follow-up visit using a structured log that classified event type, severity, timing, and relatedness to treatment in accordance with contemporary harms-reporting guidance [28].

Several procedural safeguards were incorporated to reduce bias and enhance reproducibility. Eligibility assessment followed a standardized diagnostic pathway; allocation concealment was maintained until assignment; assessors were blinded; treatment protocols were manualized; session-level adherence and device settings were documented prospectively; and all primary and secondary outcomes were prespecified before database lock. To reduce performance variability, all treating physiotherapists were trained in the intervention protocol before recruitment started. To reduce detection bias, the assessor had no access to treatment records and no involvement in intervention delivery. Rescue medication use was recorded and reviewed during follow-up to contextualize symptom trajectories. The trial database was checked against source documents before analysis, and range checks and logic checks were applied to key variables to support data integrity.

Sample size was determined a priori to ensure adequate power for both co-primary endpoints at the principal efficacy timepoint of 6 weeks. Planning was based on pairwise between-group comparisons, because the main clinical question concerned whether one active PBMT strategy outperformed the others when added to the same physiotherapy program. For VAS pain intensity, the minimum clinically important between-group difference was set at 15 mm with an assumed common standard deviation of 25 mm, corresponding to a standardized effect size of approximately 0.60, based on prior photobiomodulation trials in chronic cervical pain conditions and related cervicogenic

headache literature [16,29]. This yielded a minimum requirement of 44 participants per group under a two-sided alpha of 0.05 and 80% power. A parallel check was then performed for headache frequency, using a minimum clinically relevant difference of 2 headache days per 4-week period and an assumed standard deviation of 3.5 days. Because this endpoint required a slightly larger effective sample to maintain at least 80% power, an attrition allowance of 12% was incorporated, resulting in a target sample of 50 participants per group and 150 participants overall. This inflation was chosen to preserve adequate power for both co-primary outcomes after anticipated losses during 6-month follow-up.

All analyses were prespecified in a statistical analysis plan finalized before database lock. Statistical analyses were performed using IBM SPSS Statistics version 29.0 and R version 4.3.2. The primary analytic population was the intention-to-treat population, comprising all randomized participants analyzed according to original allocation regardless of adherence. The principal efficacy comparison was the between-group difference in change from baseline to week 6 for the two co-primary outcomes. For each co-primary endpoint, the week-6 comparison was analyzed using one-way analysis of covariance with treatment group as the fixed factor and the corresponding baseline value as covariate, consistent with recommended practice for randomized trials with baseline and follow-up quantitative measures [30]. Homogeneity of regression slopes was checked before model estimation. Because there were three planned pairwise group contrasts, Bonferroni-adjusted p values were used for pairwise post hoc comparisons, with an adjusted threshold of 0.017. The trial was interpreted as supporting superiority of one treatment strategy only if the direction of effect was concordant and statistically persuasive across both co-primary endpoints at the prespecified primary timepoint. Adjusted mean differences, 95% confidence intervals, Cohen's d for pairwise contrasts, and partial eta-squared for omnibus group effects were reported.

Longitudinal treatment trajectories across T0 to T4 were evaluated using linear mixed-effects models estimated with restricted maximum likelihood. Each model included fixed effects for group, time treated as a categorical factor, and the group-by-time interaction, together with random participant-level effects to account for within-subject correlation over repeated measurements. Competing covariance structures, including unstructured, compound symmetry, and first-order autoregressive forms, were

evaluated and the best-fitting structure was selected using Akaike's Information Criterion. The group-by-time interaction was prespecified as the main inferential test for persistence of between-group differences beyond the end of treatment. Baseline values were included as covariates in longitudinal models.

Missing data were addressed within the intention-to-treat framework using multiple imputation by chained equations under a missing-at-random assumption. Fifty imputed datasets were generated using predictive mean matching for continuous outcomes, and the imputation model included treatment group, baseline characteristics, and all observed outcome values. Final estimates were pooled using Rubin's rules [31]. Sensitivity analyses included a per-protocol analysis restricted to participants who completed at least 15 of the 18 scheduled sessions and provided valid week-6 primary-outcome data, a complete-case analysis, and a pattern-mixture sensitivity analysis using plausible delta adjustments to explore departures from the missing-at-random assumption. Secondary outcomes were analyzed using the same ANCOVA and mixed-model frameworks as the primary outcomes; because these analyses were exploratory, no multiplicity adjustment was applied across secondary endpoints. Prespecified exploratory subgroup analyses examined sex, baseline pain severity, headache chronicity, and baseline forward head posture severity by adding subgroup terms and group-by-subgroup interactions to the week-6 ANCOVA models.

Model assumptions were assessed before inferential testing. Residual normality was evaluated using Shapiro-Wilk testing together with visual inspection of quantile-quantile plots, and homogeneity of variance was examined using Levene's test. If assumptions for parametric analysis were materially violated for a primary outcome, the prespecified non-parametric alternative was the Kruskal-Wallis test followed by Dunn post hoc comparisons with Bonferroni adjustment, with rank-biserial correlations reported as effect-size measures. Baseline comparability across randomized groups was examined descriptively and inferentially using one-way analysis of variance, Kruskal-Wallis tests, or chi-squared tests as appropriate, without post-randomization covariate adjustment based solely on chance baseline imbalances.

Safety analyses summarized adverse events by treatment group, severity, and relatedness. The proportion of participants experiencing at least one adverse event was compared across groups using chi-squared testing or Fisher's exact test when cell counts

were small. No formal interim stopping rule was applied because all trial arms involved active non-invasive therapies already in clinical use; however, any serious adverse event was to be reported immediately to the ethics committee in accordance with institutional requirements.

3 RESULTS

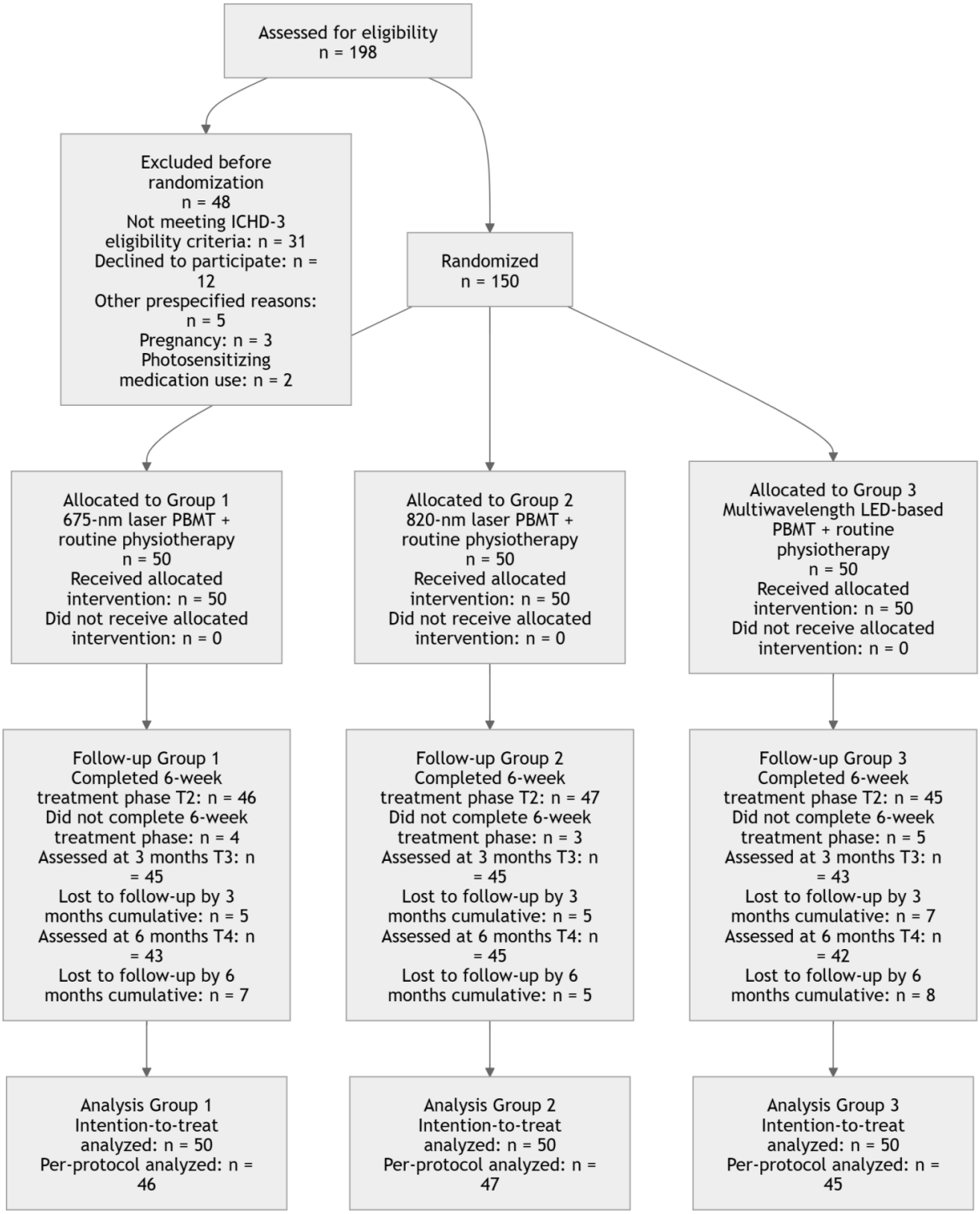
3.1 Participant flow and adherence

Between September 2024 and September 2025, 198 individuals were screened for eligibility at the Department of Physiotherapy, Sir Ganga Ram Hospital, Lahore. Of these, 48 were excluded before randomization: 31 did not meet ICHD-3 eligibility criteria, 12 declined participation, and 5 were excluded for other prespecified reasons, including pregnancy and use of photosensitizing medication. The remaining 150 participants were randomized in equal allocation to the three study groups (50 per group) and constituted the intention-to-treat population.

At the end of treatment at 6 weeks (T2), 138 participants (92.0%) had completed all 18 scheduled treatment sessions, including 46 of 50 participants (92.0%) in the 675-nm laser PBMT group, 47 of 50 (94.0%) in the 820-nm laser PBMT group, and 45 of 50 (90.0%) in the multiwavelength LED-based PBMT group. Follow-up assessments were obtained for 133 participants (88.7%) at 3 months (T3) and 130 participants (86.7%) at 6 months (T4). Overall attrition through the final follow-up was 20 participants, comprising 7 participants (14.0%) in Group 1, 5 (10.0%) in Group 2, and 8 (16.0%) in Group 3. Reported reasons for discontinuation included relocation or loss of contact (n = 8), scheduling conflicts (n = 9), and mild procedure-related discomfort (n = 3). Dropout proportions did not differ significantly between groups ($\chi^2 = 0.97$, $p = 0.62$). Mean adherence among participants who completed treatment was 17.4 of 18 sessions (96.7%). All randomized participants were retained in the intention-to-treat analyses, and missing post-baseline data were handled according to the prespecified multiple-imputation approach.

Figure 1

Consort Flowchart



3.2 Baseline characteristics

Baseline demographic and clinical characteristics were comparable across the three randomized groups, with no statistically significant between-group differences for any measured baseline variable (all $p > 0.05$), supporting successful randomization (Table 1). Across the full sample, the mean age was 38.7 years (SD 9.2), 64.0% of participants were women, and the mean duration of cervicogenic headache was 22.4 months (SD 14.6), indicating a predominantly chronic clinical population. Mean baseline VAS pain intensity was 68.5 mm (SD 12.3), and mean headache frequency was 13.8 days per 4-week period (SD 3.4). Baseline pain-related disability was substantial, with a mean NDI-U score of 30.5 (SD 5.8), and physical health-related quality of life was reduced, with a mean SF-36 physical component summary score of 36.4 (SD 7.4). Mean craniovertebral angle was 43.3° (SD 4.8), consistent with forward head posture in the overall cohort.

3.3 Primary outcomes

Mean values for the two co-primary outcomes across all assessment timepoints in the intention-to-treat population are presented in Table 2. At the prespecified primary endpoint of 6 weeks (T2), statistically significant between-group differences were observed for both pain intensity and headache frequency, with the 820-nm laser PBMT group demonstrating the greatest improvement.

For VAS pain intensity, mean values at T2 were 37.8 mm (SD 16.4) in Group 1, 21.6 mm (SD 15.8) in Group 2, and 46.2 mm (SD 17.1) in Group 3. ANCOVA adjusted for baseline VAS demonstrated a significant overall treatment effect at T2 ($F[2,146] = 48.3$, $p < 0.001$, partial $\eta^2 = 0.399$). Bonferroni-adjusted pairwise comparisons showed that Group 2 had lower pain scores than Group 1 (adjusted mean difference, -16.2 mm; 95% CI, -21.2 to -11.2; $p < 0.001$; $d = 0.87$) and Group 3 (adjusted mean difference, -24.6 mm; 95% CI, -29.6 to -19.6; $p < 0.001$; $d = 1.21$). Group 1 also showed lower pain intensity than Group 3 (adjusted mean difference, -8.4 mm; 95% CI, -13.4 to -3.4; $p = 0.003$; $d = 0.41$). Mean reductions from baseline to T2 were 30.6 mm in Group 1, 46.3 mm in Group 2, and 22.9 mm in Group 3. All three groups exceeded the prespecified minimal clinically important difference of 15 mm, but the magnitude of improvement

was greatest in Group 2. At 6 months, mean VAS scores were 48.6 mm (SD 15.2), 29.8 mm (SD 14.4), and 56.4 mm (SD 15.9), respectively, and the longitudinal mixed-effects model showed a significant group-by-time interaction ($F[8,1014] = 22.6$, $p < 0.001$), indicating sustained between-group separation over follow-up.

For headache frequency, mean values at T2 were 6.4 days per 4 weeks (SD 2.8) in Group 1, 3.8 days (SD 2.6) in Group 2, and 8.6 days (SD 3.1) in Group 3. ANCOVA adjusted for baseline headache frequency showed a significant overall treatment effect ($F[2,146] = 42.1$, $p < 0.001$, partial $\eta^2 = 0.366$). Compared with Group 1, Group 2 had 2.6 fewer headache days per 4-week period at T2 (95% CI, -3.6 to -1.6; $p < 0.001$; $d = 0.76$), and compared with Group 3, Group 2 had 4.8 fewer days (95% CI, -5.8 to -3.8; $p < 0.001$; $d = 1.18$). Group 1 also performed better than Group 3, with an adjusted mean difference of -2.2 days per 4 weeks (95% CI, -3.2 to -1.2; $p < 0.001$; $d = 0.38$). Mean reductions from baseline to T2 were 7.4 days in Group 1, 9.8 days in Group 2, and 5.5 days in Group 3. At 6 months, mean headache frequency was 9.4 days in Group 1, 5.6 days in Group 2, and 11.2 days in Group 3, and the mixed-effects model again showed a significant group-by-time interaction ($F[8,1014] = 18.4$, $p < 0.001$).

3.4 Secondary outcomes

Secondary outcome data at baseline, end of treatment, and 6-month follow-up are summarized in Table 2. The overall pattern was consistent with the primary outcomes, with the 820-nm laser PBMT group showing the largest gains across physical function, postural alignment, disability, and health-related quality of life.

Cervical flexion improved from baseline values of approximately 42° in all groups to 52.4° (SD 8.2) in Group 1, 59.2° (SD 7.6) in Group 2, and 48.6° (SD 8.6) in Group 3 at T2 (overall $p < 0.001$). At 6 months, corresponding values were 49.4°, 55.8°, and 46.4°, and the between-group difference remained significant ($p = 0.003$). Craniovertebral angle increased from approximately 43° at baseline to 48.4° (SD 4.6) in Group 1, 52.8° (SD 4.2) in Group 2, and 46.4° (SD 4.8) in Group 3 at T2 (overall $p < 0.001$). Group 2 was the only group with a mean post-treatment value exceeding 50°, whereas at T4 the means were 46.4°, 50.2°, and 44.8°, respectively, with persistent between-group differences ($p = 0.002$).

Pain-related disability also improved in all groups, but the largest change was observed in Group 2. Mean NDI-U scores decreased from 29.8 (SD 5.5) at baseline to 11.4 (SD 4.6) at T2 in Group 2, compared with reductions to 18.6 (SD 5.4) in Group 1 and 22.8 (SD 5.8) in Group 3 (overall $p < 0.001$). At 6 months, the corresponding values were 14.8, 22.4, and 27.2, respectively ($p < 0.001$). For health-related quality of life, SF-36 physical component summary scores improved from baseline means of approximately 36 to 46.4 (SD 8.4) in Group 1, 54.8 (SD 8.1) in Group 2, and 42.6 (SD 8.6) in Group 3 at T2 (overall $p < 0.001$), with sustained between-group differences at T4 ($p < 0.001$). Mental component summary scores also improved, with means at T2 of 50.2 (SD 9.1), 57.6 (SD 8.4), and 47.4 (SD 9.3), respectively (overall $p = 0.001$). Bonferroni-adjusted pairwise comparisons showed that Group 2 differed significantly from both comparator groups, whereas the difference between Groups 1 and 3 was not statistically significant for SF-36 MCS at T2 ($p = 0.09$).

3.5 Pre-specified subgroup analyses

All subgroup analyses were prespecified as exploratory. No significant group-by-subgroup interaction was identified for sex (interaction $F[2,144] = 1.14$, $p = 0.28$), headache chronicity ($F[2,144] = 1.38$, $p = 0.22$), or baseline forward head posture severity defined by craniovertebral angle 45° or less versus greater than 45° ($F[2,144] = 2.68$, $p = 0.07$). A nominally significant interaction was observed for baseline pain severity categorized as VAS 50 mm or less versus greater than 50 mm ($F[2,144] = 3.44$, $p = 0.04$), suggesting that participants with higher initial pain burden may have experienced larger absolute reductions in the 820-nm group. Because these subgroup analyses were exploratory and were not adjusted for multiplicity, this finding should be interpreted as hypothesis-generating rather than confirmatory.

3.6 Adverse events

Adverse events were actively monitored throughout treatment and follow-up. Eighteen adverse events were recorded among 150 participants. These included mild transient erythema at the treatment site in 6 participants, mild transient worsening of headache during the first two sessions in 3 participants, mild fatigue in 2 participants, and procedure-related discomfort leading to treatment discontinuation in 3 participants. No serious adverse events, device-related incidents requiring medical treatment, or unanticipated safety concerns were observed. The proportion of participants experiencing at least one adverse event was similar across groups, occurring in 5 participants (10.0%) in Group 1, 4 participants (8.0%) in Group 2, and 5 participants (10.0%) in Group 3 (Fisher exact p = 0.93), indicating comparable short-term safety across the three PBMT strategies.

Table 1

Baseline Demographic and Clinical Characteristics of Randomized Participants (N = 150)

Characteristic	Group 1 675-nm Laser PBMT + RPT (n = 50)	Group 2 820-nm Laser PBMT + RPT (n = 50)	Group 3 Multiwavelength LED-Based PBMT + RPT (n = 50)	p Value[a]
Demographic Characteristics				
Age, y, mean (SD)	38.4 (9.2)	39.1 (8.8)	38.7 (9.5)	0.91
Female sex, No. (%)	32 (64.0)	31 (62.0)	33 (66.0)	0.88
Body mass index, mean (SD)	24.8 (3.4)	25.1 (3.2)	24.6 (3.6)	0.77
Education ≥ college level, No. (%)	26 (52.0)	27 (54.0)	25 (50.0)	0.91
Clinical History				
Duration of CGH, mo, mean (SD)	22.4 (14.6)	21.8 (13.9)	23.1 (15.2)	0.84
Previous physiotherapy, No. (%)	18 (36.0)	19 (38.0)	17 (34.0)	0.87
Analgesic medication use, No. (%)	34 (68.0)	33 (66.0)	35 (70.0)	0.88
Primary Outcome Measures at Baseline				
VAS pain intensity, mm, mean (SD)	68.4 (12.3)	67.9 (11.8)	69.1 (12.7)	0.81
Headache frequency, days/4 wk, mean (SD)	13.8 (3.4)	13.6 (3.1)	14.1 (3.6)	0.72

Characteristic	Group 1 675-nm Laser PBMT + RPT (n = 50)	Group 2 820-nm Laser PBMT + RPT (n = 50)	Group 3 Multiwavelength LED-Based PBMT + RPT (n = 50)	p Value[a]
Secondary Outcome Measures at Baseline				
NDI-U score (0–50), mean (SD)	30.4 (5.8)	29.8 (5.5)	31.2 (6.1)	0.45
SF-36 PCS, mean (SD)	36.2 (7.4)	35.8 (7.1)	37.1 (7.8)	0.62
SF-36 MCS, mean (SD)	43.4 (8.2)	42.9 (8.6)	44.1 (8.9)	0.71
Cervical flexion, °, mean (SD)	41.8 (8.4)	42.2 (8.1)	41.4 (8.7)	0.87
Cervical extension, °, mean (SD)	52.4 (9.1)	53.1 (8.8)	52.8 (9.4)	0.91
Cervical rotation (ipsilateral), °, mean (SD)	38.6 (7.2)	39.1 (6.9)	38.4 (7.5)	0.84
Craniovertebral angle, °, mean (SD)	43.2 (4.8)	43.6 (4.5)	43.0 (5.1)	0.79

Abbreviations: CGH = cervicogenic headache; MCS = mental component summary; NDI-U = Neck Disability Index–Urdu version; PBMT = photobiomodulation therapy; PCS = physical component summary; RPT = routine physiotherapy; SD = standard deviation; SF-36 = Short Form-36; VAS = visual analogue scale. [a] Derived from one-way ANOVA for continuous variables or chi-squared test for categorical variables.

Table 2

Co-Primary Outcomes Across All Assessment Timepoints (Intention-to-Treat Population, N = 150)

Outcome and Timepoint	Group 1 675-nm Laser PBMT + RPT	Group 2 820-nm Laser PBMT + RPT	Group 3 Multiwavelength LED-Based PBMT + RPT	Between-Group p Value[b]
VAS Pain Intensity (mm)				
Baseline (T0)	68.4 (12.3)	67.9 (11.8)	69.1 (12.7)	0.81
3 weeks (T1)	52.1 (13.4)	41.4 (12.8)	58.2 (13.9)	<0.001
6 weeks / end of treatment (T2)[c]	37.8 (16.4)	21.6 (15.8)	46.2 (17.1)	<0.001
Change from baseline to T2	-30.6 (14.2)	-46.3 (13.8)	-22.9 (14.6)	<0.001
3 months (T3)	44.2 (15.8)	26.4 (14.9)	52.8 (16.4)	<0.001
6 months (T4)	48.6 (15.2)	29.8 (14.4)	56.4 (15.9)	<0.001
Headache Frequency (days per 4-week period)				
Baseline (T0)	13.8 (3.4)	13.6 (3.1)	14.1 (3.6)	0.72
3 weeks (T1)	9.8 (3.1)	7.4 (2.8)	11.2 (3.4)	<0.001
6 weeks / end of treatment (T2)[c]	6.4 (2.8)	3.8 (2.6)	8.6 (3.1)	<0.001
Change from baseline to T2	-7.4 (2.9)	-9.8 (2.6)	-5.5 (3.0)	<0.001
3 months (T3)	8.2 (3.0)	4.9 (2.7)	10.4 (3.3)	<0.001
6 months (T4)	9.4 (3.2)	5.6 (2.8)	11.2 (3.4)	<0.001

Data are mean (SD). Analyses were conducted in the intention-to-treat population with multiple imputation for missing post-baseline data. [b] At T2, p values are from ANCOVA adjusted for the corresponding baseline value; at T1, T3, and T4, p values are from linear mixed-effects models. [c] Prespecified primary analysis endpoint.

Table 3

ANCOVA-Adjusted Pairwise Comparisons at the Primary Endpoint (T2, 6 Weeks)

Pairwise Comparison	Adjusted Mean Difference	95% Confidence Interval	Bonferroni-Adjusted p Value	Cohen's d
VAS Pain Intensity at 6 Weeks				
Group 2 vs Group 1	-16.2 mm	-21.2 to -11.2	<0.001	0.87
Group 2 vs Group 3	-24.6 mm	-29.6 to -19.6	<0.001	1.21
Group 1 vs Group 3	-8.4 mm	-13.4 to -3.4	0.003	0.41
Headache Frequency at 6 Weeks				
Group 2 vs Group 1	-2.6 days/4 wk	-3.6 to -1.6	<0.001	0.76
Group 2 vs Group 3	-4.8 days/4 wk	-5.8 to -3.8	<0.001	1.18
Group 1 vs Group 3	-2.2 days/4 wk	-3.2 to -1.2	<0.001	0.38

VAS omnibus ANCOVA: $F(2,146) = 48.3$, $p < 0.001$, partial $\eta^2 = 0.399$. Headache-frequency omnibus ANCOVA: $F(2,146) = 42.1$, $p < 0.001$, partial $\eta^2 = 0.366$.

Table 4

Secondary Outcomes at Baseline (T0), End of Treatment (T2), and 6-Month Follow-Up (T4)

Outcome	Time	Group 1 675-nm Laser PBMT + RPT	Group 2 820-nm Laser PBMT + RPT	Group 3 Multiwavelength LED-Based PBMT + RPT	Between-Group p Value
Cervical Flexion ROM (°)	T0	41.8 (8.4)	42.2 (8.1)	41.4 (8.7)	0.87
	T2	52.4 (8.2)	59.2 (7.6)	48.6 (8.6)	<0.001
	T4	49.4 (8.8)	55.8 (8.2)	46.4 (9.1)	0.003
Craniovertebral Angle (°)	T0	43.2 (4.8)	43.6 (4.5)	43.0 (5.1)	0.79
	T2	48.4 (4.6)	52.8 (4.2)	46.4 (4.8)	<0.001
	T4	46.4 (4.9)	50.2 (4.6)	44.8 (5.2)	0.002
NDI-U (0–50)	T0	30.4 (5.8)	29.8 (5.5)	31.2 (6.1)	0.45
	T2	18.6 (5.4)	11.4 (4.6)	22.8 (5.8)	<0.001
	T4	22.4 (5.9)	14.8 (5.2)	27.2 (6.4)	<0.001
SF-36 PCS	T0	36.2 (7.4)	35.8 (7.1)	37.1 (7.8)	0.62
	T2	46.4 (8.4)	54.8 (8.1)	42.6 (8.6)	<0.001
	T4	42.8 (8.8)	50.4 (8.6)	39.6 (9.1)	<0.001
SF-36 MCS	T0	43.4 (8.2)	42.9 (8.6)	44.1 (8.9)	0.71
	T2	50.2 (9.1)	57.6 (8.4)	47.4 (9.3)	0.001
	T4	48.4 (9.4)	54.8 (8.8)	45.8 (9.6)	0.003

Data are mean (SD), intention-to-treat population. Between-group p values at T2 are from ANCOVA adjusted for baseline values; p values at T4 are from linear mixed-effects models. Secondary outcomes were prespecified as exploratory and were not adjusted for multiplicity across endpoints. For SF-36 MCS at T2, the overall between-group effect was significant, but the pairwise contrast between Groups 1 and 3 was not significant after Bonferroni adjustment ($p = 0.09$).

4 DISCUSSION

In this participant- and assessor-blinded, three-arm randomized clinical trial involving 150 adults with ICHD-3-confirmed cervicogenic headache, 820-nm near-infrared photobiomodulation therapy administered in combination with standardized physiotherapy produced the greatest improvements in both co-primary outcomes at the prespecified 6-week primary endpoint and maintained the most favorable outcome profile through 6 months of follow-up. Compared with 675-nm laser photobiomodulation and multiwavelength LED-based photobiomodulation, the 820-nm protocol was associated with larger reductions in headache frequency and pain intensity, as well as more favorable changes in neck disability, cervical mobility, postural alignment, and physical health-related quality of life. The magnitude of benefit for the primary outcomes was large, with pairwise effect sizes ranging from 0.87 to 1.21 for comparisons involving the 820-nm group. The observed treatment pattern was therefore consistent with the prespecified hypothesis that a near-infrared wavelength strategy would provide greater clinical benefit than the comparator photobiomodulation approaches when each was added to the same physiotherapy program. However, these findings should be interpreted as evidence of comparative superiority between active treatment strategies rather than proof of absolute efficacy independent of co-administered rehabilitation or non-specific treatment effects.

The present findings extend the broader literature on photobiomodulation in musculoskeletal pain while addressing a more specific clinical question that had remained unresolved in cervicogenic headache. A landmark meta-analysis by Chow et al. showed that low-level laser therapy reduced pain in acute and chronic neck pain populations, but the included studies were heterogeneous in dosimetry, anatomical targets, and diagnostic categories [32]. More recently, an umbrella review by Kang et al. supported clinically meaningful benefits of photobiomodulation across multiple musculoskeletal outcomes while also emphasizing that certainty of evidence remained limited by methodological variation and inconsistent treatment parameters [33]. Against this background, the current trial contributes new evidence in three ways. First, it focuses specifically on cervicogenic headache rather than broader neck-pain syndromes. Second, it keeps the accompanying physiotherapy program constant across all groups, thereby isolating the comparative contribution of wavelength- and device-specific photobiomodulation strategies. Third, it

directly compares two monochromatic laser protocols with a multiwavelength cluster protocol in a head-to-head randomized design, which is a more clinically informative framework than comparisons against usual care alone.

The results also expand substantially on the limited cervicogenic headache-specific photobiomodulation literature. In the previously published randomized trial by Saleh et al., laser therapy combined with physiotherapy improved pressure pain threshold and disability outcomes in cervicogenic headache, but the wavelength was not clearly specified and follow-up was short [34]. The present study suggests that the therapeutic effects attributed more generally to "laser therapy" in cervicogenic headache are not uniform across delivery strategies. At the 6-week primary endpoint, the 820-nm group achieved a mean reduction in headache frequency of 9.8 days per 4 weeks compared with 7.4 days in the 675-nm group and 5.5 days in the multiwavelength LED-based group. Likewise, VAS pain intensity decreased by 46.3 mm in the 820-nm group, compared with 30.6 mm and 22.9 mm in the other two groups. These differences were not only statistically significant but clinically meaningful, particularly given that all groups received the same standardized physiotherapy and the between-group comparison therefore reflects incremental comparative benefit attributable to the photobiomodulation strategy rather than to exercise or adjunctive physical modalities.

The treatment magnitude observed in the 820-nm group also compares favorably with the broader physiotherapy literature for cervicogenic headache. A recent network meta-analysis of physical therapist interventions for cervicogenic headache found that the best-performing combined physiotherapy approaches typically produced moderate standardized effects on pain outcomes [35]. In the present trial, the pairwise difference between 820-nm photobiomodulation and 675-nm photobiomodulation at the primary endpoint corresponded to a Cohen d of 0.87, while the difference between 820-nm photobiomodulation and the multiwavelength cluster strategy reached 1.21. Although these values should not be interpreted as direct cross-trial superiority over all non-laser interventions, they suggest that a near-infrared photobiomodulation strategy may enhance the clinical yield of a structured physiotherapy program in cervicogenic headache more than alternative light-delivery approaches. At the same time, both comparator groups also improved meaningfully from baseline, indicating that active photobiomodulation in

general may confer benefit, but that wavelength and delivery format appear to influence the size of that benefit.

The observed treatment hierarchy of 820 nm greater than 675 nm greater than multiwavelength cluster therapy is biologically plausible and consistent with established photobiomodulation theory, but it should be described as mechanistically coherent rather than mechanistically proven. Experimental work has identified cytochrome c oxidase as a major photoacceptor involved in photobiomodulation, with relevant absorption bands in both the red and near-infrared spectrum [13,14,36]. Near-infrared wavelengths are also thought to penetrate more deeply through soft tissue than visible red wavelengths, potentially improving photon delivery to deeper nociceptive and myofascial structures implicated in cervicogenic headache, including the suboccipital musculature and upper cervical zygapophyseal region [19,37]. This provides a plausible explanation for why the 820-nm protocol outperformed the 675-nm protocol despite similar surface fluence and irradiance characteristics. Nevertheless, the present trial did not directly measure tissue penetration, mitochondrial activity, inflammatory mediators, or neural sensitization, so any explanation of wavelength superiority must remain inferential and based on consistency with prior mechanistic literature rather than direct demonstration within this study.

A similar caution applies to interpretation of the multiwavelength LED-based arm. Although the cluster device delivered higher total energy per treated area, its irradiance was lower and its energy was dispersed over a substantially larger surface area than the single-point laser probes. One plausible interpretation is that this delivery format may have produced less effective photon density at clinically relevant tissue depth, thereby yielding weaker biological stimulation of deep cervical targets. It is also possible that broader spectral dispersion reduced target specificity relative to the monochromatic near-infrared probe. These are reasonable mechanistic interpretations and are broadly compatible with the biphasic dose-response model in photobiomodulation and with consensus guidance favoring near-infrared parameters for deep musculoskeletal targets [20,38]. However, the present clinical data cannot on their own distinguish among insufficient tissue penetration, lower effective irradiance at depth, altered beam characteristics, or other device-specific factors. The discussion of cluster inferiority

should therefore remain explicitly hypothesis-based rather than framed as definitive mechanistic proof.

The trial also has implications for ongoing discussions about parameter standardization in photobiomodulation research. Previous reviews have repeatedly noted that heterogeneity in wavelength, power, spot size, fluence, treatment duration, and anatomical targeting limits synthesis and reproducibility across trials [20,33,39]. The present study attempted to address this problem by transparently reporting wavelength, output power, irradiance, spot size, fluence, total energy per point or area, emission mode, pulse frequency, session duration, session frequency, and treatment targets. This level of reporting strengthens reproducibility and makes the observed treatment differences more interpretable. In particular, the 820-nm laser protocol fell within consensus-recommended near-infrared ranges proposed for chronic neck pain and deep musculoskeletal targets, whereas the 675-nm comparator represented a more superficial red-spectrum strategy and the cluster arm represented a broader mixed-wavelength delivery format [38]. The present findings therefore lend clinical support to the view that photobiomodulation parameters should not be treated as interchangeable technical details.

The secondary outcomes reinforce the primary findings and help place them in clinical context. The 820-nm group showed the greatest reduction in neck-related disability, with NDI-U scores improving from 29.8 at baseline to 11.4 at the end of treatment, a shift from severe disability into the mild disability range. This change was larger than those seen in the 675-nm and cluster groups and suggests that the superior pain reduction observed with 820 nm translated into meaningful functional improvement. Similarly, the physical component of the SF-36 improved to 54.8 in the 820-nm group at 6 weeks and remained at 50.4 at 6 months, indicating recovery toward normative physical health levels. These findings strengthen the clinical relevance of the primary outcome differences by showing that the observed analgesic effects were accompanied by broader gains in activity and function rather than by isolated changes on pain scales alone.

Interpretation of mental health-related quality of life requires more caution. Although the overall between-group difference in SF-36 mental component score was statistically significant, the pairwise difference between the 675-nm and multiwavelength cluster groups was not significant after adjustment, whereas the 820-nm group was superior to both comparators. This pattern is clinically plausible, as mental health

domains in chronic pain often improve most clearly when pain relief is both substantial and sustained [40]. Even so, mental health outcomes are inherently more variable and susceptible to external influences than pain or mobility measures, and the present trial was not designed primarily to detect between-group differences in psychological status. Accordingly, the MCS findings should be interpreted as supportive rather than central evidence of comparative therapeutic advantage.

The changes in cervical flexion and craniovertebral angle are also noteworthy because they suggest that the clinical effect of the 820-nm protocol extended beyond symptom reduction to measurable biomechanical and functional recovery. Cervical flexion improved to 59.2° in the 820-nm group at the end of treatment, exceeding gains seen in both comparator groups. Craniovertebral angle improved from 43.6° to 52.8° in the same group, with maintenance above 50° at 6 months. These data suggest that the greater symptom relief associated with 820 nm may have enabled more effective participation in the exercise-based components of the standardized physiotherapy program. That interpretation is important because it positions photobiomodulation not as a replacement for active rehabilitation, but as a modality that may facilitate rehabilitation by reducing pain-related movement limitation. This interpretation is consistent with the study design, in which all groups received the same physiotherapy and the main difference between groups lay in the photobiomodulation protocol.

An important strength of the trial is the 6-month follow-up period, which is longer than that of many previous photobiomodulation studies in musculoskeletal rehabilitation. Although some attenuation of effect occurred after the 6-week treatment period in all groups, the 820-nm group maintained the most favorable outcomes at both 3 and 6 months. For example, headache frequency in the 820-nm group rose from 3.8 days per 4 weeks at 6 weeks to 5.6 days at 6 months, yet this still represented a substantial reduction from the baseline value of 13.6 days. By contrast, the comparator groups showed greater attenuation over time. These findings suggest that the near-infrared strategy may have produced more durable clinical benefit than the alternative active protocols. However, the persistence of between-group differences should not be overinterpreted as evidence of structural biological remodeling, because the study did not include mechanistic biomarkers, imaging, or repeated physiological testing capable of confirming such processes directly.

The exploratory subgroup analyses were largely reassuring in showing that the comparative treatment pattern was broadly consistent across sex, headache chronicity, and baseline postural severity. A nominal interaction was observed for baseline pain severity, with participants reporting higher baseline pain appearing to derive greater absolute VAS reductions from the 820-nm protocol. While this is biologically plausible, the result was only marginal by conventional thresholds and arose in the context of multiple exploratory subgroup analyses without multiplicity correction. It should therefore be regarded as hypothesis-generating rather than practice-changing. Future trials specifically powered for stratified analyses would be needed before baseline pain severity could be recommended as a criterion for treatment selection.

Several limitations should be acknowledged. First, the study was conducted at a single tertiary-care center in Lahore, which may limit generalizability to other practice settings, especially primary care or lower-resource environments where treatment intensity and supervision differ. Second, despite efforts to mask participants and outcome assessors, complete blinding of the treating therapist was not realistically possible because the interventions involved different probes and operational settings. The study therefore minimized but could not eliminate performance bias. Third, the absence of a sham-control group means that the trial addresses a comparative-effectiveness question among active strategies rather than the absolute efficacy of photobiomodulation beyond placebo or usual physiotherapy alone. Fourth, missing follow-up data were handled using multiple imputation under a missing-at-random assumption. Although this was prespecified and methodologically appropriate, some uncertainty from informative dropout cannot be excluded entirely. Fifth, device output was verified using the built-in calibration approach rather than external dosimetry at every session, so small between-session variation cannot be ruled out. Sixth, no biological or imaging markers were collected to verify proposed mechanisms related to mitochondrial activation, inflammation reduction, or modulation of sensitization. As a result, the mechanistic interpretations offered here remain grounded in prior literature rather than directly tested in this trial.

External validity is mixed and should be framed carefully. On one hand, the sample characteristics, including age, sex distribution, headache chronicity, and functional impairment, are broadly compatible with published descriptions of

cervicogenic headache populations [5,41]. The use of a commercially available photobiomodulation device and clearly reported dosimetry improves reproducibility. On the other hand, the intervention package was intensive, consisting of supervised treatment three times weekly for six weeks plus a multicomponent physiotherapy program. That level of care may not be feasible in all clinical settings, so extrapolation to routine practice should be cautious. The findings are therefore most directly applicable to specialist rehabilitation environments capable of delivering structured multimodal care.

From a clinical perspective, the present results support preferential consideration of 820-nm near-infrared photobiomodulation when photobiomodulation is added to a standardized physiotherapy program for cervicogenic headache. The data do not suggest that all photobiomodulation modalities are equivalent; rather, they indicate that wavelength and delivery format appear to influence treatment response in a clinically meaningful way. At the same time, both comparator groups also achieved improvements exceeding the minimal clinically important difference for pain, which suggests that active photobiomodulation more generally may be beneficial, even if some strategies are more effective than others. For clinicians and services selecting among available probes or devices, these findings argue for more parameter-specific decision-making rather than viewing photobiomodulation as a uniform intervention class.

Future research should build on these results in a more definitive and mechanistically informative manner. A multicenter randomized trial incorporating a sham-control condition would help distinguish specific photobiomodulation effects from contextual and co-intervention effects. Trials comparing multiple fluence levels within the near-infrared range would also help determine whether the superiority of 820 nm in the present study reflects wavelength alone or wavelength-dose interaction. In addition, incorporation of inflammatory biomarkers, pressure pain thresholds, quantitative sensory testing, or imaging-based outcomes could help clarify the physiological pathways through which clinical improvement occurs. Finally, stratified trials designed prospectively to test whether baseline pain severity or other clinical phenotypes modify response could move the field toward more individualized photobiomodulation prescribing.

5 CONCLUSION

among adults with cervicogenic headache receiving the same standardized physiotherapy program, the 820-nm near-infrared photobiomodulation strategy was associated with greater reductions in headache frequency and pain intensity than 675-nm laser photobiomodulation or multiwavelength LED-based photobiomodulation. Similar graded patterns were observed across several secondary outcomes, although those analyses were exploratory. These findings provide comparative clinical evidence that wavelength and delivery format matter in photobiomodulation for cervicogenic headache, while also underscoring the need for multicenter, sham-controlled, and mechanistically enriched trials to confirm the robustness and biological basis of the observed treatment hierarchy.

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Authors' Contribution

All authors contributed equally to the development of this article.

Data availability

All datasets relevant to this study's findings are fully available within the article.

How to cite this article (APA)

Munawar, A., Ahmed, U., Bashardost, S., Ahmad, A., & Shabbir, M. (2026). THERAPEUTIC EFFICACY OF DIFFERENT WAVELENGTHS OF LOW-LEVEL

LASER THERAPY IN THE TREATMENT OF CERVICOGENIC HEADACHE: A DOUBLE-BLINDED RANDOMIZED CLINICAL TRIAL. Veredas Do Direito, 23(5), e235483. https://doi.org/10.18623/rvd.v23.5483