Enhancing non-surgical periodontal therapy: A comparative study of human placental extract gel vs. 970 nm diode laser for localized chronic moderate periodontitis

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Abstract. The present clinical study aimed to evaluate and compare the efficacy of human placental extract (HPE) gel and a 970 nm diode laser as adjuncts to non-surgical periodontal therapy in patients with localized chronic moderate periodontitis. For this purpose, 24 systemically healthy subjects were randomly assigned to three groups: Scaling and root planing (SRP) alone, SRP + HPE gel and SRP + 970 nm diode laser. Clinical parameters, including plaque index (PI), papillary bleeding index (PBI), probing pocket depth (PPD) and clinical attachment level (CAL) were recorded at baseline, 1 month and 3 months. Intergroup comparisons using non-parametric analysis demonstrated statistically significant differences in PPD and CAL at 1 and 3 months ($P<0.05$), with the SRP + HPE group illustrating the greatest improvement. No statistically significant intergroup differences were observed for PI at any time point, while PBI exhibited a significant difference only for baseline to 3-month change. Intragroup analysis revealed significant improvements over time in all parameters across all groups ($P<0.05$). The SRP + HPE group demonstrated the greatest reduction in probing depth and gain in clinical attachment, followed by the diode laser group and SRP alone. Within the limitations of the present study, both adjunctive therapies enhanced clinical outcomes compared to SRP alone, with HPE exhibiting superior regenerative potential. Further long-term studies are recommended to validate these findings.

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Introduction

Chronic periodontitis is a long standing inflammatory disease of the tissues supporting the tooth, the gingiva, periodontal ligament, cementum and alveolar bone, that progressively destroys these structures. When left unmanaged, this process results in irreversible attachment loss and, ultimately, tooth loss, with a consequent impact on oral function and overall quality of life. The condition is primarily driven by a dysbiotic subgingival biofilm, although the intensity and pattern of tissue breakdown largely depend on the host immune-inflammatory response (1).

Non-surgical periodontal therapy, particularly scaling and root planing (SRP), remains the foundation of treatment for chronic periodontitis. The concept is straightforward: Disinfect the root surface, disrupt plaque and calculus, and diminish the bacterial burden to allow tissue recovery (2). However, SRP does not consistently accomplish the task independently. Deep pockets, curved roots, furcations, or sites that remain inflamed even following debridement can all limit its effectiveness. Thus, due to these inadequacies, clinicians and researchers have been investigating and searching for other methods which can support healing. A long list of adjuncts has been tested, such as local antimicrobials, herbal preparations, probiotics, photodynamic therapy and ozone therapy. Two of the most novel and most interesting possibilities are human placental extract (HPE) and low-level laser treatment. These methods may do more than only remove plaque, as they have been reported to enhance wound healing, modulate inflammatory responses, and promote tissue regeneration through stimulation of cellular activity and growth factor release (3,4).

HPE differs from other products as it functions in a manner that mimics natural biological processes. It is derived from processed human placenta, which includes a mixture of peptides, growth factors and signaling chemicals that are already naturally known to the body (3). HPE does not function as a single-mechanism drug; instead, it functions through concurrent mechanisms to facilitate tissue regeneration and symptom management. It promotes the production of collagen by fibroblasts, stimulates the growth of new blood vessels, and generally improves the healing of periodontal pockets by enhancing tissue repair, reducing inflammation

and accelerating regeneration. HPE has been shown to exert antioxidant and anti-inflammatory effects, thus assisting in the suppression of inflammation (3,4). Currently, there are a limited number of clinical studies on HPE; however, a previous study demonstrated that the use of HPE gel following SRP led to clear improvements in attachment and pocket reduction compared to SRP alone (5). HPE does not cause an immune reaction and is safe for living organisms; thus, its use is not associated with the issues and side-effects of other biological agents (3,5). The HPE gel used in the present study was a commercially available preparation (Placentrex®, Albert David Ltd.). According to the manufacturer, each gram of the formulation contains the aqueous extract derived from 0.1 g of fresh human placenta with a total nitrogen content not exceeding 0.25% w/w, which serves as an indicator of the protein and peptide components present in the preparation. The extract contains various biologically active constituents including amino acids (such as glutamic acid, leucine and lysine), nucleotides, peptides, vitamins and growth-promoting factors, which are considered to contribute to tissue repair, angiogenesis and modulation of inflammatory responses (https://www.albertdavidindia.com/placentrex.html).

In the present study, the extract was delivered locally using a sterile absorbable gelatin sponge (Abgel®) that acted as a biodegradable carrier. The porous structure of the gelatin matrix allows the adsorption of the HPE gel and facilitates localized retention and gradual release of the bioactive components within the periodontal pocket, thereby prolonging the therapeutic effect at the treatment site.

Laser therapy, on the other hand, functions in a completely different manner. A 970 nm diode laser does not add proteins or growth factors; instead, it modifies how cells function by stimulating the energy systems of the cells. Once the light is absorbed, the mitochondria function more efficiently, ATP levels increase and oxidative stress levels decrease. The laser gives the tissues more energy while they repair (6,7). SRP and diode lasers have long been used together. Research has demonstrated that they can help reduce inflammation and speed up the process of reducing pocket depths more efficiently than SRP alone (6,8). However, not all research has produced significant results. The outcome often depends on how the laser is used, such as technique, settings and exposure time.

What is intriguing is the disparity between these two methodologies. HPE functions as a biologically intelligent framework, facilitating regeneration at the molecular scale. The diode laser does not deliver any tangible substance; it merely affects the cellular metabolism via light. SRP and HPE represent two distinct methodologies, each designed to provide SRP with the adjunctive support it occasionally requires; yet both aim to solve the same issue: Both methods aim to promote the efficient healing of periodontal tissues following SRP. However, to date, to the best of our knowledge, they have not been tested together in the same trial, particularly not in localized moderate cases where the response to treatment can vary. Currently, no study has attempted to utilize them in conjunction (7-11).

To the best of our knowledge, the present study is the first study aiming to address this gap in terms of the comparisons of the two treatment modalities and for discovering whether a biologically active gel can match, or even outperform, a laser-based approach. Addressing this gap may provide valuable clinical insight into optimizing treatment strategies for improved patient outcomes. Therefore, the present study aimed to assess and compare the clinical efficacy of HPE gel and 970 nm diode laser therapy, when used as adjunctive modalities to SRP, for the management of localized chronic moderate periodontitis.

Patients and methods

Study design. The present study was designed as a single-blinded, randomized, prospective, parallel-arm clinical trial aimed at evaluating the clinical effectiveness of HPE gel and diode laser therapy as adjuncts to SRP in patients with localized chronic moderate periodontitis. (diagnosis of stage II or III, grade B periodontitis as per the 2017 World Workshop classification) (12). The trial was carried out at the Department of Periodontology, Manipal College of Dental Sciences Mangalore, Mangalore, India, after obtaining approval from the Institutional Ethics Committee (Protocol ref. no. 24086; dated July 13, 2024). The trial was prospectively registered with the Clinical Trials Registry of India (CTRI/2025/10/096493). All procedures adhered to the Declaration of Helsinki and Good Clinical Practice guidelines (13). Written and verbal informed consent was obtained from all participants prior to inclusion.

Study population. Patients presenting to the outpatient Department of Periodontology, Manipal College of Dental Sciences Mangalore, were screened for eligibility. A total of 24 systemically healthy individuals between the ages of 25 and 65 years were selected based on the inclusion and exclusion criteria. Patient recruitment was carried out between August and September, 2024, and follow-up was completed in January, 2025.

Inclusion criteria. Patients were included if they were between 25 and 65 years of age, irrespective of sex, and diagnosed with localized chronic moderate periodontitis characterized by probing pocket depths of 4-6 mm in <30% of sites. A minimum of 15 functional teeth was required, and all included patients were diagnosed as having stage II or stage III, grade B periodontitis according to the 2017 World Workshop classification (12). Only patients who demonstrated good oral hygiene and achieved a plaque score <1 following initial supragingival therapy were considered eligible.

Exclusion criteria. The exclusion criteria included patients with systemic diseases, such as diabetes mellitus and cardiovascular diseases, which could potentially interfere with periodontal healing. Patients diagnosed with aggressive periodontitis, pregnant or lactating women, and those with a history of tobacco or alcohol use were excluded. Additional exclusion criteria comprised patients who had received periodontal therapy over the past 6 months and teeth with grade III mobility (Fig. 1).

Sample size. Using data from the study by Ganvir *et al* (14), the sample size was calculated. Assuming a clinically significant difference of 1.0 unit, a study power of 90%, and an alpha error of 5%, a minimum of 8 participants were required per group.

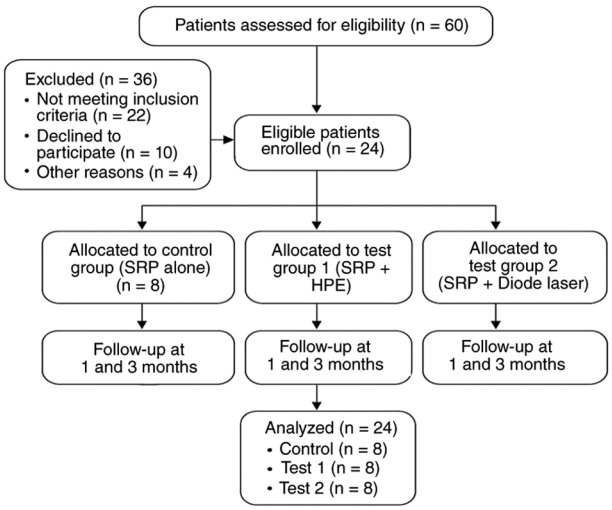

Figure 1. Patient screening and allocation flowchart (CONSORT 2010 guidelines).

Thus, the total study population was fixed at 24 patients, equally distributed across three groups.

Randomization and blinding. Block randomization was carried out using computer-generated lists created through the Sealed Envelope online tool. To maintain the allocation process concealed, sequentially numbered, opaque, sealed envelopes (SNOSE) were used. These were prepared ahead of time and handled by an investigator who did not take part in patient treatment or outcome recording. Each envelope was opened only after the patient had been enrolled, and just before the procedure, to reveal the assigned group.

Due to the nature of the interventions, the operator could not be blinded. However, the study was still single-blinded, since the examiner who recorded outcomes did not have knowledge of which treatment each patient received.

Examiner calibration. Prior to commencing the study, the examiner was calibrated to make sure the measurements would be consistent each time they were taken. To confirm that the periodontal measurements were dependable, the examiner was first calibrated using a separate set of 10 patients who were not part of the main study, but were recruited from the same hospital and presented with chronic periodontitis. For each patient, probing pocket depth (PPD) and clinical attachment level (CAL) were measured at six sites around each tooth. The same examiner repeated all measurements 48 h later, using the same technique and probe. The two recordings were considered reliable if the difference between them was not >1 mm. The level of agreement between the two measurement rounds was then assessed using Cohen's kappa statistic was calculated using the following formula:

$$\kappa = \frac{p_0 - p_e}{1 - p_e}$$

In this formula, P_0 denotes the proportion of readings that were really in concordance, whereas P_e signifies the degree of agreement that might have arisen by coincidence. The intra-examiner kappa coefficient was 0.85, indicating that the same examiner consistently recorded measurements which were reliable throughout time. A series of readings was compared with those of an experienced periodontist for additional examination. The inter examiner kappa was found to be >0.80, validating the consistency and reliability of measurements among examiners (15).

Clinical outcome measurements. Clinical parameters were recorded at three intervals: At baseline, 1 and 3 months post-treatment. A UNC-15 periodontal probe was utilized to cross-check that all the measurements were correct. The following parameters were examined: i) PPD: Measured from the gingival margin to the base of the pocket or sulcus (16). ii) CAL: Evaluated from the cementoenamel junction (CEJ) to the base of the pocket (16). When the gingival margin was positioned coronal to the CEJ, that distance was deducted from the probing depth. In the event that the margin was located apical to the CEJ, the value was added to it instead. This method guaranteed precise attachment level measurements in every circumstance. iii) Plaque index (PI): PI was recorded according to the criteria provided by Silness and Löe (17). iv) Papillary bleeding index (PBI): This was evaluated using the method described by Mühlemann (18).

The present study wished to determine the changes in PPD from the beginning of the trial to the review after 3 months. Changes in CAL, PI and PBI within the same time periods were also recorded as secondary outcomes.

Prior to commencing treatment, each participant provided information about their medical and dental history. This ensured that they were qualified to participate in the study. There was a comprehensive periodontal charting and a radiographic evaluation, and some first clinical images were obtained. Subsequently all patients received phase 1 periodontal therapy, which included oral hygiene instructions and both supragingival and subgingival SRP performed with ultrasonic and manual devices on the same day to achieve comprehensive biofilm destruction and reduce bacterial recolonization. Only patients who maintained satisfactory plaque control were advanced to the intervention stage.

Treatment methodology. Following phase I therapy and baseline recordings, patients were assigned to one of three treatment groups, as follows:

i) The control group: The control group received SRP alone. Patients in this group received full-mouth subgingival SRP, with no adjunctive therapy. Healing was allowed to occur by secondary intention (Fig. 2).

ii) Test group 1: SRP + HPE: Immediately following the completion of SRP, 1 ml HPE gel (Placentrex®, Albert David Ltd.) was prepared for local delivery. A sterile gelatin sponge (Abgel®) was trimmed under aseptic conditions using sterile scissors to obtain a few very small beads. These beads were transferred into a sterile dappen dish, and the HPE gel was dispensed directly onto them. The beads were left in contact with the gel to allow uniform adsorption of the extract onto their surface, thereby transforming them into medicated carriers suitable for placement. The medicated beads were then carefully inserted into the affected sites. A P-filling instrument (Plastic filling instrument, PF21; GDC Fine Crafted Dental) was used to place the beads into the pocket, with a

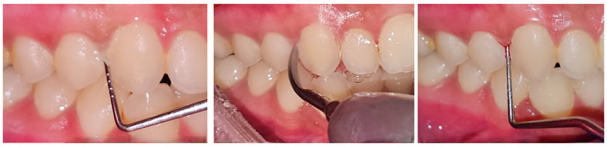

Figure 2. Control group (scaling and root planing only). Clinical images of a representative patient (32 years old, male, diagnosed with stage III, grade B periodontitis) illustrating the treated periodontal site immediately following conventional non-surgical therapy. (Left panel) Measurement of probing pocket depth at the affected site using a periodontal probe, (middle panel) scaling and root planing procedure being performed using a curette, (right panel) post-debridement assessment of the periodontal pocket using a probe.

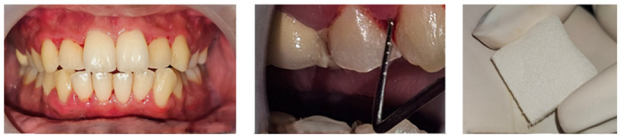

Figure 3. Preparation of HPE gel and gelatin sponge (Abgel) beads under aseptic conditions for the HPE group. Clinical images of a representative patient (38 years old, male, diagnosed with stage III, grade B periodontitis). (Left panel) Pre-operative clinical view of the affected site, (middle panel) measurement of probing pocket depth at the treatment site using a periodontal probe, (right panel) sterile gelatin sponge (Abgel) prepared and trimmed into small beads for use as a carrier for HPE gel. HPE, human placental extract.

periodontal probe helping to guide them to the deepest part of the sulcus. Following placement, a Coe-Pak periodontal dressing (COE-PAK™, cat. no. 135001; GC America Inc.) was applied to protect and retain the material. The dressing was removed at the 7-day recall visit once early healing had taken place (5) (Figs. 3-5).

iii) Test group 2: SRP + diode laser: Following SRP, diode laser therapy was performed at baseline using a 970 nm diode laser unit (Dentsply Sirona) operating in continuous wave mode at a power output of 1 W. Laser energy was delivered through a 320 μm fiber-optic tip, corresponding to a spot area of ~0.0008 cm^2. Each periodontal site was irradiated for 20 sec, delivering ~20 J of total energy, corresponding to an energy density of ~$2.5x10^4$ J/cm^2.

Prior to each procedure, the fiber tip was inspected and calibrated according to the manufacturer's recommendations to ensure consistent energy delivery. Following local anesthesia, the fiber was inserted parallel to the root surface and advanced to ~1 mm short of the pocket base, after which it was moved in slow apico-coronal sweeping motions along the inner wall of the periodontal pocket. To minimize thermal accumulation, irradiation was performed in 5-sec cycles with 2-3 sec intervals between applications. Protective eyewear was worn by both the patient and operator throughout the procedure. Of note, two additional laser applications were performed on days 3 and 7 using the same settings to maintain consistency across sessions (6) (Fig. 6).

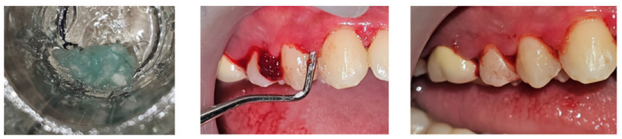

Figure 4. Placement of HPE-impregnated Abgel beads into the periodontal pocket using a P-instrument for localized drug delivery in the HPE group. Clinical images of a representative patient (38 years old, male, diagnosed with stage III, grade B periodontitis). (Left panel) Preparation of HPE-impregnated gelatin sponge (Abgel) beads in a sterile dappen dish, (middle panel) placement of the medicated beads into the periodontal pocket using a P-filling instrument, (right panel) immediate post-placement view of the treated site. HPE, human placental extract.

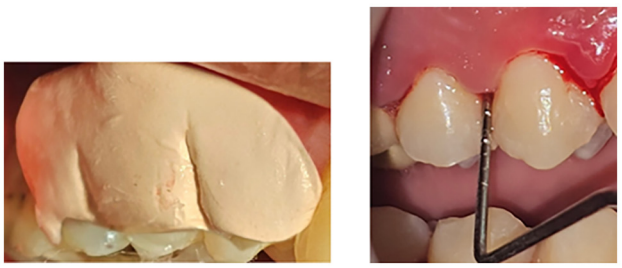

Figure 5. Application of Coe-Pak periodontal dressing over the treated site in the HPE group to secure the medicated carriers and protect the area during initial healing. Clinical images of a representative patient (38 years old, male, diagnosed with stage III, grade B periodontitis). (Left panel) Placement of Coe-Pak periodontal dressing over the treated site following insertion of HPE-impregnated beads, (right panel) post-operative assessment of the treated site using a periodontal probe. HPE, human placental extract.

Post-treatment care. All patients were instructed to rinse twice daily with 0.2% chlorhexidine gluconate (Hexidine®, ICPA Health Products Ltd.) for 2 weeks (16).

In the HPE group, a periodontal dressing (Coe-Pak) covered the treated site; thus, mechanical brushing was delayed until day 7. During this time, plaque control depended entirely on chlorhexidine rinsing. In the laser and control groups, gentle brushing with a soft-bristled toothbrush was resumed the following day. Oral hygiene instructions were reinforced at all follow-up visits, and deplaquing was performed if necessary. To avoid disturbing the healing tissues, no periodontal probing was performed before the one-month evaluation (16).

To minimize confounding variables, standardized plaque control protocols and oral hygiene instructions were implemented for all participants throughout the study period, ensuring that differences in clinical outcomes were primarily attributable to the adjunctive treatment modalities rather than variations in oral hygiene practices (Fig. 7).

Statistical analysis. Statistical analysis was performed using SPSS version 20.0 (IBM Corp.) (19). Data are expressed as the mean ± standard deviation and median (interquartile range), where appropriate. The normality of data distribution was assessed using the Shapiro-Wilk test. As the data did not follow a normal distribution ($P<0.05$), non-parametric tests were used for all analyses. Between-group (intergroup) comparisons, involving three independent treatment groups, were performed using the Kruskal-Wallis test at each time interval, as well as for change scores between time points. When statistically significant differences were observed, post hoc pairwise comparisons were conducted using Dunn's test with the Bonferroni correction to adjust for multiple comparisons. Within-group (intragroup) comparisons, involving repeated measurements within the same subjects across baseline, 1 and 3 months, were analyzed using the Friedman test. Where appropriate, pairwise comparisons between time points

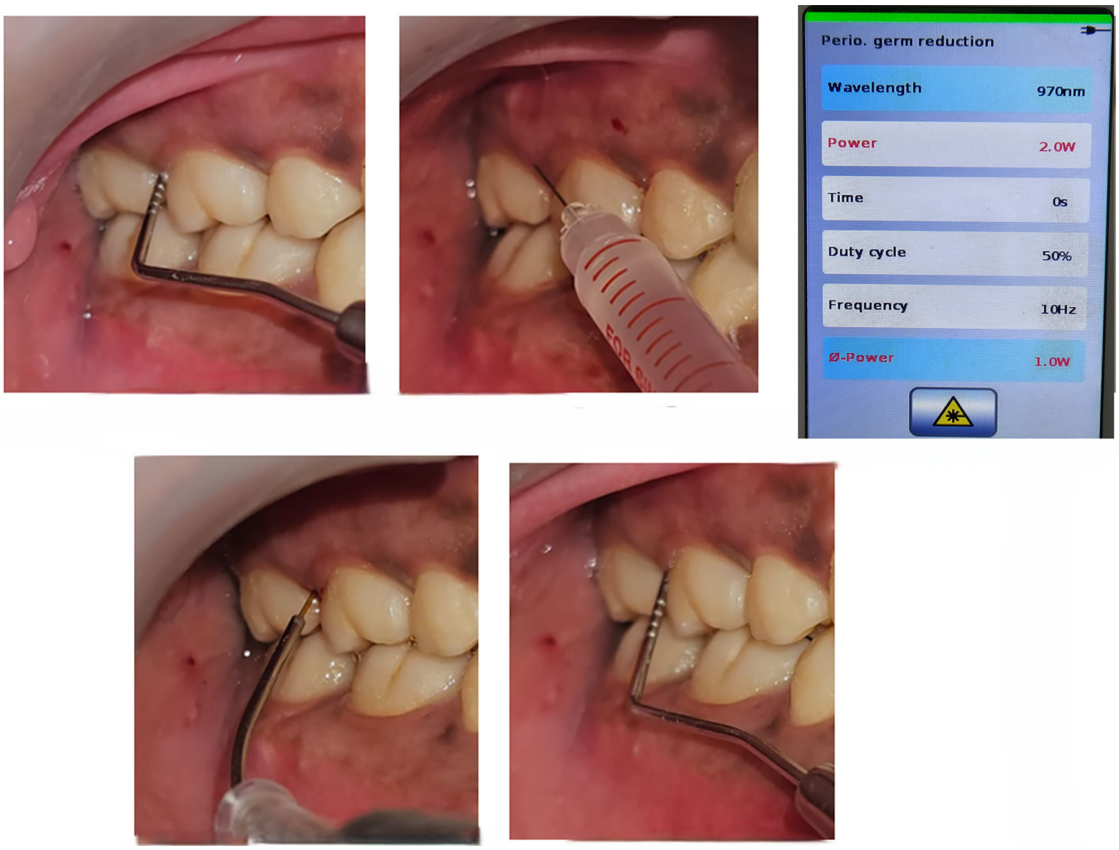

Figure 6. Application of a 970 nm diode laser in the laser group. Clinical images of a representative patient (42 years old, female, diagnosed with stage III, grade B periodontitis). (Top left panel) Measurement of probing pocket depth at the affected site using a periodontal probe, (top middle panel) administration of local anesthesia, (top right panel) display of laser settings on the device interface, (bottom left panel) laser fiber tip positioned within the periodontal pocket during treatment, (bottom right panel) post-irradiation assessment of the treated site using a periodontal probe.

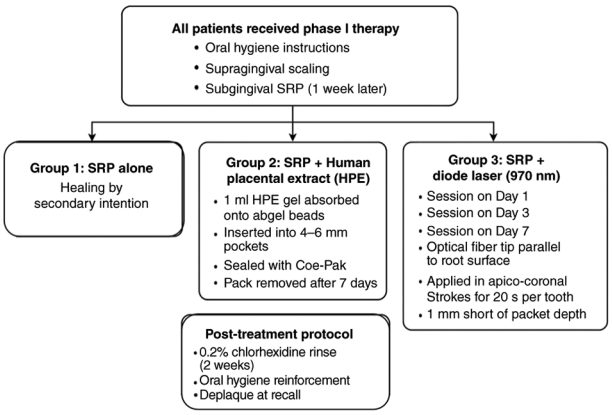

Figure 7. Summary of intervention protocols across study groups. SRP, scaling and root planning; HPE, human placental extract.

were interpreted with the Bonferroni adjustment to account for multiple testing. A P-value <0.05 was considered to indicate a statistically significant difference. Effect sizes were calculated to assess the magnitude of differences between groups.

Results

Study population and baseline characteristics. All 24 enrolled participants completed the study with no dropouts, resulting in 8 subjects per group. The mean age of the study population was 35.8±8.8 years, with a nearly equal male-female distribution. None of the participants reported systemic illness, and all were non-smokers. Baseline comparisons using the Kruskal-Wallis test revealed no statistically significant differences among the three groups for PPD (P=0.732), CAL (P=0.464), PI (P=0.676) and PBI (P=0.308), confirming that randomization produced homogeneous groups (Table I).

Changes in PPD. At baseline, there was no statistically significant difference in PPD among the three groups (P=0.732), indicating comparable initial conditions (Table II).

At 1 month, a statistically significant intergroup difference was observed (P=0.008). Post hoc pairwise comparisons using Dunn's test with the Bonferroni correction revealed significant differences between the SRP + HPE group and the SRP control group (P=0.014), as well as between the SRP + HPE group and the SRP + diode laser group (P=0.035). No statistically significant difference was observed between the control and laser groups (not significant) (Table II).

At 3 months, the intergroup difference remained statistically significant (P=0.002). Post hoc analysis demonstrated significant differences between the SRP + HPE group and the control group (P=0.007), and between the SRP + HPE group and the SRP + diode laser group (P=0.005), while no significant difference was found between the control and laser groups (not significant) (Table II).

Table I. Baseline demographic and clinical characteristics of the study population.

Parameter	HPE	Laser	SRP (control)	P-value
No. of patients	8	8	8	-
Age (years, mean ± SD)	36.5±8.11	35.0±8.8	35.75±9.48	0.944
Sex (male/female)	4/4	5/3	5/3	-
PPD (mm) baseline	4.50±1.20	4.88±0.84	4.63±0.92	0.732
CAL (mm) baseline	5.00±1.20	5.50±0.54	5.00±0.76	0.464
PI baseline	2.25±0.46	2.25±0.46	2.00±0.76	0.676
PBI baseline	2.25±0.46	2.25±0.46	1.88±0.64	0.308

SRP, scaling and root planning; HPE, human placental extract; PPD, probing pocket depth; CAL, clinical attachment level; PI, plaque index; PBI, papillary bleeding index.

Table II. Probing pocket depth at baseline, 1 and 3 months.

A, Descriptive statistics and intergroup comparisons (Kruskal-Wallis test)

Time point	Group	Mean ± SD	Median (IQR)	P-value (intergroup)	Effect size
Baseline	SRP (control)	4.625±0.916	4 (4, 5.25)	0.732	0.0271
	SRP + HPE	4.5±1.195	4.5 (3.75, 5.25)		
	SRP + diode laser	4.875±0.835	5 (4, 5.25)		
1 Month	SRP (control)	3.75±0.886	3.5 (3, 4.25)	0.008	0.4192
	SRP + HPE	2.5±0.535	2.5 (2, 3)		
	SRP + diode laser	3.625±0.916	3 (3, 4.25)		
3 Months	SRP (control)	3.5±1.069	3 (3, 4.25)	0.002	0.5589
	SRP + HPE	2±0.535	2 (2, 2)		
	SRP + diode laser	3.375±0.518	3 (3, 4)		
Δ Baseline, 3 months	SRP (control)	1.125±0.354	1 (1, 1)	0.01	0.4036
	SRP + HPE	2.5±1.069	2 (2, 3.25)		
	SRP + diode laser	1.5±0.756	2 (1, 2)		

B, Post hoc Dunn's test (Bonferroni-adjusted P-values)

Time point	Control vs. HPE	Control vs. laser	HPE vs. laser
1 Month	0.014	NS	0.035
3 Months	0.007	NS	0.005
Baseline, 3 months	0.007	0.562	0.257

Note: NS: not significant.

C, Intragroup comparisons (Friedman test)

Group	Chi-squared	df	P-value
SRP (control)	14.000	2	0.001
SRP + HPE	14.857	2	0.001
SRP + diode laser	12.667	2	0.002

SRP, scaling and root planning; HPE, human placental extract.

When comparing the reduction in PPD from baseline to 3 months, a statistically significant intergroup difference was observed (P=0.01). Post hoc analysis revealed a significant difference between the control group and the SRP + HPE

group (P=0.007), while other pairwise comparisons were not statistically significant (Table II).

Intragroup comparisons using the Friedman test demonstrated statistically significant reductions in PPD over time in all groups (SRP control: P= 0.001; SRP + HPE: P=0.001; SRP + diode laser: P=0.002) (Table II).

Descriptive analysis revealed that the mean PPD values decreased progressively from baseline to 3 months in all groups. The SRP + HPE group exhibited the greatest reduction (2.5±1.069 mm), followed by the SRP + diode laser group (1.5±0.756 mm) and the SRP control group (1.125±0.354 mm). Post hoc power analysis for PPD reduction from baseline to 3 months demonstrated a statistical power of 0.88, indicating that the study was adequately powered to detect clinically meaningful intergroup differences (Table II and Fig. 8).

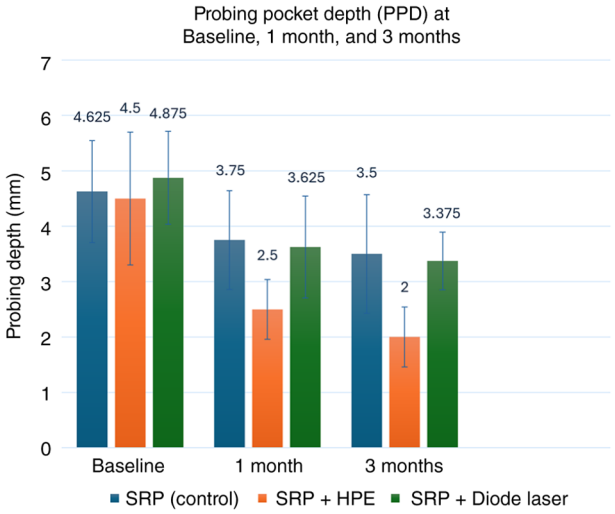

Figure 8. Bar graph demonstrating the mean ± SD probing pocket depth at baseline, 1 and 3 months for all groups. Error bars represent the standard deviation; n=8 patients per group. SRP, scaling and root planning; HPE, human placental extract.

Changes in (CAL. At baseline, there was no statistically significant difference in CAL among the three groups (P=0.464), indicating comparable initial conditions (Table III).

At 1 month, a statistically significant intergroup difference was observed (P=0.004). Post hoc pairwise comparisons using Dunn's test with the Bonferroni correction revealed significant differences between the SRP + HPE group and the SRP control group (P=0.022), as well as between the SRP + HPE group and the SRP + diode laser group (P=0.007). No statistically significant difference was observed between the control and laser groups (not significant) (Table III).

At 3 months, the intergroup difference remained statistically significant (P=0.007). Post hoc analysis demonstrated significant differences between the SRP + HPE group and the control group (P=0.026), and between the SRP + HPE group and the SRP + diode laser group (P=0.014), while no significant difference was found between the control and laser groups (not significant) (Table III).

When comparing the gain in CAL from baseline to 3 months, a statistically significant intergroup difference was observed (P=0.01). Post hoc analysis revealed a significant difference between the control group and the SRP + HPE group (P=0.007), while other pairwise comparisons were not statistically significant (Table III).

Intragroup comparisons using the Friedman test demonstrated statistically significant improvements in CAL over time in all groups (SRP control: P=0.001; SRP + HPE: P=0.001; SRP + diode laser: P=0.002) (Table III).

Descriptive analysis revealed that the mean CAL values were comparable at baseline (SRP: 5.00±0.756 mm; SRP + HPE: 5.00±1.195 mm; SRP + diode laser: 5.50±0.535 mm). At 1 month, reductions were observed in all groups, with the greatest improvement in the SRP + HPE group (3.00±0.756 mm), followed by the SRP control group (4.125±0.641 mm) and the SRP + diode laser group (4.25±0.463 mm). At 3 months, further improvements were noted (SRP: 3.875±0.991 mm; SRP + HPE: 2.50±0.926 mm; SRP + diode laser: 4.00±0.535 mm). The mean gain from baseline to 3 months was highest in the SRP + HPE group (2.50±1.069 mm), compared to the SRP + diode laser group (1.50±0.756 mm) and the SRP control group (1.125±0.354 mm). Post hoc power analysis for CAL reduction from baseline to 3 months demonstrated a statistical power of 0.88, indicating adequate ability of the study to detect clinically meaningful differences among the groups (Table III and Fig. 9).

Changes in PI. At baseline, there was no statistically significant difference in the PI among the three groups (P=0.676), indicating comparable initial conditions (Table IV).

At 1 month, no statistically significant intergroup difference was observed (P=0.600). Post hoc pairwise comparisons using Dunn's test with the Bonferroni correction confirmed the absence of significant differences between any groups (all P>0.05) (Table IV).

At 3 months, intergroup comparisons remained statistically non-significant (P=0.649), with no significant pairwise differences observed (all P>0.05) (Table IV).

When comparing the change in plaque index from baseline to 3 months, no statistically significant intergroup difference was observed (P= .481), and post hoc comparisons also did not reveal any significant differences between groups (Table IV).

Intragroup comparisons using the Friedman test demonstrated statistically significant reductions in plaque index over time in all groups (SRP control: P=0.004; SRP + HPE: P=0.001; SRP + diode laser: P=0.002) (Table IV).

Descriptive analysis revealed that the mean plaque scores decreased from baseline to 3 months in all groups. At baseline, values were comparable across groups (SRP: 2.00±0.756; SRP + HPE: 2.25±0.463; SRP + diode laser: 2.25±0.463). At 1 and 3 months, reductions were observed in all groups, with no clinically meaningful differences between them. Post hoc power analysis for plaque index changes demonstrated a statistical power of 0.20, indicating limited ability of the study to detect intergroup differences for this parameter (Table IV and Fig. 10).

Changes in PBI. At baseline, there was no statistically significant difference in the PBI among the three groups (P=0.308), indicating comparable initial conditions (Table V).

At 1 month, no statistically significant intergroup difference was observed (P=0.141). Post hoc pairwise comparisons

Table III. Mean ± SD clinical attachment level (CAL) at baseline, 1 and 3 months.

A, Descriptive statistics and intergroup comparisons (Kruskal-Wallis test)

Time point	Group	Mean ± SD	Median (IQR)	P-value (intergroup)	Effect size
Baseline	SRP (control)	5.00±0.756	5 (4.75, 5.25)	0.464	0.0668
	SRP + HPE	5.00±1.195	5.5 (4, 6)		
	SRP + diode laser	5.50±0.535	5.5 (5, 6)		
1 Month	SRP (control)	4.125±0.641	4 (4, 4.25)	0.004	0.478
	SRP + HPE	3.00±0.756	3 (2.75, 3.25)		
		SRP + diode laser	4 (4, 4.25)		
3 Months	SRP (control)	3.875±0.991	4 (3.75, 4.25)	0.007	0.433
	SRP + HPE	2.50±0.926	2.5 (2, 3)		
		SRP + diode laser	4 (4, 4)		
Δ Baseline, 3 months	SRP (control)	1.125±0.354	1 (1, 1)	0.01	0.4036
	SRP + HPE	2.50±1.069	2 (2, 3.25)		
		SRP + diode laser	2 (1, 2)		

B, Post hoc Dunn's test (Bonferroni-adjusted P-values)

Time point	Control vs. HPE	Control vs. laser	HPE vs. laser
1 Month	0.022	NS	0.007
3 Months	0.026	NS	0.014
Baseline, 3 months	0.007	0.562	0.257

Note: NS: not significant.

C, Intragroup comparisons (Friedman test)

Group	Chi-squared	df	P-value
SRP (control)	14.000	2	0.001
SRP + HPE	14.857	2	0.001
SRP + diode laser	12.667	2	0.002

SRP, scaling and root planning; HPE, human placental extract.

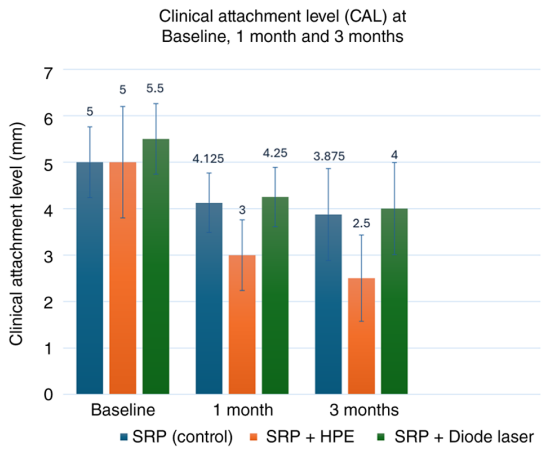

Figure 9. Bar graph demonstrating the mean ± SD clinical attachment level at baseline, 1, and 3 months for all groups. Error bars represent the standard deviation; n=8 patients per group. SRP, scaling and root planning; HPE, human placental extract.

using Dunn's test with the Bonferroni correction confirmed that there were no statistically significant differences between any groups (all P>0.05) (Table V).

At 3 months, intergroup comparisons remained statistically non-significant (P=0.130), with no significant pairwise differences observed (all P>0.05) (Table V).

However, when comparing the change in PBI from baseline to 3 months, a statistically significant intergroup difference was observed (P=0.044). Post hoc analysis did not demonstrate statistically significant pairwise differences after Bonferroni correction (all P>0.05) (Table V).

Intragroup comparisons using the Friedman test demonstrated statistically significant reductions in PBI over time in all groups (SRP control: P=0.004; SRP + HPE: P=0.001; SRP + diode laser: P=0.002) (Table V).

Descriptive analysis revealed that mean PBI values decreased from baseline to 3 months in all groups. At baseline, values were comparable across groups (SRP: 1.875±0.641;

Table IV. Plaque index (PI) at baseline, 1, and 3 months.

A. Descriptive Statistics and Intergroup Comparison (Kruskal-Wallis Test)

Time point	Group	Mean ± SD	Median (IQR)	P-value (intergroup)	Effect size
Baseline	SRP (control)	2.00±0.756	2 (1.75, 2.25)	0.676	0.0341
	SRP + HPE	2.25±0.463	2 (2, 2.25)		
	SRP + diode laser	2.25±0.463	2 (2, 2.25)		
1 Month	SRP (Control)	1.375±0.518	1 (1, 2)	0.600	0.0444
	SRP + HPE	1.25±0.463	1 (1, 1.25)		
	SRP + diode laser	1.50±0.535	1.5 (1, 2)		
3 Months	SRP (Control)	1.125±0.641	1 (1, 1.25)	0.649	0.0377
	SRP + HPE	1.125±0.641	1 (1, 1.25)		
	SRP + diode laser	1.375±0.518	1 (1, 2)		
Δ Baseline, 3 months	SRP (Control)	0.875±0.354	1 (1, 1)	0.481	0.0636
	SRP + HPE	1.125±0.641	1 (1, 1.25)		
	SRP + diode laser	0.875±0.354	1 (1, 1)		

B, Post hoc Dunn's test (Bonferroni-adjusted P-values)

Time point	Control vs. HPE	Control vs. laser	HPE vs. laser
1 Month	NS	NS	0.936
3 Months	NS	NS	1.000
Baseline, 3 months	0.884	NS	0.884

Note: NS: not significant.

C, Intragroup comparisons (Friedman test)

Group	Chi-squared	df	P-value
SRP (control)	11.143	2	0.004
SRP + HPE	13.455	2	0.001
SRP + diode laser	12.286	2	0.002

SRP, scaling and root planning; HPE, human placental extract.

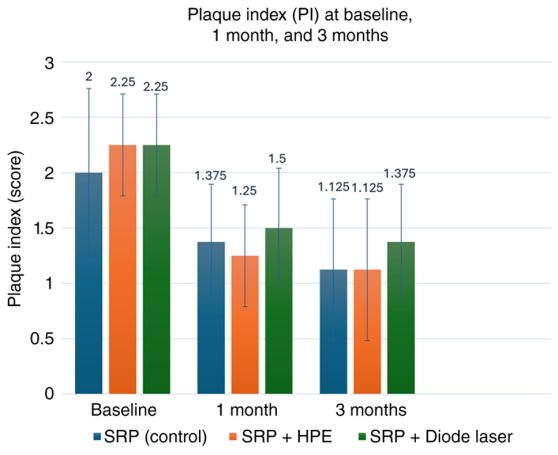

Figure 10. Bar graph demonstrating the mean ± SD plaque index at baseline, 1, and 3 months for all groups. Error bars represent the standard deviation; n=8 patients per group. SRP, scaling and root planning; HPE, human placental extract.

SRP + HPE: 2.25±0.463; SRP + diode laser: 2.25±0.463). At 1 and 3 months, reductions were observed in all groups, with the greatest improvement observed in the SRP + HPE group. Post hoc power analysis for PBI changes demonstrated a statistical power of 0.49, indicating a moderate ability of the study to detect intergroup differences for this parameter (Table V and Fig. 11).

Overall clinical improvement. To facilitate the comparisons of treatment outcomes, changes in PPD, CAL and PBI from baseline to 3 months were combined for comparative assessment (Table VI and Figs. 12-14).

The SRP + HPE group demonstrated the greatest overall improvement across key clinical parameters, followed by the SRP + diode laser group, with the SRP alone group exhibiting the least improvement. This trend is consistent with the observed intergroup differences in PPD and CAL, where the HPE group showed statistically superior outcomes.

Table V. Papillary bleeding index at baseline, 1 and 3 months.

A, Descriptive statistics and intergroup comparisons (Kruskal-Wallis test)

Time point	Group	Mean ± SD	Median (IQR)	P-value (intergroup)	Effect size
Baseline	SRP (control)	1.875±0.641	2 (1.75, 2)	0.308	0.1025
	SRP + HPE	2.25±0.463	2 (2, 2.25)		
	SRP + diode laser	2.25±0.463	2 (2, 2.25)		
1 Month	SRP (control)	1.25±0.707	1 (1, 2)	0.141	0.1701
	SRP + HPE	1.00±0.00	1 (1, 1)		
	SRP + diode laser	1.50±0.535	1.5 (1, 2)		
3 Months	SRP (control)	1.00±0.756	1 (0.75, 1.25)	0.130	0.1775
	SRP + HPE	0.75±0.463	1 (0.75, 1)		
	SRP + diode laser	1.375±0.518	1 (1, 2)		
Δ Baseline, 3 months	SRP (control)	0.875±0.354	1 (1, 1)	0.044	0.2723
	SRP + HPE	1.50±0.756	1 (1, 2)		
	SRP + diode laser	0.875±0.354	1 (1, 1)		

B, Post hoc Dunn's test (Bonferroni-adjusted P-values)

Time point	Control vs. HPE	Control vs. laser	HPE vs. laser
1 Month	0.795	NS	0.146
3 Months	NS	0.703	0.134
Baseline, 3 months	0.091	NS	0.091

Note: NS: not significant.

C, Intragroup comparisons (Friedman test)

Group	Chi-squared	df	P-value
SRP (control)	11.143	2	0.004
SRP + HPE	15.077	2	0.001
SRP + diode laser	12.286	2	0.002

SRP, scaling and root planning; HPE, human placental extract.

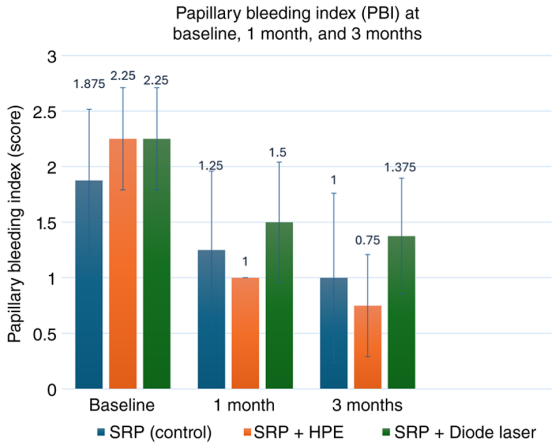

Figure 11. Bar graph demonstrating the mean ± SD reduction in probing pocket depth from baseline to 3 months for all groups. Error bars represent the standard deviation; n=8 patients per group. SRP, scaling and root planning; HPE, human placental extract.

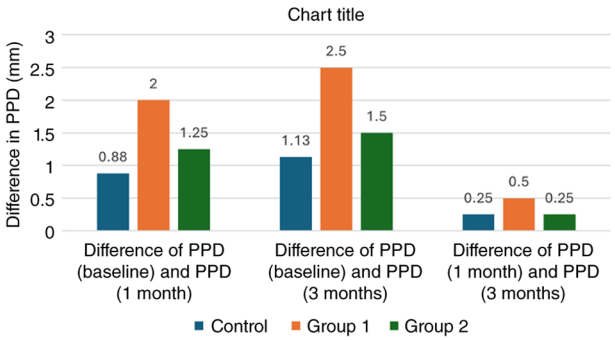

Figure 12. Bar graph demonstrating the mean improvement in the key parameter (PPD) at 3 months for all treatment groups. PPD, probing pocket depth; SRP, scaling and root planning; HPE, human placental extract.

Both adjunctive therapies enhanced clinical outcomes beyond those achieved by SRP alone. The SRP + HPE group

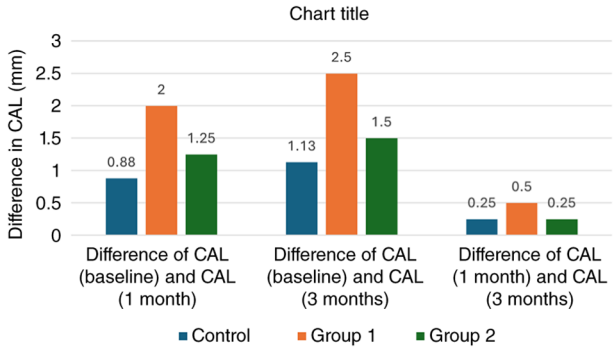

Figure 13. Bar graph demonstrating the mean improvement in the key parameter (CAL) at 3 months for all treatment groups. CAL, clinical attachment level; SRP, scaling and root planning; HPE, human placental extract.

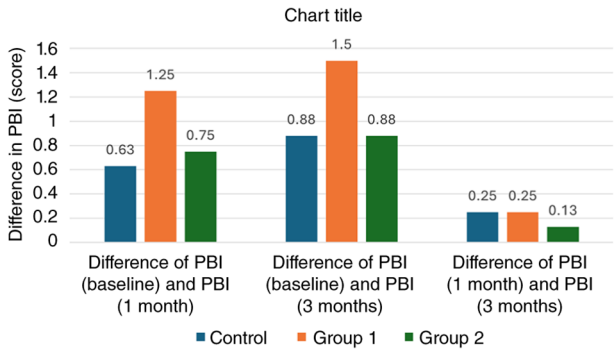

Figure 14. Bar graph demonstrating the mean improvement in key parameter (PBI) at 3 months for all treatment groups. PBI, papillary bleeding index; SRP, scaling and root planning; HPE, human placental extract.

demonstrated greater reduction in probing depth, improved attachment gain and numerically greater reduction in bleeding scores. The SRP + diode laser group also exhibited measurable clinical benefits, consistent with previous studies on its role in periodontal therapy (6,7,20).

These findings support the concept that biologically active agents may provide stronger regenerative benefits compared to photobiomodulation alone (3,5,20-22). No patient in any group reported adverse effects or post-treatment complications.

Discussion

The present study investigated two supplementary methods, HPE and a 970 nm diode laser, utilized alongside routine SRP for localized chronic periodontitis. As expected, SRP alone resulted in clinical improvement; however, the addition of either adjunctive therapy produced superior outcomes. Among the three groups, the greatest overall improvement was observed in the HPE group. It resulted in greater reductions in probing depth, higher attachment gains, and a numerically greater reduction in bleeding indices (23). The diode laser also demonstrated clinical benefits, although these were less pronounced compared to HPE.

The positive response to HPE can be explained by its biological characteristics. HPE contains a variety of biologically active components, including growth factors, peptides, nucleotides, amino acids and cytokines. Several growth-promoting molecules, such as epidermal growth factor, fibroblast growth factor and transforming growth factor-β have been reported in placental derivatives and are known to play critical roles in tissue regeneration. These factors stimulate fibroblast proliferation, enhance collagen synthesis, promote angiogenesis and facilitate extracellular matrix remodeling. Additionally, placental extracts exhibit anti-inflammatory and antioxidant properties, which may reduce the production of pro-inflammatory cytokines within periodontal tissues. The combined regenerative and anti-inflammatory effects may contribute to the greater clinical attachment gain and reduction in bleeding observed in the HPE group. In their study, Sharma *et al* (5) also reported that HPE performed effectively as an adjunct to SRP, with greater reduction in PPD and improved attachment gain compared to SRP alone. The early reduction in bleeding observed in the HPE group may reflect the anti-inflammatory properties of the extract. Previous research has demonstrated that placental derivatives reduce pro-inflammatory cytokine levels and restore antioxidant balance, which may explain the more consistent healing response observed in this study (3,23).

The diode laser group also demonstrated improved outcomes compared with SRP alone, which is consistent with previous reports on diode laser therapy (6,21,24). The therapeutic effects of diode lasers in periodontal therapy are mainly attributed to their photothermal and photobiomodulatory actions. At wavelengths of ~970 nm, laser energy is readily absorbed by pigmented tissues and hemoglobin, allowing effective bacterial reduction within the periodontal pocket. In addition to its antimicrobial effect, low-level laser irradiation can stimulate mitochondrial activity in host cells, increasing adenosine triphosphate production and enhancing cellular metabolism. This photobiomodulation promotes fibroblast proliferation, collagen synthesis, and improved microcirculation, thereby accelerating tissue repair and reducing inflammatory responses. These mechanisms may explain the improved probing depth reduction observed in the laser group compared with SRP alone. However, the magnitude of improvement was lower than that observed in the HPE group, possibly due to the relatively transient nature of the photobiomodulatory effects (24).

Plaque scores remained comparable across all groups throughout the study period. This suggests that the observed clinical improvements were attributable to the adjunctive therapies rather than differences in oral hygiene practices. Previous studies have similarly demonstrated that appropriately selected adjuncts can enhance the outcomes of SRP (20,22).

The S3 clinical recommendations from the European Federation of Periodontology state that SRP remains the gold standard for non-surgical periodontal therapy, while adjunctive modalities may provide additional benefits in selected cases (20). The effectiveness of laser therapy may vary depending on parameters, such as wavelength, energy settings, clinical environment and operator skill, which may explain the variability in reported outcomes across studies. A recent study indicated that diode lasers can reduce bleeding and probing depth, although the magnitude of improvement is often limited (25).

Table VI. Mean change (Δ) in key parameters from baseline to 3 months.

Group	ΔPPD (mm) (mean ± SD)	ΔCAL (mm) (mean ± SD)	ΔPBI (mean ± SD)	Rank (overall)
SRP + HPE	2.5±1.069	2.5±1.069	1.5±0.756	1st
SRP + diode laser	1.5±0.756	1.5±0.756	0.875±0.354	2nd
SRP (control)	1.125±0.354	1.125±0.354	0.875±0.354	3rd

SRP, scaling and root planning; HPE, human placental extract.

Cost and accessibility also influence clinical applicability. Laser devices may be costly and less accessible in certain clinical settings. By contrast, HPE is relatively cost-effective, biologically compatible and easy to apply. There is growing interest in biologically active adjuncts that promote tissue regeneration rather than solely mechanical debridement (3,26). HPE represents a promising option in this context, as it combines conventional non-surgical therapy with biologically driven regenerative support. Future research is required to explore the combined use of both modalities to evaluate potential synergistic effects.

The present study had certain limitations which should be mentioned. The findings of the present study should be interpreted within the context of its design. This investigation was conducted as a preliminary clinical study aimed at exploring the potential benefits of HPE gel and diode laser therapy as adjuncts to SRP. Although statistically significant improvements were observed, the relatively modest sample size may limit the generalizability of the results. Future randomized clinical trials including larger cohorts (≥30 participants per group) would help further validate these observations. In addition, the 3-month follow-up period primarily reflects the early phase of periodontal healing, and longer observation periods of 6-12 months would be valuable for assessing the long-term stability of treatment outcomes. The present study employed a single-blinded design, and while examiner calibration was performed to ensure measurement reliability, the possibility of minor observational bias cannot be completely excluded. Furthermore, the present study focused mainly on clinical parameters. Future studies may incorporate microbiological assessments, inflammatory biomarker evaluation, and patient-reported outcome measures to provide deeper insight into the biological mechanisms underlying treatment response. Despite these considerations, the present study provides preliminary clinical evidence supporting the adjunctive potential of HPE gel and diode laser therapy in non-surgical periodontal management, which may serve as a foundation for further research in this area.

In conclusion, in the context of the present study, adjunctive application of HPE in conjunction with SRP produced the most favorable clinical outcomes, including greater reduction in probing pocket depth and improved clinical attachment gain. Diode laser therapy also demonstrated clinical benefits compared with SRP alone, although the magnitude of improvement was lower than that observed with HPE. SRP alone resulted in expected clinical improvement but did not show the additional benefits observed with adjunctive therapies. Within the limitations of this study, HPE appears to be a promising adjunctive modality for non-surgical periodontal therapy. Further long-term studies with larger sample sizes are required before these findings can be generalized to routine clinical practice.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

SS contributed to the conceptualization of the study, in the study methodology, data collection, investigation, statistical analysis, and the drafting of the manuscript. DK contributed to the conceptualization of the study, the study supervision, data validation, data interpretation, and the critical revision of the manuscript. NJS contributed to the study methodology, study supervision, resource provision, data validation, and the critical review of the final version of the manuscript. SS and DK confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

The study protocol was approved by the Institutional Ethics Committee of Manipal College of Dental Sciences Mangalore, Manipal Academy of Higher Education, Mangalore, India (Protocol ref. no. 24086; dated July 13, 2024). The clinical trial was prospectively registered with the Clinical Trials Registry of India (CTRI/2025/10/096493). Written informed consent was obtained from all participants prior to study inclusion. All procedures were conducted in accordance with the Declaration of Helsinki (2013 revision).

Patient consent for publication

Written informed consent for the publication of clinical details and images was obtained from all participants.

Competing interests

The authors declare that they have no competing interests.

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