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The Clinical and Biochemical Effects of Er,Cr:YSGG Laser as an adjunct to Scaling and Root Planing in Management of Chronic Periodontitis

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Introduction: Chronic periodontitis, a widespread inflammatory condition, compromises the supporting structures of teeth through the progressive destruction of the periodontal ligament and alveolar bone. This damage is primarily initiated by the buildup of bacterial biofilm on tooth surfaces, triggering a host immune response that leads to tissue deterioration. While scaling and root planing (SRP) are standard treatments, there is a need to explore adjunctive therapies that can enhance these outcomes. The laser therapy both soft tissue lasers and hard tissue lasers, has shown promise in enhancing the outcomes of SRP by targeting and reducing bacterial biofilm more efficiently. But however, the biochemical parameters such as inflammatory markers and enzymes involved in tissue destruction after application of Er,Cr: YSGG laser remains unexplored. Aim: The objective of the study was to investigate the additional benefits of incorporating the Erbium, chromium-doped yttrium, scandium, gallium and garnet laser (Er,Cr: YSGG laser) with traditional scaling and root planing (SRP) in the treatment of chronic periodontitis. Specifically, this research seeks to evaluate how the laser impacts biochemical markers indicative of inflammation and tissue destruction along with clinical outcomes such as pocket depth reduction and attachment level gains. By examining these parameters, the study aims to provide a comprehensive assessment of the effectiveness of the Er,Cr:YSGG laser as a supplementary treatment modality, potentially leading to improved therapeutic strategies for managing chronic periodontitis. Materials and Methods: The study was performed at Saveetha Dental College, in Chennai, Tamil Nadu, India. The study was conducted for a duration of 3 months from November 2023 to February 2024.Thirty patients who were diagnosed with chronic periodontitis were included in the study. They were divided into two groups. The first group included fifteen patients who were subjected to scaling and root planing (SRP) alone. The second group included fifteen patients who were treated with Er,Cr:YSGG laser as an adjunct to scaling and root planing. Clinical parameters like clinical attachment level(CAL), periodontal probing depth(PPD) were assessed at baseline and 3 months after the non surgical periodontal therapy. Biochemical parameter C-reactive protein levels were evaluated at baseline and 3 months after periodontal therapy. Statistical analysis was done using IBM SPSS Statistics for

Windows, version 23. Intergroup analysis was done using independent t-test and intra-group analysis was done using a paired t-test. Statistical significance was set at a p-value of less than 0.05. Results: The mean probing depth scores were 5.69 ± 0.04 mm and 5.69 ± 0.35 mm in the SRP group and Er,Cr:YSGG laser group respectively at baseline. The periodontal probing depth scores were 5.01 ± 0.02 mm and 3.80 ± 0.58 in the SRP group and Er, Cr:YSGG laser group respectively after 3 months. There was a statistically significant difference between SRP and SRP with Er,Cr:YSGG group at the end of 3 months with a p value of 0.01*. The mean clinical attachment level scores were 7.55 ± 0.02 mm and 7.56 ± 0.03 mm in the SRP group and Er,Cr:YSGG laser group respectively at baseline. The CAL scores were 6.97 ± 0.08 mm and 5.96 ±0.52 mm in the SRP and Er,Cr:YSGG laser groups respectively at the end of 3rd month indicating a statistically significant difference between the intervened group and the control group with a p-value of 0.03*. The mean CRP levels were 2.41 ± 0.05 ng/ml and 2.41 ± 0.36 ng/ml in the SRP and Er,Cr:YSGG laser groups respectively in the baseline. The CRP levels were 2.42 ± 0.40 ng/ml and 2.18 ± 0.12 ng/ml in the SRP and Er,Cr:YSGG laser group respectively at the end of 3 months which was statistically significant with a p-value of 0.04*. Conclusion: The integration of Er, Cr: YSGG laser therapy as an adjunct to traditional scaling and root planing (SRP) has demonstrated significant clinical and biochemical benefits in the management of periodontal disease. This combination therapy showed marked reduction in biochemical marker of inflammation, indicating a systemic anti-inflammatory effect. Additionally clinical parameters also demonstrated reduced probing depths and enhanced attachment levels, compared to SRP alone. These findings suggest that the Er, Cr: YSGG laser enhances the effectiveness of SRP, promoting better periodontal health and potentially offering a more comprehensive approach to periodontal therapy.

Keywords: non-surgical periodontal therapy, C-reactive protein, Erbium lasers, Clinical attachment level, Periodontal probing depth.

1. Introduction

Periodontitis is a complex inflammatory disease triggered by bacteria, causing progressive damage to the supporting structures of teeth, which includes bone loss and attachment breakdown [1]. The main focus of periodontitis treatment involves eliminating the causative factors such as bacterial biofilm, smear layer, and subgingival deposits. This promotes the restoration of healthy periodontal attachment to the disease-free cementum [2]. Conventional non-surgical periodontal therapy subgingival scaling and root planing (SRP) performed manually are efficacious but mostly being insufficient, particularly in advanced periodontal disease. Previous literature suggests that surgical periodontal therapy is more efficacious than SRP specifically for pockets measuring six millimeters or deeper[3].

Traditional periodontal therapy involves subgingival instrumentation, which may include the application of antibiotics administered systemically or locally, mouthwashes and lasers either alone or in combination. Patients undergoing standard periodontal therapy along with an additional treatment modality have shown greater reductions in bacterial levels and improved clinical healing outcomes [4]. These adjunctive products aim to enhance clinical outcomes and potentially prevent the need for surgical intervention leading to a comprehensive mangament of chronic periodontitis.

Laser therapy is proposed as a beneficial approach for non-surgical periodontal treatment, offering advantages such as shorter treatment duration, improved patient compliance, bacteriolytic effects, and potentially reducing the necessity for flap surgery [5]. This suggests that laser therapy might be more effective in addressing deeper periodontal pockets compared

to conventional non-surgical methods. However, there is limited scientific evidence supporting these assertions [6,7]. Furthermore, variations in types of laser, power settings, energy configurations, and therapeutic regimen pose challenges for comparing studies and drawing definitive conclusions regarding the overall efficacy of laser therapy for periodontitis [8].

The American Academy of Periodontology conducted a thorough Best Evidence Consensus (BEC) systematic review to evaluate the current literature on laser therapy for periodontitis treatment [9]. According to their findings, laser therapy, in conjunction with traditional periodontal treatment, may provide a small incremental gain in clinical outcomes compared to non-surgical periodontal treatment alone for moderate to severe chronic forms of periodontitis. This benefit translates to a reduction of less than one millimeter in probing pocket depth and clinical attachment level.

In the field of periodontics, there is a widely embraced understanding that erbium lasers can be competently employed for both non-surgical and surgical periodontal interventions while reducing the occurrence of significant side effects or complications [10]. Erbium lasers, exemplified by the erbium, chromium-doped yttrium, scandium, gallium and garnet (Er, Cr:YSGG) laser with a wavelength of 2780 nm and the erbium-doped yttrium-aluminium-garnet (Er:YAG) laser with a wavelength of 2940 nm, have showcased their efficacy in non-surgical and surgical periodontal therapy due to their capacity to induce minimal thermal effects, penetrate tissues shallowly, cause limited tissue trauma and provoke a subtle inflammatory reaction, consequently promoting rapid wound healing [11].

From a biochemical point of view, periodontal disease is characterized by quantitative changes in the concentration of biomarkers which signify inflammation of the diseased area [12]. C-reactive protein (CRP) is a pentameric plasma protein found in both vertebrates and many invertebrates[13]. It plays a crucial role in the body's systemic response to inflammation, serving as a significant biomarker in medical research. Numerous studies have demonstrated a positive link between chronic periodontitis and elevated serum CRP levels [14][15]. This association is biologically plausible due to the release of inflammatory mediators such as interleukin-1(IL-1), interleukin-6 (IL-6), and tumor necrosis factor alpha (TNF-α) during periodontitis, which can stimulate hepatocytes to produce CRP. This connection underscores the role of CRP as a potential indicator in medical research focused on periodontal health and systemic inflammation. Thus, the aim of this study is to assess the application of Er,Cr:YSGG laser used adjunctively with SRP and compare with conventional SRP, to evaluate the laser's potential to reduce inflammation and promote tissue regeneration by evaluating the C-reactive protein levels in gingival crevicular fluid and to assess the clinical parameters like clinical attachment level (CAL); probing depth (PD) in Chronic periodontitis patients. By assessing periodontal parameters and inflammatory markers, the research seeks to elucidate the potential advantages of this combined approach, providing insights into its effectiveness in improving periodontal health and contributing to the development of more comprehensive treatment protocols.

2. Materials and Methods

Study Population

The research was conducted at the Department of Periodontics, Saveetha Dental College in Chennai, Tamil Nadu, India. The study protocol obtained approval from the Institutional Ethical Committee at Saveetha Dental College in Chennai, with the ethical clearance number IHEC/SDC/PERIO-2102/23/078. Before participating, all individuals provided informed and comprehensive consent. The study included 30 patients who were diagnosed with chronic periodontitis. The sample size was determined using G power 3.0 software, aiming for 80% statistical power. Group A, consisted of fifteen individuals who received subgingival scaling and root planing (SRP) and were instructed to maintain regular oral hygiene practices along with scaling. Group B, included fifteen participants who underwent Er,Cr:YSGG laser application as an adjunct to SRP.

Inclusion and Exclusion Criteria

The inclusion criteria were as follows: 1)systemically healthy patients; 2) individuals with generalized or localized chronic periodontitis, possessing a minimum of 20 teeth, having at least 3 sites with probing depth (PD) $\geq$ 5 mm [16]; 3) patients aged 30-50 years of age in good general health; The exclusion criteria were: 1) individuals who are chronic smokers; 2) individuals who have systemic diseases impacting the periodontium such as diabetes mellitus and cardiovascular disease; 3) individuals who take medications which are known to induce gingival enlargements like amlodipine, cyclosporine, phenytoin; 4) pregnant women were excluded.

Clinical Protocols

Scaling and Root Planing

Each patient received initial periodontal therapy, which commenced with full-mouth supragingival scaling during their first appointment. At the subsequent treatment session (after 7 days), full-mouth subgingival scaling and root planing (SRP) were performed using universal curettes 2R & 2L and 4R & 4L (Hu-Friedy) and a ultrasonic handpiece with piezoelectric technology, administered under local anesthesia with 2% lidocaine containing 1:100,000 epinephrine. The SRP procedures concluded when the operator determined that the surfaces of root were sufficiently smooth and thoroughly debrided, assessed using a William's probe (Figure 1a,1b,1c).

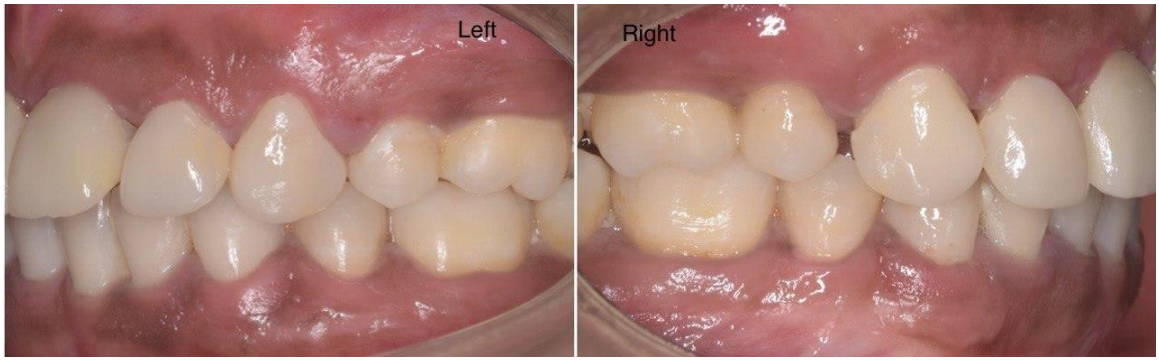

FIGURE 1a: Pre operative picture of left lateral and right lateral side before scaling and root planing in SRP group showing inflammation.

FIGURE 1b: Intra operative picture of left lateral and right lateral side in scaling and root planing group showing thorough instrumentation of the root surface with universal curette (2R,2L and 4R,4L).

FIGURE 1c: Post operative picture of left lateral and right lateral side in scaling and root planing group showing complete removal of calculus, plaque and biofilm from the root surfaces and periodontal pockets.

Er, Cr:YSGG laser as an adjunct to SRP

In this investigation, an Er,Cr:YSGG laser device (Waterlase, Biolase, USA) was utilized,

emitting photons at a wavelength of 2780 nm with the duration of the pulse ranging from 140 to 200 microseconds and a frequency of 20 Hz [17]. Initially, standard SRP is performed using ultrasonic and hand instruments to remove plaque, calculus, and biofilm from tooth surfaces and periodontal pockets. Following SRP, the Erbium Chromium, YSGG laser is employed to enhance periodontal debridement and promote tissue healing. The laser therapy was carried out for full mouth in the same sitting. The laser parameters are typically set to 1 W of power, with air and water settings adjusted to 10% and 15% respectively, to ensure efficient cooling and prevent thermal damage. A Z-6 model laser tip, measuring 9 mm in length and 600 µm in diameter, is inserted into the periodontal pocket. The inner epithelial lining of the pocket is meticulously removed to the full pocket depth, along with 5 mm of the outer epithelial layer.

The laser is operated parallel to the long axis of the root surfaces, moving from the coronal to the apical aspect to ensure thorough debridement. Root surface conditioning is achieved by angling the laser tip at 5–15° towards the root, moving it back and forth to achieve adequate acid-etching and smoothness. This process not only removes residual debris but also promotes better attachment of the periodontal tissues. This protocol leverages the antimicrobial and biostimulatory effects of the Erbium Chromium, YSGG laser, aiming to reduce inflammation, enhance healing, and improve clinical outcomes in periodontal therapy (Figure 2a-2d).

FIGURE 2a: Pre and post operative picture of scaling and root planing in laser group before application of Erbium, Chromium, yttrium, scandium, gallium and garnet laser (Er,Cr:YSGG laser)

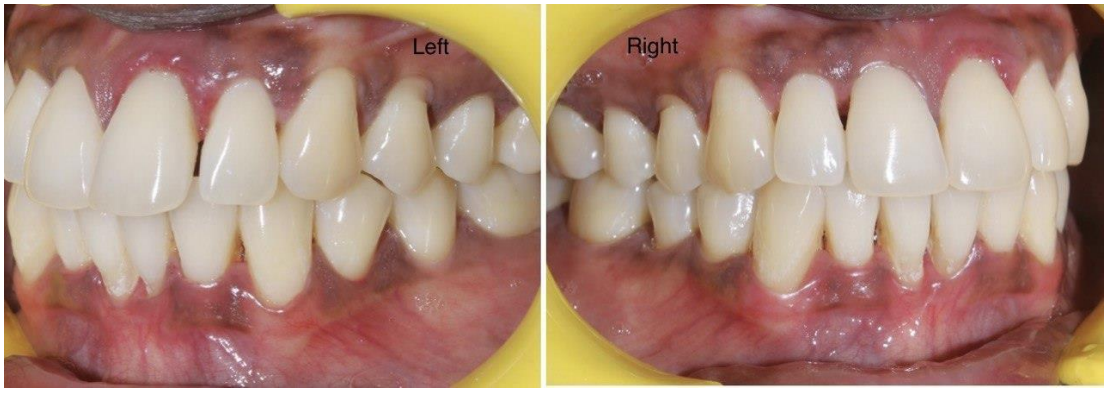

FIGURE 2b: Pre operative picture of left lateral and right lateral side after scaling and root planing in laser group before application of Er, Cr:YSGG laser after thorough instrumentation of the root surface with universal curette (2R,2L and 4R,4L).

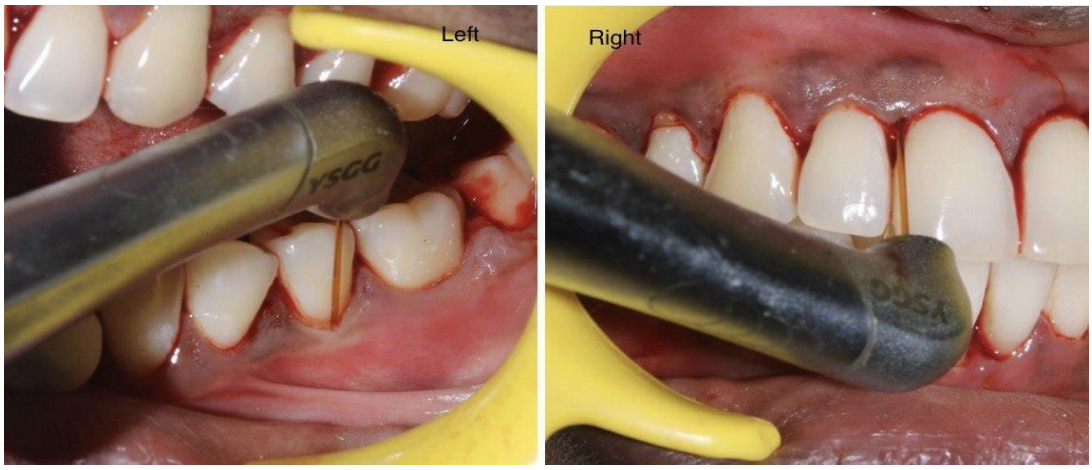

FIGURE 2c: Intra operative picture of left lateral and right lateral side in laser group showing removal of granulation tissue from inner epithelial lining and de-epithelizing the outer epithelium upto the pocket depth with Er, Cr: YSGG laser

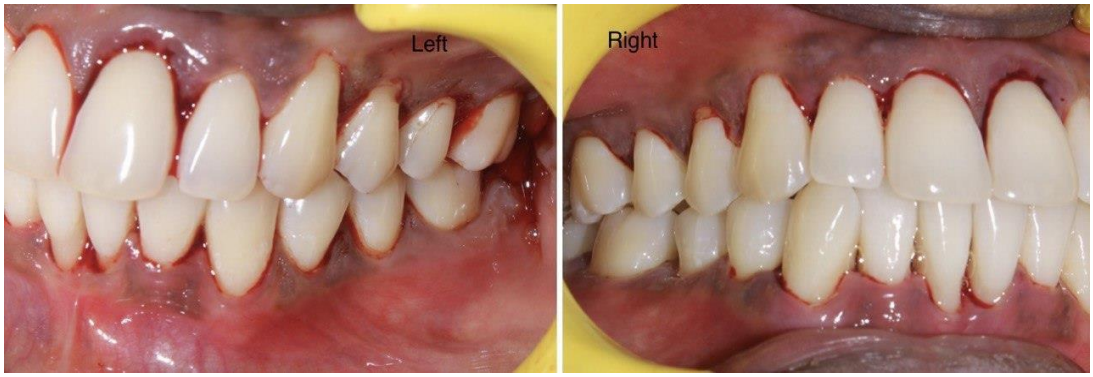

FIGURE 2d: Post operative picture of left lateral and right lateral side in laser group after removing granulation tissue from the inner epithelial lining with Er, Cr:YSGG laser

Gingival Crevicular Fluid Collection and Processing (GCF)

To prepare for sampling, the crevicular site was dried and isolated using a cotton roll. A precise amount of gingival crevicular fluid (GCF) was collected by carefully inserting a calibrated 1–5-microvolume capillary pipette into the test site, ensuring the pipette tip was positioned outside the crevicular space. The collected fluid was promptly transferred into plastic vials containing phosphate-buffered saline (PBS) and then frozen at -70°C for storage. Subsequently, CRP levels within the GCF samples were analyzed using a sandwich enzyme-linked immunosorbent assay (ELISA) kit (Calbiotech, Inc., El Cajon, USA), following the manufacturer's instructions. GCF was collected at baseline before the commencement of periodontal therapy and 3 months after the periodontal therapy to check CRP levels.

Clinical Parameters

Periodontal Probing Depth (PPD)

Periodontal probing involves gently inserting the William's probe into the sulcus or clinical pocket alongside the tooth's long axis, applying controlled pressure to advance it into the tissue along the tooth's surface [18]. The probe is systematically moved around the tooth, examining each of the six surfaces: distofacial, facial, mesiofacial, distolingual, lingual, and mesiolingual, to identify areas of deepest penetration. During this process, the probe is positioned within the periodontal pocket, and the PPD is measured from the margin of the gingiva to the base of the periodontal pocket. PPD was recorded at baseline and 3 months after the non-surgical periodontal therapy.

Clinical Attachment Level (CAL)

The clinical attachment level is determined by measuring the distance from the cemento-enamel junction (CEJ) to the base of the periodontal pocket [19]. To calculate CAL, any gingival recession is added to the recorded PPD, or if there is gingival hyperplasia, it is subtracted from the PPD. These adjustments account for changes in the gingival position relative to the CEJ and provide a more accurate measurement of attachment loss. CAL was recorded at baseline and 3 months after the non-surgical periodontal therapy.

C-reactive protein Level

CRP levels were measured in the gingival crevicular fluid at baseline and 3 months after the periodontal therapy which was evaluated by sandwich enzyme-linked immunosorbent assay (ELISA) (Figure 3).

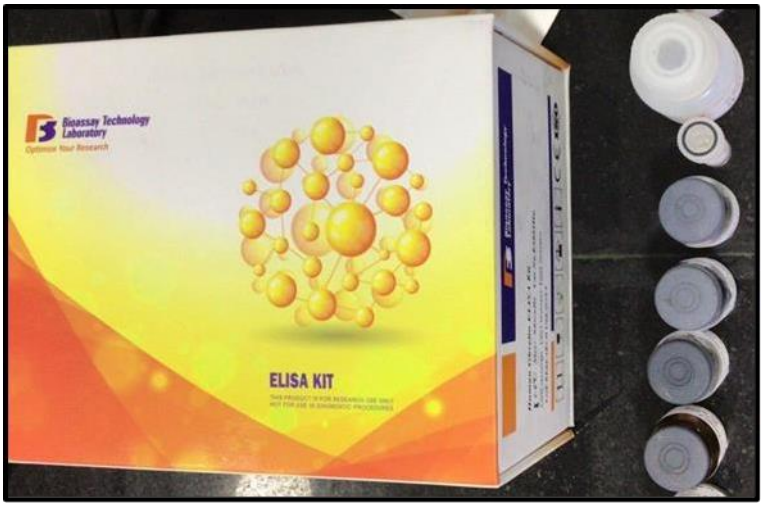

FIGURE 3 : ELISA kit

Statistical analysis

The study assessed the mean and standard deviations of scores obtained. To analyze differences in probing pocket depth (PPD), clinical attachment level (CAL), and C-reactive protein (CRP) levels between baseline and 3 months within the same group, a paired t-test was

utilized. Additionally, an independent t-test was employed to compare these parameters between different groups. Statistical analysis was conducted using Statistical Package for Social Sciences (SPSS) software version 23 (IBM Corp., Armonk, NY, USA). A significance level of $p < 0.05$ was chosen to determine statistical significance in the study findings.

3. RESULTS

The study included 30 patients who were diagnosed with chronic periodontitis. They were divided into two groups, with 15 participants in each group. The mean age of included participants was 34.5 ± 3.67 years. The review picture of SRP and laser group are as below (Figure 4 and Figure 5).

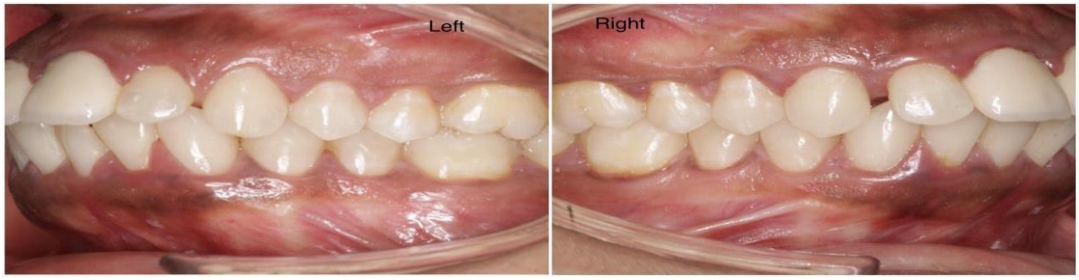

FIGURE 4: 3 months review picture in left and right lateral side of scaling and root planing group

FIGURE 5: 3 months review picture in left and right lateral side of laser group

Periodontal Probing Depth scores (PPD)

The mean probing depth scores were 5.69 ± 0.04 mm and 5.69 ± 0.35 mm in the SRP group and Er,Cr:YSGG laser group respectively at baseline. This inferred most of the patients had advanced periodontitis in the baseline. The periodontal probing depth scores were 5.01 ± 0.02 mm and 3.80 ± 0.58 in the SRP group and Er, Cr:YSGG laser group respectively after 3 months. The results of the present study indicated that the PPD scores were statistically significant between the control and the experimental group at the end of 3 months with a p-value of 0.01*(Table 1).

Study groups	Periodontal Probing depth scores in mm(Scaling &root planing group)	Periodontal Probing depth scores in mm(SRP+Er,Cr:YSGG laser group)	p-value
	Mean±SD	Mean±SD	
Baseline	5.69±0.04	5.69±0.35	0.91

3 months	5.01±0.02	3.80±0.58	0.01*
p-value (Baseline vs 3 months)	0.19	0.02*	

TABLE 1: Depicts the mean and standard deviation of periodontal probing depth scores between the studied groups

Clinical Attachment Level (CAL)

The mean CAL scores were 7.55 ± 0.02 mm and 7.56 ± 0.03 mm in the SRP group and Er,Cr:YSGG laser group respectively at baseline. This revealed most of the included participants had advanced periodontitis in the baseline. The CAL scores were 6.97 ± 0.08 mm and 5.96 ±0.52 mm in the SRP and Er,Cr:YSGG laser groups respectively at the end of 3rd month. Therefore, the CAL scores were statistically significant between the control and the intervened groups at the end of 3 months with a p-value of 0.03*(Table 2).

Study groups	Clinical attachment level scores in mm(Scaling &root planing group)	Clinical attachment level scores in mm(SRP+Er,Cr:YSGG laser group)	p-value
	Mean±SD	Mean±SD	
Baseline	7.55±0.02	7.56±0.03	0.36
3 months	6.97±0.08	5.96±0.52	0.03*
p-value (Baseline vs 3 months)	0.28	0.01*	

TABLE 2: Depicts the mean and standard deviation of clinical attachment level scores between the studied groups

C-reactive protein levels (CRP)

The mean CRP levels were 2.41 ± 0.05 ng/ml and 2.41 ± 0.36 ng/ml in the SRP and Er,Cr:YSGG laser groups respectively in the baseline. This indicated that the included patients had severe inflamamtion in the baseline. The CRP levels were 2.42 ± 0.40 ng/ml and 2.18 ± 0.12 ng/ml in the SRP and Er,Cr:YSGG laser group respectively at the end of 3 months. The scores were statistically significant between the control group and experimental groups at the end of 3 months with a p-value of 0.04*(Table 3).

Study groups	C-reactive protein levels in ng/ml(Scaling &root planing group)	C-reactive protein levels in ng/ml(SRP+Er,Cr:YSGG laser group)	p-value
	Mean±SD	Mean±SD	
Baseline	2.41±0.05	2.41±0.36	0.30
3 months	2.42±0.40	2.18±0.12	0.04*
p-value (Baseline vs 3 months)	0.43	0.03*	

TABLE 3: Depicts the mean and standard deviation of CRP levels between the studied groups

4. DISCUSSION

In this study, both the test and control groups received mechanical therapy using subgingival scalers and universal curettes, with all participants receiving thorough oral hygiene instructions beforehand. The test group additionally received Er, Cr: YSGG laser treatment as

an adjunct to scaling and root planing. The Er, Cr: YSGG laser group showed favorable outcomes in terms of clinical parameters and inflammatory markers when compared to SRP group.

The selection of a therapeutic laser for periodontal treatment is influenced by various factors, including the specific procedure being conducted, the intended clinical goals, and the practitioner's preferences. The integration of laser-assisted periodontal therapy into nonsurgical periodontal treatment aims to enhance treatment outcomes compared to traditional methods, promoting improved healing and potentially reducing the necessity for future surgical interventions [20]. In this study, erbium family lasers were used as an adjunct to scaling and root planing. Er,Cr: YSGG lasers, characterized by their longer wavelength, are particularly effective for procedures that necessitate shallow tissue penetration, and exhibiting a minimally invasive technique for treatment of deep periodontal pockets [21]. Additionally, these lasers exhibit a strong affinity for hydroxyapatite crystals. The laser tip was kept parallel to the root surface and directed away from adjacent teeth. This orientation helps to confine the laser energy to the targeted area. Moreover a sweeping, back-and-forth motion was employed to ensure even treatment while avoiding prolonged exposure to any single spot, which could harm neighboring structures. These precautions were taken to minimize its effect on adjacent tooth surface.

The study revealed a substantial reduction in CAL scores in the group that received intervention compared to the control group with a p value of 0.03*. This reduction in CAL scores indicates a reduction in the severity of periodontal inflammation. Specifically, CAL scores significantly decreased from baseline to 3 months in the intervened group, whereas the group that underwent SRP also showed a decrease in scores compared to baseline, though this change was not statistically significant. These findings are in accordance with previous research conducted by Gutknecht et al.[22]. The observed improvement in scores can be attributed to factors such as enhanced cell proliferation and re-attachment of periodontal ligament cells to the root surface, eradication of endotoxins of the root surface, and efficacious calculus removal using erbium lasers without causing tissue carbonization or charring[23].

The results regarding probing pocket depth (PPD) showed a notable decrease in scores from the baseline assessment to the 3-month follow-up in the experimental group compared to the control group, with a statistically significant difference observed with a p value of 0.01*. The reduction in PPD scores within the intervened group may be linked to the elimination of intracellular and extracellular bacteria in the affected areas, highlighting erbium laser decontamination as a promising treatment option for periodontal disease [24]. This suggests that erbium lasers play a substantial role in addressing periodontal inflammation. Additionally, according to Sanz-Sanchez et al., 2016 concluded that Er,Cr:YSGG exhibits antibacterial properties against Aggregatibacter actinomycetemcomitans and Porphyromonas Gingivalis [25]. These results provide further evidence supporting the antimicrobial effectiveness of erbium lasers. These findings were also concluded by Banafsheh Poormoradi et al. 2021 who reported that Er,Cr:YSGG when used as an adjunct to SRP showed a substantial decrease in CAL and PPD scores when compared to chlorhexidine mouthwash as an adjunct to SRP on halitosis in chronic periodontitis patients[26].

The CRP levels also revealed a noteworthy reduction in scores from baseline to 3 months

between the test group and the control group with a p value of 0.04*. As per Kumar et al., the concentration of CRP in gingival crevicular fluid (GCF) holds greater importance and validates the inflammatory nature of chronic periodontitis [27]. Nonsurgical periodontal intervention proved efficacious in diminishing CRP levels in GCF. Furthermore, C-reactive protein present in GCF, is indicative of inflammation severity, collagen breakdown, and bone remodeling and exhibited correlations with clinical manifestations of periodontal disease [28]. Several researches have showcased a distinct positive link between chronic periodontitis and increased serum levels of CRP. These studies have also indicated that following non-surgical periodontal therapy, although CRP levels decreased from baseline values, the reduction was not statistically significant[29,30].

In contrast, Ide et al.,investigated whether circulating levels of C-reactive protein (CRP) decrease after treating periodontitis but did not detect a decrease in circulating CRP following scaling and root planing [31]. One possible explanation for the sustained elevation of CRP after SRP is that this treatment may be inadequate to halt the progression of periodontal disease in all individuals with periodontitis. Moreover, complete eradication of microorganisms from deep, inaccessible periodontal pockets may not be achievable solely through SRP. Therefore, in this study Er,Cr:YSGG laser was used as an adjunct to SRP to achieve enhanced biochemical outcomes. According to author's best knowledge, this is the first study to evaluate CRP levels in chronic periodontitis patients where erbium lasers were used as an adjunct to SRP. The results showed a statistically significant reduction in CRP levels in laser treated group when compared to non-intervened group validating Er,Cr:YSGG laser as a valuable tool in periodontal therapy.

Nevertheless, a limitation of the present study is that to validate and extend these findings, future studies with larger sample sizes are required.

5. CONCLUSION

Nonsurgical treatment of chronic periodontitis using Er, Cr:YSGG laser along with scaling and root planing (SRP) proved notably more effective than SRP alone in reducing pocket depth (PD), clinical attachment loss (CAL), and C-reactive protein (CRP) levels at a 3-month follow-up. Consequently, employing Er, Cr:YSGG laser as an adjunct contributed to improved clinical and biochemical outcomes in chronic periodontitis patients. However, the durability of these positive effects over the long term remains uncertain, necessitating further research with extended follow-up periods.

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