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REVIEW ARTICLE

Efficacy of Er:YAG laser in the treatment of chronic periodontitis: systematic review and meta-analysis

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Abstract Scaling root planing (SRP) has been proven efficacious as the traditional treatment approach for chronic periodontitis. However, important limitations such as difficult access in deep pockets, grooves, and furcations have led to the development of new therapeutic strategies. The erbium-doped:yttrium-aluminium-garnet (Er:YAG) laser is one of the most promising laser types for periodontal therapy. Its efficacy in radicular debris removal and root smoothing has been proven in vitro. However, the clinical effectiveness of the Er:YAG laser remains controversial. The aim of the present systematic review was to systemically assess the scientific evidence for the effectiveness of Er:YAG laser compared to SRP in the treatment of chronic periodontitis. Electronic database searches of MEDLINE, Cochrane Controlled Clinical Trial Register, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, CINAHL, Science Direct, ISI Web of Science, and SCOPUS were performed, as well as hand-searching of relevant journals through December 23, 2010. Quality assessment was made according to the CONSORT guidelines. The systematic review was performed according to the QUOROM statement and Cochrane Collaboration recommendations. Meta-analyses of the clinical attachment level gain, probing depth reduction, and changes in gingival recession were performed using weighted mean differences for continuous data with 95% confidence intervals, nested in a random effect model. No statistically significant differences were found in any of the investigated clinical parameters among the five random controlled trials (RCTs) entered into the study, indicating that there was no evidence of effectiveness. However, significant heterogeneity, a high risk of bias in three of the five included studies, and methodological shortcomings indicate that the results should be considered with caution. Future long-term, well-designed RCTs are needed to assess the scientific evidence of Er:YAG laser efficacy as an alternative treatment strategy to SRP.

Keywords Laser · Er:YAG · Chronic periodontitis · Meta-analysis

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Introduction

Chronic periodontitis, an inflammatory disease characterized by clinical attachment loss, alveolar bone loss, and periodontal pocket formation, is caused by mixed infections with the subgingival microbiota being organized as a biofilm [1]. Hence, the major goal of periodontal treatment is the removal of bacterial deposits and calculus from root surfaces of affected teeth [2, 3]. Periodontal nonsurgical treatment based on scaling root planing (SRP) consists of the elimination of plaque, calculus, and bacterial debris from the root surface. Generally, SRP is accomplished by hand- or power-driven instruments, which are equally effective [4, 5]. However, traditional therapy has several known limitations and disadvantages, such as difficult access in furcations, grooves, concavities, and deep pockets [6–8], high time and physical effort requirements for hand instrumentation [9], and contaminated aerosol formation when using ultrasonic scalers [10].

Recently, several types of lasers have been suggested as alternative or adjunctive treatments to SRP. Indeed, compared to the traditional therapeutic armamentarium, laser

use offers various advantageous characteristics, such as bleeding control, selective calculus ablation, as well as bactericidal and detoxification effects against periodontopathic pathogens [11–13]. However, the use of lasers is more expensive than traditional therapies [14]. Among the different types of lasers tested, the erbium-doped:yttrium-aluminium-garnet (Er:YAG) laser appears to be one of the most promising for use with periodontal treatment. The Er:YAG laser is able to ablate both soft and hard tissues [15]. Its wavelength (2,940 nm) is ideal for absorption by hydroxyapatite and water, which evaporate into the irradiated hard tissues after laser exposure. This evaporation causes a microexplosion of the same tissues. Therefore, the ablation effect probably is unrelated to thermal effects [16, 17], with minimal thermal rise within the pulp [18].

Several in vitro and in vivo studies have investigated the ability of the Er:YAG laser to perform calculus and plaque removal and root smoothing [18–21]. Crespi et al. [19], Eberhard et al. [18], and Frentzen et al. [20] reported significant reductions in calculus and periodontopathic flora with the Er:YAG laser. Although different results were found when comparing Er:YAG to SRP, these differences could be due to the clinical handling of the Er:YAG laser tip. In particular, the angulation of the tip [22], as well as the proximity of the handpiece tip to the root surface, the time of application, and the power settings have a paramount influence on the amount of root substance removed [11].

Although the in vitro removal capability of the Er:YAG laser has been proven, its clinical efficacy remains questionable. Results from randomized clinical trials (RCTs) have shown divergent clinical outcomes in the initial treatment of chronic periodontitis. Crespi et al. [23] reported a significant reduction in clinical parameters at 6 months in the Er:YAG group compared to the group treated by SRP with ultrasonic scalers. Using similar laser parameters, Schwarz et al. [24] and Sculean et al. [25] did not report any significant differences at 6 months in clinical attachment level (CAL) or probing depth (PD) between patients treated with the Er:YAG laser or SRP. A recent systematic review [26] focused on laser treatment in nonsurgical periodontal therapy found that Er:YAG laser monotherapy could be expected to have similar short- and long-term clinical outcomes as SRP. However, this review considered the evidence supporting Er:YAG use to be weak. Furthermore, a consensus report of the European Workshop on Periodontology [27] clearly indicated the limited evidence of Er:YAG clinical effectiveness and the need for further studies.

To the best of our knowledge, no meta-analysis has been performed on the use of Er:YAG laser in the treatment of periodontal disease. A systematic review and meta-analysis seem to be appropriate methods of assessing the scientific evidence on the actual outcomes of the clinical effectiveness and safety of the Er:YAG laser as a monotherapy for chronic periodontitis. Therefore, the first aim of this systematic review was to address the following focused question: "What is the efficacy of Er:YAG, when used as alternative treatment to SRP in the treatment of patients with chronic periodontitis?" A secondary aim was to survey the literature in relation to the clinical safety of Er:YAG treatment

Materials and methods

This systematic review and meta-analysis were conducted in accordance with the guidelines of the QUOROM statement [28] and the Cochrane Collaboration recommendations [29].

Search strategy

The following electronic databases were searched from their earliest records until January 5, 2011: MEDLINE, Cochrane Controlled Clinical Trial Register (CCCTR), Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effects (DARE), CINAHL, Science Direct, ISI Web of Science, and SCOPUS. To minimize the potential for reviewer bias, screening was performed independently by two reviewers (FS and AP). The level of agreement between reviewers was determined by the Cohen k test, assuming k=0.61 as an acceptable agreement score [30, 31]. Disagreement regarding inclusion or exclusion of the retrieved papers was resolved by discussion.

The databases were searched using the following search format, using Boolean operators and asterisk symbol (*) as truncation: (Intervention) ("Lasers, Solid-State"[Mesh] OR "Erbium"[Mesh] OR "Lasers"[Mesh] OR "Laser Therapy"[Mesh] OR erbium OR erbium yag OR erbium yttrium aluminum garnet OR erbium-yttrium-aluminum-garnet OR er yag) AND (Outcome) (periodontal non surgical treatment OR periodontal non-surgical therapy OR scaling root planing OR dental scaling OR periodontal treatment OR periodontal therapy OR "Dental Scaling"[Mesh] OR "Root Planing"[Mesh] OR "Dental Prophylaxis"[Mesh] OR dental deposit* OR papillary bleeding index OR sulcus bleeding OR bleeding on probing OR gingival index OR periodontitis OR periodontal disease* OR periodontal pocket* OR pocket depth OR plaque index OR dental plaque OR dental calculus OR attachment loss OR clinical attachment level OR alveolar bone loss OR "Periodontitis"[Mesh] OR "Chronic Periodontitis"[Mesh] OR "Periodontal Diseases"[Mesh] OR "Periodontal Pocket"[Mesh] OR "Periodontal Attachment Loss"[Mesh] OR "Tooth Mobility"[Mesh]).

Table 1 Categories used to assess the quality of selected studies

Category	Description	Grading
A	Sample size calculation, estimating the minimum number of participants required to detect a significant difference among compared groups	0=did not exist/not mentioned/not clear 1=was reported, but not confirmed 2=reported and confirmed
B	Randomization and allocation concealment methods	0=clearly inadequate 1=possibly adequate 2=clearly adequate
C	Clear definition of inclusion and/or exclusion criteria	0=no 1=yes
D	Completeness of follow-up (specified reasons for withdrawals and dropouts in each study group)	0=no/not mentioned/not clear 1=yes/no withdrawals or dropouts occurred
E	Experimental and control groups comparable at study baseline for important prognostic factors	0=no 1=unclear/possibly not comparable for one or more important prognostic factors 2=clearly adequate
F	Presence of masking	0=no 1=unclear/not complete 2=yes
G	Appropriate statistical analysis	0=no 1=unclear/possibly not the best method applied 2=yes

Additionally, the following journals were searched manually, from their earliest records to December 2010: *Journal of Periodontology*, *International Journal of Periodontics and Restorative Dentistry*, *Journal of Clinical Periodontology*, *Journal of Dental Research*, *Journal of Periodontal Research*, *Periodontology 2000*, *Journal of Dentistry*, *Journal of American Dental Associations*, *Journal of Clinical Dentistry*, *Lasers in Medical Science*, *Lasers in Surgery and Medicine*, *Clinical Oral Investigations*, and *Photomedicine and Laser Surgery*. No language restriction was applied.

The references of all selected full-text articles and related reviews were scanned. The corresponding authors were contacted to obtain missing, unclear, or unpublished data.

Study inclusion and exclusion criteria

The study selection process was performed by two reviewers (FS and RG) in two phases. In the first phase, the studies were analyzed according to the following inclusion criteria (A):

A.1 Randomized controlled clinical trials
A.2 Studies comparing Er:YAG laser with manual or ultrasonic SRP alone
A.3 Studies involving human adult subjects (age≥18 years)
A.4 Patients with chronic periodontitis

Table 2 Abstracts retrieved by electronic, manual, and reference searching

Database	Overall number of search outcomes	Number of searchoutcomes without overlap
PubMed (Basis)	855	-
Science Direct	3	2
Cochrane Controlled Clinical Trials Register	142	5
Cochrane Database of Systematic Reviews	33	0
Database of Abstracts of Reviews of Effects	2	0
CINAHL	93	23
ISI Web of Science	151	25
Handsearch	2	0
Reference review articles	1	0
Reference selected articles	0	0

Table 3 Studies excluded and reason for exclusion

Study	Year of publication	Criteria for exclusion	Type of study
Gursoy-Mert et al. [39]	2010	A.1	Case report
Braun et al. [40]	2010	B.4	Randomized clinical trial
Gómez et al. [42]	2009	A.1	In vitro study
Schwarz et al. [26]	2008	A.1	Systematic review
Lopes et al. [43]	2008	B.6	Part of Lopes et al. 2010
Ishikawa et al. [44]	2008	A.1	Review
Crespi et al. [23]	2007	B.2	Randomized clinical trial
Derdilopoulou et al. [1]	2007	B.4	Randomized clinical trial
Moghare Abed et al. [45]	2007	A.1	In vitro study
Cobb et al. [46]	2006	A.1	Review
Tomasi et al. [47]	2006	B.3	Randomized clinical trial
Schwarz et al. [48]	2006	A.1	In vitro study
Chanthaboury et al. [14]	2005	A.1	Review
Crespi et al. [49]	2005	A.1	In vitro study
Van As [50]	2004	A.1	Review
Ishikawa et al. [51]	2004	A.1	Review
Eberhard et al. [18]	2003	A.1	In vitro study
Schwarz et al. [53]	2003	A.2	Randomized clinical trial
Ishikawa et al. [54]	2003	A.1	Review
RSTCAAP [55]	2002	A.1	Review
Lioubavina-Hack et al. [56]	2002	A.1	Review
Frentzen et al. [20]	2002	A.1	In vitro study
Folwaczny et al. [57]	2000	A.1	In vitro study
Watanabe et al. [58]	1996	A.1	Clinical trial

Only studies that fulfilled all of the inclusion criteria (A) were admitted to the second phase. In phase II, the preselected studies were analyzed according to the following exclusion criteria (B):

B.1 Data not reported as mean ± SD
B.2 Patients with systemic disease, or who consumed antibiotics or medications that are known to affect periodontal tissue or treatment within the last 6 months, or who underwent periodontal treatment within the last 6 months
B.3 Follow-up of<6 months
B.4 No outcome of interest
B.5 Insufficient information on laser device and energy settings
B.6 Duplicate studies

Authors contact process

The authors of the articles that satisfied the inclusion criteria were contacted via e-mail to retrieve missing data and information. If no answer was received, then a second e-mail was forwarded at 2 weeks after the first e-mail was sent. One month after the first contact, if the study met one or more exclusion criteria and no or incomplete answers were sent by the authors, then the article was excluded.

Outcome measures

The primary outcomes of interest assessed to answer the focused question were CAL gain (mm) and PD reduction (mm) between the test and control groups. The secondary outcomes of interest were changes in plaque index (PI), gingival index (GI), bleeding on probing (BoP), full-mouth plaque score, and full-mouth bleeding score. Adverse events, microbiological changes, and laboratory findings were evaluated as reported by the authors.

Data extraction

Data were collected by two independent reviewers (FS and AM). The following data were extracted from the included studies: year of publication, country, study design, demographic characteristics of participants, number of patients per intervention group, inclusion criteria, diagnostic criteria, laser characteristics, adverse events, microbiological outcomes, and follow-up. If data were presented numerically (in tables or text) and graphically (in figures), then only numeric data were considered for extraction. The

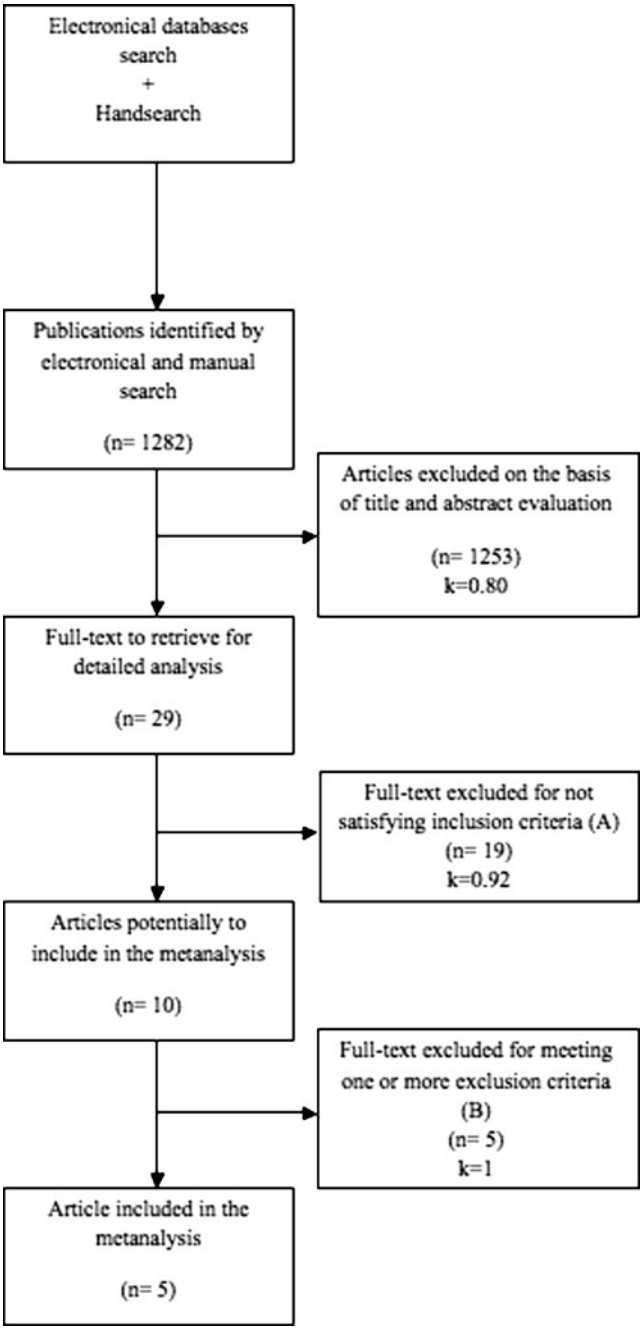

Fig. 1 Flowchart of the search strategy

reviewers cross-checked all extracted data. Disagreements were resolved by discussion until consensus was reached.

Quality assessment of selected studies

A quality assessment of all selected studies was performed by two reviewers (FS and AP) according to the revised recommendations of the CONSORT statement for the evaluation of RCTs [32] (Table 1). Quality assessment was performed in two different phases. In particular, phase I of quality assessment was based on the published full-text article, while all studies were reconsidered in phase II according to the supplementary information provided by the corresponding authors. After determining the scores during phase II of quality assessment, an overall estimation of plausible risk of bias (low, moderate, or high) was obtained for each selected study. In brief, a low risk of bias was estimated when all of the criteria were met. A moderate risk was considered when≥1 criteria were partly met. A high risk of bias was estimated when≥1 criteria were not met (*Cochrane Handbook for Systematic Reviews of Interventions*, Version 5.0.2, http://www.cochrane-handbook.org).

Statistical analysis

For each intervention group, the differences between the pre- and postintervention means of the outcomes of interest were calculated with the following formulas [33]: $\Delta CAL = CAL_2 - CAL_1$, where ΔCAL is CAL gain, CAL_2 is the mean value of CAL at the end of follow-up, and CAL_1 is the mean value of CAL at baseline; $\Delta PD = PD_2 - PD_1$, where ΔPD is PD reduction, PD_2 is the mean value of PD at the end of follow-up, and PD_1 is the mean value of PD at baseline. For the secondary outcomes, changes between pre- and postintervention were calculated from $\Delta GR = GR_2 - GR_1$, where ΔGR is the change in gingival recession, GR_1 is the mean value of GR at baseline, and GR_2 is the mean value of GR at the end of follow-up.

If the standard deviation of the pre- and postintervention mean difference was not reported in the study, then it was calculated according to the following formula: $SD = \sqrt{(SD_1^2 + SD_2^2 - 2r \times SD_1 \times SD_2)}$, where SD^2 is the standard deviation of the difference between the pre- and postintervention mean values, SD_1 is the standard deviation of the mean value at baseline, SD_2 is the standard deviation of the mean value at the end of follow-up, and r is the correlation coefficient (assumed to be 0.5). If studies provided the standard errors of the mean (SE), then the SD was calculated based on the sample size (N), according to the following formula: $SE = SD/\sqrt{N}$.

Data were combined for meta-analysis using a statistical software package (RevMan software, version 5.0, The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen, Denmark). The effect size was estimated and reported as the mean difference (MD) for continuous variables. Weight was calculated in individual studies as described above. Briefly, the MD values were nested in a random effect model (Der Simonian & Laird model), with corresponding Z-statistics. The p values and 95% confidence intervals (CIs) were calculated. For WMD, $p < 0.05$ was considered statistically significant.

Heterogeneity was assessed using the χ^2-based Q-statistic method and I^2 measurement. A significant heterogeneity was

Table 4 Characteristics of the included studies

Characteristic		Reference				
		[15]	[41]	[25]	[52]	[24]
Country		Italy	Brazil	Germany	Germany	Germany
Study design		RCT, SM, QD	RCT, SM, QD	RCT, SM	RCT, SM	RCT, SM
Population		26 patients (mean age: 50.5± 11.7 years)	19 patients (31–55 years)	20 patients (29–62 years)	20 patients (28–79 years)	20 patients (28–79 years)
		706 teeth	76 teeth		100 teeth	100 teeth
		1,582 sites	76 sites	1,306 sites	600 sites	600 sites
Inclusion criteria		Chronic periodontitis	Chronic periodontitis	Chronic periodontitis	Chronic periodontitis	Chronic periodontitis
		PD≥4 mm, smoking<10 cigarettes per day	PD≥5 mm, non-smokers	PD≥4 mm, non-smokers	PD≥4 mm, non-smokers	PD≥4 mm, non-smokers
Intervention		Test 1: Laser +SRP	Test 1: SRP+laser	Test: Laser	Test: Laser	Test: Laser
		Test 2: Laser	Test 2: Laser	Control: SRP	Control: SRP	Control: SRP
		Control 1: SRP	Control 1: SRP			
		Control: 2	Supragingival prophylaxis	Control: 2 No treatment		
Laser type		Er:YAG	Er:YAG	Er:YAG	Er:YAG	Er:YAG
		Fiber tip Ø 0.5×10 mm	Chisel tip Ø 1.1× 0.5 mm	Feedback, Chisel tips Ø 1.1×0.5 mm, 1.65× 0.5 mm	Chisel tips Ø 1.1×0.5 mm, 1.65× 0.5 mm	Chisel tips Ø 1.1×0.5 mm, 1.65× 0.5 mm
Laser parameters		Wavelength 2.94 μm, frequency 10 Hz, energy level 150 mJ/pulse	Wavelength 2.94 μm, frequency 10 Hz, energy level 100 mJ/pulse, fluency 12.9 J/cm^2/pulse	Wavelength 2.94 μm, frequency 10 Hz, energy level 160 mJ/ pulse	Wavelength 2.94 μm, frequency 10 Hz, energy level 160 mJ/pulse	Wavelength 2.94 μm, frequency 10 Hz, energy level 160 mJ/pulse
Evaluation intervals		3, 6 months	1, 3, 6, 12 months	3, 6 months	12, 24 months	3, 6 months
Clinical outcome at 6 months (at 12 months)						
CAL gain	Laser	0.2±1.9 (−)	0.6±1.21 (0.68±1.1)	1.11±1.01 (−)	- (1.8±1.21)	1.9±1.05 (−)
	SRP	0.5±1.8 (−)	1.35±1.41 (1.41±1.3)	1.11±1.09 (−)	- (0.9±1.24)	1.0±1.0 (−)
	Laser+SRP	0.5±1.7 (−)	-	-	-	-
	SRP+laser	-	1.07±1.77 (1.15±1.4)	-	-	-
	Prophylaxis	0.1±1.9 (−)	-	-	-	-
	No treatment	-	-	-	-	-
PD reduction	Laser	0.7±1.66 (−)	1.54±1.21 (1.66±1.15)	1.52±0.57 (−)	- (1.9±0.57)	2.0±0.65 (−)
	SRP	0.9±1.51 (−)	2.23±1.34 (2.29±1.21)	1.57±0.69 (−)	- (1.5±1.12)	1.6±0.65 (−)
	Laser+SRP	1.2±1.6 (−)	-	-	-	-
	SRP+laser	-	2.1±1.44 (2.19±1.37)	-	-	-
	Prophylaxis	0.7±1.7 (−)	-	-	-	-
	No treatment	-	-	-	-	-
Changes in GR	Laser	–0.6±0.37 (−)	0.61±0.37 (0.56±0.35)	–0.41±0.16 (−)	– (0.1±0.75)	0.1±0.75 (−)
	SRP	–0.5±1.21 (−)	0.57±0.59 (0.53±0.57)	–0.46±0.2 (−)	– (0.6±0.75)	0.5±0.8 (−)
	Laser+SRP	–0.7±1.1 (−)	-	-	-	-
	SRP+laser	-	0.66±0.79 (0.69±0.71)	-	-	-
	Prophylaxis	–0.5±1.2 (−)	-	-	-	-
	No treatment	-	-	-	-	-

Table 4 (continued)

Characteristic	Reference				
	[15]	[41]	[25]	[52]	[24]
Microbiological outcome	-	PCR technique. At 6 and 12 months, significant reductions in Aa, Pg, Pn, and Tf in SRP+laser group, significant reduction in Aa in laser group, no significant reduction in SRP group	-	Dark field microscopy. At 12 months, significant intragroup reduction of spirochetes and increase of cocci and nonmotile rods, but no significant intergroup differences	Dark field microscopy. At 6 months, increasing percentage of motile rods and decreasing percentage of cocci in both groups, but no significant difference between groups

indicated by $p<0.1$ because of the moderate insensitivity of the Q statistic [34]. The value of I^2 ranged from 0 to 100, with larger values (≥75%), suggesting high heterogeneity [35].

The forest plots for each meta-analysis present the raw data (means, SDs and sample sizes) for each arm per included study. Point estimates and CIs for the chosen effect measure are shown as blocks and lines, respectively. The heterogeneity statistic (I^2), total number of participants per group, overall average effect (MD and Z-statistics) in the random effect model, and percent weight given to each study are also shown in the forest plots.

The presence of publication bias was investigated for each outcome of interest with two methods. Visual detection was used to analyze the funnel plot [36], while quantitative analysis was performed using the regression asymmetry test [37] and the trim-and-fill method [38]. All analyses of publication bias were made using Stata 10 Intercooled (StataCorp LP, College Station, TX, USA).

Results

Study selection

A total of 1,282 potentially relevant titles and abstracts were found during the electronic and manual searches (Table 2). During the first stage of study selection, 1,253 publications were excluded based on evaluation of the title and abstract (inter-reviewer agreement $k=0.80$). During the second phase, the complete full-text articles of the remaining 29 publications [1, 14, 15, 18, 20, 23–26, 39–58] were thoroughly evaluated. A total of 19 papers [14, 18, 20, 26, 39, 42, 44–46, 48–51, 53–58] were excluded during this second stage as they did not fulfill the inclusion criteria (A) ($k=0.92$). Five full-texts articles [1, 23, 40, 43, 47] of the remaining ten publications were excluded because they met≥1 of the exclusion criteria (B) ($k=1$) (Table 3). Finally, a total of five studies [15, 24, 25, 41, 52] fulfilled the required selection criteria of both phases and were included in the present review. A flowchart for the study selection process is shown in Fig. 1. The main characteristics of the three included studies are summarized in Table 4.

Descriptive results

All included studies were clinical RCTs using a split-mouth design. One study [52] represented the long-term follow-up of another included study [24]. All studies compared Er:YAG laser to SRP in the treatment of chronic periodontitis, although different energy levels (ranging from 100 to 160 mJ/pulse) and fiber tip diameters (ranging from 1.1×0.5 mm to 1.65×0.5 mm) were used. Four RCTs [15, 24, 25, 41] reported CAL gain, PD reduction, and GR changes at 6 months, while two studies [41, 52] reported these outcomes at 12 months. Changes in PI, GI, and BoP were evaluated in all studies. Two studies [15, 25] reported the full-mouth plaque score and only one study [15] reported the full-mouth bleeding score; however, since different types of indices were used, it was not possible to pool these outcomes into the metaanalysis. Microbiological data were provided by three studies [24, 41, 52]. No laser-related side-effects or adverse events were reported by the included studies.

Rotundo et al. compared the clinical effects of Er:YAG laser alone (Laser), Er:YAG laser in combination with SRP (Laser+SRP), SRP alone (SRP), or subgingival prophylaxis (S). A total of 27 patients were randomly allocated to receive Laser+SRP (Test 1), Laser (Test 2), SRP (Control 1), or S (Control 2). One patient dropped out of the study; therefore, the analysis was performed on 26 patients. The CAL, PD, BoP, Rec, and PI (Ainamo & Bay, 1975) values were recorded at baseline and at 3 and 6 months after treatment. For CAL gain and PD reduction, higher values were achieved by Laser+SRP and SRP, followed by Laser and S. Changes in GR results were similar among treatments. No statistically significant difference in CAL was

Table 5 Quality assessment of selected studies prior to and after contact (parentheses) with corresponding authors

Reference	*A (0–2)	*B (0–2)	*C (0–1)	*D (0–1)	*E (0–2)	*F (0–2)	*G (0–2)	Estimated risk of bias
[15]	2	2	1	1	2	2	2	Low (Low)
[41]	2	2	1	1	2	2	2	Low (Low)
[25]	0	0	1	1	2	0	2	High (High)
[52]	0	0	1	1	2	2	2	High (High)
[24]	0	0	1	1	2	2	2	High (High)

found among treatments, with the exception of SRP and Laser+SRP compared to S. The authors concluded that no additional benefit was found when the Er:YAG laser was used alone or as an adjunct to SRP.

Lopes et al. compared four treatment modalities: SRP+Laser (Test 1), Laser (Test 2), SRP (Control 1), and No treatment (Control 2). Clinical and microbiological parameters were recorded. With regard to clinical parameters, CAL, PD, BoP, GR, PI, and GI (Ainamo & Bay, 1975) were registered at baseline and at 1, 3, 6, and 12 months after treatment. The results at 6 and 12 months showed significant improvements in the CAL, PD, GR, and BoP values in all groups, but no significant difference was found among treatment groups. The PI was significantly reduced at 6 and 12 months for all treatments, except for control, but no significant difference among treatments was detected. A significant reduction in GI was retrieved for SRP+Laser and SRP. Microbiological findings at 6 months after treatment showed significant reductions in *Aggregatibacter actinomycetemcomitans* (*Aa*), *Porphyromonas gingivalis* (*Pg*), *Tannerella forsythia (Tf)*, and *Prevotella nigrescens* (*Pn*) in the SRP+Laser group, while only *Aa* was reduced in the Laser group. The results at 12 months were similar, with additional reductions of *Prevotella intermedia* (*Pi*) and *Pg* in the SRP+Laser and Laser group, respectively. The authors considered Er:YAG laser, either as a monotherapy or in addition to SRP, to be an effective alternative treatment for the reduction and control of microorganism proliferation.

Sculean et al. and Schwarz et al. [24, 52] used similar designs, comparing Er:YAG (Test) laser monotherapy to SRP (Control). However, Sculean et al. compared a fluorescence-controlled (InGaAs) Er:YAG laser to SRP performed with an ultrasonic device, while Schwarz compared Er:YAG without fluorescence to SRP performed with hand instruments. At 6 months, Sculean et al. reported a significant improvement in the mean values of BoP, PD, and CAL, but no significant difference was observed between the groups.

In contrast, at 6 months, Schwarz et al. reported significant improvements in CAL gain, PD reduction, BoP, PI (Silness & Löe, 1964), and GI (Löe & Silness, 1963) within groups, as well as significant differences between groups for all clinical parameters except PI and GI, in favor of the Laser group. Deeper pockets (PD≥7 mm) showed greater improvement than moderate (4 mm<PD<6 mm) or shallow (1 mm<PD<3 mm) pockets. The improved results were maintained at the 12- and 24-month follow-ups. With regard to microbiological out-

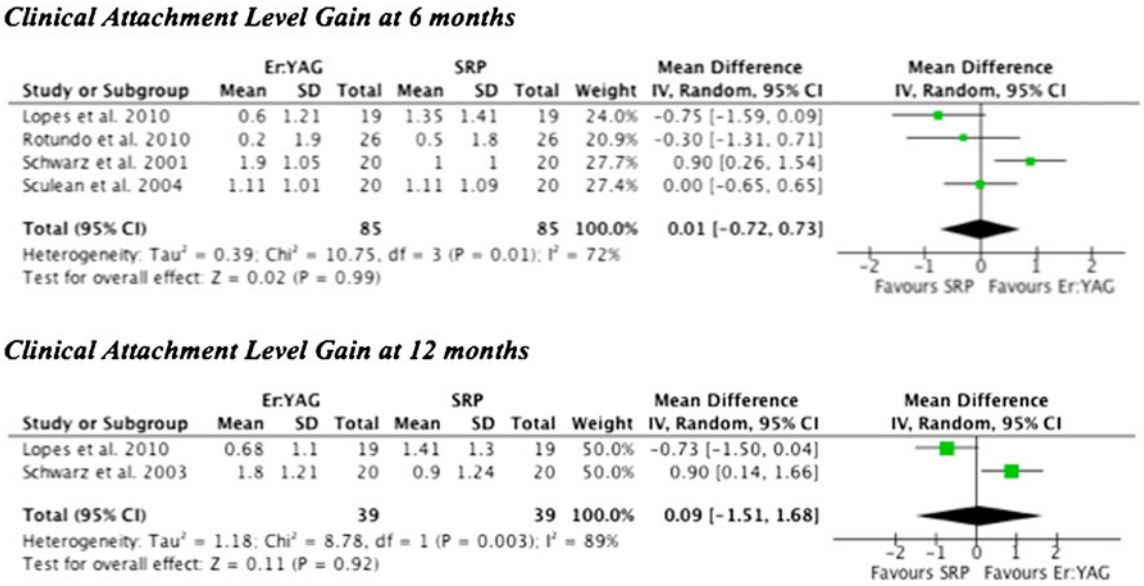

Fig. 2 CAL gain at 6 and 12 months

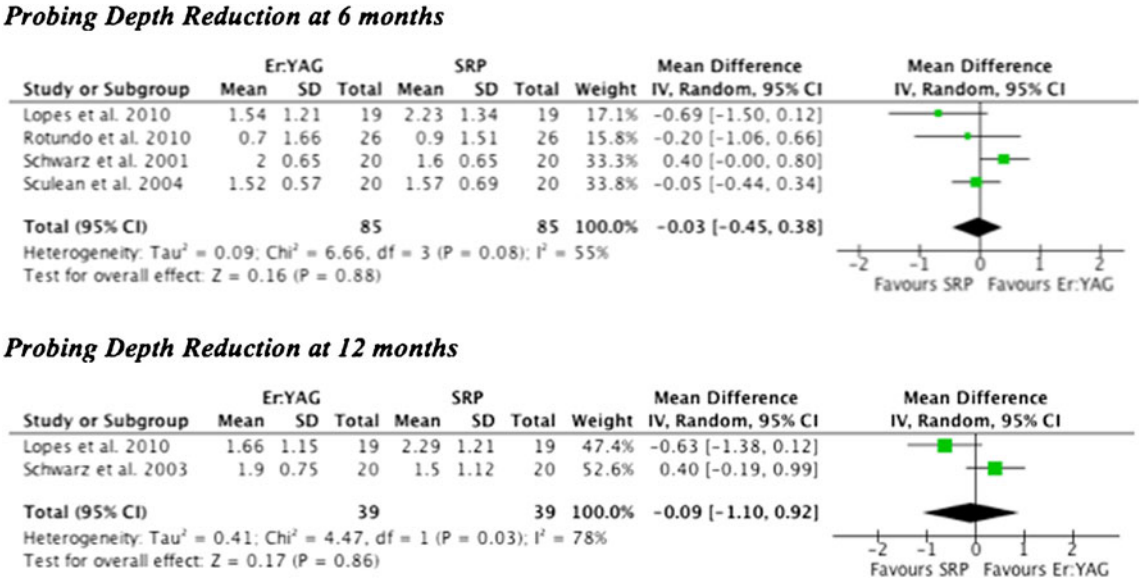

Fig. 3 PD reduction at 6 and 12 months

comes, both the Laser and Control groups showed a significant increase in cocci and nonmotile rods and a decrease in motile rods and spirochetes, but no significant differences were observed between the groups. At 12 months after treatment, the number of motile rods was almost identical to the baseline score in both groups. At 24 months, an increasing percentage of spirochetes and decreasing percentage of cocci and nonmotile rods were observed in both treatment groups; however, no significant difference was found between the groups.

Quality assessment

The results of the quality assessment of all selected studies before and after contact with the corresponding authors are presented in Table 5. In particular, even after contacting the authors, sample size calculation (A) and information on the randomization and allocation concealment method (B) were only available and confirmed for Rotundo et al. [15] and Lopes et al. [41]. All studies provided sufficient information on the inclusion and exclusion criteria used (C). The completeness of the follow-up period was reported in all studies (D); the experimental and control groups were comparable at baseline for important prognostic factors (E) in all the studies. Before the authors were contacted, masking was clear in all studies, excepted for Sculean et al. [25]. All of the studies fully satisfied the remaining criterion (G). The risk of bias before contact with the authors was estimated to be high for

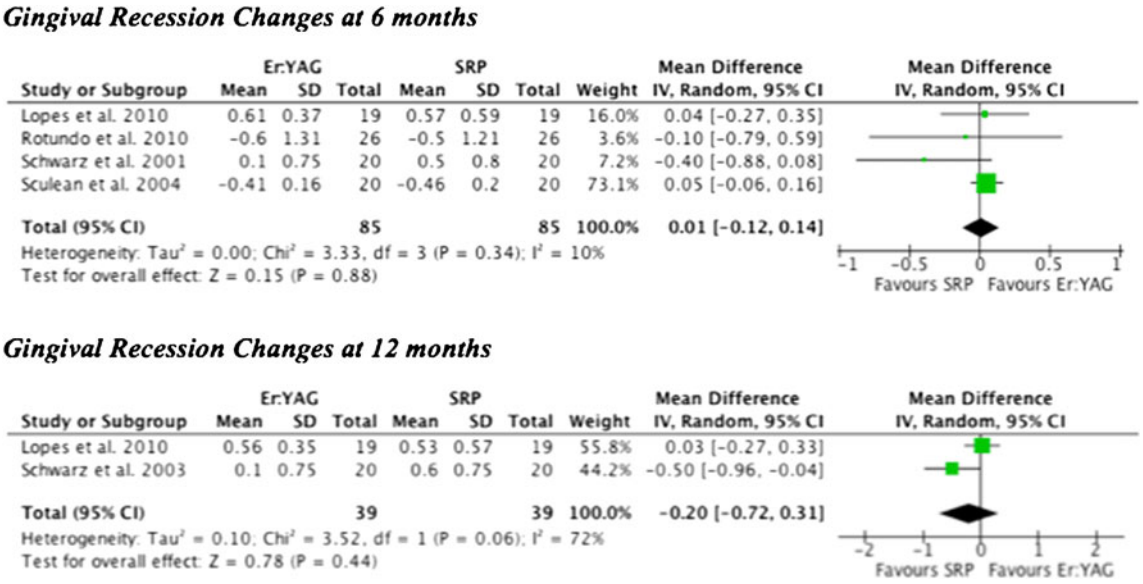

Fig. 4 GR changes at 6 and 12 months

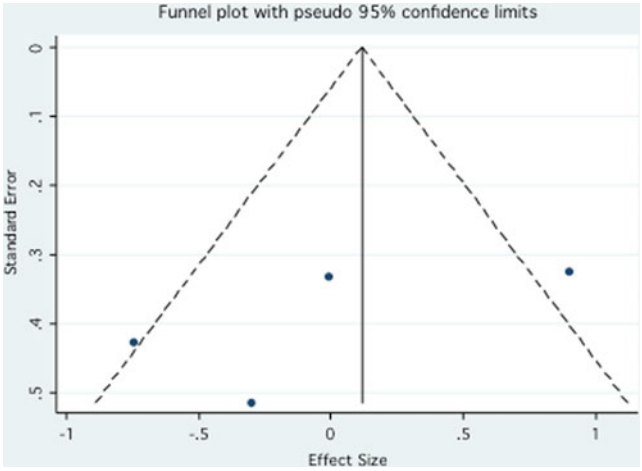

Fig. 5 Funnel plot for CAL gain outcome

three studies [24, 25, 52] and low for two studies [15, 41] (k=1.0) (Table 5).

Meta-analyses

The results of meta-analyses for the primary outcomes are reported in Figs. 2 and 3. The CAL gain at 6 months was extracted from all included studies, while at 12 months it was extracted from only 2 studies [41, 52]. No significant differences were observed between Er:YAG and SRP (MD=0.01, 95% CI range: –0.72 to 0.73, p=0.99), but moderate heterogeneity was detected (χ^2=10.75, p=0.01, I^2=72%) (Fig. 2). Similar results were found at 12 months, with an MD of 0.09 (95% CI range: –1.51 to 1.68, p=0.92) with a high heterogeneity between studies (χ^2=8.78, p=0.003, I^2=89%) (Fig. 2).

A reduction in PD was reported in all selected studies. At 6 months, no statistically significant difference was observed between groups (MD=−0.03, 95% CI range: –0.45 to 0.38, p=0.88), and no heterogeneity was detected (χ^2=6.66, p=0.08, I^2=55%) (Fig. 3). The results at 12 months were comparable to those at 6 months (MD=−0.09, 95% CI range: –1.10 to 0.92, p=0.86) with χ^2 = 4.47 (p=0.03, I^2=78%) (Fig. 3).

All studies showed changes in GR in the control and test groups. At 6 months, no significant differences were observed between the Laser and SRP groups (MD=0.01, 95% CI range: –0.12 to 0.14, p=0.88), with no evidence of heterogeneity (χ^2=3.33, p=0.34, I^2=10%) (Fig. 4). At 12 months, the MD was −0.2 (95% CI range: –0.72 to 0.31, p=0.44) with χ^2=3.52 (p=0.06, I^2=72%) (Fig. 4).

Subgroup analysis and metaregression were not performed, considering the small number of included studies. The funnel plots for CAL gain and other outcomes of interest did not show asymmetry (Fig. 5). However, the regression asymmetry test did not suggest a publication bias for the investigated outcomes of interests (Table 6). In addition, the difference between the original estimate and the adjusted effect size according to the trim-and-fill effect procedure remained nonsignificant for all calculated outcomes of interest. The trim-and-fill method for CAL gain, PD reduction, or changes in GR did not show missing study.

Discussion

A systematic review and meta-analysis were conducted to evaluate the effectiveness of the Er:YAG laser in the treatment of chronic periodontitis as an alternative therapeutic strategy to SRP. Five RCTs, with a total of 85 patients and 3,564 sites, were entered in the meta-analysis to investigate CAL gain, PD reduction, and GR changes in the Er:YAG laser and SRP groups. All studies reported significant intragroup improvement in clinical and microbiological parameters in patients treated with the Er:YAG laser. However, three studies [15, 25, 41] did not report a significant difference between Er:YAG laser and SRP groups in CAL gain, PD reduction, or GR changes. Schwarz et al. reported significant differences in the same clinical parameters at short- [24] and long-term intervals [52]. The meta-analysis revealed no significant differences for any investigated parameter at 6 and 12 months (Figs. 2–4), suggesting that there was no evidence of the superior effectiveness of the Er:YAG laser compared to SRP. This finding is consistent with previously published studies [1, 15, 25, 41, 46, 47] showing a lack of adjunctive benefits when the Er:YAG laser is used as an alternative to SRP. No meta-analysis of microbiological data could be made, since microbiological outcomes were focused on different types of microbiota and were analyzed with different techniques. Considering that different results were obtained by the included studies, this outcome needs to be analyzed in detail in future studies.

Table 6 Quantitative analysis for publication bias assessments

	Original meta-analysis		Trim-and-fill analysis		
Outcome	MD (95% CI)	p	MD (95% CI)	Studies trimmed/total studies	Egger regression p
CAL gain	0.01 (−0.72 to 0.73)	0.99	0.004 (−0.72 to 0.72)	0/4	0.34
PD reduction	−0.03 (0.45 to 0.38)	0.88	−0.033 (−0.452 to 0.385)	0/4	0.87
GR changes	−0.05 (−0.15 to 0.05)	0.31	−0.01 (−0.12 to 0.14)	0/4	0.28

An important issue uncovered in the meta-analysis is the moderate–high significant heterogeneity. The funnel plot and trim-and-fill analyses revealed no evidence of publication bias. Nevertheless, heterogeneity could be explained by differences among the included studies in terms of the types of fiber tips, energy settings, times of laser application, and differences in patient smoking habits. However, due to the limited number of studies included, no subgroup analysis or meta-regression could be performed.

With regard to the safety of the Er:YAG laser, all of the studies reported no side-effects or adverse events throughout the entire study period with the employed energy settings. This finding is consistent with observations of previous studies and of a recent systematic review [26]. No cost/benefit analysis could be performed, since studies included in the meta-analysis did not consider this issue. However, since laser represents a more expensive treatment than traditional ones [14], this is an important issue to address.

Methodological quality analysis revealed a high risk of bias for three of the five included studies. An inadequate randomization method was the most important quality shortcoming, while the lack of a sample size calculation could have contributed to the low power for three studies [24, 25, 52]. Another important methodological issue was the study design. All of the included studies adopted a split-mouth design, with randomization of the mouth sides instead of the patients. This design presumably reduces the error variance of the experiment, yielding a higher statistical power [59] and necessitating a smaller number of patients for the trial [60]. However, comparisons made on a within-patient basis have potential disadvantages, because treatments may affect the experimental site in unexpected ways (i.e., carry-across effects) [26]. Therefore, unless a priori knowledge indicates that no carry-across effects exist, reported estimates of the treatment efficacy may be biased [60].

Previous reviews [14, 26, 46, 51] have underlined the questionable use of Er:YAG laser in the treatment of chronic periodontitis, reporting weak [26] or inconsistent [46] evidence of its effectiveness. However, none of these previous reviews included a meta-analysis. The present evidence-based systematic review was different in three respects. First, only the Er:YAG laser was investigated, and the investigation was performed with a specific search strategy. Second, additional well-designed RCTs with low risks of bias [15, 41] were included. Third, an appropriate meta-analysis was performed that was based on the random effect model (Der Simonian & Laird model), heterogeneity, and publication bias analysis.

The results of this meta-analysis should be considered in light of its shortcomings. The low methodological quality for three of the five included studies, limited number of studies, and moderate-high heterogeneity indicate that the results are not unbiased and reliable. We concur with the recommendations of Schwarz et al. [26] that future well-designed clinical RCTs with adequate power are needed to address the effectiveness of Er:YAG laser treatment compared to SRP in chronic periodontitis treatment. Future studies should also address microbiological data, cost and time analyses, and long-term follow-up results.

Conclusions

This systematic review and meta-analysis, performed according to the guidelines of the QUOROM statement and Cochrane Collaboration recommendations, did not find evidence for the superior effectiveness of Er:YAG laser use compared to SRP in chronic periodontitis treatment. Considering the major qualitative limitations of the meta-analysis, our results should be interpreted with caution. Future long-term, well-designed RCTs are needed to assess the scientific evidence of Er:YAG laser efficacy as a monotherapy for chronic periodontitis.

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