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A Systematic Review and Meta-Analysis of the Effect of Various Laser Wavelengths in the Treatment of Peri-Implantitis

Georgios A Kotsakis, DDS, Resident*, Ioannis Konstantinidis, DDS, Doctoral Candidate†, Ioannis K. Karoussis, DDS, MS, Dr. med dent. Assistant Professor ‡, Xiaoye Ma, MS, Doctoral Candidate§, Haitao Chu, Ph.D., Associate Professor§

* Division of Periodontology, University of Minnesota, Minnesota, MN, United States

† Division of Prosthodontics, Technical University of Dresden, Dresden, Germany

‡ Department of Periodontology, National and Kapodistrian University of Athens, Athens, Greece

§ Division of Biostatistics, School of Public Health, University of Minnesota, Minnesota, MN, United States

Objectives: The primary aim of this systematic review was to address the following focused question: ‘’is laser therapy as a monotherapy, or as an adjunctive therapy an efficacious treatment modality for patients with peri-implantitis?’’

Material and Methods: The PubMed database of the US National Library of medicine and the Cochrane Central Register of Controlled Trials (CENTRAL) were electronically searched and complemented by manual searches up to June 2013.

Results: The search yielded 137 titles and abstracts. Following initial screening, 15 out of 137 publications were scrutinized during the second phase of the review. In the second phase, 9 articles were excluded from the analysis and 6 controlled, clinical studies were selected.

Narrative synthesis of the results revealed that non-surgical laser treatment with a single application of either an Er:YAG (2,940 nm) laser, or a diode laser (660 nm) in combination with a phenothiazine chloride dye is efficient in controlling inflammation around treated implants for at least 6-months following intervention, while it only has a mild effect on reduction in probing depth (PD) and gain in clinical attachment level (CAL). There is limited information regarding the clinical application of CO_2 laser (10.6 μm) in the surgical treatment of peri-implantitis, however its use may be promising. A meta-analysis could only be performed for the efficacy of Er:YAG laser (2,940 nm wavelength) due to the heterogeneity of the studies and the limited number of data available. Meta-analysis did not reveal statistically significant evidence for treatment effects in reducing PD and CAL levels in comparison to controls.

Conclusions: Based on the limited currently available information any superiority of laser treatment in comparison to conventional treatment of peri-implantitis could not be identified. Considering the high heterogeneity and the low number of included studies we cautiously conclude that non-surgical laser therapy may be investigated as phase I therapy for the treatment of peri-implantitis. Future research should emphasize on detailed description of the specific laser characteristics and power settings in clinical studies.

KEYWORDS:

Peri-implantitis, lasers, systematic review, meta-analysis

Even though dental implants are a successful treatment modality, failures may occur.[1,2] Peri-implantitis is the most common reason for a late failure and can occur even after years of successful osseointegration.[3,4]

Despite the structural differences between periodontal and peri-implant tissues[5] there are many similarities in the microbiota that is responsible for the development of periodontal and peri-implant diseases.[6,7] Peri-implantitis is defined as an inflammatory disease that is characterized by loss of supporting bone around a functioning implant.[8,9] Microorganisms residing on the implant surface are considered to be the primary etiologic factor of peri-implantitis.[10,11] The role of microbial plaque accumulation in the development of peri-implantitis has been well documented.[10-14] On the contrary, the ideal method of implant surface decontamination in order to re-establish the health of peri-implant tissue remains to be determined.[15]

Removal of bacterial deposits is essential in the treatment of peri-implant infections and various therapeutic approaches have been described in the literature including mechanical debridement, disinfection with chemotherapeutic agents and laser therapy.[16,17] Recently, there has been a plenitude of scientific data regarding the use of laser irradiation to achieve titanium surface decontamination and thus research is focusing in their potential use in the treatment of peri-implantitis.[18-20] Results from an in vitro study have shown that Er:YAG, CO_2 and diode lasers can achieve high, or even complete elimination of surface bacteria on contaminated titanium surfaces.[18] In vitro data have shown that CO_2 and diode lasers do not cause any surface alterations following irradiation.[19,20] Er:YAG laser can also be used for implant treatment without harming the titanium surface if proper settings are applied.[19, 20]

Despite the amount of published data reporting on the treatment of peri-implantitis using different laser wavelengths there has been no systematic assessment of their efficacy. Therefore, the aim of this review was to address the question **‘’is laser therapy as a monotherapy, or as an adjunctive therapy, an efficacious treatment modality for patients with peri-implantitis? ‘‘.**

MATERIALS & METHODS

Search Strategy:

The PubMed database of the US National Library of medicine, the EMBASE database and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched for available data. The search included articles published from January 1990 up to and including June 2013. Articles available online in electronic form ahead of print were considered eligible for inclusion. For the purposes of the present study the definition of peri-implantitis described in the 1st European Workshop on Periodontology and reviewed at the 6th Workshop was utilized.[21,22] Based on this definition peri-implantitis was defined as the presence of inflammation of the mucosa and loss of supporting bone around an implant in function.[21,22]

The first phase of the evaluation of the literature included an electronic search using the following combination of terms and key words: (‘‘Peri-implantitis’’ OR ‘‘periimplantitis’’) OR (‘‘peri-implant’’ OR ‘‘periimplant’’) AND ‘’laser’’.

Two reviewers performed the screening independently (G.K., I.K.) after reviewing the title and the abstract of each potentially relevant article for inclusion according to specific inclusion criteria. The full texts of all articles considered as potentially relevant

by at least one reviewer where obtained for eligibility evaluation against the predetermined inclusion criteria.

Inclusion criteria. During the initial selection, titles and abstracts were reviewed for eligible articles. Inclusion of an article was based on the following criteria:

- English language
- Human studies
- Prospective, controlled, clinical studies reporting data from at least 10 patients
- Use of Laser therapy as monotherapy or as an adjunct in the treatment of peri-implantitis
- Report of (or report of data allowing the calculation of) clinical indexes of peri-implant disease, including clinical attachment level (CAL) and probing depth (PD)
- Follow-up of at least 6-months following treatment

The electronic search was complemented by manual search of the following journals between January 1990 to June 2013: *Clinical Implant Dentistry and Related Research, Clinical Oral Implants Research, Journal of Clinical Periodontology, Journal of Dental Research, Journal of Periodontology, Lasers in Medical Science, Lasers in Surgery and Medicine, Photomedicine and Laser Surgery (previously, Journal of Clinical Laser Medicine & Surgery), The International Journal of Oral & Maxillofacial Implants, The International Journal of Periodontics and Restorative Dentistry.*

Lastly, the reference list of each of the selected full-text articles was reviewed for article titles suggesting treatment of peri-implantitis with the use of laser as adjunct or as monotherapy. If required, an attempt was made to contact the corresponding authors for obtaining missing, unclear or unpublished data.

Outcome Variables

The primary outcome variables assessed were the clinical attachment level gain (ΔCAL) and the reduction in probing depth (ΔPD).

Selection of Studies\Data Extraction

For the final phase of selection the full-text articles of all potentially relevant studies were acquired and evaluated independently by the two reviewers. If more than one article corresponded to the same clinical study only the most recent article was considered for inclusion.

Any disagreement between the reviewers regarding final inclusion of an article was resolved by discussion. In case of a disagreement that was not resolved, the opinion of a third experienced reviewer (I.K.K.) would be asked for and would be considered final. If the disagreement persisted, it would be reported and analyzed in the results of this study. κ scores (Cohen's kappa coefficient) were employed to determine the level of agreement between the two reviewers.[23]

The two reviewers using a standardized process and specially designed data-extraction forms individually conducted data extraction from the selected studies according to the approach reported in a previous systematic review.[24]

Briefly, the main characteristics of each study (study design, number of patients/implants included, treatment approach, laser characteristics, adjunctive treatment, type of intervention and outcome measures) and clinical outcomes of studies were reported. Any data related to adverse events were recorded. Again any disagreement between the reviewers would be resolved by discussion.

Quality Assessment of Included Studies

A specific protocol was used independently by the two reviewers for the qualitative assessment of the screened articles. The clinical studies included in this study were assessed utilizing criteria from the revised CONSORT statement for evaluation of randomized-controlled trials according to the protocol described in a systematic review by Schwarz et al. (2008).[25,26]

The aim of the quality assessment was to review randomization, masking, follow-up, statistical analysis and report of outcomes for the selected studies. A cumulative score was formed for each study following quality assessment and an overall estimation of risk of bias was assigned to each included randomized clinical trial. Studies where all of the criteria were met were assigned a low risk of bias.[26] A moderate risk was considered when at least one of the criteria was partially met and a high risk of bias was estimated when one or more of the criteria were not met.[26] (Supplemental figure 1)

Statistical Analysis

Meta-analyses were conducted separately for each of the two primary outcomes: CAL and PD. Subgroup effects were studied using meta-regression comparing surgical and non-surgical groups. Heterogeneity among the studies of each outcome were assessed using the χ^2 test and I^2 statistic.[27] Outcome measures were combined with a fixed-effects model in the absence of heterogeneity, or with a random-effects model in the presence of heterogeneity with a p-value < 0.05.[28] Forest plots were produced reporting weighted average of outcomes with 95% confidence interval, and overall treatment effects and subgroup effects at a significance level of 0.05. All above statistical analyses were carried out by a statistical software.**k** Regression tests for funnel plots asymmetry were conducted to explore potential publication bias.[29]

RESULTS:

A total of 136 titles and abstracts were identified following electronic search using the specific combination of terms and keywords. The manual search of the journals mentioned above added one potentially relevant article to the search for a total number of 137 titles.[30] After the first phase of selection 122 articles were excluded based on the title and the abstract. Inter-examiner agreement was high. (Cohen's kappa statistic for inter-reviewer agreement: k = 0.91)

For the second phase, the complete full-text articles of all studies selected (15) in the first phase were scrutinized.[30-44] Throughout this procedure the full-texts of these studies

were reviewed independently and twice by two reviewers (G.K. and I.K.) and selection was based on the predetermined inclusion criteria.

A total of 9 publications were excluded during this stage of selection (k=0.88).[30-38] (Table 1) Reference checking of relevant reviews and included studies revealed no additional papers. Six publications (6 studies) fulfilled the inclusion criteria and were included in this systematic review.[39-44] (Figure 1, Table 2)

Results of Quality Assessment

One of the six studies was a controlled clinical study[39], while five were randomized controlled clinical studies.[40-44] Three studies were assessed as having a high risk of bias[39,42,43], one as having a moderate risk of bias[44] and two as having low risk of bias.[40,41]

Subdivision of Included Studies

Data were subdivided into 3 categories based on the type of laser investigated in each study. (Supplemental table 1)

- 4 publications reported on results of Er:YAG treatment using a 2,940 nm wavelength.[40-43]

In three of the four publications the same laser system was utilized for implant surface decontamination.[41-43] The remaining study utilized a different Er:YAG laser system with the same wavelength and similar power settings.[40] This was the only study where access flap surgery was employed as a treatment approach; in all other studies Er:YAG irradiation was performed in a non-surgical manner.

In this study the researchers assessed the effect of Er:YAG laser application in comparison to mechanical cleaning with plastic curettes and application of cotton pellets moistened with sterile saline.[40] Evaluation of reduction in PD revealed statistically significant difference in both groups at 12-months, but only the control group demonstrated a significant effect in PD reduction at the 24-months interval. Connective tissue attachment loss (CA loss) and BOP values were significantly reduced in both groups at 12-months, while only the BOP values remained statistically significantly reduced at 24-months.

Renvert et al. (2011) [41] performed decontamination with an air-abrasive as a control to compare the efficacy of Er:YAG laser as a monotherapy in the non-surgical treatment of peri-implantitis in 100 sites. At 6-months post-treatment they could not find any significant intergroup or intragroup reduction in peri-implant probing depth measurements, but found a significant decrease in bleeding on probing around implants allocated in both groups.

Two studies evaluated the same treatment approach utilizing Er:YAG laser for the non-surgical treatment of peri-implantitis.[42,43] Mechanical debridement with plastic curettes and administration of a chemotherapeutic agent (0.2% chlorhexidine) was utilized in the control group. Findings from the above studies suggest that a significant reduction in PD and CA loss can be expected following this type of treatment of peri-implantitis at 6-months post-intervention, but this reduction is not maintained at the 12-month interval. The mean reduction in PD and CA loss was less than 1mm in both

studies.[42,43] No difference between the test and control groups was noted. Reduction in BOP was significant in comparison to baseline in both studies and was significantly more with the application of Er:YAG laser treatment.[42,43]

- 1 prospective study reported on the use of CO_2 laser treatment[39]

Deppe *et al.* (2007) [39] reported the outcomes of CO_2 laser treatment on 29 implants in the test group that were followed for at least 6-months at the observation endpoint. The treatment approach in the ''test'' subgroups included disinfection using CO_2 laser irradiation with a 10.6 µm wavelength. Implants in the control group (n=25) were treated with conventional decontamination. Each group was further divided in two subgroups receiving either adjunctive soft tissue resection or guided bone regeneration. At the post-treatment evaluation all treatment approaches were significantly effective in reducing PD in comparison to baseline. However attachment levels were substantially reduced only in the bone augmentation subgroups of each group and not in the soft tissue resection subgroups. In the soft tissue resection-conventional treatment subgroup the attachment levels remained unchanged, while there was a 0.8 mm gain in the soft tissue resection-laser treatment subgroup. The inter-subgroup variation in CAL was diminished between conventional treatment and laser treatment in the bone augmentation subgroups. CO_2 laser treatment was successful in halting the progression of CA loss in all cases of surgical treatment, but it was significantly more successful than conventional decontamination only when combined with soft tissue resection.

- 1 randomized clinical trial reported on the use of photodynamic therapy[44]

In this study the efficiency of a combination of a diode laser with a wavelength of 660 nm and power density of 100 mW with a phenothiazine chloride dye, namely photodynamic therapy (PDT), in non-surgical treatment of peri-implantitis was investigated. The dual application of PDT with a 1-week interval was compared to a single application of minocycline hydrochloride microspheres in the peri-implant sulci. A total of 20 implants per group with a diagnosis of early peri-implantitis were evaluated in this study. All implants had probing depths in the range of 4-6 mm with active bleeding on probing and radiographic sings of bone loss. Pockets in both test groups were irrigated with 3% hydrogen peroxide in addition to the randomly allocated treatment modality. No statistically significant reduction was noted for either of the groups in regards to clinical attachment levels in comparison to baseline as well as between two groups. Both treatment modalities resulted in similar and statistically significant reductions in probing depth at 6-months even though the magnitude of reduction was not clinically significant (PDT group: 0.36 mm). Complete resolution of inflammation as determined by the presence of bleeding on probing was unpredictable with either of the two treatment approaches.

Adverse events associated with laser treatment were only reported in one study.[39] In this study, four implants that were treated with CO_2 irradiation and bone augmentation were eventually lost due to chronic infection.[39] (Table 3)

Meta-Analysis

The heterogeneity between the types of intervention used in each study (laser wavelength) allowed for only one meta-analysis. Owing to the adequate number of

studies with the use of Er:YAG laser using relatively homogenous inclusion/exclusion criteria, a meta-analysis could be conducted for the results of Er:YAG laser treatment at the 6-month post-intervention observation interval. Regression tests for funnel plots asymmetry suggested no evidence of publication bias for CAL and PD (p=0.49, 0.812, respectively).

Figures 2, 3 present the forest plots and summary estimates for weighted mean difference of CAL and PD between the treatment and control groups. For CAL and PD outcomes, three studies were included in the meta-analysis as non-surgical group[41-43] and one study was included as surgical group.[40] Tests for overall heterogeneity returned to be non-significant for CAL and PD (p=0.12 and p=0.31). Thus, the fixed effects models were applied for CAL and PD outcomes.[27] The pooled effect sizes in CA loss after 6-months for the non-surgical group, for the surgical group and for all studies were found to be non-significant (p=0.22, p=0.14 and p=0.09, respectively). No statistically significant evidence for treatment effects in reducing PD level were found for the non-surgical group, surgical group, and all studies (p=0.97, p=0.16 and p=0.7, respectively. There was no evidence for subgroup difference between surgical and non-surgical treatments in CA loss and PD reduction (p=0.36 and p=0.17, respectively).

DISCUSSION

The present systematic review included 6 clinical studies that reported on outcomes of laser therapy in the treatment of peri-implantitis.[39-44] The predefined criteria set for selection of relevant studies allowed only for the inclusion of prospective, controlled clinical studies with adequate number of subjects and follow-up time so as to maintain a high level of evidence.[45] Narrative synthesis of the results revealed that all included studies reported improvement in the peri-implant condition of implants treated with the various laser wavelengths. Due to the lack of longitudinal data on implant survival in most of the included studies, CAL and PD were used as relevant surrogates.

The magnitude of reduction in PD and CA loss varied among studies based on the type of intervention (surgical versus non-surgical).[39-44] In four out of six studies a non-surgical approach was utilized.[41-44] Non-surgical interventions revealed decreases in CA loss and PD that were generally less than 1mm.[41-44] Results showed that the use of either Er:YAG laser (2,940 nm), or photodynamic therapy with a diode laser (660 nm) in a non-surgical manner were potent in reducing mucosal inflammation and to some extent the probing depth around implants diagnosed with peri-implantitis.[41-44] This reduction was significant up to 6-months post-treatment, but waned after 12-months had elapsed.[42] Since a limited effect of non-surgical laser therapy exists in PD and CA loss reduction, while its potency in reducing peri-implant inflammation is significant, there may be merit in the investigation of non-surgical laser treatment as phase I peri-implantitis therapy.

In the remaining two studies that employed a surgical approach the reduction in clinical parameters was at least two-fold comparing to studies that used a non-surgical treatment approach.[39,40] This observation is consistent with the conclusions of other reviews that have compared the effect of type of intervention on peri-implantitis treatment outcome.[46, 47] There seems to be a consensus among researchers that non-surgical treatment has limited efficacy in yielding clinically significant improvement in

the treatment of peri-implantitis, thus surgical treatment should be considered the preferred approach.[48]

As previously mentioned, the benefit of laser treatment should be investigated as a prequel to surgical treatment. The reduction of the microbial load in the peri-implant pocket during initial laser therapy with a non-surgical approach could potentially further increase the efficiency of surgical treatment applied in an environment with halted inflammation. Alternatively, as Persson *et al.* (2011)[37] have previously suggested, based on the significant short-term effect of non-surgical laser treatment a repetition of the laser application may be advantageous. Findings from this review showed that non-surgical therapy is efficient at controlling peri-implant inflammation for at least 6-months post-intervention.[41-44] Based on this knowledge, a relevant research question would be to identify the ideal repetition intervals for application of laser therapy on the contaminated implant surface until a state of health is re-established and can be maintained.

A limitation of the present systematic review and meta-analysis is that the heterogeneity of data relevant to laser wavelengths, energy settings and laser application techniques did not allow for a quantitative synthesis of data from all the included studies. The ''all-inclusive'' use of the term laser therapy has to be revisited in future studies. Each laser wavelength and its specific pulse energy at the tip are parameters that define a singular treatment modality. It is not scientifically accurate to compare the efficacy of different laser wavelengths under the generic term ''laser treatment'' as this may lead to misleading conclusions. In general most of the studies under-reported the mode of laser-beam application, peak laser power and contact time. As previously stressed, information on laser wavelength is necessary, but not sufficient to convey enough information on how treatment was rendered and additional data regarding the pulse energy transmitted at the fiber tip are pivotal on treatment outcome. As an example, the safe application of the same laser wavelength (2.94 μm) may become unsafe by causing cracks and decrease in the roughness of an implant with just a 200 mJ increase in its energy.[19]

It seems that identification of appropriate parameters for laser application in the treatment of peri-implantitis must precede controlled studies comparing the efficacy of laser therapy to conventional implant treatment modalities. Variables such as wave mode, diameter of optic fiber, pulse energy and pulse duration are among others that may significantly modify the thermal events associated with laser treatment and lead to titanium surface alterations.[19] Subsequently, modified surface structure may alter host tissue response to the treated titanium surface, thus masking the decontamination effect that laser therapy has to offer.[18,49] Therefore study design of future clinical trials should include identification of the ideal parameter settings that yield the best efficiency to toxicity ratio for the specific laser wavelength utilized as determined by proof-of-principle, or pilot studies. It is obvious that explicit report of power settings and mode of application is of paramount importance in clinical studies assessing the efficacy of laser treatment.

Another factor that may exert significant influence over host-response to treatment and was underreported in the included studies is smoking.[50]

It has been previously shown that smoking has a deleterious effect on response to peri-implantitis treatment in a dose-dependent manner.[51] Available information regarding

the impact of smoking on the outcomes of laser therapy in the treatment of peri-implantitis are missing from the literature. Previous studies in periodontal treatment have shown that laser therapy may provide additional benefits for smokers, even though results are equivocal.[52,53,54]

A further limitation of this review is that a number of included studies used confounding factors such as, hydrogen peroxide, chlorexhidine or plastic curettes in combination with laser treatment. It has been previously reported that these interventions may negatively interfere with the biocompatibility of titanium surfaces.[55,56,57] Thus, future research studies should be designed to assess the efficiency of a specific laser wavelength by ruling out other confounding variables that may interfere with the outcome, such as chemotherapeutic or mechanical agents. Additionally, the use of such confounding factors in the treatment of patients in each control group warrants interpretation of results of the meta-analysis with caution. Researchers should attempt to use the simplest and most universally accepted treatment modality, such as the use of sterile saline for disinfection as a control intervention when attempting to assess laser treatment efficacy.[56]

CONCLUSIONS

We conclude that based on the limited currently available information any superiority of laser treatment in comparison to conventional treatment of peri-implantitis could not be identified. Considering the high heterogeneity and the low number of included studies we cautiously conclude that non-surgical laser therapy may be investigated as phase I therapy for the treatment of peri-implantitis. Future research should emphasize on detailed description of the specific laser characteristics and power settings in clinical studies.

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Correspondence address: (e-mail can be published), George A. Kotsakis, DDS, Advanced Education Program in Periodontology, University of Minnesota, 515 Delaware Street SE, Minneapolis, MN 55455, (651) 395-9200, kotsa001@umn.edu

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Figure 1.

Process through the stages of the present systematic review and meta-analysis modified from the QUOROM statement flowchart[22]

Figure 2.

Forest plot for selected studies reporting CAL changes after 6-months of treatment

Footnote: Weighted mean differences were estimated by a fixed effects model. Mean difference > 0 indicates better treatment effect in laser group than control group.

Figure 3.

Forest plot for selected studies reporting PD changes after 6-months of treatment.

Footnote: Weighted mean differences were estimated by a fixed effects model. Mean difference > 0 indicates better treatment effect in laser group than control group.

Table 1.

Studies excluded in the second phase of selection with reasons for the exclusion of each study.

Excluded studies	**Reason for exclusion**
Deppe et al.[30]	Non-english language
Romanos & Netwig[31]	Insufficient clinical data reported
Bach et al.[32]	Insufficient clinical data reported
Schwarz et al.[33]	Non-english language
Schwarz et al.[34]	Uncontrolled study
Sennhenn- Kirchne et al.[35]	Ex vivo study design
Romanos & Netwig[36]	Different definition of peri-implant disease
Persson et al.[37]	Same study population as Renvert et al. [41]
Schwarz et al.[38]	Same study population as Schwarz et al.[40]

Table 2

Study	Study design	Treatment approach	Intervention		Adjuctive Intervention	Patients/ Implants at baseline	Number of Dropouts	Follow-up period (months)
Schär et al.[44]	RCT	Non-surgical	Test group	Photodynamic treatment (HELBO)	Mechanical debridement with titanium curettes and glycine-based powder air polishing and irrigation with 3% hydrogen peroxide	20 patients/ 20 implants	0	6
			Control group	Local delivery of minocycline microspheres	Same as test group	20 patients/ 20 implants		
Schwarz et al.[40]	RCT	Surgical	Test group	Er: YAG laser	Implantoplasty at the supracrestally exposed implant threads	15 patients/ 19 implants	1	24
			Control group	Plastic curettes and cotton pellets soaked with sterile saline	Same as test group	15 patients/ 16 implants	5	
Renvert et al.[41]	RCT	Non-surgical	Test group	Er:YAG laser	No	21 patients/ 55 implants	0	6
			Control group	Air abrasive	No	21 patients/ 45 implants		
Deppe et al.[39]	Prospective clinical study	Surgical	Test group	CO_2 laser application with soft tissue resection or bone augmentation	Air-powder abrasive application supracrestally	19 patients/ 39 implants	0	5-59
			Control group	Conventional decontamination with soft tissue resection or bone augmentation	Same as test group	13 patients/ 34 implants		
Schwarz et al.[42]	RCT	Non-surgical	Test group	Er:YAG laser	No	10 patients/ 20 implants	0	12

			Control group	Mechanical debridement with plastic curettes and 0,2% chlorhexidine	No	10 patients/ 20 implants		
Schwarz et al.[43]	RCT	Non-surgical	Test group	Er: YAG laser	No	10 patients/ 16 implants	0	6
			Control group	Mechanical debridement with plastic curettes and 0,2% chlorhexidine	No	10 patients/ 16 implants	2	

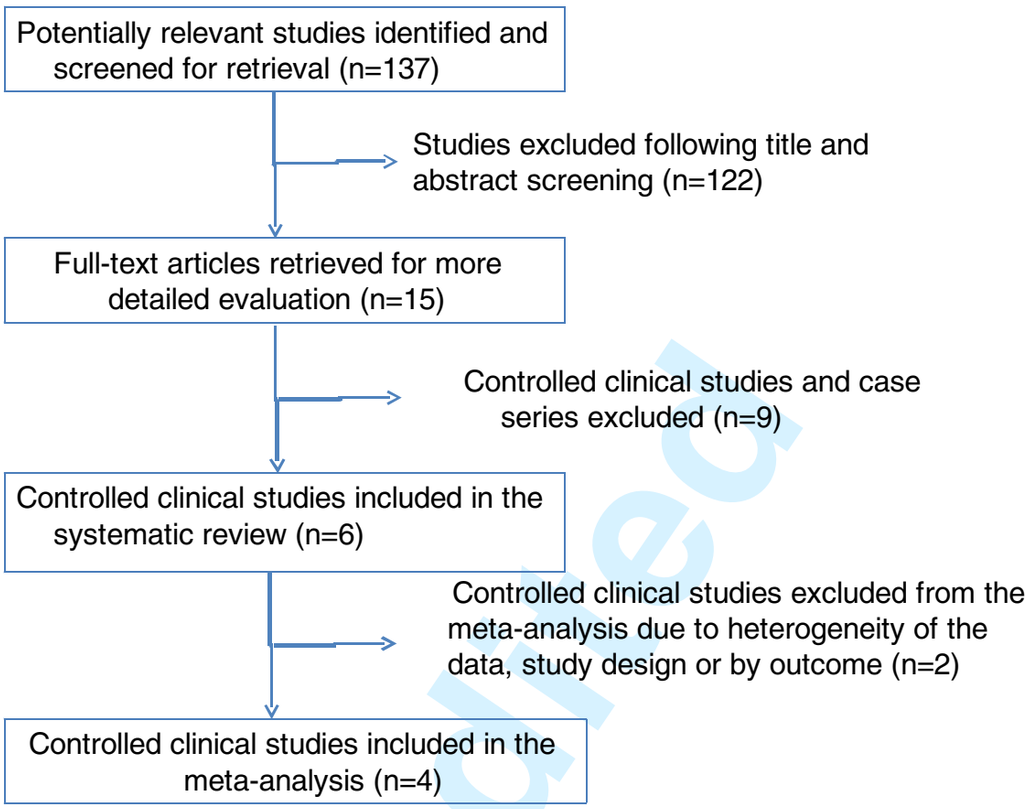
Table 3

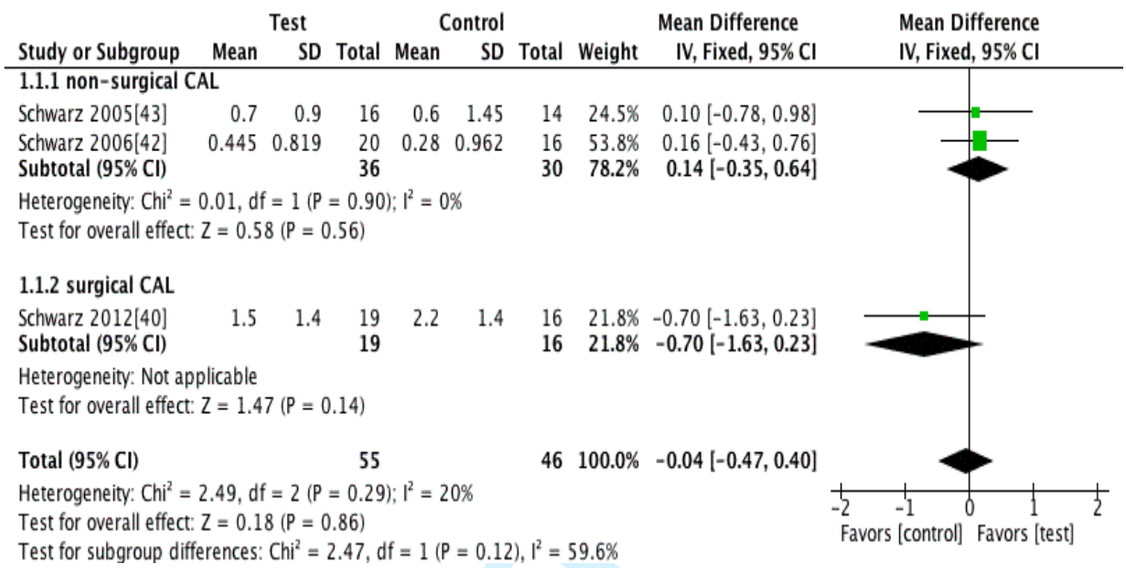
Study	Intervention		Probing depth (PD) Mean±SD (mm)			Clinical attachment level (CAL) Mean±SD (mm)			Adverse events
			Baseline	Outcome	Difference	Baseline	Outcome	Difference	
Schär et al.[44]	Test group	Mechanical debridement with titanium curettes and glycine-based powder air polishing and photodynamic treatment	4.19±0.55	3.83±0.58	N.R*	2.66±0.73	2.50±0.77	N.R*	None related to laser treatment
	Control group	Mechanical debridement with titanium curettes and glycine -based powder air polishing and local delivery of minocycline	4.39±0,77	3.90±0.78	N.R*	2.72±0,72	2.53±0.65	N.R*	
Schwarz et al.[40]	Test group	Er:YAG laser	5.1±1.6	3.4±0.6	1.7±1.4	6.4±2.0	4.9±1,1	1.5±1.4	None related to laser treatment
	Control group	plastic curettes and cotton pellets soaked with sterile saline	5.5±1.8	3.1±0.6	2.4±1.5	6.7±2.2	4.5±1,4	2.2±1.4	
Renvert et al.[41]	Test group	Er:YAG laser	5.7±1.7	5.1±1.5	0.8 ±0.5	N.R*	N.R*	N.R*	None related to laser treatment
	Control group	Air abrasive	6.3±2.0	5.6±1.8	0.9±0.9	N.R*	N.R*	N.R*	
Deppe et al.[39]	Test group	CO2 laser with soft tissue resection or augmentation	5.7±1.4	3.5±1.5	N.R*	7.2±1.3	5.1±1.1	N.R*	Chronic infection remained in a site treated with CO_2 laser and bone augmentation and all 4 implants at the site were eventually lost

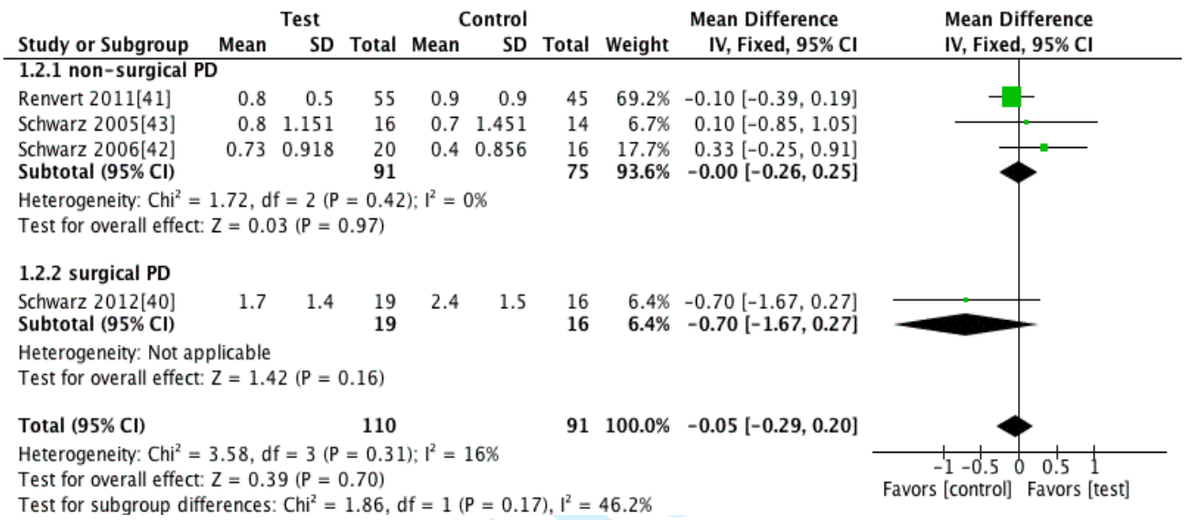
	Control group	Conventional decontamination with soft tissue resection or with augmentation	5.7±1.8	3.4±1.2	N.R*	7.1±1.3	5.4±6.7	N.R*	Severe infection occurred in a site with advanced peri-implantitis that was treated with conventional decontamination and bone augmentation. The infection led to loss of 4 implants in this case.
Schwarz et al.[42]	Test group	Er:YAG laser	5.25±1.02‡	4.52±0.79‡	0.73±0.9	5.88±0.8‡	5,4±0.8‡	0.4±0.81	None related to laser treatment
	Control group	Mechanical debridement with plastic curettes and 0.2% chlorhexidine	5.21±0.91‡	4.81±0.79‡	0.4±0.9	5.82±1.1‡	5.54±0.9‡	0.28±0.96	
Schwarz et al.[43]	Test group	Er:YAG laser	5.4±1.2	4.6±1.1	0.8±1.15†	5.8±0.9	5.1±0.9	0.7±0.9†	None related to laser treatment
	Control group	Mechanical debridement with plastic curettes and 0.2% chlorhexidine	5.5±1.5	4.8±1.4	0.7±1.45†	6.2±1.5	5.6±1.4	0.6±1.5†	

N.R*: Not reported, †Calculated by the authors, ‡Reported following contact with the original author

[k] Review Manager (RevMan). Version 5.2. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2012.


Potentially relevant studies identified and screened for retrieval (n=137)
Studies excluded following title and abstract screening (n=122)
Full-text articles retrieved for more detailed evaluation (n=15)
Controlled clinical studies and case series excluded (n=9)
Controlled clinical studies included in the systematic review (n=6)
Controlled clinical studies excluded from the meta-analysis due to heterogeneity of the data, study design or by outcome (n=2)
Controlled clinical studies included in the meta-analysis (n=4)


Test
Control
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Fixed, 95% CI
IV, Fixed, 95% CI
1.1.1 non-surgical CAL
Schwarz 2005[43] 0.7 0.9 16 0.6 1.45 14 24.5% 0.10 [-0.78, 0.98]
Schwarz 2006[42] 0.445 0.819 20 0.28 0.962 16 53.8% 0.16 [-0.43, 0.76]
Subtotal (95% CI) 36 30 78.2% 0.14 [-0.35, 0.64]
Heterogeneity: Chi² = 0.01, df = 1 (P = 0.90); I² = 0%
Test for overall effect: Z = 0.58 (P = 0.56)
1.1.2 surgical CAL
Schwarz 2012[40] 1.5 1.4 19 2.2 1.4 16 21.8% -0.70 [-1.63, 0.23]
Subtotal (95% CI) 19 16 21.8% -0.70 [-1.63, 0.23]
Heterogeneity: Not applicable
Test for overall effect: Z = 1.47 (P = 0.14)
Total (95% CI) 55 46 100.0% -0.04 [-0.47, 0.40]
Heterogeneity: Chi² = 2.49, df = 2 (P = 0.29); I² = 20%
Test for overall effect: Z = 0.18 (P = 0.86)
Test for subgroup differences: Chi² = 2.47, df = 1 (P = 0.12), I² = 59.6%
-2
-1
0
1
2
Favors [control]
Favors [test]


Test
Control
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Fixed, 95% CI
IV, Fixed, 95% CI
1.2.1 non-surgical PD
Renvert 2011[41] 0.8 0.5 55 0.9 0.9 45 69.2% -0.10 [-0.39, 0.19]
Schwarz 2005[43] 0.8 1.151 16 0.7 1.451 14 6.7% 0.10 [-0.85, 1.05]
Schwarz 2006[42] 0.73 0.918 20 0.4 0.856 16 17.7% 0.33 [-0.25, 0.91]
Subtotal (95% CI) 91 75 93.6% -0.00 [-0.26, 0.25]
Heterogeneity: Chi² = 1.72, df = 2 (P = 0.42); I² = 0%
Test for overall effect: Z = 0.03 (P = 0.97)
1.2.2 surgical PD
Schwarz 2012[40] 1.7 1.4 19 2.4 1.5 16 6.4% -0.70 [-1.67, 0.27]
Subtotal (95% CI) 19 16 6.4% -0.70 [-1.67, 0.27]
Heterogeneity: Not applicable
Test for overall effect: Z = 1.42 (P = 0.16)
Total (95% CI) 110 91 100.0% -0.05 [-0.29, 0.20]
Heterogeneity: Chi² = 3.58, df = 3 (P = 0.31); I² = 16%
Test for overall effect: Z = 0.39 (P = 0.70)
Test for subgroup differences: Chi² = 1.86, df = 1 (P = 0.17), I² = 46.2%
-1 -0.5 0 0.5 1
Favors [control] Favors [test]