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ABSTRACT

This systematic review and meta-analysis assessed the efficacy of lasers in reducing dentin hypersensitivity (DH) as compared with placebo or no treatment. Seven electronic databases and a manual search resulted in 2,538 unique publications. After selection, 13 studies were included in the meta-analysis. A CONSORT-based quality assessment revealed that 3 and 10 studies were at low and high risk of bias, respectively. A random-effects model with the generic inverse variance standardized mean difference (SMD) was used because of expected heterogeneity. Meta-analyses of the baseline-end of follow-up changes in pain revealed no differences for Er,Cr:YSSG *vs.* placebo (SMD = 2.49; 95% CI, -0.25 to 5.22; $p = .07$) but did reveal differences in favor of lasers for Er:YAG *vs.* placebo (SMD, 2.65; 95% CI, 1.25 to 4.05; $p = .0002$), Nd:YAG *vs.* placebo (SMD, 3.59; 95% CI, 0.49 to 6.69; $p = .02$), and GaAlAs *vs.* placebo (SMD, 3.40; 95% CI, 1.93 to 4.87; $p < .00001$). High and significant heterogeneity was found for all comparisons. In conclusion, Er:YAG, Nd:YAG, and GaAlAs lasers appear to be efficacious in reducing DH. However, given the high heterogeneity of the included studies, future randomized controlled clinical trials are needed to confirm these results.

KEY WORDS: dentin sensitivity, low-level laser therapy, dentin-desensitizing agents, laser semiconductor, solid-state lasers, review.

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Lasers for the Treatment of Dentin Hypersensitivity: A Meta-analysis

INTRODUCTION

Dentin hypersensitivity (DH) is a frequently reported dental condition that is typically characterized by short, sharp pain, which cannot be ascribed to any other form of dental defect or pathology, arising from exposed dentin in response to thermal, evaporative, tactile, osmotic, or chemical stimuli (Holland *et al.*, 1997). The prevalence of DH ranges from 4% to 74% (Rees and Addy, 2002), depending on the population screened. Its pathogenesis remains unclear. A commonly supported mechanism for DH is the hydrodynamic theory, which assumes that painful stimulation increases fluid flow within the dentinal tubules, causing the activation of resident baroreceptors (Brannström *et al.*, 1967). Based on this theory, the ideal treatment for DH should reduce fluid flow within the dentinal tubules or block the pulp nerve response (Holland *et al.*, 1997). Accordingly, several approaches have been proposed for in-office DH therapy, such as desensitizing agents (Lan *et al.*, 1999), iontophoresis, adhesives, and resins (Porto *et al.*, 2009).

Lasers have been recently proposed for the in-office treatment of DH. The exact mechanism of action of lasers in DH is not clearly understood, although several theories have been proposed. For low-intensity lasers (*e.g.*, GaAlAs), the irradiation may have a photo-bio-modulating effect on cellular activity, increasing the deposition of tertiary dentin by odontoblastic cells (Ladalaro *et al.*, 2004). Middle-output-power lasers (*e.g.*, Er:YAG, Nd:YAG, and Er,Cr:YSSG) may reduce or obliterate the dentinal tubules (Sgolastra *et al.*, 2011). For Er:YAG and Er,Cr:YSSG, the efficacy in reducing DH is thought to be related to the thermo-mechanical ablation mechanism and to the high absorption of their wavelengths by water (Hossain *et al.*, 1999; Braun *et al.*, 2010; Yilmaz *et al.*, 2011c). These effects may lead to the evaporation of the superficial layer of dentinal fluid, reducing the flow within the dentinal tubules. The dentin may be fused due to exposure to Nd:YAG laser, solidifying into a glazed, non-porous surface (Birang *et al.*, 2007; Dilsiz *et al.*, 2010a). Nd:YAG irradiation can also directly act at the nerve level by blocking C and A β fibers (Orchardson *et al.*, 1997).

Previous studies have sought to analyze the efficacy of lasers in treating DH. Sgolastra *et al.* (2011) and He *et al.* (2011) performed systematic reviews of this question. These authors could not clarify whether the effectiveness of the laser was superior to that of a placebo, but they did highlight that laser application was safe and without adverse events. A more recent meta-analysis (Lin *et al.*, 2013) found that the use of lasers was superior to that of a placebo in the treatment of DH. However, these authors did not stratify the results according to the type of laser, and they argued that different lasers may not have the same effects on reducing DH.

For assessment of whether lasers are efficacious in reducing DH when compared with a placebo or no treatment, the literature must be evaluated systematically. Therefore, the primary aim of the present systematic review and meta-analysis was to assess the efficacy of lasers, stratified according to

laser type, on changes in pain level, when compared with a placebo or no treatment. The secondary aim was to assess the safety of the laser application and the occurrence of adverse events.

MATERIALS & METHODS

This systematic review was conducted in agreement with recommendations of the Cochrane Collaboration (Higgins and Green, 2011) and the principles of the PRISMA statement (Moher *et al.*, 2009).

Search Strategy

A thorough search of the literature was performed in the computerized databases of MEDLINE, Cochrane Controlled Clinical Trial Register, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects (DARE), CINAHL, Science Direct, and SCOPUS, through February 10, 2013. Two blinded reviewers (FS and AP) independently performed the study-selection process. Inter-reviewer reliability was determined by Cohen's *k* test, with an assumed acceptable threshold value of 0.61 (Landis and Koch, 1977a,b). Discrepancies with regard to the inclusion or exclusion of studies were resolved by discussion between the reviewers who selected the studies.

The databases were searched with the following search algorithm, in which Boolean operators were used and the asterisk symbol (*) indicated truncation: In the CINAHL, Cochrane Controlled Clinical Trial Register, Cochrane Database of Systematic Reviews, and DARE databases, the MeSH terms were not used.

A manual search was performed of issues from the past 15 years of the following journals: *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 Endodontics*, *International Journal of Endodontics*, *Journal of the American Dental Association*, *Journal of Clinical Dentistry*, *Lasers in Medical Science*, *Lasers in Surgery and Medicine*, *Clinical Oral Investigations*, and *Photomedicine and Laser Surgery*. To avoid selection bias, no restrictions were applied with regard to language or year, and the references of all selected full-text articles and related reviews were scanned. The corresponding authors were contacted, as needed, to find unpublished material or obtain missing data.

Eligibility Criteria

The study-selection process was performed by two blinded reviewers (FS and RG) in 2 phases. In the first phase, the studies were analyzed according to the following inclusion criteria: (1) randomized controlled clinical trials (RCTs); (2) studies comparing laser treatment of DH with placebo or no treatment; and (3) studies conducted on adult humans (age > 18 yrs). Only studies that met all of the inclusion criteria were admitted to the second phase, which consisted of analysis of the pre-selected studies according to the following exclusion criteria: (1) studies including patients with systemic diseases or who had undergone treatment or were taking drugs that could alter pain perception; (2) studies that did not assess DH by scale or score; and (3) studies not reporting numerical data.

Outcome Variables

Based on the results of the search, 4 comparisons were possible: (1) Er,Cr:YSSG vs. placebo, (2) Er:YAG vs. placebo, (3) Nd:YAG vs. placebo, and (4) GaAlAs vs. placebo.

The primary outcome of interest was the change in the baseline-end of follow-up pain level. Secondary outcomes of interest included cost-effectiveness analysis.

Quality Assessment

The quality assessment of the methodology of all of the included studies (Table 1) was performed independently by two blinded reviewers (FS and AM) according to the revised recommendation of the CONSORT statement. The level of inter-reviewer agreement was calculated as reported above. After the scores had been determined, an overall estimation of plausible risk of bias (low, moderate, or high) was performed for each selected study. Low risk of bias was estimated when all of the criteria were met, a moderate risk was estimated when one or more criteria were partly met, and a high risk of bias was estimated when one or more criteria were not met (Higgins and Green, 2011).

Statistical Analysis

Data were combined for the meta-analysis by a statistical software package (RevMan software, version 5.2, The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen, Denmark). Mean differences (MD), 95% confidence intervals (CIs), and standard errors (SEs) were entered for all studies to combine data from parallel and split-mouth studies (Lesaffre *et al.*, 2007). Because the main outcome of interest was reported on different scales, the pooled effect size was calculated by the generic inverse variance standardized mean difference (SMD). For split-mouth studies, an intrapatient correlation coefficient of 0.5 was assumed.

Because of the expected interstudy heterogeneity, a random-effects model (Der Simonian and Laird model) with the corresponding Z-statistics was used. The *p* values and 95% CIs were calculated. A level of $p < .05$ was considered statistically significant. The χ^2 -based Q-statistic method and I^2 measurement were used to assess the heterogeneity, and the level of significance was assumed to be $p < .1$. However, because of the moderate insensitivity of the Q statistic, only an I^2 value of 0% was considered reliable to detect the absence of heterogeneity. Forest plots for each meta-analysis were used to present the raw data (means, SDs, and sample sizes) for each arm of the study.

RESULTS

Search

The electronic and manual searches resulted in 4,602 articles, including 885 in MEDLINE, 68 in the Cochrane Central Register of Controlled Trials, 160 in the Cochrane Database of Systematic Review, 4 in DARE, 659 in CINAHL, 561 in the ISI Web of Science, 2,265 in Science Direct, and 126 in SCOPUS. After duplicates were removed, 2,538 articles were identified (inter-reviewer agreement, $k = 0.84$). In total, 2,499 articles were excluded based on evaluation of the title and abstract. Of

Table 1. Categories for Assessing 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 = 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

Table 2. List of Excluded Studies and Reasons for Exclusion

Study	Exclusion Criterion	Type of Study
Talesara <i>et al.</i> , 2012	A.2	Randomized clinical trial
Ehlers <i>et al.</i> , 2012	A.2	Randomized clinical trial
Umberto <i>et al.</i> , 2012	A.2	Randomized clinical trial
Flecha <i>et al.</i> , 2013	A.2	Randomized clinical trial
Sgolastra <i>et al.</i> , 2011	A.1	Systematic review
He <i>et al.</i> , 2011	A.1	Systematic review
Dilsiz <i>et al.</i> , 2010b	A.2	Randomized clinical trial
Maamary <i>et al.</i> , 2009	A.1	Clinical trial
Aranha <i>et al.</i> , 2009	A.2	Randomized clinical trial
Kara and Orbak, 2009	A.2	Randomized clinical trial
Dilsiz <i>et al.</i> , 2009	A.2	Randomized clinical trial
Ipci <i>et al.</i> , 2009	A.2	Randomized clinical trial
Birang <i>et al.</i> , 2008	B.2	Randomized clinical trial
Ladalaro <i>et al.</i> , 2004	A.1	Controlled clinical trial
Noya <i>et al.</i> , 2004	A.1	Clinical trial
Ciaramicoli <i>et al.</i> , 2003	A.1	Controlled clinical trial
Marsilio <i>et al.</i> , 2003	A.1	Clinical trial
Corona <i>et al.</i> , 2003	A.1	Controlled clinical trial
Yonaga <i>et al.</i> , 1999	A.2	Randomized clinical trial
Moritz <i>et al.</i> , 1998	A.1	Randomized clinical trial
Moritz <i>et al.</i> , 1996	A.1	Controlled clinical trial
Lan and Liu, 1996	A.1	Clinical trial
Gelskey <i>et al.</i> , 1993	B.3	Randomized clinical trial
Renton-Harper and Midda, 1992	A.1	Controlled clinical trial
Yamaguchi <i>et al.</i> , 1990	A.1	Controlled clinical trial
Sato <i>et al.</i> , 1989	A.1	Clinical trial

the 39 articles assessed for eligibility, 24 were excluded for not satisfying one or more inclusion criteria, and 2 articles were excluded for meeting one or more exclusion criteria. The list of

the excluded studies and the reasons for exclusion are provided in Table 2. Finally, 13 studies qualified for inclusion in the systematic review and meta-analysis (inter-reviewer agreement,

$k = 1$). The PRISMA flowchart of the complete study-selection process is illustrated in Fig. 1.

Description of Included Studies

All of the included studies were RCTs comparing one type of laser with a placebo or no treatment. All publications were in English. Nine were split-mouth studies, whereas 4 studies adopted a parallel design (Table 3). In 4 studies (Gerschman *et al.*, 1994; Birang *et al.*, 2007; Orhan *et al.*, 2011; Yilmaz *et al.*, 2011a), the setting of the study was not clearly reported. The remaining studies performed the research at a university, except for 1 study (Sicilia *et al.*, 2009), in which patients came from both university and private clinics.

The method used to diagnose DH varied widely among the included studies. All of the included RCTs assessed DH through evaporative stimulation, except one study (Birang *et al.*, 2007) that assessed DH through tactile stimulation. Four studies (Gerschman *et al.*, 1994; Sicilia *et al.*, 2009; Vieira *et al.*, 2009; Aranha and Eduardo, 2012) also assessed DH by tactile stimulation. All studies reporting the evaporative assessment of DH used a syringe air blast, although the time of exposure and the intensity of stimulation varied. Studies performing the tactile assessment of DH used different methods of evaluation. Scraping and pressure on the dental surface with periodontal probe or dental explorer were the most commonly used methods. As the instrument for recording DH, 2 studies (Schwarz *et al.*, 2002; Sicilia *et al.*, 2009) used a verbal rating scale (VRS), and the remaining 11 studies used a visual analog scale (VAS) that varied from 0 to 5 or 10 cm.

The lasers and the laser parameters/settings that were used in the studies varied greatly (Table 3). The follow-up ranged from immediately to 6 mos after treatment. Four studies (Gentile and Gregghi, 2004; Birang *et al.*, 2007; Dilsiz *et al.*, 2009; Aranha and Eduardo, 2012) did not report any information about the occurrence of adverse events; 1 study (Gerschman *et al.*, 1994) reported the occurrence of pain after the application of laser; and the remaining studies reported no relevant adverse events. Cost-effectiveness analysis could not be performed because no article analyzed this issue.

Risk of Bias in Included Studies

The results of the CONSORT-based quality analysis are illustrated in Table 4. Three studies (Sicilia *et al.*, 2009; Yilmaz *et al.*, 2011a,b) were at low risk of bias; all of the remaining studies were considered to be at high risk of bias. The most frequent unsatisfactory criteria were the lack of a sample size calculation (Criterion A) and inadequate or unreported methods of randomization and allocation concealment (Criterion B). All of the studies satisfied Criterion E. All studies except one (Gerschman *et al.*, 1994) satisfied Criterion G.

Effects of Intervention

Fig. 2 shows the results of the meta-analyses in terms of the Forest plots for baseline-end of follow-up changes in pain level

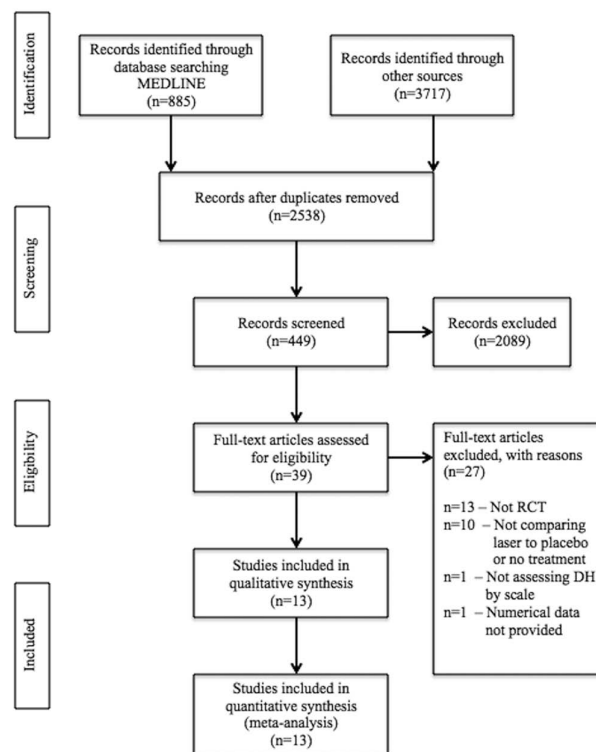


Figure 1. PRISMA flowchart of the search strategy.

for various laser-type vs. placebo comparisons. For Er,Cr:YSSG vs. placebo, the meta-analysis result from 3 studies demonstrated a non-significant change (SMD, 2.49; 95% CI, -0.25 to 5.22; $p = .07$). The meta-analysis result from 4 studies for Er:YAG vs. placebo (SMD, 2.65; 95% CI, 1.25 to 4.05; $p = .0002$), the result from 3 studies for Nd:YAG vs. placebo (SMD, 3.59; 95% CI, 0.49 to 6.69; $p = .02$), and the result from 8 studies for GaAlAs vs. placebo (SMD, 3.40; 95% CI, 1.93 to 4.87; $p < .00001$) each indicated a significant change in pain level in favor of laser use. High and significant heterogeneity was present in all 4 comparisons (Fig. 2). No cost-effectiveness analysis could be performed because none of the included studies reported any information on this issue.

DISCUSSION

Summary of Main Findings

The aim of the present systematic review and meta-analysis was to assess the efficacy of laser use for the in-office treatment of DH, when compared with a placebo or no treatment. The results seemed to support the efficacy of laser use in reducing DH, with the exception of Er,Cr:YSSG, which did not show any significant difference compared with placebo. With regard to the absence of statistical significance for the Er,Cr:YSSG vs. placebo comparison, it should be stressed that only 3 studies were included in that meta-analysis; therefore, the power to detect significant differences could have been low.

Table 3. Characteristics of the Included Studies

Study (setting)	Design	Mean age (range, yrs)	N (F/M)	Intervention (laser settings)	Follow-up after tx	Adverse Events
Aranha and Eduardo, 2012 (U)	SM	NR	28 (NR)	ErYAG (0.64 W) ErCrYSSG (0.25 W) ErCrYSSG (0.5 W) Placebo laser	1 wk, 1 mo	NR
Birang <i>et al.</i> , 2007 (NR)	SM	NR	9 (4/5)	ErYAG (1 W, 15 Hz) NdYAG (100 mJ, 3 Hz) Placebo laser	T0, 1, 3, 6 mos	NR
Dilsiz <i>et al.</i> , 2009 (U)	SM	34 ± 9.8 (18–52)	24 (13/11)	ErYAG (2940 nm, 60 mJ/pulse, 2 Hz, 20 sec) NdYAG (1064 nm, 100 mJ/pulse, 15 Hz, 100 sec) GaAlAs (808 nm, 100 mW, 20 sec) No treatment	30 min, 2 wks, 1, 2 mos	NR
Gentile and Greggi, 2004 (U)	PI	NR (20–52)	32 (22/10)	GaAlAs (670 nm, 15 mW, 4 J/cm ² , 120 sec) Placebo laser	T0	NR
Gerschman <i>et al.</i> , 1994 (NR)	PI	37.5 (15–65)	71 (NR)	GaAlAs (830 nm, 30 mW, 1.8 J, 620 sec) Placebo laser	T0	Pain immed. after tx in two patients
Lier <i>et al.</i> , 2002 (U)	SM	NR (26–66)	17 (14/3)	NdYAG (4 W, 120 sec) Placebo laser	1 wk, 1, 4 mos	None
Orhan <i>et al.</i> , 2011 (NR)	PI	34.31 ± 3.17 (21–51)	16 (8/8)	GaAlAs (655 nm, 25 mW, 4 J/cm ² , 160 sec) Placebo laser	1 d, 1 wk	None
Schwarz <i>et al.</i> , 2002 (U)	SM	36 (23–56)	30 (16/14)	ErYAG (80 mJ, 3 Hz) No treatment	1 wk, 2, 6 mos	None
Sicilia <i>et al.</i> , 2009 (U & PC)	PI	41.67 (19–70)	45 (27/18)	GaAlAs (810 nm, 1.5–2.5 mW, 60 sec) Placebo laser	15, 30 min, 2, 4 days, 1, 2 wks, 1, 2 mos	None
Vieira <i>et al.</i> , 2009 (U)	SM	NR (24–68)	24 (23/7)	GaAlAs (660 nm, 30 mW, 120 sec) Placebo	T0, 3 mos	None
Yilmaz <i>et al.</i> , 2011a (NR)	SM	44 ± 9.7 (18–60)	51 (29/22)	ErCrYSSG (2780 nm, 0.25 W, 20 pulses/sec, 30 sec) GaAlAs (810 nm, 30 mW, 60 sec) No treatment	T0, 1 wk, 1, 3 mos	None
Yilmaz <i>et al.</i> , 2011b (U)	SM	41 (18–58)	48 (26/22)	GaAlAs (500 mW, 60 sec) Placebo laser	T0, 1 wk, 1, 3, 6 mos	None
Yilmaz <i>et al.</i> , 2011c (U)	SM	NR	42 (24/18)	ErCrYSSG (0.25 W, 20 kHz, 30 sec) Placebo laser	T0, 1 wk, 1, 3 mos	None

"Setting" indicates whether the study was performed in a university (U) or private clinic (PC) setting. T0, immediately after treatment (tx). SM, split-mouth; PI, parallel; NR, not reported.

The results obtained here are consistent with those from a previous meta-analysis (Lin *et al.*, 2013), which showed that lasers were significantly more effective than placebo at reducing DH. However, that previous meta-analysis did not consider the different types of lasers and argued that different laser types may not all have the same effect. The results are in contrast to those from our previous systematic review (Sgolastra *et al.*, 2011) in

which we could not exclude the presence of a placebo effect. This discrepancy could be attributed to the very low number of studies (3) included in our previous systematic review. Moreover, no quantitative analysis could be performed in our previous study.

In this study, a high and significant heterogeneity was found for all comparisons. This high heterogeneity could be attributed

Table 4. CONSORT-based Quality Analysis of the Included Studies

Study	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
Aranha and Eduardo, 2012	0	0	1	0	2	0	2	High
Birang <i>et al.</i> , 2007	0	2	1	0	2	2	2	High
Dilsiz <i>et al.</i> , 2009	0	0	1	0	2	2	2	High
Gentile and Gregghi, 2004	0	0	1	0	2	0	2	High
Gerschman <i>et al.</i> , 1994	0	0	1	1	2	0	0	High
Lier <i>et al.</i> , 2002	0	0	1	0	2	2	2	High
Orhan <i>et al.</i> , 2011	0	2	1	1	2	2	2	High
Schwarz <i>et al.</i> , 2002	0	0	1	1	2	2	2	High
Sicilia <i>et al.</i> , 2009	2	2	1	1	2	2	2	Low
Vieira <i>et al.</i> , 2009	0	0	1	1	2	2	2	High
Yilmaz <i>et al.</i> , 2011a	2	2	1	1	2	2	2	Low
Yilmaz <i>et al.</i> , 2011b	2	0	1	1	2	2	2	High
Yilmaz <i>et al.</i> , 2011c	2	2	1	1	2	2	2	Low

Letters refer to categories of quality assessment, as described in Table 1.

to various important discrepancies among the included studies, such as differences in the study design (parallel vs. split-mouth), laser parameters/settings, methods of DH assessment, types of stimulation, and follow-up times. The split-mouth design has the potential advantages of reducing the error variance of the experiment and providing a higher statistical power (Lesaffre *et al.*, 2007), while allowing a smaller number of patients to be included in the trial (Hujoel and DeRouen, 1992). However, comparisons made on a within-patient basis have important disadvantages, because treatments may affect the experimental site in unpredictable ways (*i.e.*, carry-over effects). Furthermore, it has been suggested that split-mouth trials showed deficiencies in reporting and in the application of correct statistical procedures (Lesaffre *et al.*, 2007). Therefore, unless *a priori* knowledge indicates that no carry-over effects exist, the reported estimates of the treatment efficacy should be considered to be biased (Hujoel and DeRouen, 1992).

Differences in the DH assessment methods (*i.e.*, tactile vs. evaporative stimulation) could have led to discrepancies in the levels of reproducibility among the studies, contributing to the high level of heterogeneity. Compared with tactile stimulation, evaporative stimulation is thought to be a more reproducible method for assessing DH (Ide *et al.*, 2001). The studies differed in the scale used for the assessment of DH (VAS vs. VRS). VRS is a more restrictive scale than VAS, and its reliability depends on the ability

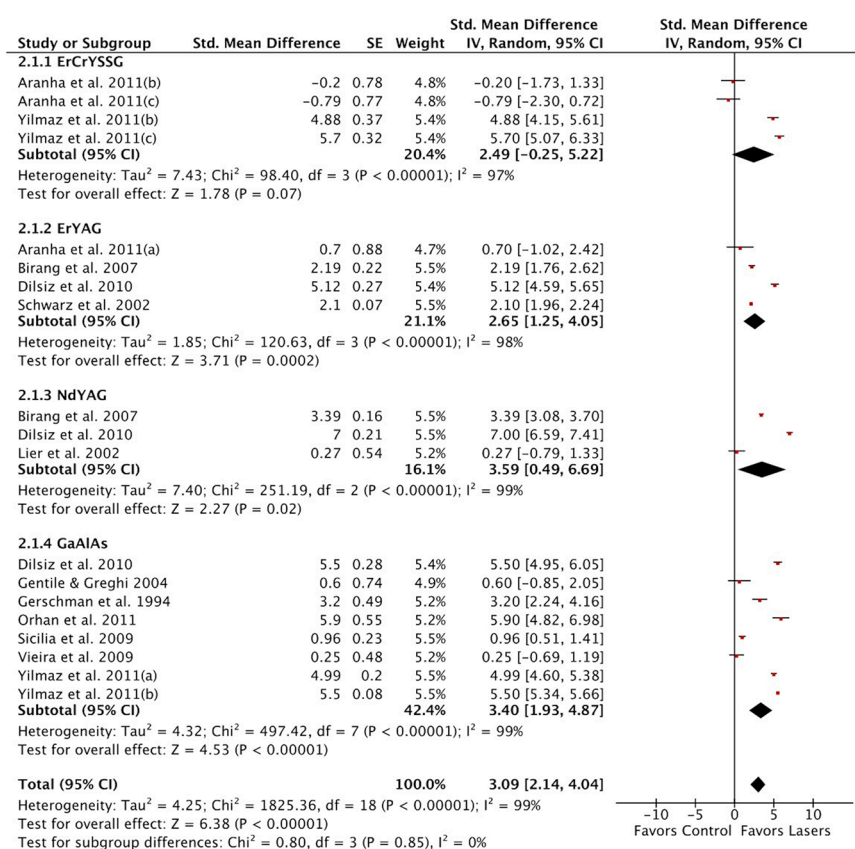


Figure 2. Forest plot for changes in pain levels.

of the patient to define the pain. Therefore, the reliability of VRS cannot always be considered meaningful (Holland *et al.*, 1997). The laser parameters/settings also differed considerably among the studies. However, since no optimal or standardized parameters have been suggested in the literature, it is difficult to state which parameters are more adequate and which may have negatively influenced the results of the studies.

With regard to the occurrence of adverse events, none of the included studies that addressed this issue reported the occurrence of any adverse events, with the exception of 1 study (Gerschman *et al.*, 1994) that reported the occurrence of pain after the laser application. This result is consistent with that of a previous systematic review (He *et al.*, 2011) that failed to retrieve important in-office laser adverse events.

Quality of the Evidence

The CONSORT-based quality analysis revealed that only 3 studies (Sicilia *et al.*, 2009; Yilmaz *et al.*, 2011a,b) were at low risk of bias. The most frequently unsatisfied criterion was the calculation of sample size (Criterion A), which could have contributed to the low statistical power of the studies at high risk of bias (Table 4). The second-most commonly unsatisfied criterion was inadequacy or absence of a randomization method. The randomization process is performed to assign participants to study groups, such that the groups are balanced for known and unknown risk factors to minimize bias (Pihlstrom *et al.*, 2012). Inadequate randomization methods could influence the reliability of the randomization itself, thereby introducing a bias into the study. The present meta-analysis included rigorous inclusion/exclusion criteria and used a wide search strategy with no language restrictions.

Limitations of the Meta-analysis

The present systematic review had some important limitations. A high degree of heterogeneity was found, which could influence the final results of the meta-analysis. Three out of 4 of the comparisons performed had a low number of included studies, which may have contributed to a low power for the meta-analyses. Finally, important discrepancies were found among the included studies that may prevent us from reaching reliable conclusions.

Implications for Research

The present systematic review highlighted the need for additional, well-planned RCTs to examine the efficacy of laser treatment for DH. Such RCTs should have an adequate sample size calculation, clearly describe the randomization process, adopt a continuous scale (*e.g.*, VAS) to record changes in DH, and preferably use an evaporative method to stimulate DH.

Implications for Clinical Practice

Er:YAG, Nd:YAG, and GaAlAs lasers could be efficacious in reducing DH when compared with a placebo. However, considering the important limitations of the present meta-analysis, no clinical recommendation can be given.

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