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Lasers to prevent dental caries: a systematic review

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ABSTRACT

Objective To assess the effectiveness of lasers (at sub-ablative parameters) in reducing caries incidence compared with traditional prophylactic interventions (TPIs) when used alone or together with other TPIs such as pits and fissures sealant or fluoride gels or varnishes.
Design A systematic review. Data sources include Medline (via PubMed), Embase, Web of Science and the Cochrane Library (December 2019).
Eligibility criteria Only randomised trials (RCTs) and controlled clinical trials (CCTs) dealing with prophylactic lasers use (vs TPI or untreated teeth) were considered as eligible. We excluded in vitro and ex vivo studies.
Data extraction Eligible studies were selected and data extracted independently by two reviewers. Risk of bias was assessed adopting the Cochrane Risk of Bias tool. Data on caries incidence, sealant retention, fluoride uptake, adverse events, treatment duration, patients' discomfort and cost-effectiveness ratio was extracted.
Data analysis Extracted data were presented narratively due to the heterogeneity of included studies.
Results Seven RCTs and two CCTs, all with an evident risk of bias, met inclusion criteria, pooling together 269 individuals and 1628 teeth. CO_2, neodymium-doped yttrium aluminium garnet, erbium-doped yttrium aluminum garnet (Er:YAG), erbium, chromium: yttrium scandium gallium garnet (Er,Cr:YSGG) and Argon lasers were used. In the permanent dentition, lasers only when used in combination with TPIs were effective in reducing caries when compared with untreated teeth (risk ratio (RR)=0.44 (0.20–0.97); Er:YAG laser) or with TPIs used alone (RR=0.39 (0.22–0.71); CO_2 laser). Moreover, Argon laser significantly improved the fluoride uptake into the enamel surfaces (ANalysis Of VAriance (ANOVA) tests: 95%, p<0.0001). Likewise, sealant retention improved when acid etching was performed on previously irradiated enamel fissures by CO_2 laser (RR=0.63 (0.38–1.04)) or Er:YAG laser (RR=0.54 (95% CI: 0.34 to 0.87)). In addition, laser resulted safe and well tolerated by patients.
Conclusion Despite some positive indications, an inadequate level of evidence was found in the included studies concerning the lasers' effectiveness in preventing caries. Further studies with a higher methodological quality level are required.

Strengths and limitations of this study

- ► This review systematically and with rigorous methodological procedures addressed the topic of laser use to prevent caries.
- ► Cochrane Risk of Bias (RoB) tool was adopted to evaluate the RoB of the included studies.
- ► The original Cochrane RoB was adopted rather than the recent Cochrane RoB2.
- ► The study protocol was not registered in the International prospective register of systematic reviews (PROSPERO).
- ► Few studies were found with a wide number of described types of laser (high heterogeneity), which hindered any meta-analysis of data.

INTRODUCTION

Dental caries represent a relevant public health problem due to its universally high prevalence among both children and adults. In a worldwide epidemiological evaluation performed in 2010, untreated caries in permanent teeth was the most prevalent disease compared with all other illnesses.[1] Prophylactic interventions against caries are strongly recommended by the WHO.[2] The most universally used of traditional prophylactic interventions (TPIs) against caries are the application of sealant on enamel pits and fissures of molars[3] and the topical administration of high fluoride gel or varnish.[4 5] Laser might represent an alternative or complementary prophylactic treatment to TPIs to improve the prevention of caries.

Laser in dentistry was used in different fields such as conservative,[6] endodontics,[7] periodontology,[8] implantology,[9] oral surgery,[10] etc. Laser, in recent years, has also been used for prophylactic purposes against caries at sub-ablative levels, energy enough to modify enamel structure but without any tissue ablative capacity. Since the 1980s, laser light has been shown to be able to modify the structure of superficial dental enamel tissues.[11] When the laser light at sub-ablative energy interacts with the enamel, it produces a superficial and instantaneous increase in temperature from 100°C to 1600°C inducing structural tissue modification.[11] In particular, the laser light interacts with water and hydroxyapatite, two chromophores of the enamel. The water inside the irradiated enamel decreases its concentration,[12] particularly of its molecules around the hydroxyapatite crystals with a consequent decrease of tissue permeability,[13] including the penetration of acids produced by caries bacteria.[14] Moreover, when hydroxyapatite is irradiated, the content of its chemical components is modified: the calcium and phosphate ions increase[14] while the carbonate ions decrease.[12] These changes increase the chemical stability of the irradiated hydroxyapatite.[14 15] In particular, the loss of calcium carbonates increases the degree of enamel crystallinity with an improvement in its structural proprieties.[16]

The use of the laser has demonstrated further validity in vitro: increasing the absorption of fluoride in the enamel and improving sealant retention when used in combination with acid gel for etching enamel pits and fissures.[17]

The above-mentioned laser properties noted above have motivated our further interest in evaluating the prophylactic capacity of this tool in preventing caries, even in vivo studies.

OBJECTIVES

The first objective of this review was to verify whether the use of laser at sub-ablative energy induces enamel modification sufficient to improve it in the following ways: resistance against caries and fluoride uptake and retention of sealant materials by improving traditional etching procedures. The second objective was to determine whether laser use was safe for the dental pulp vitality, and moreover whether participants assessed as acceptable this intervention.

METHODS

Study design

It is a systematic review of scientific literature. The reporting of this study follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Inclusion criteria

Type of studies

Only clinical trials were included, excluding any in vitro study. Likewise, ex vivo studies (where teeth were examined after their extraction or exfoliation) were excluded. Both randomised controlled trials (RCTs) and controlled clinical trials (CCTs) carried out in humans were included. Among RCTs, both parallel-group and split-mouth clinical trials were considered eligible. The minimum or maximum follow-up times of studies were not considered as an exclusion criterion.

Type of participants

Participants, irrespective of age and gender, with sound primary and/or permanent teeth (without caries or other treatments such as fillings, prosthetic manufactures or orthodontic brackets and/or bands), who had undergone laser prophylaxis (primary prevention) interventions on enamel coronal surfaces, were considered.

Type of interventions

Intervention group was any laser application (specific to increasing the resistance against demineralisation of enamel) alone or in combination with any TPI.

Control group was no treatment, placebo alone or in combination with any TPI, or any TPI alone.

Type of outcomes

Primary outcomes

Incidence of caries, enamel fluoride uptake, sealant retention and adverse effects (ie, irreversible dental pulpitis or necrosis, and dental abscess) were primary outcomes.

Secondary outcomes

Operator preference, participant discomfort, treatment duration and cost effectiveness were secondary outcomes.

Studies selection

A comprehensive search to identify all relevant studies, regardless of language, was carried out in the following database (December 2019): Medline (via PubMed), Embase, Web of Science and Cochrane Library. The PubMed search strategy (adapted to each database) is reported in online supplemental appendix 1. All the references were collected in the EndNote V.X7 software and duplicates were removed.

Two reviewers (SP and BC) independently screened titles and abstracts in the above-mentioned databases, which met the inclusion criteria. Disagreements were resolved through discussion between the two researchers, and when a resolution was not obtained a third reviewer was consulted (SC). Once the full texts of the chosen records were obtained, two additional reviewers (GL and MO), working independently, deleted those deemed not useful for the review. In case of disagreement, a third reviewer was consulted (SC).

Data extraction

The same two reviewers (GL and MO) who assessed the eligible studies for this review independently performed data extraction and in case of disagreement a third researcher was consulted (SC). From included studies, data concerning authors, year of publication, country and setting, as well as the number of participants, age and gender were extracted. Moreover, data describing the adopted interventions in both experimental and control groups (with the different devices or materials used) were extracted.

In outcomes such as incidence of caries, sealant retention and adverse events, data of incidence was extracted, that is, the number of cases of new caries, sealant filling detachments and pulpitis episodes in either teeth or sealants of each sample group tested during the duration of the studies. In addition, fluoride intake data was measured in terms of the ratio or difference between the mean values of enamel fluoride content (parts per million) before and after each surgery. Treatment duration data were recorded in terms of the average time (s) elapsed during each treatment from start to finish. Patients' discomfort average (measured with specific graded rating scales) or incidence (individuals experiencing distress) as data was also extracted.

Assessment of risk of bias in included studies

In the included studies a 'risk of bias' (RoB) was assessed by two researchers (MO and IA) with independent evaluations. In the case of lack of final agreement, a third researcher was consulted (SC). For this type of assessment, the recommendations formulated in Chapter 8 of the Cochrane Handbook for Systematic Reviews of Interventions[18 19] were followed. RoB assessment involved the following domains: selection bias (sequence generation and allocation concealment), performance bias, detection bias, attrition bias and selective outcome reporting bias. The RoB judgement for each outcome was expressed in three degrees: low RoB, unclear RoB and high RoB.

Statistical analysis

The effectiveness and safety of laser prophylactic intervention was calculated for dichotomous outcomes between the treatment and control groups measuring the risk ratio (RR) with a 95% CI, while for continuous data we calculated the mean difference (MD) with 95% CI. In case of studies with similar populations, interventions, comparators and outcomes, we have planned to carry out meta-analyses using the Review Manager V.5.3 software. We would have combined relative risks for dichotomous data and MDs for continuous data, using the random-effects method (DerSimonian and Laird inverse variance).

Data synthesis

Due to the high heterogeneity of type of lasers and outcome measures, we did not perform meta-analyses and presented the results in a narrative way.

Patient and public involvement

No patient involved.

RESULTS

We identified 1224 records through the literature search, which were reduced to 825 records when duplicates were removed. Thirty-three records were assessed to fulfil the selection criteria and, therefore, selected as valid to be obtained in their full text version. The level of consistency found (kappa coefficient of agreement) between two reviewers performing the initial screening of records was high (κ value=0.93). After the full text examination, nine studies (10 publications[20–29]) meeting the inclusion criteria were included (figure 1 and table 1), while the remaining 23 studies were excluded due to the reasons reported in the online supplemental appendix 2. The study carried out by Nammour *et al* was described in two publications.[25 26] All nine studies[20–29] were written in English.

Included studies

The nine included studies were published between 1996 and 2015. Seven studies were RCTs[21–28] while the remaining two studies were CCTs.[20 29] All the studies had a split-mouth design where both intervention and control groups were represented by teeth located in opposite sides of single dental arcs rather than in different patients. Characteristics of included studies are reported in tables 1 and 2.

Participants

Pooling the participants from all the nine included studies, 269 individuals were obtained and 1628 teeth were tested. The number of enrolled participants in each study varied from 12 to 51. Excluding Nammour's two papers,[25 26] where the buccal surface of anterior teeth was treated, in the other eight trials only the occlusal surface of posterior teeth (molars and premolars) was tested for the laser evaluation. In five studies, the treatments were carried out in children[20 21 24 27 29] while in the remaining studies young adults were enrolled.

Treatments

In all nine studies, the lasers were employed with sub-ablative parameters, with a low level of fluency ranging from 10 J/cm^2 to 85 J/cm^2. In three studies, the CO_2 laser was adopted[20 22 28]; in two studies, the neodymium-doped yttrium aluminium garnet (Nd:YAG) laser was used[27 29]; in another study, the argon (two publications) laser was employed[25 26]; in one study, the erbium-doped yttrium aluminum garnet (Er:YAG) laser was used[21] and in the last two studies,[23 24] the erbium, chromium: yttrium scandium gallium garnet (Er,Cr:YSGG) laser was used. To support the use of laser prophylactic interventions, other interventions were adopted in the included studies such as 1.23% acidulated phosphate fluoride gel or foam,[27 29] enamel pit and fissure resin sealant,[28] and 5% fluoride varnish.[20]

RoB assessment of the body of evidence

The RoB assessment was carried out through the Cochrane RoB tool[18 19] (figure 2). Two studies[20 29] were considered to be at high risk of selection bias because they were CCTs without any randomisation procedure for the participants' allocation in both control and intervention groups. The remaining seven studies (eight publications) were RCTs,[21–28] but only one reported adequate concealment of allocation.[22]

All studies were at high risk of performance bias (blinding of participants and personnel) due to the nature of treatments. Moreover, four out of nine studies[20 25 26 29] did not describe the presence of blinded assessors for evaluating outcomes with an unclear risk of detection bias.

In terms of attrition bias, four out of nine included studies which presented a high risk of this type of bias[20 21 27 28] due to participants drop-out varying from 18% to 50% in a time period ranging from 12 months to 4 years. When the selective outcome reporting bias was considered, all the trials were considered as having an unclear risk of this bias given that none of them evaluated

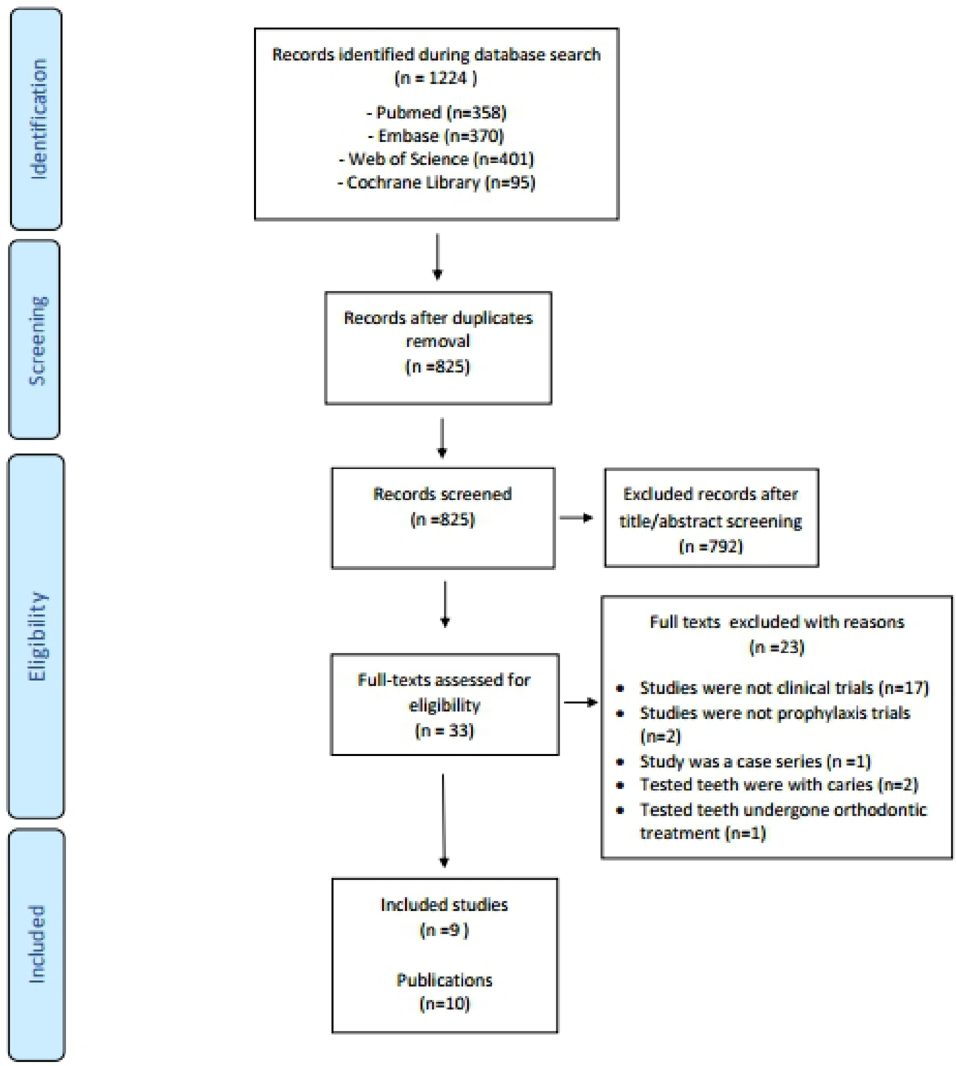

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram.

all the primary outcomes (specifically incidence of caries and adverse events).

Effectiveness of treatments

Caries incidence

Four studies reported this outcome.[20 21 27 29] Three studies were carried out on permanent teeth (molar and premolars)[20 21 29], while one study considered only primary molars.[24] CO_2, Nd:YAG and Er:YAG lasers were the type of devices used in these four included studies.

Permanent teeth

The three studies were all carried out on children with ages ranging between 6 and 11 years. The number of enrolled participants varied from 28 to 51 with an overall of 558 teeth examined, and the duration of the studies ranged from 1 year to 4 years.

When laser was used alone (CO_2 laser),[20] it did not result effective in reducing caries incidence on untreated teeth (RR=0.89 (95% CI: 0.40 to 1.97), p=0.77).

Conversely, when laser was combined with TPIs, it resulted effective as demonstrated in two studies.[20 21] In the first of these two studies,[20] CO_2 laser combined with the sealants (compared with a control group of untreated teeth) contributed to the reduction, with a statistical relevance, of the caries incidence with a preventable fraction of 78% (RR=0.22 (95% CI: 0.05 to 0.94), p=0.02). In the second study,[21] Er:YAG laser, combined with sealants (intervention group) and compared with the same sealants used alone (control group), resulted in a caries incidence reduction of 56% (RR=0.44 (95% CI: 0.20 to 0.97), p=0.03).

In a further study,[29] laser (Nd:YAG laser) in combination with acidulated phosphate fluoride gel (intervention group) was compared with this fluoride gel used alone (control group). Also in this case, laser combined with fluoride gel resulted more effective than gel alone with a caries incidence reduction of 61% (RR=0.39 (95% CI: 0.22 to 0.71), p=0.001).

Primary teeth

In the only study where primary teeth were treated,[27] 35 children were enrolled and 280 first and second primary molars were treated. Four interventions were used as follows: Nd:YAG laser; 1.23% phosphate acidulated

Table 1 Main characteristics of included studies population

Author(s) and year	Type of study	Country	Participants (n)	Teeth (n)	Age (years)	Gender (n)	Setting
Brugnera *et al* 1997[20]	CCT split-mouth design	Brazil	28	112 permanent first molars	6–11	Not reported	Not reported
Durmus *et al* 2017[21]	RCT split-mouth design	Turkey	51	204 permanent first molars	7–10	27 males 24 females	University Paediatric Dental Clinic
Goodis *et al* 2004[22]	RCT split-mouth design	USA	24	74 erupted upper and lower third molars	21–34	11 males 13 females	University Dental Clinic
Karaman *et al* 2013[23]	RCT split-mouth design	Turkey	16	112 teeth (63 molars and 49 premolars)	20–23	1 male 15 females	University Dental Clinic
Kumar *et al* 2016[24]	RCT split-mouth design	India	50	200 permanent first molars	6–12	Not reported	University Paediatric Dental Clinic
Nammour *et al* 2003 and 2005[25 26]	RCT split-mouth design	Belgium	12	98 unspecified anterior permanent teeth	Not reported	Not reported	Not reported
Raucci-Neto *et al* 2015[27]	RCT split-mouth design	Brazil	35	416 first and second primary molars	7–8	Not reported	University Paediatric Dental Clinic
Walsh 1996[28]	RCT split-mouth design	Australia	20	170 permanent molars and premolars	15–38	13 males 7 females	University Preventive Dental Clinic
Zezell *et al* 2009[29]	CCT split-mouth design	Brazil	33	242 premolars and lower molars	7–15	Not reported	University Paediatric Dental Clinic

CCT, controlled clinical trial; RCT, randomised controlled trial.

fluoride gel and 5% fluoride varnish and sealants. Nd:YAG was used alone or in association with each of the other three interventions. The control group comprised untreated teeth. The study duration was 1 year. Only when laser was used alone, it was found able to significantly reduce caries incidence with mean values of 70% (RR=0.30; (95% CI: 0.11 to 0.78), p=0.004).

Sealant retention

Four studies described this outcome.[20 21 23 28] Sealant retention was assessed by comparing two different types of enamel etching, laser light irradiation (laser etching) and traditional acid gel apposition (acid etching). Two types of comparisons were performed: (a) laser light used alone was compared with acid gel and (b) laser light in addition to acid gel was compared with acid gel.

Laser etching combined with acid etching versus acid etching alone

The following two studies[20 22] compared the combined etching procedure (laser light and acid gel) with traditional acid etching.

In the two studies, the number of patients enrolled ranged from 28 to 42 with a total number of 224 teeth. The duration of the studies ranged from 18 months to 24 months.

In both these studies, laser light combined with acid gel resulted in better etching than acid gel used alone in terms of sealant retention. In fact, when CO_2 laser in addition of acid gel was used,[20] a reduction from 19 (n=19/28) to 12 (n=12/28) detachments was found, with a 37% of drop-out decrease (RR=0.63 (95% CI: 0.38 to 1.04), p=0.059). Similarly, when Er:YAG laser was combined with acid gel,[21] there was a 46% of detachment reduction (RR=0.54 (95% CI: 0.34 to 0.87)), passing from 35 (n=35/84) to 19 (n=19/84) sealant fillings, which fell out during the period of follow-up visits.

Laser etching versus acid etching

Three studies[23 24 28] dealt with this topic. In these trials, the number of participants varied from 16 to 50 and their ages from 6 years to 23 years, with only a single study evaluating children.[24] A total of 438 permanent molars and

Table 2 Main characteristics of included studies interventions

Author(s) and year	Intervention group	Control group	Lasers characteristics
Brugnera *et al* 1997[20]	1. Nd:YAG laser 2. Sealant 3. Nd:YAG laser+sealant	No treatment	CO_2 Pulsed emission; rate repetition: 7 Hz; pulse duration: 20 ms
Durmus *et al* 2017[21]	Er:YAG laser+orthophosphoric acid	Orthophosphoric acid	Er:YAG laser Wavelength: 2.94 µm; non-contact mode; pulse energy: 120 mJ; repetition rate: 10 Hz; spot size: 0.6 mm
Goodis *et al* 2004[22]	1. High energy CO_2 (4.8 J) 2. Low energy CO_2 (2.4 J)	Sham procedure	CO_2 laser Wavelength: 9.6 mm; pulse duration: 5–8 µs; rate repetition: 10 Hz; energy density: 1.5 J/cm^2; pulse energy: 12 mJ
Karaman *et al* 2013[23]	Er,Cr:YSGG laser	Orthophosphoric acid	Er,Cr:YSGG laser Wavelength: 2.78 µm; pulsed emission; no contact mode; spot size: 600 µm; repetition rate: 10 Hz; power: 125 W
Kumar *et al* 2016[24]	Er,Cr:YSGG laser	Orthophosphoric acid	Er,Cr:YSGG laser Wavelength: 2.78 µm; pulsed emission; no contact mode; spot size: 600 µm; repetition rate: 20 Hz; power: 1.5 W
Nammour *et al* 2003 and 2005[25 26]	1. Fluoride gel 2. Argon laser+fluoride gel	No treatment	Argon laser Continuous emission; energy density: 10.74 J/cm^2; spot size: 11 mm; irradiation duration: 30 s; pulse power: 340 mW
Raucci-Neto *et al* 2015[27]	1. Nd:YAG laser 2. Nd:YAG laser+fluoride gel 3. Nd:YAG laser+fluoride variant 4. Sealant	1. Fluoride varnish 2. Fluoride gel 3. No treatment	Nd:YAG laser Wavelength: 1.064 vm; pulsed emission; spot size: 300 µm; pulse duration: 100 µs; rate repetition: 10–100 Hz; irradiation duration: 30 s; energy density: 73.9 J/cm^2; power: 50 W
Walsh 1996[28]	CO_2 laser	Orthophosphoric acid	CO_2 laser Pulsed emission; spot size: 800 µm; rate repetition: 20 Hz; pulse duration: 20 ms; power: 5 W; irradiation duration: 7 s
Zezell *et al* 2009[29]	1. Nd:YAG laser 2. Sealant 3. Nd:YAG laser+sealant	No treatment	CO_2 laser Pulsed emission; rate repetition: 7 Hz; pulse duration 20 ms

Er,Cr:YSGG, erbium, chromium: yttrium scandium gallium garnet; Er:YAG, erbium-doped yttrium aluminum garnet; Nd:YAG, neodymium-doped yttrium aluminium garnet.

premolars were evaluated. The duration of the studies ranged from 1 year to 3 years.

In this topic, similar results were found: in all three studies,[23 24 28] there was no statistically significant difference between the laser light etching and the acid etching with regard to sealant filling drop-out. In the first of the three studies, in fact, in which Er,Cr:YSGG laser was used, 9 out of 56 sealant fillings (n=9/56) were detached in the intervention group (laser etching), while 8 out of 56 in the control group (acid etching) showed no significant difference between the two groups (RR=0.87 (95% CI: 0.37 to 2.06)).[23] Likewise in the second study,[24] where again Er,Cr:YSGG laser was used, in both acid and laser etching groups, the same number of detachments (78/100) were found. In the third study,[28] similar to the other two, 2 sealant fillings out of 96 were detached in the laser etching group (n=2/96), while 4 out of 74 were detached in the acid etching group, with no significant difference (RR=0.39 (95% CI: 0.07 to 2.05), p=0.24).

Fluoride uptake into the enamel surfaces

One study (two publications) carried out by Nammour *et al* reported on this outcome.[25 26] Twelve participants were enrolled in this trial and 98 upper permanent anterior teeth were tested. In the intervention group, argon laser irradiation was performed before 1.23% acidulated phosphate fluoride gel administration. In the control group, only fluoride gel was administered. The fluoride uptake was evaluated at 1 week and after 6 months. The intervention group showed a higher degree of fluoride adsorption than the control group, with statistically significant differences both at 1 week and at 6 months (ANalysis Of VAriance (ANOVA) tests=95%, p<0.0001; R^2=0.9751—Bartlett's statistic corrected=134 and p<0.0001).

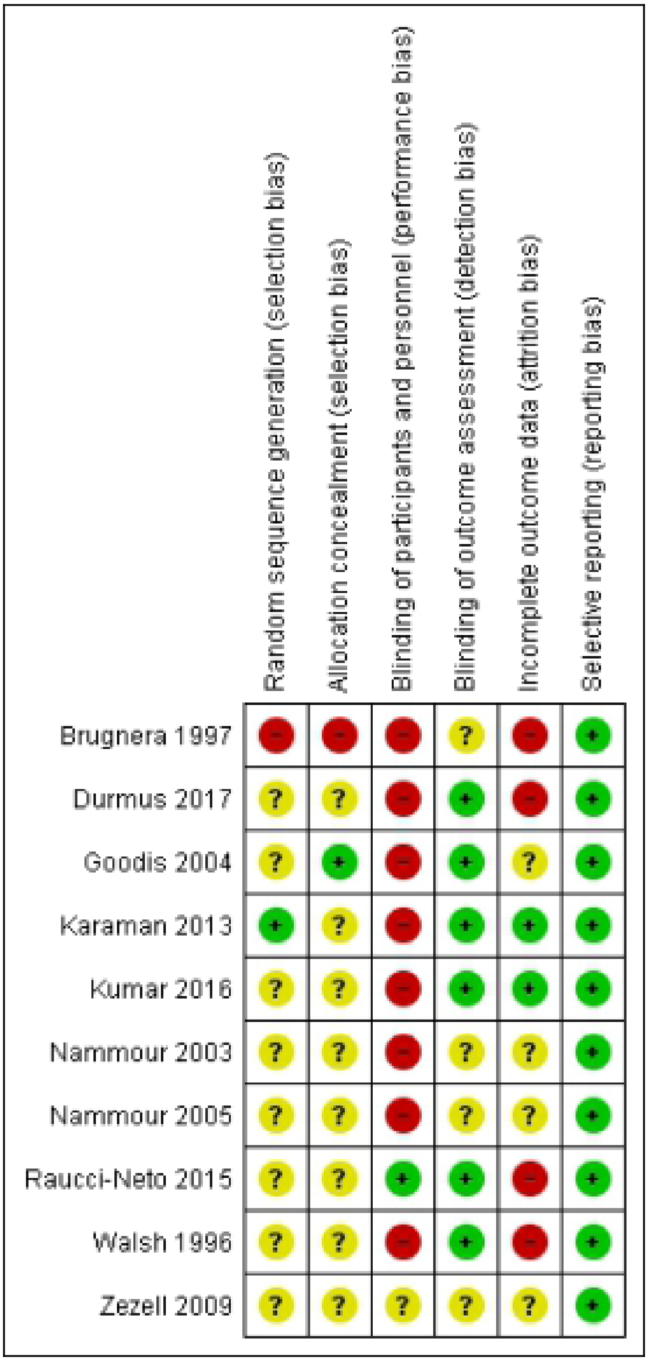

Figure 2 Risk of Bias summary of included studies.

Adverse events

Two trials investigated dental pulp health after laser irradiation.[22 28] A total of 44 participants, aged 15–38 years, were enrolled in the two studies and 174 permanent molars and premolars (including third molars) were examined by clinical evaluation (symptomatology) as well as with electrical and thermal pulp vitality tests. Control radiographs were also taken in one of the two studies.[22] In the two studies, there was only one case of reversible pulpitis 3 days after treatment.

Treatment duration

In the studies where this outcome was described, the laser irradiation duration varied as follows: 7 s,[28] 10 s[24] up to 30 s.[20 25–27] In the remaining included studies, the time employed for laser irradiation was no reported. In addition, in none of the studies was a comparison between laser and other interventions in terms of treatment duration performed.

Patients' discomfort

In the only study reporting this outcome, both Er,Cr:YSGG laser and orthophosphoric acid were equally well accepted by patients (p=1). The Visual Analogue Scale mean score measuring the patients' discomfort, indeed, resulted very low for both laser or acid etching procedures, with the same value of 0.33 (SD=2.22).[23]

Cost-effectiveness ratio

This outcome was not reported in any of the included studies.

All results related to each outcome were synthesised in table 3.

DISCUSSION

The aim of this study was to carry out a systematic review of scientific literature to search evidence supporting the use of lasers at sub-ablative irradiation energy levels for preventing dental caries. The sub-ablative energy level can be defined as an amount of energy not able to ablate the dental tissues but sufficient to modify their structure. Although a cut-off value between ablative and sub-ablative energies has not yet been precisely established in the literature, nevertheless on the basis of the data found both in this review and another two similar ones,[17 30] the energy density value of the sub-ablative lasers never exceeds 100 mJ/cm^2.

In our systematic literature review, nine studies (10 publications), which met the inclusion criteria, were found. A possible limitation was that in all trials many outcomes showed either unclear or high RoB; therefore, also the degree of confidence in their results was low. In addition, due to the limited number of studies found for each tested laser (with a small sample of enrolled participants), there were also doubts on the results' precision. Moreover, methodological limitations on the review process should also be mentioned due to the absence of a study protocol publication prior to performing the present study's final version. In addition, the use of the original RoB assessment rather than its last version (RoB2) could be considered a further methodological limitation. However, some interesting conclusion might be drawn out from this review as reported below.

Summary of evidences

Based on the data found in our review, when sub-ablative laser was used on permanent teeth as a prophylactic intervention against caries, it was clinically effective only

Table 3 Results for each outcome in the included studies

Author(s) and Year	Study duration	Caries incidence	Sealant retention	Fluoride uptake	Adverse events (irreversible dental pulpitis)	Other outcomes
Brugnera *et al* 1997[20]	48 months	Permanent teeth (a) CO_2 laser alone vs untreated teeth: caries incidence reduction of 11% (RR=0.89 (95% CI: 0.40–1.97), p=0.77), not statistically relevant difference and (b) CO_2 laser+sealants vs untreated teeth: caries incidence reduction of 78% (RR=0.22 (95% CI: 0.05–0.94), p=0.02), statistically relevant difference	Permanent teeth CO_2 laser etching+acid etching vs acid etching: sealant drops-out reduction of 37%(RR=0.63 (95% CI: 0.38–1.04), p=0.059), not statistically relevant difference			Cost effectiveness: not described; patients' discomfort: not reported; duration of treatment: no comparison was made between the intervention and control groups
Durmus *et al* 2017	18 months	Permanent teeth Er:YAG laser+sealants vs sealants: caries incidence reduction of 56% (RR=0.44 (95% CI: 0.20–0.97), p=0.03), statistically relevant difference	Permanent teeth Er:YAG laser etching+acid etching vs acid etching: sealant drops-out reduction of 46% (RR=0.54 (95% CI: 0.34–0.87), p=0.01), statistically relevant difference			Cost effectiveness: not described; patients' discomfort: not reported; duration of treatment: no comparison was made between the intervention and control groups
Goodis *et al* 2004[22]	1 month				No episodes of irreversible dental pulpitis (n=0/96 irradiated teeth) when CO_2 laser was used	Cost effectiveness: not described; patients' discomfort: not reported; duration of treatment: no comparison was made between the intervention and control groups
Karaman *et al* 2013[23]	24 months		Permanent teeth Er,Cr:YSGG laser etching vs acid etching: sealant drops-out reduction of 13%(RR=0.87 (95% CI: 0.37–2.06); p=0.75), not statistically relevant difference			Cost effectiveness: not described; patients' discomfort: Er,Cr:YSGG laser vs sealants, not statistically relevant difference was found (measured with VAS); duration of treatment: no comparison was made between the intervention and control groups
Kumar *et al* 2016[24]	12 months		Permanent teeth Er,Cr:YSGG laser etching vs acid etching: same number of sealant drops-out (n=78/100) not statistically relevant difference			Cost effectiveness: not described; patients' discomfort: not reported; duration of treatment: no comparison was made between the intervention and control groups

Continued

Table 3 Continued

Author(s) and Year	Study duration	Caries incidence	Sealant retention	Fluoride uptake	Adverse events (irreversible dental pulpitis)	Other outcomes
Nammour *et al* 2003 and 2005[25 26]	1 week 6 months			Permanent teeth Laser+1.23% acidulated phosphate fluoride gel vs 1.23% acidulated phosphate fluoride: enamel fluoride uptake increased four times (ANOVA tests=95%, $p<0.0001$; $R^2=0.9751$— Bartlett's statistic corrected=134 and $p<0.0001$) not statistically relevant difference		Cost effectiveness: not described; patients' discomfort: not reported; duration of treatment: no comparison was made between the intervention and control groups
Raucci-Neto *et al* 2015[27]	12 months	Primary teeth Nd:YAG laser vs untreated teeth: caries incidence reduction of 70% (RR=0.30 (95% CI: 0.11 to 0.78)), statistically relevant difference Sealants vs untreated teeth caries incidence reduction of 33% (RR=0.67 (95% CI: 0.35 to 1.26), p=0.19), not statistically relevant difference				Cost effectiveness: not described; patients' discomfort: not reported; duration of treatment: no comparison was made between the intervention and control groups
Walsh 1996[28]	18 months		Permanent teeth CO_2 laser etching vs acid etching: sealant drops-out reduction of 61%(RR=0.39 (95% CI: 0.07 to 2.05), p=0.24), not statistically relevant difference		No episodes of irreversible dental pulpitis (n=0/96 irradiated teeth) when CO_2 laser was used	Cost effectiveness: not described; patients' discomfort: not reported; duration of treatment: no comparison was made between the intervention and control groups
Zezell *et al* 2009[29]	12 months	Permanent teeth Nd:YAG laser+1.23% acidulated phosphate fluoride gel vs 1.23% acidulated phosphate fluoride gel: caries incidence reduction of 61%(RR=0.39 (95% CI: 0.22 to 0.71), p=0.001), statistically relevant difference				Cost effectiveness: not described; patients' discomfort: not reported; duration of treatment: no comparison was made between the intervention and control groups

ANOVA, ANalysis Of VAriance; Er,Cr:YSGG, erbium, chromium: yttrium scandium gallium garnet; Er:YAG, erbium-doped yttrium aluminum garnet; Nd:YAG, neodymium-doped yttrium aluminium garnet; RR, risk ratio; VAS, Visual Analogue Scale.

if used in association with a TPI such as sealant or fluoride gel. Laser combined with a TPI, indeed, reduces the incidence of caries by reinforcing enamel, and moreover it reduces the detachment of sealant fillings from the dental enamel surfaces. Conversely, when the laser was used alone, it did not improve enamel resistance against caries or sealants retention.

Laser, therefore, instead of being an alternative to TPIs, should be considered a prophylactic intervention able to improve the effectiveness of TPIs. TPIs, indeed, although effective in reducing caries, show some clinical limitations according to the literature. Sealants, for example, present 5%–10% of fillings detachment per year[31] while a high content of fluoride gels or varnishes present a potential chronic and acute toxicity[32] and additionally required repeated applications, which can be difficult among subjects with low education and socioeconomic status, where this disease is particularly prevalent.[33 34] Laser might contribute to reduce these limitations, decreasing the number of detachment cases. In addition, laser when combined with fluoride varnishes and gels (favouring the fluoride uptake of four times) might increase their effectiveness against caries, with a theoretical possibility of limiting both the dosage and the number of dental visits required for administrating fluoride. The absorption of fluorine affects its positive clinical action by increasing the enamel content of the fluorapatite, making it more resistant against acid demineralisation.[35]

In the only study where laser was used on primary teeth, it seemed effective in reducing caries incidence, also when used alone, with better results than in permanent teeth. This difference of effectiveness could be explained by considering the difference in enamel structure shown in permanent and primary dentitions. However, the paucity of information (one single study with few participants) makes this all hypothetical.

There were no studies that described the cost-effectiveness outcome, resulting in a significant lack of relevant information, considering that the laser being a high-tech device could most likely require higher costs than TPIs.

Similar studies in the literature

In the literature, two reviews dealt with the use of lasers as a prophylactic intervention, one in vitro[17] and the other in vivo.[30] The in vitro review showed that the intervention of some types of lasers (CO_2, argon, diodes and Er,Cr:YSGG lasers) used alone or in combination with TPIs was able to reinforce the enamel against acid demineralisation (acids similar or analogous to those of caries). In fact, the enamel treated with laser light, after being subjected to cycles of demineralisation in acid solutions, showed a lower loss of minerals (spectroscopic analysis), a lower loss of surface hardness (microhardness tests) and a lower average depth of cavity lesions (scanning electron microscopy and light polarised microscope evaluations) compared with untreated enamel. The in vitro review, therefore, presented a number of advantages only partially confirmed by our in vivo review.

The second review[30] we found, which exclusively analysed clinical trials, evaluated the laser clinical efficacy in etching enamel with results similar to our review: the laser used alone did not increase the retention rate of sealant fillings, conversely when used in addition to TPIs it improved this retention. Moreover, as in our review, the laser at sub-ablative levels was as well accepted by patients as were TPIs.

Finally, the use of laser in prophylaxis is part of a very modern vision of dentistry, based on prevention instead of caries reparative treatments as recommended by the most important scientific societies in this field (eg, American Pediatric Dentistry). More generally, the scientific dental community in recent times has been oriented towards an approach to caries based on minimally invasive interventions,[36] aimed at maximum tissue preservation, and in this new approach prophylaxis has assumed a central role never played in the past.

CONCLUSIONS

Despite both the limited number of studies (few participants) and the evident RoB found in all outcomes considered in this review, lasers used at sub-ablative energy level in combination with TPIs resulted in an increased caries prevention effectiveness compared with TPIs alone or to untreated teeth. However, until now, there was not sufficient evidence for recommending the use of laser as an alternative clinical solution compared with traditional caries prophylactic interventions. Finally, the safety of lasers was evaluated in a few of the studies reporting the absence of side effects such as irreversible dental pulp phlogosis or necrosis. High-quality methodological studies are required to obtain a more thorough knowledge of all topics considered in this study. Studies also including outcomes such as patients' discomfort and cost-effectiveness ratio would be required.

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Contributors The authors SP, BC and SC conceived the original idea for this study. The remaining three authors (GL, MO and IA) established both the search strategy and the study protocol. Moreover, SP and BC screened titled and abstracts of records obtained from literature databases, independently, in order to obtain their full texts. GL and MO screened independently the full texts. In case of disagreement, SC was consulted. GL and MO performed data extraction from the selected full texts. IA and MO performed the risk of bias assessment. All authors revised critically the manuscript and approved its final version.

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Appendix 1. PubMed search strategy

Search	Pubmed Query	Items found
#1	"Lasers"[Mesh]	50,960
#2	"Low-Level Light Therapy"[Mesh]	5,588
#3	laser dentistry	11,394
#4	#1 OR #2 OR #3	60,823
#5	"Tooth Demineralization"[Mesh]	47,022
#6	dental caries	57,825
#7	#5 OR #6	58,866
#8	"prevention and control"[Subheading]	1,263,961
#9	"Dental Prophylaxis"[Mesh]	7,624
#10	sealant[Title/Abstract] AND retention[Title/Abstract]	436
#11	caries[Title/Abstract] AND prevention[Title/Abstract]	6,012
#12	#8 OR #9 OR #10 OR #11	1,272,343
#13	#4 AND #7 AND #12	384
#14	#4 AND #7 AND #12 Filters: Humans	312
#15	laser[Title/Abstract] AND caries[Title/Abstract] AND prevention[Title/Abstract] Filters: Humans	105
#16	(laser[Title/Abstract] AND (sealant[Title/Abstract] OR enamel[Title/Abstract]) AND retention[Title/Abstract]) Filters: Humans	37
#17	#14 OR #15 OR #16	358

Appendix 2. List of excluded studies with reasons

Study ID	Reasons for exclusion
1. Ana 2007	The study is not a clinical trial
2. Aderson 2002	The study is not a clinical trial
3. Apel 2004	The study is not a clinical trial
4. Bahar 1994	The study is not a clinical trial
5. Bahrololoomi 2019	The study was not a clinical trial
6. Blankenau 1999	The study is not a clinical trial
7. Correa Alfonso 2013	The study is not a clinical trial
8. Cozean 1997	No prophylaxis intervention was performed in this study
9. Genovese 2008	No prophylaxis intervention was performed in this study
10. Güçlü 2018	The included studies undergone orthodontic treatment
11. Gorton 2003	The study is not a clinical trial
12. Harazaki 2001	The included teeth in the study were not all sound
13. Hicks 2004	The study is not a clinical trial
14. Hicks 2004	The study is not a clinical trial
15. Kato 2003	This study was a case series without any control group
16. Neto 2015	The study is not a clinical trial
17. Raucci-Neto 2015b	The study is not a clinical trial
18. Rechmann 2011	The study is not a clinical trial
19. Rechmann 2013	The included teeth in the study were not all sound
20. Roshkind 2008	The study is not a clinical trial
21. Seino 2015	The study is not a clinical trial
22. Stern 1972	The study is not a clinical trial
23. Stern-Oliveira 2006	The study is not a clinical trial