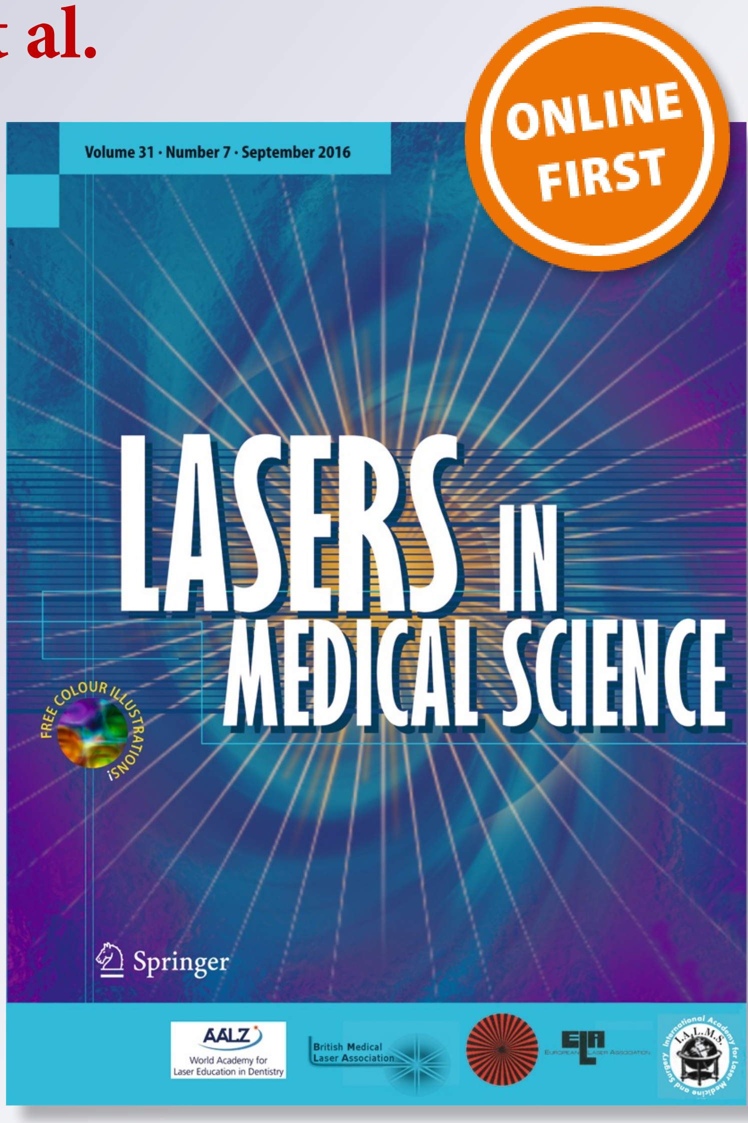
Role of laser irradiation in direct pulp capping procedures: a systematic review and meta-analysis

Fawad Javed, Sergio Varela Kellesarian, Tariq Abduljabbar, Elham Gholamiazizi, Changyong Feng, Khaled Aldosary, Fahim Vohra, et al.

Lasers in Medical Science

ISSN 0268-8921

Lasers Med Sci
DOI 10.1007/s10103-016-2077-6



Springer

Lasers Med Sci
DOI 10.1007/s10103-016-2077-6

REVIEW ARTICLE

Role of laser irradiation in direct pulp capping procedures: a systematic review and meta-analysis

Fawad Javed [1] · **Sergio Varela Kellesarian** [1] · **Tariq Abduljabbar** [2] · **Elham Gholamiazizi** [3] · **Changyong Feng** [4] · **Khaled Aldosary** [5] · **Fahim Vohra** [2] · **Georgios E. Romanos** [6,7]

Received: 14 May 2016 / Accepted: 12 September 2016

Abstract A variety of materials are available to treat exposed dental pulp by direct pulp capping. The healing response of the pulp is crucial to form a dentin bridge and seal off the exposed pulp. Studies have used lasers to stimulate the exposed pulp to form tertiary dentin. The aim of the present systematic review and meta-analysis was to evaluate the evidence on the effects of laser irradiation as an adjunctive therapy to stimulate healing after pulp exposure. A systematic literature search was conducted up to April 2016. A structured search using the keywords "Direct pulp capping," "Lasers," "Calcium hydroxide pulp capping," and "Resin pulp capping" was performed. Initially, 34 potentially relevant articles were identified. After removal of duplicates and screening by title, abstract, and full text when necessary, nine studies were included. Studies were assessed for bias and data were synthetized using a random-effects meta-analysis model. Six studies were clinical, and three were preclinical animal trials; the follow-up period ranged from 2 weeks to 54 months. More than two thirds of the included studies showed that laser therapy used as an adjunct for direct pulp capping was more effective in maintaining pulp vitality than conventional therapy alone. Meta-analysis showed that the success rate in the laser treatment group was significantly higher than the control group (log odds ratio = 1.737; 95 % confidence interval, 1.304–2.171). Lasers treatment of exposed pulps can improve the outcome of direct pulp capping procedures; a number of confounding factors may have influenced the outcomes of the included studies.

Keywords Calcium hydroxide · Direct pulp capping · Lasers · Resin pulp capping

✉ Fawad Javed
fawad_javed@urmc.rochester.edu

1 Department of General Dentistry, Eastman Institute for Oral Health, University of Rochester, Rochester, NY, USA

2 Department of Prosthetic Dental Science, College of Dentistry, King Saud University, Riyadh, Saudi Arabia

3 Department of Mechanical Engineering, Pennsylvania State University, Capital College, PA, USA

4 Department of Biostatistics and Computational Biology, School of Medicine and Dentistry, University of Rochester Medical Center, Rochester, NY, USA

5 Dental Department, King Khaled University Hospital, King Saud University, Riyadh, Saudi Arabia

6 Department of Oral Surgery and Implant Dentistry, Dental School, Johann Wolfgang Goethe, University of Frankfurt, Frankfurt, Germany

7 Department of Periodontology, School of Dental Medicine, Stony Brook University, Stony Brook, NY, USA

Introduction

Pulpal exposure is often encountered during routine restorative procedures such as caries excavation and cavity and crown preparations [1–3]. Depending on the size and the extent of hemorrhage, the exposure can be treated using pulp capping techniques, pulpotomy or pulpectomy [4, 5]. Of these methods, pulp capping has been shown to have a predictable outcome in the management of pulpal exposures [6, 7]. Pulp capping is an attempt to maintain the vitality of the exposed pulp by inducing a healing response. This response is mediated by the stimulation of the pulp tissue to form a reparative dentin bridge which seals the pulp from bacterial contamination [8]. A variety of materials have been used in an attempt to stimulate odontoblasts in the exposed pulp to secrete reparative dentine [9]. Calcium hydroxide ($Ca[OH]_2$), resins, glass ionomer cement (GIC), mineral trioxide aggregate (MTA), formocresol, and

Published online: 23 September 2016

antibiotics have been applied on exposed pulps with variable success [10–12]. However, some studies [13, 14] have also focused on the effects of dental lasers on pulp healing after pulp exposure.

Laser treatment has been shown to amplify the oral wound healing process by stimulation of neural cell regeneration following injury, pain attenuation, endorphin release, and modulation of the immune system [15, 16]. This is attributed to the photo-excitation of singlet oxygen in the tissues caused by laser irradiation, which stimulates DNA and RNA formation [17]. Furthermore, laser irradiation is known to stimulate mineralization in dental pulp cells [18–20]. It has been demonstrated that laser therapy can induce odontoblast to lay down tertiary dentin and form a dentin bridge to wall off an exposed pulp [21]. Studies [14, 22–24] have assessed the efficacy of lasers as an adjunctive treatment in the management of pulp exposures. Cengiz et al. [24] reported a significantly higher success rate in teeth treated with lasers and conventional pulp capping materials than teeth treated with conventional pulp capping materials only. Similarly, exposed pulps of teeth treated with $Ca(OH)_2$ and laser therapy were shown to have a significantly higher success rate than exposed pulps of teeth treated with $Ca(OH)_2$ in the study by Santucci et al. [25]. However, Suzuki and co-workers [23] reported no difference in the wound healing between the pulps of teeth treated with laser and adhesive resin when compared to treatment with adhesive resin only and $Ca(OH)_2$ only. Similarly, Hasheminia et al. [26] studied the effects of laser irradiation of the exposed pulp with MTA or $Ca(OH)_2$ application and reported no difference in the healing response when compared to $Ca(OH)_2$ application alone.

There appears to be some debate on the efficacy of laser therapy used as an adjunct to pulp capping procedures. Therefore, the aim of this review was to systematically evaluate the evidence on the effects of laser irradiation as an adjunctive therapy to stimulate healing after pulp exposure.

Materials and methods

Focused question

The guidelines from Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) [27] were used to construct the focused question. The question addressed according to the Participants, Interventions, Control, Outcomes (PICO) principle was—"What is the efficacy of lasers compared to conventional therapy for direct pulp capping procedures?"

(P) Participants: Subjects must have exposed pulps treated with direct pulp capping procedures
(I) Types of interventions: The intervention of interest was the use of lasers for the direct pulp capping
(C) Control intervention: Subjects with exposed pulps treated with direct pulp capping procedures without lasers
(O) Outcome measures: Pulp vitality and healing response to laser therapy for direct pulp capping at the end of the follow-up period.

Selection criteria

The eligibility criteria were as follows: (a) Controlled clinical studies; (b) retrospective chart reviews; (c) experimental studies, comparing the effects of lasers used for direct pulp capping against conventional pulp capping. Review papers, in vitro studies, conference abstracts, letters to the editor, case reports, commentaries, interviews, and updates were excluded.

Search strategy

Electronic database searches were performed using different combinations of Medical Subject Headings (MeSH) terms and free text words: (1) direct pulp capping; (2) lasers; (3) calcium hydroxide pulp capping; (4) resin pulp capping; (5) clinical trials; (6) randomized controlled trials; (7) retrospective studies. Electronic database of MEDLINE/PubMed, EMBASE, Scopus, ISI Web of knowledge, and Google-Scholar were searched for articles addressing the focused question. There were no time restrictions. Titles and abstracts of retrieved articles were screened for eligibility by two authors (VR and SVK). Full texts of articles obtained from the previous step were evaluated for inclusion. The reference lists of relevant articles were hand searched for additional studies. Data was extracted from studies that answered our inclusion criteria. The data was tabulated as follows (1) study design; (2) participants; (3) intervention; (4) controls; (5) follow-up periods; and (6) outcomes measures.

Study selection

The search protocol is presented in Fig. 1. A total of 34 studies were initially identified. Eleven papers were selected after screening of the titles and abstracts for full-text evaluation. Two studies which did not fit the eligibility criteria were excluded at this step and nine studies were included in this systematic review. For the quantitative analysis, animal studies were excluded. Appendix A contains the excluded studies with reason for exclusion in parenthesis.

Quality assessment of included studies

The Critical Appraisal Skills Program (CASP) Cohort Study Checklist [28] was used to conduct a quality assessment of the included studies. The CASP tool is based on 12 specific criteria, which are as follows: (1) study issue is clearly

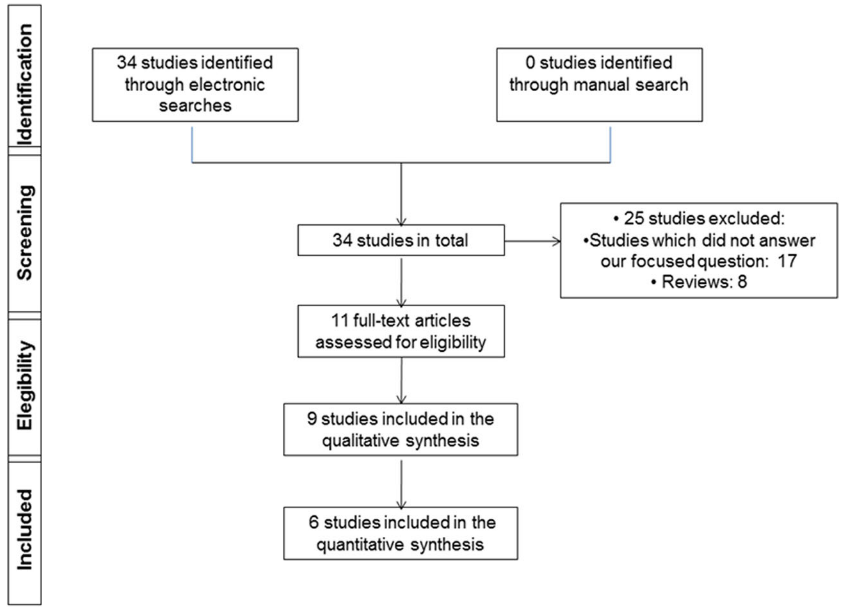


Fig. 1 Article selection flow chart for the systematic review according to PRISMA guidelines

focused; (2) cohort is recruited in an acceptable way; (3) exposure (laser irradiation of exposed pulp) is accurately measured; (4) outcome (pulp vitality and healing response) is accurately measured; (5) confounding factors are addressed; (6) follow-up is long and complete; (7) results are clear; (8) results are precise; (9) results are credible; (10) results can be applied to the local population; (11) results fit with available evidence; and (12) there are important clinical implications. A response of either Yes, No, or cannot tell was given to each criterion. A study could have a maximum score of 12.

Statistical analysis

Data from the clinical studies was extracted for the quantitative analysis. In the meta-analysis, Mantel-Haenszel method was used to estimate an overall odds ratio of success of pulp capping with versus without laser irradiation, from different studies. The forest plot was used to show the 95 % confidence interval of the log odds ratio in each individual study and that of the combined log odds ratio.

Results

Clinical studies

General characteristics

Out of the six clinical studies [13, 14, 22, 24, 25, 29] included, five were randomized controlled trials [13, 14, 22, 24, 29] and one study had a cohort design [25]. The numbers of participants ranged from 10 to 260 subjects with mean ages ranging between 14.5 and 34.8 years. In the clinical studies [13, 14, 22, 24, 25, 29], one study reported the gender of the participants [24]. The follow-up duration ranged between 4 and 54 months. Five studies [13, 14, 22, 29] compared the efficacy of $Ca(OH)_2$ with adjunct laser therapy verses $Ca(OH)_2$ alone for direct pulp capping. Santucci et al. [25] evaluated the outcomes of lasers and restorative adhesive resin versus $Ca(OH)_2$ for direct pulp capping procedures. In the study by Cengiz et al. [24], the two test groups which underwent adhesive treatment efficacy of adhesive $Ca(OH)_2$ treatments with and without adjunct laser therapy were compared. Both anterior and posterior teeth were treated in three studies [14, 22, 29]. In two studies [13, 25], types of teeth treated were not reported. Three studies [13, 14, 24] reported to size of pulp exposure, which ranged between 0.1 and 1.5 mm (Table 1).

Laser parameters

Two studies [13, 14] used the carbon dioxide (CO_2) lasers, in two studies [24, 29]. Erbium, chromium-doped yttrium, scandium, gallium, and garnet (Er,Cr:YSGG) laser was used. In the study by Olivi et al. [29], Er,Cr:YSGG and Er:YAG lasers were assessed. In two studies [22, 25], low level diode lasers were used. In the studies by Olivi et al. [29], Cengiz et al. [24], and Yazdanfar et al. [22], laser therapy was performed in defocused, hard tissue, and continuous wave modes, respectively. In three studies [13, 14, 25], the mode of laser delivery was not reported. Two studies reported the diameter of the optic fiber, which was 320 μm [25] and 400 μm [22]. Wavelength of the laser used was reported in four studies [13, 14, 22, 29], which ranged between 808 and 10,600 nm. Power of the laser used ranged between 0.5 and 5 W [13, 14,

Table 1 Characteristics of studies included

Authors	Study design	Participants		Intervention and control	Size of the exposure—mean (range) in mm	Follow-up (months)	Outcome measures
		Number	Age mean (range) in years	Study groups			Success rate—% of vital teeth at final follow-up
Clinical studies							
Cengiz et al. [24]	RCT	Test 1, 15 Test 2, 15 Control 1, 15 Control 2, 15	28 (18–41)	Test 1, laser + $Ca(OH)_2$ Test 2, laser + resin Control 1, $Ca(OH)_2$ Control 2, resin	NA (0.5–1.5)	6	Test 1, 100 % Test 2, 100 % Control 1, 73 % Control 2, 67 %
Moritz et al. [13]	RCT	Test, 100 Control, 100	Test, 34.4 (8–74) Control, 33.9 (9–68)	Test, laser + $Ca(OH)_2$ Control, $Ca(OH)_2$	0.6 (0.1–1.5)	12	Test, 89 % Control, 68 %
Moritz et al. [14]	RCT	Test, 130 Control, 130	Test, 34.8 (15–65) Control, 33.9 (9–68)	Test, laser + $Ca(OH)_2$ Control, $Ca(OH)_2$	0.6 (0.1–1.2)	24	Test, 93 % Control, 68 %
Olivi et al. [29]	RCT	Test 1, 34 Test 2, 30	Test 1, 14.5 (11–18) Test 2, NA (19–40)	Test 1a, 2a, laser + $Ca(OH)_2$ Test 1b, 2b, laser + $Ca(OH)_2$ Control 1c, 2c, $Ca(OH)_2$	NA	48	Test 1a, 2a, 80 %, 80 % Test 1b, 2b, 75 %, 70 % Control 1c, 2c, 63 %, 50 %
Santucci et al. [25]	Cohort	Test, 64 Control, 29	NA	Test, laser + resin Control, $Ca(OH)_2$	NA	54	Test, 90.3 % Control, 43.6 %
Yazdanfar et al. [22]	RCT	Test, 5 Control, 5	26 (14–40)	Test, laser + RM-GIC Control, RM-GIC	NA	12	Test, 100 % Control, 60 %
Experimental studies							
Hasheminia et al. [26]	Animal study	9 cats 36 teeth	NA	Test 1, laser + MTA Test 2, laser + $Ca(OH)_2$ Control, MTA	NA	4	No difference among test and control groups
Jayawardena et al. [30]	Animal study	Rats 76 teeth	NA	Test, laser + $Ca(OH)_2$ Control, $Ca(OH)_2$	NA	0.5	Increased reparative dentin formation in test group compared to control group
Suzuki et al. [23]	Animal study	42 rats 75 teeth	8–9 weeks	Test, laser + resin Control, resin Control, $Ca(OH)_2$	NA (0.2–0.4)	1	No difference among test and control groups

RCT randomized controlled trial, *NA* not available, *$Ca(OH)_2$* calcium hydroxide, *MTA* mineral trioxide aggregate, *RM-GIC* resin modified glass ionomer cement

22, 24, 25, 29]. Five studies [13, 14, 24, 25, 29] reported the pulse interval of the lasers used, which ranged between 1 and 140 μs. Olivi et al. [29] and Cengiz et al. [24] reported the duration of laser application, which was 60 and 10 s, respectively.

Outcomes

Direct pulp capping with adjunct laser therapy yielded a success rate of up to 100 % as compared to when pulp capping was performed without adjunct laser therapy [13, 14, 22, 24, 25, 29].

Quality assessment of studies

Quality assessment showed that all studies [13, 14, 22, 24, 25, 29] had scores ranging between 8 and 10. Shortcomings of all studies were as follows: (a) confounders remained unaddressed (item 5 in CASP Score protocol) and (b) it remained unclear if the studies fitted the available evidence or not (item 11 ion CASP score).

Experimental studies

General characteristics

Three experimental studies [23, 26, 30] were included, out of which two studies [23, 30] were performed in rats and one in cats [26]. Age of animals was reported in one study [23], in which the rats were 8 to 9 weeks old. In studies by Suzuki et al. [23], Hasheminia et al. [26], and Jayawardena et al. [30], efficacy of resin, MTA, and $Ca(OH)_2$, respectively, in direct pulp capping with and without adjunct laser therapy was assessed. Studies on rats were performed on maxillary first molars, and in the study by Hasheminia et al. [26], pulp capping was performed on canines. Size of the pulp exposure was reported by one study [23], which ranged between 0.2 and 0.4 mm. The follow-up duration ranged between 2 weeks and 4 months [23, 26, 30] (Table 1).

Laser parameters

In studies by Hasheminia et al. [26] and Jayawardena et al. [30], Er:YAG laser (2940 nm) used a fiber tip with a diameter of 600 μm. In the study by Hasheminia et al. [26], laser was delivered as a very long pulse, and in the study by Jayawardena et al. [30], the laser was delivered in contact mode. Suzuki et al. [23] used CO_2 laser (10,600 nm) at 0.5 W in a super-pulse mode using a thick diameter fiber (740 μm). Pulse interval and energy fluence were reported by Suzuki et al. [23] and Hasheminia et al. [26], which were 200 μs and 0.69 J/cm^2 and 700 μs and 71 J/cm^2. The laser frequency were reported by Hasheminia et al. [26] and Jayawardena et al. [30], which were 3 and 10 Hz, respectively. Duration of laser application was reported by Suzuki et al. [23] and Hasheminia et al. [26], which was 1.5 and 15 s, respectively (Table 2).

Outcomes

Two studies [23, 26] reported that outcomes of direct pulp capping when performed with or without adjunct laser therapy are comparable. Results by Jayawardena et al. [30] reported increased reparative dentin formation when direct pulp capping was performed using $Ca(OH)_2$ with adjunct Er:YAG laser as compared to when $Ca(OH)_2$ was used alone (Table 1).

Quality assessment of studies

Quality assessment showed that all studies [23, 26, 30] had scores ranging between 8 and 10. Shortcomings of all studies were as follows: (a) confounders remained unaddressed (item 5 in CASP Score protocol); (b) short-term follow-up (item 6 in CASP score); and (c) it was difficult to assess the clinical significance of the experimental results (item 10 in CASP score) (Table 3).

Meta-analysis

After data extraction, six studies [13, 14, 22, 24, 25, 29] were included in the meta-analysis of the weighted mean differences of pulpal healing with and without laser therapy (Table 4). The remaining three studies [23, 26, 30] were excluded from the meta-analysis as they were experimental preclinical studies. Figure 2 presents the forest plots and summary estimates for log odds ratio of success rate of direct pulp capping procedures with versus without laser irradiation, respectively. The Mantel-Haenszel combined odds ratio shows that the success rate in the treatment group is significantly higher than the control group (log odds ratio = 1.737; 95 % confidence interval, 1.304–2.171) (Table 4).

Discussion

According to Arany et al. [31], low level laser therapy (LLLT) (approximately 800 nm) activates latent growth factor complex and transforming growth factor beta-1, which differentiate host stem cells thereby promoting tissue regeneration. Furthermore, experimental results on rat models have demonstrated a significant increase in dentin regeneration following LLLT [31]. It has also been reported that the application of lasers on the exposed pulpal tissue promotes healing by increasing cellular motility and mesenchymal cell proliferation [32–34]. Authors of the present systematic review and meta-

Table 2 Laser parameters

Authors	Type of laser	Mode	Diameter of optic fiber (in µm)	Laser wavelength (in nm)	Power (in W)	Pulse interval duration (in µs)	Frequency (in Hz)	Energy fluence (J/cm^2)	Duration of laser application (in s)
Clinical studies									
Cengiz et al. [24]	Er,Cr:YSGG	Hard tissue	–	–	0.5	140	20	–	10
Moritz et al. [13]	CO_2 laser	–	–	10,600	1	1	–	–	–
Moritz et al. [14]	CO_2 laser	–	–	10,600	1	1	–	–	–
Olivi et al. [29]	Er,Cr:YSGG	Defocused	–	2780	3–5	20	20	–	60
	Er:YAG	Defocused		2940	1.5–2	–	3	–	60
Santucci et al. [25]	Nd:YAG	–	320	–	1.75	20	–	–	–
Yazdanfar et al. [22]	Diode	Continuous wave	400	808	1.5	–	–	–	–
Experimental studies									
Hasheminia et al. [26]	Er:YAG	Very long pulse	600	2940	–	700	3	71	15
Jayawardena et al. [30]	Er:YAG	Contact mode	600	2940	–	–	10	–	–
Suzuki et al. [23]	CO_2 laser	Super-pulse mode	740	10,600	0.5	200	–	0.698	1.5

CO_2 carbon dioxide, *Er, Cr:YSGG* erbium, chromium: yttrium-scandium-gallium-garnet, *Er:YAG* erbium-doped yttrium aluminum garnet, *Nd:YAG* neodymium-doped yttrium aluminum garnet

Table 3 Quality assessment of the included studies

Authors	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12	Total quality score out of 12
Clinical studies													
Cengiz et al. [24]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Cannot tell	Yes	9
Moritz et al. [13]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Cannot tell	Yes	10
Moritz et al. [14]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Cannot tell	Yes	10
Olivi et al. [29]	Yes	No	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Cannot tell	Yes	8
Santucci et al. [25]	Yes	No	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Cannot tell	Yes	8
Yazdanfar et al. [22]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Cannot tell	Yes	10
Experimental studies													
Hasheminia et al. [26]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Cannot tell	Yes	8
Jayawardena et al. [30]	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	No	Cannot tell	Yes	7
Suzuki et al. [23]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Cannot tell	Yes	8

Table 4 Estimated log odds ratio and Mantel-Haenszel combined odds ratio

Study	Estimate	SE	95 % CI	Sample size	Type
Moritz et al. [13]	1.443	0.396	0.667 to 2.220	200	Single
Moritz et al. [14]	1.859	0.393	1.088 to 2.629	260	Single
Santucci et al. [25]	2.476	0.569	1.362 to 3.591	93	Single
Olivi et al. [29]	0.906	0.570	−0.211 to 2.023	64	Single
Yazdanfar et al. [22]	1.792	1.748	−1.634 to 5.218	10	Single
Cengiz et al. [24]	3.230	1.481	0.328 to 6.132	60	Single
MH_LOR	1.737	0.221	1.304 to 2.171	687	Combined

analysis applauds these results since nearly 80 % of the studies [13, 14, 22, 24–26, 29] showed that adjunct laser therapy is more effective in maintaining pulp vitality than conventional therapy (using Ca[OH]$_2$, MTA or resin, etc.) alone. It is hypothesized that rise in tissue temperature caused by laser application stimulates tissue microcirculation thereby enhancing tissue regeneration [35, 36]. However, among the studies included, there was a lack of standardization in the laser parameters. It is noteworthy that among the studies included in the present systematic review and meta-analysis, there were two modalities of laser irradiation—one that used high power lasers and interacted with tissues by increasing temperature, and the other that used low power lasers or defocused high power lasers that did not increase tissue temperature, but biomodulated tissues, accelerated wound healing, and modulated inflammation. In the studies by Moritz et al. [13, 14], CO_2 laser (10,600 nm) was used as an adjunct to direct pulp capping procedures. The 24-month follow-up results showed 93 % success in terms tooth vitality among teeth that received laser therapy as an adjunct to pulp capping [13, 14]; however, these studies [13, 14] did not report whether the laser was delivered in a focused or defocused mode. Moreover, in these studies [13, 14], other critical parameters such as duration of laser application and diameter of fiber were also not reported. It may therefore be argued that the same laser when applied for longer durations using a focused mode may demonstrate significantly different results as compared to those reported in studies by Moritz et al. [13, 14]. Yazdanfar et al. [22] used LLLT (808 nm) as adjuncts to their pulp capping protocol and reported 100 % success at 12 months of follow-up. This suggests that low as well as high power lasers may be used as adjuncts to conventional pulp capping procedures; however, it is essential to standardize the laser parameters. Further well-designed clinical trials are warranted in this regard. The outcomes of experimental studies [13, 14, 23] included in the present review were controversial. It is likely that this dissimilarity could be related to the short follow-up duration of the experimental studies. Studies [37, 38] have shown that pulp healing is more predictable with a smaller exposure and in younger patients. In addition, other factors that have been reported to influence direct pulp capping procedures include the following: (a) controlling pulpal bleeding after exposure and prior to placing the pulp capping agent [39]; (b) cause of exposure: exposures caused by mechanical reasons are more likely to survive pulp capping procedures than exposures caused by caries [39]; (c) control of moisture and

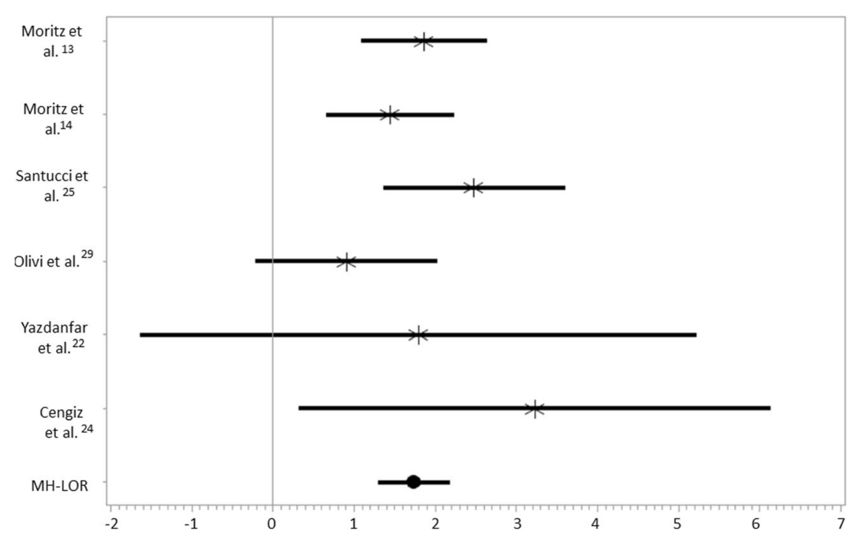


Fig. 2 Forest plot using Mantel-Haenszel method for 95 % confidence interval of individual study and of the combined log odds

contamination in the dentin adjacent to the site of exposure [39]. The age of the patients reported in the included studies [13, 14, 22, 24, 29] ranged between 9 and 68 years. The size of the pulp exposure varied from 0.1 mm to greater than 1.5 mm [13, 14, 23, 24], and was not consistently reported. Moreover, in these studies [13, 14, 22, 24, 29], cause of exposure remained unclear. In order to reach a consensus on efficacy of laser irradiation on pulpal tissue, reporting and standardization of these variables is necessary.

$Ca(OH)_2$ is considered to be the gold standard for pulp capping and is shown to have consistent outcomes in dentin bridge formation to seal off the exposed pulp [40, 41]. In these studies, [13, 14, 29, 30] $Ca(OH)_2$ was placed over the pulp in the test groups after laser irradiation. One study [26] used MTA along with laser therapy for direct pulp capping and found no difference among the different groups in terms of pulpal healing. Data from recent meta-analysis [12, 42] show that MTA has a higher success rate in direct pulp capping as compared to $Ca(OH)_2$. Considering the high success rate of pulp capping with MTA and $Ca(OH)_2$, it is unclear how to identify the contribution of laser application in the improvement of outcomes in the test group. This suggests that further studies with well-defined experimental and control group are needed.

Conclusion

It appears that lasers treatment of exposed pulps can improve the outcome of direct pulp capping procedures. However, the exact mechanism of this effect remains unclear.

Compliance with ethical standards The authors declare that they have no conflict of interest. The study was approved by the Research Ethics Committee of the College of Dentistry, King Saud University, Riyadh, Saudi Arabia. This is a systematic review article; therefore, an informed consent was not required. This article does not contain any studies with human participants or animals performed by any of the authors. The authors extend their sincere appreciations to Deanship of Scientific Research at King Saud University for its funding of this prolific research group (PRG-1437-38)

Appendix A: List of excluded studies, with reason for exclusion in parenthesis

- Stefanova VP, Tomov GT, Tsanova S (2015) Morphological Study Of Border Area Of Pulp-Capping Materials And Er:YAG Laser Prepared Hard Dental Surface. Folia medica 57 (1):49-55. doi:10.1515/folmed-2015-0019 (Focused question not answered)
- Poggio C, Ceci M, Dagna A, Beltrami R, Colombo M, Chiesa M (2015) In vitro cytotoxicity evaluation of different pulp capping materials: a comparative study. Arhiv za higijenu rada i toksikologiju 66 (3):181-188. doi:10.1515/aiht-2015-66-2589 (Focused question not answered)
- Kurtzman GM (2015) Evolution of Comprehensive Care, Part 4. Direct Restorations. Dentistry today 34 (8):22, 24, 26-27 (Focused question not answered)
- Komabayashi T, Ebihara A, Aoki A (2015) The use of lasers for direct pulp capping. Journal of oral science 57 (4):277-286. doi:10.2334/josnusd.57.277 (Review)
- Arany PR, Cho A, Hunt TD, Sidhu G, Shin K, Hahm E, Huang GX, Weaver J, Chen AC, Padwa BL, Hamblin MR, Barcellos-Hoff MH, Kulkarni AB, D JM (2014) Photoactivation of endogenous latent transforming growth factor-beta1 directs dental stem cell differentiation for regeneration. Science translational medicine 6 (238):238ra269. doi:10.1126/scitranslmed.3008234 (Focused question not answered)
- Yilmaz Y, Keles S, Mete A (2013) Temperature changes in the pulpal chamber and the sealing performance of various methods of direct pulp capping of primary teeth. European journal of pediatric dentistry: official journal of European Academy of Pediatric Dentistry 14 (2):95-100 (Focused question not answered)
- Huth KC, Hajek-Al-Khatar N, Wolf P, Ilie N, Hickel R, Paschos E (2012) Long-term effectiveness of four pulpotomy techniques: 3-year randomized controlled trial. Clinical oral investigations 16 (4):1243-1250. doi:10.1007/s00784-011-0602-3 (Focused question not answered)
- de Assuncao Pinheiro IV, Borges BC, de Lima KC (2012) In vivo assessment of secondary caries and dentin characteristics after traditional amalgam restorations. European journal of dentistry 6 (3):263-269 (Focused question not answered)
- Cannon M, Wagner C, Thobaben JZ, Jurado R, Solt D (2011) Early response of mechanically exposed dental pulps of swine to antibacterial-hemostatic agents or diode laser irradiation. The Journal of clinical pediatric dentistry 35 (3):271-276 (Focused question not answered)
- Masuda-Murakami Y, Kobayashi M, Wang X, Yamada Y, Kimura Y, Hossain M, Matsumoto K (2010) Effects of mineral trioxide aggregate on the differentiation of rat dental pulp cells. Acta histochemica 112 (5):452-458. doi:10.1016/j.acthis.2009.05.001 (Focused question not answered)
- Kneist S, Schmidt F, Callaway A, Willershausen B, Rupf S, Wicht M, Thiede B (2010) Diversity of Lactobacillus species in deep carious lesions of primary molars. European archives of pediatric dentistry: official journal of the European Academy of Pediatric Dentistry 11 (4):181-186 (Focused question not answered)
- Ferriello V, Faria MR, Cavalcanti BN (2010) The effects of low level diode laser treatment and dental pulp-capping materials on the proliferation of L-929 fibroblasts. Journal of oral science 52 (1):33-38 (Focused question not answered)
- Mohammadi Z (2009) Laser applications in endodontics: an update review. International dental journal 59 (1):35-46 (Review)
- Fuks AB (2008) Vital pulp therapy with new materials for primary teeth: new directions and Treatment perspectives. Pediatric dentistry 30 (3):211-219 (Review)
- Parker S (2007) Surgical laser use in implantology and endodontics. British dental journal 202 (7):377-386. doi:10.1038/bdj.2007.284 (Review)
- Srinivasan V, Patchett CL, Waterhouse PJ (2006) Is there life after Buckley's Formocresol? Part I – a narrative review of alternative interventions and materials. International journal of pediatric dentistry / the British Pedodontic Society [and] the International Association of Dentistry for Children 16 (2):117-127. doi:10.1111/j.1365-263X.2006.00688.x (Focused question not answered)
- Olivi G, Genovese MD (2006) Erbium chromium laser in pulp capping treatment. J Oral Laser Appl 6 (4):291-299 (Focused question not answered)
- Huth KC, Paschos E, Hajek-Al-Khatar N, Hollweck R, Crispin A, Hickel R, Folwaczny M (2005) Effectiveness of 4 pulpotomy

techniques–randomized controlled trial. Journal of dental research 84 (12):1144-1148 (Focused question not answered)

- Stabholz A, Sahar-Helft S, Moshonov J (2004) Lasers in endodontics. Dental Clinics of North America 48 (4):809-832, vi. doi:10.1016/j.cden.2004.05.012 (Review)
- Matsumoto K (2000) Lasers in endodontics. Dental Clinics of North America 44 (4):889-906, viii (Review)
- Kimura Y, Wilder-Smith P, Matsumoto K (2000) Lasers in endodontics: a review. International endodontic journal 33 (3):173-185 (Review)
- Dabrowska E, Zdanowicz-Wiloch J, Pawinska-Magnuszewska M, Stokowska W (1997) Intravital treatment of the pulp with simultaneous laser biostimulation. Roczniki Akademii Medycznej w Bialymstoku (1995) 42 (1):168-176 (Focused question not answered)
- Walsh LJ (1994) Clinical evaluation of dental hard tissue applications of carbon dioxide lasers. Journal of clinical laser medicine & surgery 12 (1):11-15. doi:10.1089/clm.1994.12.11 (Focused question not answered)
- Meese G, Holzel B, Engelmann U (1991) [Micro-plasma treatment of dental pulp in animal experiments]. Deutsche Stomatologie (Berlin, Germany: 1990) 41 (12):479-481 (Focused question not answered)
- Wilder-Smith P (1988) The soft laser: therapeutic tool or popular placebo? Oral surgery, oral medicine, and oral pathology 66 (6):654-658 (Review)

References

1. Ding J, Ebihara A, Watanabe S, Iino Y, Kokuzawa C, Anjo T, Suda H, Sumi Y (2014) Application of optical coherence tomography to identify pulp exposure during access cavity preparation using an Er:YAG laser. Photomed Laser Surg 32(6):356–359. doi:10.1089/pho.2013.3688
2. Browning WD, Chan DC, Swift EJ Jr (2013) Critical appraisal: approaches to caries removal: what the clinical evidence says. J Esthet Restor Dent 25(2):141–151. doi:10.1111/jerd.12022
3. Ring AL (1969) [The problem of pulp injuries following inlay and crown preparation with specific reference to Durelon]. Zahnarzt 13(2):3–8, passim
4. Hafez AA, Cox CF, Tarim B, Otsuki M, Akimoto N (2002) An in vivo evaluation of hemorrhage control using sodium hypochlorite and direct capping with a one- or two-component adhesive system in exposed nonhuman primate pulps. Quintessence Int 33(4):261–272
5. Cox CF, Tarim B, Kopel H, Gurel G, Hafez A (2001) Technique sensitivity: biological factors contributing to clinical success with various restorative materials. Adv Dent Res 15:85–90
6. Queiroz AM, Assed S, Leonardo MR, Nelson-Filho P, Silva LA (2005) MTA and calcium hydroxide for pulp capping. J Appl Oral Sci 13(2):126–130
7. Cvek M (1978) A clinical report on partial pulpotomy and capping with calcium hydroxide in permanent incisors with complicated crown fracture. J Endod 4(8):232–237. doi:10.1016/s0099-2399(78)80153-8
8. Swift EJ, Trope M, Ritter AV (2003) Vital pulp therapy for the mature tooth—can it work? Endod Top 5(1):49–56
9. Ricucci D, Loghin S, Lin LM, Spangberg LS, Tay FR (2014) Is hard tissue formation in the dental pulp after the death of the primary odontoblasts a regenerative or a reparative process? J Dent 42(9):1156–1170. doi:10.1016/j.jdent.2014.06.012
10. Malkondu O, Karapinar Kazandag M, Kazazoglu E (2014) A review on biodentine, a contemporary dentine replacement and repair material. Biomed Res Int 2014:160951. doi:10.1155/2014/160951
11. Schwendicke F, Brouwer F, Schwendicke A, Paris S (2016) Different materials for direct pulp capping: systematic review and meta-analysis and trial sequential analysis. Clin Oral Investig. doi:10.1007/s00784-016-1802-7
12. Zhu C, Ju B, Ni R (2015) Clinical outcome of direct pulp capping with MTA or calcium hydroxide: a systematic review and meta-analysis. Int J Clin Exp Med 8(10):17055–17060
13. Moritz A, Schoop U, Goharkhay K, Sperr W (1998) The CO_2 laser as an aid in direct pulp capping. J Endod 24(4):248–251. doi:10.1016/s0099-2399(98)80106-4
14. Moritz A, Schoop U, Goharkhay K, Sperr W (1998) Advantages of a pulsed CO_2 laser in direct pulp capping: a long-term in vivo study. Lasers Surg Med 22(5):288–293
15. Sardari F, Ahrari F (2016) The effect of low-level helium-neon laser on oral wound healing. Dent Res J (Isfahan) 13(1):24–29. doi:10.4103/1735-3327.174693
16. Kathuria V, Dhillon JK, Kalra G (2015) Low level laser therapy: a panacea for oral maladies. Laser Ther 24(3):215–223. doi:10.5978/islsm.15-RA-01
17. Karu T, Kalendo G, Letokhov V (1981) Control of RNA synthesis rate in tumour cell HeLa by action of a low-intensity visible light of copper laser. Lettere Al Nuovo Cimento (1971–1985) 32(2):55–59
18. Matsui S, Takeuchi H, Tsujimoto Y, Matsushima K (2008) Effects of Smads and BMPs induced by Ga-Al-As laser irradiation on calcification ability of human dental pulp cells. J Oral Sci 50(1):75–81
19. Matsui S, Tsujimoto Y, Matsushima K (2007) Stimulatory effects of hydroxyl radical generation by Ga-Al-As laser irradiation on mineralization ability of human dental pulp cells. Biol Pharm Bull 30(1):27–31
20. Ohbayashi E, Matsushima K, Hosoya S, Abiko Y, Yamazaki M (1999) Stimulatory effect of laser irradiation on calcified nodule formation in human dental pulp fibroblasts. J Endod 25(1):30–33. doi:10.1016/s0099-2399(99)80395-1
21. Tate Y, Yoshiba K, Yoshiba N, Iwaku M, Okiji T, Ohshima H (2006) Odontoblast responses to GaAlAs laser irradiation in rat molars: an experimental study using heat-shock protein-25 immunohistochemistry. Eur J Oral Sci 114(1):50–57. doi:10.1111/j.1600-0722.2006.00261.x
22. Yazdanfar I, Gutknecht N, Franzen R (2015) Effects of diode laser on direct pulp capping treatment : a pilot study. Lasers Med Sci 30(4):1237–1243. doi:10.1007/s10103-014-1574-8
23. Suzuki M, Ogisu T, Kato C, Shinkai K, Katoh Y (2011) Effect of CO(2) laser irradiation on wound healing of exposed rat pulp. Odontology 99(1):34–44. doi:10.1007/s10266-010-0140-5
24. Cengiz E, Yilmaz HG (2016) Efficacy of erbium, chromium-doped: yttrium, scandium, gallium, and garnet laser irradiation combined with resin-based tricalcium silicate and calcium hydroxide on direct pulp capping: a randomized clinical trial. J Endod 42(3):351–355. doi:10.1016/j.joen.2015.11.015
25. Santucci PJ (1999) Dycal versus Nd:YAG laser and Vitrebond for direct pulp capping in permanent teeth. J Clin Laser Med Surg 17(2):69–75. doi:10.1089/clm.1999.17.69
26. Hasheminia SM, Feizi G, Razavi SM, Feizianfard M, Gutknecht N, Mir M (2008) A comparative study of three treatment methods of direct pulp capping in canine teeth of cats: a histologic evaluation. Lasers Med Sci 25(1):9–15. doi:10.1007/s10103-008-0584-9
27. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, Clarke M, Devereaux PJ, Kleijnen J, Moher D (2009) The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions:

explanation and elaboration. BMJ 339:b2700. doi:10.1136/bmj.b2700

28. Zeng X, Zhang Y, Kwong JS, Zhang C, Li S, Sun F, Niu Y, Du L (2015) The methodological quality assessment tools for preclinical and clinical studies, systematic review and meta-analysis, and clinical practice guideline: a systematic review. J Evid Based Med 8(1): 2–10. doi:10.1111/jebm.12141
29. Olivi G, Genovese MD, Maturo P, Docimo R (2007) Pulp capping: advantages of using laser technology. Eur J Paediatr Dent 8(2):89–95
30. Jayawardena JA, Kato J, Moriya K, Takagi Y (2001) Pulpal response to exposure with Er:YAG laser. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 91(2):222–229. doi:10.1067/moe.2001.111943
31. Arany PR, Cho A, Hunt TD, Sidhu G, Shin K, Hahm E, Huang GX, Weaver J, Chen AC, Padwa BL, Hamblin MR, Barcellos-Hoff MH, Kulkarni AB, D JM (2014) Photoactivation of endogenous latent transforming growth factor-beta1 directs dental stem cell differentiation for regeneration. Sci Transl Med 6 (238):238ra269. doi:10.1126/scitranslmed.3008234
32. Ginani F, Soares DM, Barreto MP, Barboza CA (2015) Effect of low-level laser therapy on mesenchymal stem cell proliferation: a systematic review. Lasers Med Sci 30(8):2189–2194. doi:10.1007/s10103-015-1730-9
33. AlGhamdi KM, Kumar A, Moussa NA (2012) Low-level laser therapy: a useful technique for enhancing the proliferation of various cultured cells. Lasers Med Sci 27(1):237–249. doi:10.1007/s10103-011-0885-2
34. Eduardo Fde P, Bueno DF, de Freitas PM, Marques MM, Passos-Bueno MR, Eduardo Cde P, Zatz M (2008) Stem cell proliferation under low intensity laser irradiation: a preliminary study. Lasers Surg Med 40(6):433–438. doi:10.1002/lsm.20646
35. Schindl A, Heinze G, Schindl M, Pernerstorfer-Schon H, Schindl L (2002) Systemic effects of low-intensity laser irradiation on skin microcirculation in patients with diabetic microangiopathy. Microvasc Res 64(2):240–246
36. Schindl A, Schindl M, Pernerstorfer-Schon H, Kerschan K, Knobler R, Schindl L (1999) Diabetic neuropathic foot ulcer: successful treatment by low-intensity laser therapy. Dermatology 198(3):314–316
37. Honegger D (1979) Contrôle clinique à long terme du coiffage pulpaire direct:(réalisé par les étudiants de la SMD, Genève). Impr. Berichthaus
38. Reuver J (1992) 592 Pulpaüberkappungen in einer zahnärztlichen Praxis-eine klinische√ Prüfung (1966–1990). Dtsch Zahnärztl 47: 29–32
39. Hilton TJ (2009) Keys to clinical success with pulp capping: a review of the literature. Oper Dent 34(5):615–625. doi:10.2341/09-132-0
40. Ji YM, Jeon SH, Park JY, Chung JH, Choung YH, Choung PH (2010) Dental stem cell therapy with calcium hydroxide in dental pulp capping. Tissue Eng Part A 16(6):1823–1833. doi:10.1089/ten.TEA.2009.0054
41. Uses of calcium hydroxide: an online study guide (2008). J Endod 34 (5 Suppl):e87-92. doi:10.1016/j.joen.2007.07.023
42. Li Z, Cao L, Fan M, Xu Q (2015) Direct pulp capping with calcium hydroxide or mineral trioxide aggregate: a meta-analysis. J Endod 41(9):1412–1417. doi:10.1016/j.joen.2015.04.012