TITLE: Photo-Activated Disinfection Therapy for Dental Surgery: Review of the Clinical Effectiveness

DATE: 11 September 2013

CONTEXT AND POLICY ISSUES

The oral cavity harbors more than 700 prokaryote species;[1] most of these species are normal flora of the healthy oral cavity.[2] Some of these microorganisms are responsible for oral pathologies. Bacteria such as *Actinobacillus actinomycetemcomitans, Prevotella intermedia, Porphyromonas gingivalis, Treponema denticola,* and *Tannerella forsythia* are responsible for common forms of periodontal diseases,[3] and *Bacteroides, Peptostreptococcus,* and *microaerophilic Streptococcus species* may cause osteomyelitis of the jaw.[4]

During a surgical intervention, disinfection of the oral cavity is attempted by using different chemical solutions such as chlorhexidine and iodine. This is done to prevent, or at least reduce the risk of wound infections or bacteremia following the surgical intervention.[5] In the case of periodontal and endodontic treatments, mechanical cleaning of the affected surfaces are believed to be the gold standard.[6]

Photodynamic antimicrobial chemotherapy or light-activated disinfection is a technology based on the production of free oxygen radicals capable of affecting the membranes of microorganisms.[7] The technique is composed of a photosensitizer substance that can be activated with a suitable wave length and light source. The photosensitizer, usually toluidine blue, is activated with a light source. After its activation, it produces energy capable of transforming the surrounding oxygen into free radicals. The free radical then attacks the exposed microorganisms.[7]

Photodynamic chemotherapy may be used in dentistry to reduce the bacterial load in cases of periodontal lesions and during root canals. Another potential use of this technique is as a pre-surgical disinfection method for the oral cavity to prevent oral flora from penetrating the bone and submucosal tissues during surgery. This disinfection method may also be useful during surgical periodontal treatments.

The objective of the current review is to evaluate the efficacy of photoactive disinfection in the context of dental surgery as a pre-surgical disinfection method or as an adjunct for the surgical periodontal treatment.

RESEARCH QUESTIONS

What is the evidence for the clinical effectiveness and safety of photo-activated disinfection therapy (PDT) to reduce the bacterial load and decrease surgical infections for patients undergoing dental surgery?

KEY FINDINGS

Two studies were included that evaluated the technology as an adjunct to surgical periodontal treatment. The available evidence showed that the use of this technology as an adjunct to the surgical periodontal treatment did not ameliorate patient's outcomes more than what was seen with the conventional surgical periodontal treatment.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2013, Issue 7), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI (Health Devices Gold), Canadian and major international health technology agencies, as well as a focused Internet search. No methodological filters were applied to limit retrieval by publication type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2008 and August 13, 2013.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed for relevance. Full texts of relevant titles and abstracts were retrieved and assessed for inclusion. The final article selection was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Patients undergoing dental surgery
Intervention	Photo-activated disinfection therapy
Comparator	Any form of bacterial decolonization prior to surgery
Outcomes	Reduction of patients' bacterial load Decrease in surgical site infections
Study Designs	Health technology assessment, systematic reviews, meta-analyses, randomized and non-randomized controlled trials

Exclusion Criteria

Studies were excluded if they did not evaluate photo-activated disinfection therapy in the context of dental surgery. Studies with more recent updates were considered duplicates; the most recent update was considered the primary publication, and previous versions were used as secondary source of data.

Critical Appraisal of Individual Studies

The methodological quality of the included randomized controlled trials was evaluated using the SIGN50 checklist for controlled studies.[8] For the included studies a numeric score was not calculated. Instead, the strengths and limitations of the study were described.

SUMMARY OF EVIDENCE

Quantity of Research Available

A total of 239 potential citations were identified by searching the bibliographic databases, with 234 citations being excluded during the title and abstract screening based on their irrelevance to the questions of interest. The full text documents of the remaining five articles were retrieved. Of the five articles, one did not meet the inclusion criteria and was excluded, leaving four articles that reported on two randomized controlled trials.

A PRISMA diagram demonstrating the study selection process is presented in Appendix I. Additional references of potential interest are provided in Appendix V.

Summary of Study Characteristics

Four articles that reported on two randomized-controlled trials that addressed the review question were included in this report.[9-12] Details on studies characteristics are tabulated in Appendix II.

Souza et al. conducted their RCT in Brazil, and they evaluated the efficacy of photo-activated disinfection as adjunct to surgical and non-surgical periodontal treatments.[9] The included patients (N=15 patients for 15 molars) had bilateral class III furcation defects, and randomization was done on the basis of split mouth method. The periodontal treatment was conducted in two stages. The first stage was an initial non-surgical scaling and root planning; the photo-activated disinfection group received photodynamic therapy in addition to the non-surgical treatment. In the second stage after 45 days, all patients had a flap surgery and debridement of the defect; the photo-dynamic disinfection group received photodynamic therapy in addition to the surgical treatment. The trial evaluated the outcomes in terms of change in volume of the gingival crevicular fluid, bleeding on probing, change in gene expression of inflammatory and modeling factors and change in concentration of transforming growth factor β-1 in the crevicular fluid. The gene expression of inflammatory precursors, volume of gingival fluids and the concentration of transforming growth factor β-1 are surrogate markers of inflammation in the periodontal tissues. When these tissues are invaded by pathogenic microorganism, they produce and release inflammatory precursors. Variations in these precursors can be used as surrogate outcomes to evaluate the efficacy of periodontal treatment. Results were published by Souza et al.[9] and Andrade et al.[10]

De Angelis et al. conducted their RCT in Italy, and it evaluated the benefits of photo-activated disinfection in the treatment of peri-implantitis.[11] According to the clinical presentation of the case, patients received either non-surgical (N= 61) or surgical (N = 19) treatment. Patients, from both treatment options, were randomized equally to a conventional surgical and non-surgical treatment group without PDT or to a conventional treatment plus photo-activated disinfection group. The trial evaluated treatment outcomes in terms of implant failure, recurrence of peri-implantitis, re-treatment, adverse events and complications, changes in marginal bone level and pocket probing depth, and safety.[11] Results were published by De Angelis et al.[11] and Esposito et al.[7]

Summary of Critical Appraisal

Details on studies appraisal are tabulated in Appendix III.

The trial by Souza et al. employed a computer-generated randomization sequence.[9] One investigator evaluated the outcomes for all included patients, and this was done to avoid any subjective differences in the evaluation. Limits of the trial included a sample size based on convenience and not on statistical power calculation. Another potential limitation was that blinding of the evaluator to treatment group was not specified.[9] The analysis of results was not complete and could not be used to withdraw conclusions; the analysis of findings was based mainly on single-time evaluations. The differences between the treatment groups did not consider or adjust for the baseline values of each outcome. The calculation of changes from baseline for each group and the difference in these changes would have been more appropriate.

The trial by De Angelis et al. employed a computer-generated randomization sequence.[11] The investigator who evaluated the outcomes was blinded to the treatment allocation. The trial size was based on statistical power calculation; however, the article did not provide any justification for the common standard deviation used for this calculation. Other potential limitations of the trial was use of unstandardized surgical treatment protocol: the investigators had the choice of reducing marginal bone and eliminating unsupported implant spirals.[11] This additional procedure could affect the treatment outcomes. Because it was not provided for all patients systematically, it could bias the results favoring patients who had their implants smoothed and patients who had alveolar bone osteoplasty.

Summary of Findings

Details on study findings are tabulated in Appendix III.

Souza et al.[9] and Andrade et al.[10] reported that the difference between the treatment groups in the gene expression for the inflammatory precursors and seven tissue modulating factors (out of eleven) were not statistically significantly different between the treatment groups; the results for the other five genes were statistically significant. The concentration of transforming growth factor β-1 in the crevicular fluid was not statistically different between the two groups. On the other hand, the volume of the crevicular fluid was statistically significantly lower in the photodynamic group; however, the baseline value for the photodynamic group was lower than that of the control group, the difference between groups in terms of change from baseline volume was not evaluated in the trial. Bleeding on probing and probing depth were not statistically significantly different between the treatment groups.

De Angelis et al.[11] and Esposito et al.[7] reported that light-activated disinfection and the control groups were not statistically significantly different in any of the evaluated outcomes after 4 months and one year of follow-up.

Limitations

The available evidence is limited to two small trials. This might be due to the fact that photo-dynamic disinfection is a new technology, and its application in dental surgery is not common. Another limitation of this review is that the included trials evaluated the use of photo-dynamic disinfection as an adjunct to surgical treatment. We did not identify any studies on the use of photodynamic disinfection technology for pre-surgical oral disinfection. The two studies were conducted in adults; we did not find information on the use of PDT in children. Surgical site infection was an outcome of interest; however, none of the included studies evaluated this outcome explicitly.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

This report aimed to review the evidence of effectiveness of photo-dynamic disinfection in reducing the bacterial load and decrease surgical infections for patients undergoing dental surgery. Two studies were included that evaluated the technology as an adjunct to surgical periodontal treatment.

With respect to the effectiveness of photodynamic disinfection, the available evidence showed that the use of this technology as an adjunct to surgical periodontal treatment was not statistically significantly different than conventional treatment in improving periodontal treatment outcomes. We did not identify any studies on the use of photodynamic disinfection technology for pre-surgical oral disinfection.

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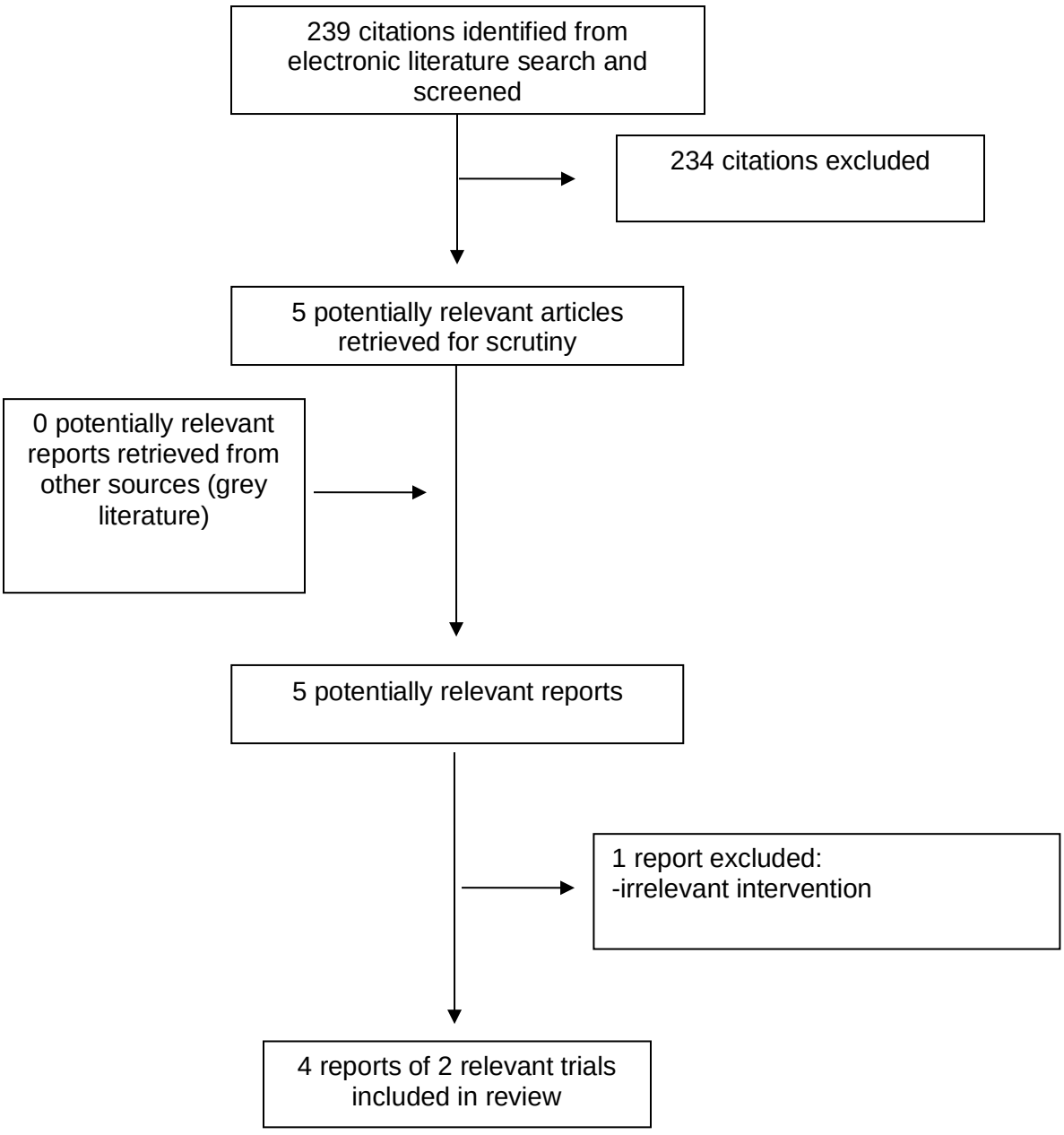
APPENDIX I: SELECTION OF INCLUDED STUDIES



APPENDIX II: CHARACTERISTICS OF THE INCLUDED STUDIES

Study objective and design	Population	Intervention	Comparator	Outcomes
Souza et al. 2013[9] and Andrade et al. 2013[10] – Brazil				
To test the efficacy of efficacy of PDT as adjunct therapy to non-surgical and surgical periodontal treatment. Randomized controlled trial using the split mouth technique	Fifteen periodontal patients with bilateral lower molars with class III furcation lesion and scheduled for extraction. 6 males and 9 females Age: from 36 to 65 years	**N= 15 molars** **Initial therapy:** Non-surgical scaling and root planning and antimicrobial photodynamic therapy. **Surgical therapy (45 days after the initial therapy):** Flap surgery accompanied with scaling and root planning and antimicrobial photodynamic therapy.	**N= 15 molars** **Initial therapy:** Non-surgical scaling and root planning. **Surgical therapy (45 days after the initial therapy):** Flap surgery accompanied with scaling and root planning	Outcomes were evaluated 45 days after the initial therapy and 21 days after the surgical therapy: • Change in gene expression during periodontal wound healing • Change in concentration of transforming growth factor-β1 in the gingival crevicular fluid • Change in volume of the gingival crevicular fluid • Bleeding on probing
De Angelis et al. 2012[11] and Esposito et al. 2013[7] – Italy				
To evaluate the benefits of light-activated disinfection as adjunct therapy to non-surgical or surgical treatment of peri-implantitis Randomized controlled trial – Four dental centers/ investigators	Eighty patients with at least one implant affected by peri-implantitis[a] 38 males and 42 females Age: from 25 to 80 years (mean 59 years)	**N= 40 patients/ implants** **Surgical treatment[b] (n = 9):** Flap surgery, curettage of the defect, debridement of the implant surface, and light activated disinfection **Non-surgical treatment[c] (n = 31)** Debridement of the implant surface with hand and/or mechanical instruments	**N = 40 patients/ implants** **Surgical treatment[b] (n = 10):** Flap surgery, curettage of the defect, and debridement of the implant surface **Non-surgical treatment[c] (n= 30)** Debridement of the implant surface with hand and/or mechanical instruments	• Implant failure (defined as primary outcome) – evaluated up to 5 years • Recurrence of peri-implantitis[d] (defined as primary outcome)[e] • Complications and adverse events • Re-treatment (defined as primary outcome) • Change in marginal bone level • Changes in pocket probing depth[e].

[a] peri-implantitis was defined as at least 3 mm of bone loss from the baseline radiographs and the presence of infection (with pus exudation and/or soft tissue swelling and/or redness)
[b] surgical treatment was provided for patients with implants that had marginal bone loss > 5 mm. Bone removal and elimination of the unsupported implant threads could be performed at the discretion of the operator.
[c] non-surgical treatment was provided for implants with marginal bone loss of 3 to 5 mm
[d] recurrent peri-implantitis was defined as additional bone loss of at least 2 mm
[e] outcome evaluated after 1, 3 and 5 years

APPENDIX III: CRITICAL APPRASIAL OF THE INCLUDED STUDIES

Strengths	Limitations
Souza et al. 2013[9] and Andrade et al. 2013[10] – Brazil	
Randomized sequence was generated by a computer. Outcome assessment was done by one investigator to avoid discrepancies in measurements. However, it was not specified that this investigator was blinded to the treatment allocation.	The size of the trial (number of patients) was based on convenience, and it was not based on power calculation. Therefore, the trial might be underpowered to detect the differences in outcomes between the two treatment groups.
De Angelis et al. 2012[11] and Esposito et al. 2013[7] – Italy	
Outcomes' assessor was blinded with regards to the treatment group. Sample size was based on power calculation. However, this calculation used a common standard deviation of a change in marginal bone level equal to 1.5; the report did not provide any justifications for this choice. Furthermore, the trial was powered to detect a1 mm deference in change of bone levels; the use of a standard deviation larger than the expected difference itself might indicate the potential of skewed distribution of results. In this case, the *t-test* used for the comparison is not suitable; a non-parametric test would have been more appropriate. Randomized sequence was generated by a computer, and one investigator managed this sequence. The investigator was not involved in the selection and treatment of the patients.	Sequential outcome assessment was planned, but there were no adjustment for the statistical testing criteria. The level of significance should be reduced with each sequential evaluation. All statistical comparisons were conducted at the 0.05 level of significance. This could potentially conclude that the results were statistically significant when the results were not in reality. Surgical treatment protocol was not standardized. The investigators had the choice of reducing marginal bone and eliminated unsupported implant spirals. These two factors might affect the outcomes of treatment. However, these two factors were not systematically reported or considered in outcomes assessment.

APPENDIX IV: MAIN FINDINGS OF THE INCLUDED STUDIES

<table>
<tr><th>Study findings</th><th>Conclusions/ Comments</th></tr>
<tr><td colspan="2">Souza et al. 2013[9] and Andrade et al. 2013[10] – Brazil</td></tr>
<tr><td>
<table>
<tr><th>Outcome measure</th><th>Photodynamic group (N= 15)</th><th>Control group (N= 15)</th><th>Difference between group</th></tr>
<tr><td colspan="4">Gene expression; mRNA level/β-actin (SD)[a]</td></tr>
<tr><td colspan="4">Inflammatory precursors</td></tr>
<tr><td>TNF-α</td><td>3.63 (1.23)</td><td>4.29 (1.33)</td><td rowspan="8">Not statistically significant</td></tr>
<tr><td>Il-1β</td><td>3.54 (0.79)</td><td>3.55 (0.98)</td></tr>
<tr><td>Il-4</td><td>1.85 (0.76)</td><td>2.16 (0.94)</td></tr>
<tr><td>Il-10</td><td>1.42 (0.55)</td><td>1.21 (0.25)</td></tr>
<tr><td>Il-4/ TNF-α</td><td>0.57 (0.30)</td><td>0.58 (0.38)</td></tr>
<tr><td>Il-4/ Il-1β</td><td>0.55 (0.31)</td><td>0.67 (0.34)</td></tr>
<tr><td>Il-10/ TNF-α</td><td>0.47 (0.33)</td><td>0.32 (0.14)</td></tr>
<tr><td>Il-10/ Il-1β</td><td>0.42 (0.19)</td><td>0.37 (0.15)</td></tr>
<tr><td colspan="4">Tissue modulating factors</td></tr>
<tr><td>MMP-2</td><td>3.26 (0.89)</td><td>4.23 (0.97)</td><td>Statistically significant</td></tr>
<tr><td>TIMP-2</td><td>2.75 (0.52)</td><td>2.88 (0.59)</td><td rowspan="4">Not statistically significant</td></tr>
<tr><td>MMP-2/TIMP-2</td><td>1.21 (0.36)</td><td>1.53 (0.45)</td></tr>
<tr><td>Type I collagen</td><td>2.18 (1.56)</td><td>1.55 (0.54)</td></tr>
<tr><td>RANKL</td><td>2.21 (0.95)</td><td>1.67 (1.10)</td></tr>
<tr><td>Alkaline phosphatase</td><td>1.93 (1.42)</td><td>1.13 (1.18)</td><td rowspan="2">Statistically significant</td></tr>
<tr><td>Osteoprotegrin</td><td>0.84 (0.45)</td><td>0.30 (0.26)</td></tr>
<tr><td>Osteoprotegrin/RANKL</td><td>4.34 (4.03)</td><td>0.23 (0.16)</td><td rowspan="3">Not statistically significant</td></tr>
<tr><td>Osteopontin</td><td>1.04 (0.89)</td><td>1.30 (0.86)</td></tr>
<tr><td>Osteocalcin</td><td>2.96 (1.02)</td><td>3.08 (0.96)</td></tr>
<tr><td>Bone sialoprotein</td><td>3.98 (1.04)</td><td>3.81 (1.17)</td></tr>
<tr><td colspan="4">Concentration of TGF-β1, pg/μL (SD)</td></tr>
<tr><td>Baseline:</td><td>45.6 (100.2)</td><td>25.6 (50.4)</td><td rowspan="2">Not statistically significant</td></tr>
<tr><td>Post-surgery</td><td>170.0 (534.4)</td><td>18.5 (31.5)</td></tr>
<tr><td>Difference from baseline</td><td colspan="2">Not statistically significant</td><td>Not reported</td></tr>
<tr><td colspan="4">Volume of gingival crevicular fluid, μL (SD)</td></tr>
<tr><td>Baseline:</td><td>2.75 (2.2)</td><td>3.11 (2.4)</td><td>Not statistically significant</td></tr>
<tr><td>Post-surgery</td><td>2.34 (1.8)</td><td>3.0 (2.0)</td><td>Statistically significant</td></tr>
<tr><td>Difference from baseline</td><td colspan="2">Not statistically significant</td><td>Not reported</td></tr>
<tr><td colspan="4">Bleeding on probing – results post-surgery were not reproted</td></tr>
<tr><td>Baseline:</td><td>100%</td><td>100%</td><td rowspan="2">Not statistically significant</td></tr>
<tr><td>Post-initial therapy</td><td>80%</td><td>86%</td></tr>
<tr><td>Difference from baseline</td><td colspan="3">Not reported</td></tr>
<tr><td colspan="4">Probing depth, mm</td></tr>
<tr><td>Baseline:</td><td>7.07 (1.6)</td><td>6.80 (1.6)</td><td rowspan="2">Not statistically significant</td></tr>
<tr><td>Post-surgery</td><td>6.20 (2.1)</td><td>6.27 (1.7)</td></tr>
<tr><td>Difference from baseline</td><td colspan="2">Statistically significant</td><td>Not reported</td></tr>
</table>
</td><td>Authors' conclusions
The trial authors concluded that photodynamic therapy had additional effect after surgical periodontal treatment. Positive effects were reported in terms of the volume of the gingival crevicular fluid and some tissue modulating genes. However, the authors raised some doubts about the clinical relevance of these differences.

Reviewer's comments:
The analysis of findings was based mainly on single-time evaluations. The differences between the treatment groups did not consider/ adjust for the baseline values of each outcome. The calculation of changes from baseline for each group and the difference in these changes (for each outcome) would have been more appropriate to withdraw conclusions.</td></tr>
<tr><td colspan="2">Il-1β = Interleukin-1β ; Il-4 = Interleukin-4 ; Il-10 = Interleukin-10 ; GCF = gingival crevicular fluid; MMP-2 = Matrixproteinase-2 ; RANKL = Receptor activator of nuclear factor-kB ; TGF-β1 = transforming growth factor-β1; TIMP-2 = Tissue inhibitor of MMP-2; TNF-α = Tumor necrosis factor-α

[a] All gene expression values were reported at 21 days after surgical intervention; baseline values were not reported. Differences between groups were not adjusted for baseline values</td></tr>
</table>

<table>
<tr><th>Study findings</th><th>Conclusions/ Comments</th></tr>
<tr><td colspan="2">De Angelis et al. 2012[11] and Esposito et al. 2013[7] – Italy</td></tr>
<tr><td>
<table>
<tr><th>Outcome measure</th><th>Light-activated disinfection (N= 40)[a]</th><th>Control treatment (N= 40)[a]</th><th>Difference between groups</th></tr>
<tr><td colspan="4">Implant failure, n/N</td></tr>
<tr><td>Four months</td><td>0</td><td>0</td><td></td></tr>
<tr><td>One year</td><td>1/37</td><td>0/40</td><td>Not statistically significant</td></tr>
<tr><td colspan="4">Treatment complication, n/N</td></tr>
<tr><td>Four months</td><td>2/40[b]</td><td>1/40[c]</td><td rowspan="2">Not statistically significant</td></tr>
<tr><td>One year</td><td>1/37[d]</td><td>0/40</td></tr>
<tr><td colspan="4">Recurrence of peri-implantitis, n/N</td></tr>
<tr><td>One year</td><td>3/37</td><td>3/40</td><td>Not statistically significant</td></tr>
<tr><td colspan="4">Retreatment, n/N</td></tr>
<tr><td>Four months</td><td>15/40</td><td>16/40</td><td rowspan="2">Not statistically significant</td></tr>
<tr><td>One year</td><td>29/37</td><td>33/40</td></tr>
<tr><td colspan="4">Mean plaque scores, mean (SD)</td></tr>
<tr><td>Pre-operative</td><td>2.18 (1.53)</td><td>2.15 (1.64)</td><td></td></tr>
<tr><td>Four months</td><td>0.97 (1.14)</td><td>0.93 (1.23)</td><td rowspan="2">Not statistically significant</td></tr>
<tr><td>One year</td><td>0.89 (0.94)</td><td>0.93 (0.94)</td></tr>
<tr><td colspan="4">Mean marginal bleeding scores, mean (SD)</td></tr>
<tr><td>Pre-operative</td><td>2.95 (1.32)</td><td>2.68 (1.25)</td><td></td></tr>
<tr><td>Four months</td><td>1.03 (1.33)</td><td>1.10 (1.33)</td><td rowspan="2">Not statistically significant</td></tr>
<tr><td>One year</td><td>1.35 (1.32)</td><td>1.28 (1.11)</td></tr>
<tr><td colspan="4">Mean marginal bone level, mean (SD) – mm</td></tr>
<tr><td>Pre-operative</td><td>4.5 (1.8)</td><td>4.9 (2.1)</td><td></td></tr>
<tr><td>Change at one year (from baseline)</td><td>0 (1.3), p=1.00</td><td>-1.3 (1.3), p=0.54</td><td>Not statistically significant</td></tr>
<tr><td colspan="4">Mean pocket probing depth, mean (SD) – mm</td></tr>
<tr><td>Pre-operative</td><td>6.2 (1.6)</td><td>6.5 (2.2)</td><td></td></tr>
<tr><td>Change at four months (from baseline)</td><td>1.08 (1.78), p= 0.001</td><td>1.20 (1.86), p<0.001</td><td rowspan="2">Not statistically significant</td></tr>
<tr><td>Change at one year (from baseline)</td><td>1.1 (2.0), p=0.001</td><td>0.95 (1.9), p=0.003</td></tr>
</table>
</td><td>Authors' conclusions
The trial authors concluded that the use of light-activated disinfection technology as adjunct with mechanical treatment of peri-implantitis did not improve any clinical outcome after one year of follow-up</td></tr>
<tr><td colspan="2">[a] Only 19 implants were treated surgically; 9 in the Light-activated disinfection group and 10 in the control group. There were no subgroup results for the surgically treated implants.
[b] the two complications were wound dehiscence and post-surgical swelling
[c] the reported complication was post-surgical swelling
[d] the reported complication was an abscess</td></tr>
</table>

APPENDIX V: SUMMARY OF STUDIES ON THE USE OF PHOTO-ACTIVATED DISINFECTION IN NON-SURGICAL CONTEXT

The objective of this section is to summarize studies that evaluated the efficacy of photo-activated disinfection therapy in non-surgical dental interventions. The summary is based on the published abstracts, and the full texts were not retrieved.

A total of 31 studies were identified in the literature; 26 controlled trials and five systematic reviews (**Table 2**). All identified studies evaluated the efficacy of photodynamic therapy in the context of the periodontal therapy. Patients with chronic or aggressive periodontitis and patients with peri-implantitis were evaluated in these studies. The majority of studies evaluated the photodynamic therapy as an adjunct to the non-surgical periodontal treatment; comparisons were made with the non-surgical treatment without the photodynamic therapy. The overall results of the reviewed abstracts indicated that the use of phototherapy as an adjunct to the non-surgical treatment did not ameliorate the periodontal outcomes more than what was recorded for the non-surgical treatment alone.

In conclusion, and within the limits of this summary, the available evidence does not support the use of photodynamic therapy or disinfection as an adjunctive therapy for periodontitis.

Table 2: Characteristics of the Included Studies (from abstracts)

Study objective and design	Population	Intervention	Comparator	Outcomes
Arweiler et al 2013[13]				
To evaluate the short-term effects of nonsurgical periodontal therapy with additional photodynamic therapy Randomized controlled trial	Thirty-six patients with aggressive periodontitis	- Non-surgical treatment plus photodynamic therapy - N = 18 patients	Non-surgical treatment plus antibiotics (amoxicillin + metronidazole for 7 days) N = 18 patients	After 3 months, systemic administration of antibiotics resulted in significantly higher reduction of probing depth and a lower number of deep pockets compared to photodynamic therapy
Queiroz et al. 2013[14]				
to investigate the adjunctive effect of antimicrobial photodynamic therapy to non-surgical periodontal therapy Randomized controlled trial	Twenty patients with chronic periodontitis	- Non-surgical treatment plus photodynamic therapy - N = 20 teeth	Non-surgical treatment N = 20 teeth	• There was no statistically significant difference between groups in terms of probing depth or clinical attachment level.
Balata et al. 2013[15]				
to evaluate the effects of photodynamic therapy as an adjunct to full-mouth ultrasonic debridement. Randomized controlled trial	Twenty-two patients with severe chronic periodontitis	Full-mouth ultrasonic debridement plus photodynamic therapy N = not reported	Full-mouth ultrasonic debridement N = not reported	• After six months, there were not statistically significant difference between groups in bleeding on probing pocket depth or clinical attachment level
Muller et al. 2013[16]				
To assess the efficacy of photodynamic therapy as adjunctive therapy for residual periodontal pockets Randomized controlled trial	Twenty-eight patients with residual periodontal pockets after initial periodontal therapy with ultrasonic instrumentation	- Photodynamic therapy applied twice a week (N = 28 teeth) - Photodynamic therapy applied once a week (N = 28 teeth)	Placebo therapy (without activating the laser/light source) (N = 28 teeth)	• It was reported that C-reactive protein was significantly lower only if the laser had been activated twice. • All other outcomes did not differ between groups significantly
Bassetti et al. 2013[17]				
To evaluate the efficacy of photodynamic therapy on the initial peri-implantitis Randomized controlled trial	Forty patients with initial peri-implantitis	- Non-surgical treatment plus photodynamic therapy - N = 20 implants	Non-surgical treatment plus locally delivered minocycline microspheres N = 20	• No statistically significant differences were observed between groups after 12 months with respect to clinical, microbiological and host-derived parameters

Table 2: Characteristics of the Included Studies (from abstracts)

Study objective and design	Population	Intervention	Comparator	Outcomes
Sgolastra et al. 2013[18]				
To evaluate the efficacy of photodynamic therapy on chronic periodontitis Systematic review and meta-analysis	Fourteen randomized controlled trials	- Non-surgical scaling and root planning plus photodynamic therapy	Non-surgical scalling and root planning alone	• The use of photodynamic therapy produced a difference of 0.19 mm in probing depth and 0.37 mm in clinical attachment level. These differences were statistically significant but they don't present clinically significant differences
Macedo et al 2103[19]				
to evaluate the efficacy of photodynamic therapy in the treatment of chronic periodontitis in diabetic patients randomized controlled trial	Thirty patients with chronic periodontitis and uncontrolled diabetes	- Non-surgical treatment plus doxycycline plus photodynamic therapy - N = 15 patients	Non-surgical treatment plus doxycycline N = 15	• After three months, the groups didn't differ significantly in terms of probing depth, bleeding on probing of clinical attachment level. • The photodynamic group showed statistically significant reduction of the HbA1C; the difference in change from baseline was 0.47 (the unit of change in HbA1C was not reported in the abstract)
Mongardini et al. 2012[20]				
To evaluate the efficacy of photodynamic therapy on the periodontal outcomes for patients with chronic periodontitis Randomized controlled trial	Thirty patients with residual periodontal pockets during the maintenance phase of treatment	- Non-surgical treatment plus photodynamic therapy - N = 30 teeth	Non-surgical treatment N = 30 teeth	• At one week, the photodynamic group showed statistically significantly lower rate of bleeding on probing and probing depths. However, these differences were evaluated at the end of the study, but these differences were not evaluated in terms of change from baseline.
Bassir et al. 2013[21]				
To evaluate the efficacy of photodynamic therapy in the treatment of chronic periodontitis Controlled trial (randomization was not reported)	Sixteen patients affected by moderate to severe chronic periodontitis	- Non-surgical treatment plus photodynamic therapy conducted one week after the non-surgical treatment - N = 16 mouth quadrants (number of teeth was not reported)	- Non-surgical treatment - N = 16 mouth quadrants (number of teeth was not reported)	• There were no significant differences among groups in terms of changes of clinical parameters in any time interval

Table 2: Characteristics of the Included Studies (from abstracts)

Study objective and design	Population	Intervention	Comparator	Outcomes
Dilsiz et al. 2013[22]				
To evaluate the clinical effects of photodynamic therapy on the outcomes of chronic periodontitis Randomized controlled trial	Twenty-four patients with untreated chronic periodontitis	- Non-surgical treatment plus photodynamic therapy - N = 24 teeth	- Non-surgical treatment - N = 24 teeth	• There were no significant differences between the photodynamic group and the non-surgical treatment group in terms of changes of clinical parameters
Schar et al. 2013[23]				
To evaluate the efficacy of photodynamic therapy in the treatment of peri-implantitis Randomized controlled trial	Forty subjects with initial peri-implantitis, i.e. pocket probing depths 4-6 mm with concomitant bleeding on probing and marginal bone loss ranging from 0.5 to 2 mm between delivery of the reconstruction and pre-screening appointment	- Non-surgical treatment plus photodynamic therapy - N = 20	- Non-surgical treatment plus locally delivered minocycline microspheres - N = 20	• Between-group comparisons revealed no statistically significant differences at baseline, 3 and 6 months in terms of bleeding on probing, clinical attachment level or mucosal recession
Berakdar et al. 2012[24]				
To evaluate the clinical effects of photodynamic therapy on the outcomes of chronic periodontitis Randomized controlled trial	Twenty-two patients with chronic periodontitis and at least four teeth with probing depth ≥ 5mm	- Non-surgical treatment plus photodynamic therapy - N = 44 teeth	- Non-surgical treatment - N = 44 teeth	• The photodynamic group showed numerically greater reduction in probing depth (0.5mm of difference); however, the statistical significance of this difference was not reported. • Results for bleeding on probing and clinical attachment level were not reported in the abstract
Noro Filho et al. 2012[25]				
To evaluate the efficacy of photodynamic therapy in the treatment of periodontitis in HIV patients Randomized controlled trial	Twelve HIV patients with periodontitis; the type of periodontitis was not reported in the abstract	- Non-surgical treatment plus photodynamic therapy - N = not specified	- Non-surgical treatment - N = not specified	• Patients in the photodynamic group presented a higher probing depth reduction and clinical attachment level gain than those in the non-surgical treatment group at 45 days and 3 and 6 months. • It was not specified if these differences were for the change from baseline or just for each time point.

Table 2: Characteristics of the Included Studies (from abstracts)

Study objective and design	Population	Intervention	Comparator	Outcomes
Giannopoulou et al. 2012[26]				
To evaluate the efficacy of photodynamic therapy on the treatment of residual periodontal pockets Randomized controlled trial	Thirty-two patients with a history of previous treatment for periodontitis and the persistence of sites with probing depths >4 mm and bleeding on probing	- Non-surgical treatment plus photodynamic therapy - N = not specified	- Non-surgical treatment - N = not specified	• No significant differences were observed among the treatment modalities at any time point in terms of levels of interleukin-17, basic fibroblast growth factor, granulocyte colony-stimulating factor, granulocyte macrophage colony-stimulating factor, or macrophage inflammatory protein 1-alpha
Cappuyns et al. 2012[27]				
To evaluate the efficacy of photodynamic therapy on the treatment of residual periodontal pockets Randomized controlled trial	Thirty-two patients with a history of previous treatment for periodontitis and the persistence of sites with probing depths >4 mm and bleeding on probing	- Non-surgical treatment plus photodynamic therapy - N = not specified	- Non-surgical treatment - N = not specified	• The abstract did not report the differences between groups in terms of pocket probing depth, bleeding on probing, or gingival recession; these outcomes were monitored over 6 months
Theodoro et al. 2012[28]				
To evaluate the long term efficacy of photodynamic therapy in chronic periodontitis Randomized controlled trial	Thirty three patients with chronic periodontitis	- Non-surgical treatment plus photodynamic therapy - N = not specified	- Non-surgical treatment - N = not specified	• There were no significant difference between the groups in terms of visible plaque index, bleeding gingival index, bleeding on probing, probing depth, gingival recession or clinical attachment level • The photodynamic group showed a significant reduction in the percentage of sites positive for all bacteria
Novaes et al. 2012[29]				
To evaluate the efficacy of photodynamic therapy in the treatment of aggressive periodontitis Randomized controlled trail	Ten patients with aggressive periodontitis	- Photodynamic therapy - N = not specified	- Non-surgical treatment - N = not specified	• The photodynamic group was more effective in reducing numbers of A. actinomycetemcomitans • The non-surgical treatment was more efficient in reducing the presence of periodontal pathogens of the Red Complex

Table 2: Characteristics of the Included Studies (from abstracts)

Study objective and design	Population	Intervention	Comparator	Outcomes
Al-Zahrani et al. 2011[30]				
To evaluate the efficacy of photodynamic therapy in patients with chronic periodontitis Randomized controlled trial	Twenty smoker patients with moderate to severe periodontitis A total of 54 teeth were randomized	- Non-surgical treatment plus photodynamic therapy - N = not specified	- Non-surgical treatment - N = not specified	• A statistically significant greater reduction in probing depth and clinical attachment level in the photodynamic group compared to the control group was found at the 3-month follow up. • These differences were evaluated at 3 months, but these differences were not evaluated in terms of change from baseline.
Herrera et al. 2011[31]				
To evaluate the efficacy of photodynamic therapy for chronic periodontitis Systematic review and meta-analysis	Four randomized controlled trials	- Non-surgical treatment plus photodynamic therapy	- Non-surgical treatment	• At 12 weeks, the photodynamic group showed a statistically significant improvement of the clinical attachment level (0.29 mm). The clinical significance of this difference was not ascertained • Results for probing depth and gingival recession were not reported
Herrera et al. 2011[31]				
To evaluate the efficacy of photodynamic therapy for chronic periodontitis Systematic review and meta-analysis	Five randomized controlled trials	- Photodynamic therapy with or without non-surgical treatment	- Non-surgical treatment or no treatment	**Clinical attachment level** • Studies that compared photodynamic therapy to no treatment found no difference in clinical attachment level • whereas those that compared photodynamic therapy plus non-surgical treatment to those receiving just the non-surgical treatment gave a statistically significant difference (0.34 mm). **Probing depth** • Three studies that compared photodynamic therapy alone to non-surgical treatment alone showed a reduction in probing depth in favour of the non-surgical treatment

Table 2: Characteristics of the Included Studies (from abstracts)

Study objective and design	Population	Intervention	Comparator	Outcomes
				(difference of 0.21mm) • In three studies that compared photodynamic therapy plus non-surgical treatment to non-surgical treatment alone the difference was 0.25 mm
Ge et al. 2011[32]				
To evaluate the clinical effects of photodynamic therapy in the treatment of chronic periodontitis Controlled trial (randomization was not specified)	Fifty-eight patients with chronic periodontitis	- Non-surgical treatment plus one session of photodynamic therapy (N was not specified) - Non-surgical treatment plus two sessions of photodynamic therapy (N was not specified)	- Non-surgical treatment (N was not specified)	• There were no differences between the three groups in terms of probing depth or clinical attachment level • Photodynamic group showed reduction in the number of bleeding sites on probing at the 12-week evaluation
Sigusch et al. 2010[33]				
To evaluate the efficacy of photodynamic therapy in patients with chronic periodontitis Randomized controlled trial	Twenty-four patients with localized chronic periodontitis, in whom only F. nucleatum was detected by baseline polymerase chain reaction after non-surgical treatment	- Photodynamic therapy - N = not specified	- Placebo - N = not specified	• The photodynamic therapy showed significant reductions in reddening, bleeding on probing, and mean probing depth and clinical attachment level • The F. nucleatum DNA concentration was found to be significantly reduced compared to the baseline level in the photodynamic group
Azarpazhooh et al. 2010[34]				
was to evaluate the effectiveness of photodynamic therapy for the treatment of periodontitis systematic review and meta-analysis	Five randomized controlled trials	- Photodynamic therapy with or without non-surgical treatment	Non-surgical treatment or no treatment	• Photodynamic therapy as an independent treatment or as an adjunct to non-surgical treatment versus a control group of non-surgical treatment did not demonstrate statistically or clinically significant advantages
Atieh 2010[35]				
To evaluate the effectiveness of photodynamic therapy for	Four randomized controlled trials	- Non-surgical treatment plus photodynamic therapy	Non-surgical treatment	• The use of photodynamic therapy in conjunction with non-surgical treatment was associated with

Table 2: Characteristics of the Included Studies (from abstracts)

Study objective and design	Population	Intervention	Comparator	Outcomes
the treatment of periodontal diseases Systematic review and meta-analysis				significantly greater attachment gain (mean difference 0.29 mm), and greater reduction in probing depth (mean difference 0.11) • It was not clear if these difference were fort eh change from baseline or just for the 12-week assessment
Ruhling et al. 2010[36]				
To evaluate the efficacy of photodynamic therapy in chronic periodontitis Randomized controlled trial	Fifty four patient with chronic periodontitis and at least two persistent pockets after initial non-surgical treatment	- Photodynamic therapy alone - N = 25	- Non-surgical treatment (second session) - N = 29	• There was no difference between the two treatment modalities in terms of probing depth after three months from therapy
Al-Zahrani et al. 2009[37]				
To evaluate the efficacy of photodynamic therapy for the treatment of chronic periodontitis in diabetic patients Randomized controlled trial	Forty-five patients with type 2 diabetes and moderate to severe chronic periodontitis	- Non-surgical treatment plus photodynamic therapy (N =15) - sd	- Non-surgical treatment (N =15) - Non-surgical treatment plus doxycycline (N =15)	• No significant differences in periodontal parameters and glucose levels were detected among the three groups
Lulic et al. 2009[38]				
To evaluate the efficacy of the repeated photodynamic therapy on the treatment of chronic periodontitis Randomized controlled trial	Ten maintenance patients with 70 residual pockets – patients already had initial non-surgical treatment	- Photodynamic therapy (applied five times in two weeks) - N = no specified	- Placebo therapy - N = not specified	• At six months, the photodynamic therapy group showed greater reduction in probing depth, gain in clinical attachment level and decrease in bleeding on probing. • It was not clear if these differences were from baseline or within the treatment groups at the final follow-up visit (at 6 months)
Polansky et al. 2009[39]				
To evaluate the photodynamic therapy for its bactericidal potential and clinical effect in the	Fifty-eight subjects with chronic periodontitis and at least three active periodontal pockets 5mm or deeper	- Non-surgical treatment plus photodynamic therapy - N = not specified	- Non-surgical treatment - N = not specified	• The intergroup difference was not significant in terms of probing depth or bleeding on probing • For the microbial parameters, no

Table 2: Characteristics of the Included Studies (from abstracts)

Study objective and design	Population	Intervention	Comparator	Outcomes
treatment of periodontitis Randomized controlled trial				significant difference was found between the test and the control group
Chondros et al. 2009[40]				
To evaluate the clinical and microbiological effects of the adjunctive use of PDT in non-surgical periodontal treatment Randomized controlled trial	Twenty-four patients receiving regularly supportive periodontal therapy	- Non-surgical treatment plus photodynamic therapy - N = Not specified	- Non-surgical treatment N = Not specified	• At 3 months and 6 months, a statistically significantly higher improvement of BOP was found in the test group. • At 3 months after therapy, the microbiological analysis showed a statistically significant reduction of Fusobacterium nucleatum and Eubacterium nodatum in the test group. • At 6 months, statistically significantly higher numbers of Eikenella corrodens and Capnocytophaga species were detected in the test group.
Christodoulides et al. 2008[41]				
To evaluate the clinical and microbiologic effects of the adjunctive use of PDT to non-surgical periodontal treatment Randomized controlled trial	Twenty-four subjects with chronic periodontitis	- Non-surgical treatment plus photodynamic therapy - N = not specified	- Non-surgical treatment - N = not specified	• At 3 and 6 months after treatment, there were no statistically significant differences between the groups with regard to clinical attachment level, probing depth, plaque score, or microbiologic changes
Braun et al. 2008[42]				
To assess the effect of adjunctive antimicrobial photodynamic therapy in chronic periodontitis Controlled trial	Twenty patients with untreated chronic periodontitis	- Non-surgical treatment plus photodynamic therapy - N = 20 patients (40 mouth quadrants)	- Non-surgical treatment - N = 20 patients (40 mouth quadrants)	• After 3 months, there was no difference between the groups in terms of gingival recession. • Differences in relative attachment level, probing depth or bleeding on probing were not reported in the abstract