INPLASY PROTOCOL

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Clinical efficacy of single and multiple applications of antimicrobial photodynamic therapy in periodontal maintenance: A systematic review and network meta-analysis

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Review question / Objective: **For patients exhibiting residual periodontal pockets and included into regular SPT, do adjunctive aPDT applications to SRP result in greater clinical improvements, compared to SRP alone?**
Condition being studied: **Periodontitis.**
Information sources: **A database of unpublished studies (OpenGray [http://www.opengrey.eu/]) was searched. In addition, all of the included full-text studies' references were screened to find additional relevant publications. Furthermore, a manual search of the following scientific journals was performed: Journal of Periodontology, Journal of Periodontal Research, Journal of Clinical Periodontology, International Journal of Periodontics and Restorative Dentistry, Periodontology 2000, Journal of Photochemistry and Photobiology, Photomedicine and Laser Surgery, Lasers in Surgery and Medicine, Lasers in Medical Science and Photodiagnosis and Photodynamic Therapy.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 6 January 2021 and was last updated on 6 January 2021 (registration number INPLASY202110022).

INTRODUCTION

Review question / Objective: **For patients exhibiting residual periodontal pockets and included into regular SPT, do adjunctive aPDT applications to SRP result in greater clinical improvements, compared to SRP alone?**

Rationale: **Numerous studies have demonstrated that aPDT can be an effective adjunct in managing a non-treated periodontal disease. However, the evidence**

of its effectiveness as an adjunct in periodontal maintenance is scarce. Therefore, the aim of a current systematic review is to evaluate the clinical efficacy of application of aPDT when used adjunctively to SRP, as compared to SRP alone, in treating periodontal patients, enrolled into regular SPT.

Condition being studied: Periodontitis.

METHODS

Search strategy: A database of unpublished studies (OpenGray [http://www.opengrey.eu/]) was searched. In addition, all of the included full-text studies' references were screened to find additional relevant publications. Furthermore, a manual search of the following scientific journals was performed: Journal of Periodontology, Journal of Periodontal Research, Journal of Clinical Periodontology, International Journal of Periodontics and Restorative Dentistry, Periodontology 2000, Journal of Photochemistry and Photobiology, Photomedicine and Laser Surgery, Lasers in Surgery and Medicine, Lasers in Medical Science and Photodiagnosis and Photodynamic Therapy.

Participant or population: Patients diagnoses with recurrent periodontitis and included into supportive periodontal therapy.

Intervention: SRP+aPDT (SA or MA). (SRP - scaling and root planing, aPDT - antimicrobial photodynamic therapy, MA - multiple applications, SA - single application).

Comparator: SRP + aPDT (SA) vs. SRP + aPDT (MA) vs. SRP alone (SRP - scaling and root planing, aPDT - antimicrobial photodynamic therapy, MA-multiple applications, SA-single application.

Study designs to be included: Randomized controlled clinical trials (RCTs) with parallel or split-mouth designs with a minimum of 3 months of a follow-up.

Eligibility criteria: During the first stage of study selection, the titles and abstracts were screened and evaluated according to the following inclusion criteria: • RCTs comparing the effectiveness of aPDT to SRP in patients, diagnosed with residual periodontal pockets. • Patients enrolled in regular periodontal maintenance programs. • Parallel and split-mouth design studies included systemically healthy patients. • The presence of a control group, receiving SRP either alone or with a placebo. • The test group received the same SRP as a control group, plus the aPDT (SA or MA). • SRP was carried out by manual or sonic scaling. • The study reported on PD and/or CAL changes before and after treatment as mean values with standard deviations. • The follow-up ≥ 3 months. • Written in the English language. At the second stage, the full texts of potentially eligible articles were reviewed and evaluated according to the following exclusion criteria: • Studies including patients with systemic diseases. • Patients were receiving initial periodontal treatment rather than supportive periodontal therapy. • Studies carried out aPDT as a monotherapy. • Studies did not report on the clinical treatment outcomes, including changes in PD and/or CAL.

Information sources: A database of unpublished studies (OpenGray [http://www.opengrey.eu/]) was searched. In addition, all of the included full-text studies' references were screened to find additional relevant publications. Furthermore, a manual search of the following scientific journals was performed: Journal of Periodontology, Journal of Periodontal Research, Journal of Clinical Periodontology, International Journal of Periodontics and Restorative Dentistry, Periodontology 2000, Journal of Photochemistry and Photobiology, Photomedicine and Laser Surgery, Lasers in Surgery and Medicine, Lasers in Medical Science and Photodiagnosis and Photodynamic Therapy.

Main outcome(s): The primary outcome variable was PD reduction; the secondary outcome variable included CAL gain.

Data management: From the selected articles fulfilling the inclusion criteria, the following data was retrieved to data extraction templates: • General information: country, study design, included patients' periodontal status, time of involvement in maintenance programs, number of participants, follow-up time, and patients' gender, smoking status and age . • The number of patients included in the final analysis, treatment protocols in control and test groups, laser types, parameters, type of photosensitizers and clinical outcomes are presented in Table 3. The mean values and standard deviations of changes in PD reduction and CAL gain, following the treatment, in both the test and control groups, were extracted for the data analysis and are also presented in Table 3.

Quality assessment / Risk of bias analysis: The quality of all included studies was assessed during the data-extraction process, which involved evaluating the methodological elements that could influence each study's outcome. The Cochrane Collaboration's two-part tool for assessing the risk of bias was used to assess bias across the studies and to identify papers with intrinsic methodological and design flaws . The following items were evaluated as posing a low, high or unclear risk of bias: random sequence generation, concealing allocations, blinded participants/personnel, incomplete outcome data, selective reporting outcomes and other potential risks of bias. The degree of bias was categorized as low risk if all criteria were met, moderate risk when one criterion was missing and high risk if two or more criteria were missing.

Strategy of data synthesis: First, a traditional pairwise meta-analysis will be performed. The random-effect model will be utilized, incorporating the assumption that different studies were evaluated differently, but had related treatment effects. The included studies' continuous variables (PD and CAL) will be categorized in groups and analyzed using the Review Manager software (version 5.2.8, Copenhagen, Denmark, 2014). The intervention effects' estimates will be expressed as weighted mean difference (WMD) with 95% confidence intervals (CIs). Chi-squared tests will evaluate the heterogeneity, which will be considered as low for values ≤ 25%, moderate for values between 25% and 50% and high for values > 50%.

Subgroup analysis: A random-effect network using Bayesian-framework Markov-chain Monte Carlo methods will be created using ADDIS 1.16 (https://gemtc.drugis.org). The continuous data of each parameter (PD and CAL) were evaluated in a network specifying the relationship between the studies' MDs and combining direct and indirect comparisons of the different treatment types. The data will be considered statistically significant when $P < 0.05$, with a 95% CI. The probability of the best clinical effect for each type of treatment modality will be assessed by calculating each treatment group's MD, comparing them to arbitrary standard controls, and counting the proportion of iterations of the Markov chain of the MD ranking for treatments.

Sensibility analysis: Inconsistency between direct and indirect comparisons will be accessed through the node-splitting model.

Language: English.

Country(ies) involved: Lithuania, Brasil, Switzerland.

Keywords: systematic review, periodontitis, residual pockets, periodontal maintenance, photodynamic therpy.

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