INPLASY PROTOCOL

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Corresponding author:
Túlio Ferrisse

tuliomferrisse@gmail.com

Author Affiliation:
São Paulo University (UNESP), School of Dentistry, Araraquara.

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The effectiveness of curcumin-mediated antimicrobial photodynamic therapy for oral disinfection: a systematic review and meta-analysis of randomized clinical trials

Ferrisse, TM[1]; Dias, LM[2]; De Oliveira, AB[3]; Jordão, CC[4]; Mima, EGO[5]; Pavarina, AC[6].

Review question / Objective: What the accuracy of curcumin-mediated antimicrobial photodynamic therapy in microbial load?

Eligibility criteria: The inclusions criteria for the systematic review were: the utilized of curcumin-mediated antimicrobial photodynamic therapy for oral microbial load reduction, curcumin not associated with any nanoparticle and randomized clinical trials. Additionally, the exclusion criteria were: in vitro, animal, observational and pre-clinical studies, non-randomized clinical trials, review articles, letters to the editor, personal opinions, book chapters, articles written in other languages.

Information sources: Electronic databases, contact with authors, trial registers.

INTRODUCTION

Review question / Objective: What the accuracy of curcumin-mediated antimicrobial photodynamic therapy in microbial load?

Condition being studied: The oral cavity comprises hundreds of microorganism located mainly in teeth, gingival sulcus, tongue, buccal mucosa, soft palates and tonsils, which provides enriching

environments for microbial communities. In normal symbiosis situations, these microorganisms act directly or indirectly favoring the health of the host. However, in situations that the balance of the finely tuned crosstalk between the oral microbiota, immune cells and the epithelium was harmed, some microorganisms express their pathogenicity and can cause local and systemic infections. The presence of the opportunist microorganism and poor oral hygiene or difficult in perform a good oral hygiene (e.g. surfaces of dental materials such as resign composites, amalgams and orthodontic appliances) lead an abnormal proportion in oral microbiome and, therefore, the emergence of infection may occur. Currently, due to the resistance, tolerance and persistent found in many of oral microorganism against the traditional antimicrobials therapies, there is a need to look at new possibilities for treatment approaches. In this scenario, the antimicrobial photodynamic therapy (aPDT) is a good option for therapies approaches, since that, the development of resistance to aPDT has not yet been observed. Natural compounds are enriched with chlorophyll that favors photodynamic effects due to high quantum yield of singlet oxygen, being the Curcumin (Curcuma longa) one of the most natural compounds studied as PS in aPDT. Curcumin is activated by blue light (405-460 nm) and requires some modifications in his structure to be used in aPDT on account of the hydrophobic structure. Thus, to better synthetized the scientific information about the clinical application of curcumin-mediated antimicrobial photodynamic therapy on microbial load in randomized clinical trials (RCT) is necessary.

METHODS

Search strategy: Two independent examiners were calibrated to perform the steps of articles selection. The independent examiners conducted an electronic search in PubMed, Science Direct, Scopus, SciELO, Lilacs, Cochrane Library and Embase. The following search terms for PubMed, Science Direct and Embase were

"(((antimicrobial photodynamic therapy) OR (photodynamic therapy)) AND (curcumin)) AND (Clinical trials)", for Scopus were "((((antimicrobial AND photodynamic AND therapy) OR (photodynamic AND therapy)) AND (curcumin)) AND (clinical AND trials))", and for SciELO, Lilacs and Cochrane Library two search terms were used "(((antimicrobial photodynamic therapy) OR (photodynamic therapy)) AND (curcumin)) AND (Clinical trials)" and "((((antimicrobial AND photodynamic AND therapy) OR (photodynamic AND therapy)) AND (curcumin)) AND (clinical AND trials))". The kappa calibration between the examiners was considered "almost perfect" agreement (0.91/p <0.01). In addition, a handing searching was conducted thought the other relevant journals in photodynamic therapy area and also in ClinicalTrials.gov. The Mendeley Reference Software® was used to delete duplicate articles. Data were extracted from selected articles after the eligibility step was done, after that; the articles were analyzed and discussed. Any possibility of disagreement during the process was solved before proceeding to the next steps, by reaching a consensus.

Participant or population: Human and oral microbial population.

Intervention: Curcumin-mediated antimicrobial photodynamic therapy.

Comparator: aPDT mediated with another photosensitizer with exception of curcumin or topical application of traditional antimicrobial solutions (e.g. chlorhexidine) or only placebo.

Study designs to be included: Randomized clinical trials.

Eligibility criteria: The inclusions criteria for the systematic review were: the utilized of curcumin-mediated antimicrobial photodynamic therapy for oral microbial load reduction, curcumin not associated with any nanoparticle and randomized clinical trials. Additionally, the exclusion criteria were: in vitro, animal, observational and pre-clinical studies, non-randomized

clinical trials, review articles, letters to the editor, personal opinions, book chapters, articles written in other languages.

Information sources: Electronic databases, contact with authors, trial registers.

Main outcome(s): The primary outcome was the microbial load (in percentage or in CFU log10), and the secondary outcomes were i) demographic data such as; sample size, gender, systemic health conditions, ii) authors, microorganism evaluated, PS concentration, source, wave-length, energy fluency, pre-irradiation time and duration of irradiation, plaque index (PI) and gingival bleeding index (GBI). The present study aimed to answer the following focused questions: what the accuracy of curcumin-mediated antimicrobial photodynamic therapy in microbial load.

Quality assessment / Risk of bias analysis: For this part, the Delphi list criteria were used to access the quality of clinical trials included in the present systematic review. Two independent examiners performed this evaluation. Any possibility of disagreement was solved by a third examiner. In the risk of bias assessment was used the RoB 2 tool for clinical trials. Two independent examiners performed this evaluation. Any possibility of disagreement was solved reaching a consensus.

Strategy of data synthesis: All steps according to Prisma guideline will be carried out, and the information extracted from the included articles will be attached in a table.

Subgroup analysis: None.

Sensitivity analysis: None.

Country(ies) involved: Brazil.

Keywords: Photodynamic therapy; antimicrobial photodynamic therapy; curcumin; sistematic review; meta-analysis, oral microorganisms; oral polimicrobial biofilm.

Contributions of each author:
Author 1 - Túlio Ferrisse - Conceptualization, Methodology, Validation, Formal analysis, Investigation, Resources, Data Curation, Writing - Original Draft, Writing - Review & Editing, Visualization.
Email: tuliomferrisse@gmail.com
Author 2 - Luana Dias.
Author 3 - Analú Oliveira.
Author 4 - Claudia Jordão.
Author 5 - Ewerton Mima.
Author 6 - Ana Claudia Pavarina.