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Systematic review and meta-analysis of the antioxidant capacity of lycopene in the treatment of periodontal disease

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López-Valverde, N[1]; López-Valverde, A[2]; Aragoneses, JM[3]; de Sousa, BM[4]; Rueda, JAB[5].

Corresponding author:
Nansi López-Valverde

nlovalher@usal.es

Author Affiliation:
University of Salamanca.

ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 September 2023 and was last updated on 30 September 2023.

INTRODUCTION

Review question / Objective There seems to be an interrelation between low antioxidant levels and PD and the aim of our meta-analysis was to evaluate, in randomized clinical studies, the antioxidant effect of lycopene in the treatment of this pathology.
The research question was formulated according to the PICOS strategy: "In patients with PD, does the antioxidant action of lycopene have a clinically significant additional effect when used alone or as an adjuvant to conventional treatment? Interventional studies in adult humans with PD (P) comparing conventional periodontal treatment with the ad-dition of lycopene (I) versus patients who had only received conventional periodontal treatment (C) were included to observe the effects of periodontal treatment (O); only randomized clinical studies (S) were considered.

Rationale There are no meta-analyses analyzing the antioxidant effectiveness of lycopene (RCTs) on periodontal disease.

Condition being studied Lycopene is a lipophilic carotenoid, a natural antioxidant, found in certain vegetables and fruits, such as tomatoes, grapes, watermelons, papayas, and blueberries. Different properties have been attributed to it, such as anticarcinogenic, cardioprotective, anti-inflammatory, antihypertensive, and above all, a potent antioxidant action. Precisely, this potent antioxidant action is associated with a lower risk of chronic diseases and it has been shown that high concentrations of lycopene in serum, are associated with lipid peroxidation and a decrease in protein oxidation. At the cellular level it has been shown that, lycopene, has proliferative effects on osteoblasts, increasing bone re-generation, as well as an inhibitory effect on osteoclastic formation and resorption, which could be very useful in tissue engineering, since lycopene could increase

the quality and speed of new bone formation in periodontal treatments.

METHODS

Participant or population Subjects with periodontal disease receiving lycopene treatment.

Intervention Conventional periodontal treatment + lycopene.

Comparator Conventional periodontal treatment.

Study designs to be included RCTs.

Eligibility criteria a) RCTs (single or double-blind) conducted in patients with PD defined as bleeding, bone loss ≥2 mm and/or suppuration to peri-implant probing (≥ 4 mm).b) Studies comparing the efficacy of adjuvant treatment with local/systemic lycopene versus single surgical or non-surgical treatment, in PDc) Articles in English language.

Information sources PubMed/MEDLINE; WOS; EMBASE.

Main outcome(s) After exclusion, 7 studies were finally selected and collected for meta-analysis. PPD was evaluated by five studies, three of which were in favor of the experimental group, without statistical significance (p = 0.90). CAL was evaluated by four studies, although only two were in favor of the experimental group without statistical significance (p=0.24). Similarly, the group that evaluated BOP, obtained 2 studies in favor of the intervention without statistical significance (p = 0.13). PI was evaluated by six studies and was the only group where the intervention obtained statistical significance (p=0.003), with 5 studies in favor of the intervention. In the group of studies that evaluated UA, only the study by Wasti et al. was in favor of the intervention but without statistical significance (p=0.79). Finally, the group that evaluated GI, with 2 studies in favor of the experimental group and better performance of this group, although without established statistical significance (p=0.71). Heterogeneity was high in all studies, exceeding 80%.

Additional outcome(s) The analysis of the parameters evaluated in the selected studies, with respect to the follow-up periods, PPD analysis was statistically significant (p=0.03 and p=0.07, respectively) in the short- and medium-term studies. Similarly, BOP estimates were statistically sig-nificant in the short- and medium-term studies (p=0.008 and p=0.03, respectively) and PI was statistically significant in the short- and medium-term (p=0.0003 and p=0.01, respec-tively). GI assessment was statistically significant at both short-term (p=0.002) and me-dium-term (p=0.02) follow-up. Heterogeneity was low in the overall CAL assessment (I2=16.7%). All other assessments, whether short-, medium- or long-term, showed high heterogeneity >50.

Quality assessment / Risk of bias analysis Cochrane Risk of Bias Tool (RoB2). The domains "random sequence generation" (selection bias), "blinding of participants and personnel" (performance bias), "allocation concealment" (selection bias) and "blinding of outcome assessment" (detection bias). The domains "incomplete outcome data" (attrition bias) and "selective reporting" (reporting bias) were met by only two studies. None of the studies reported the domain "other bias".

Strategy of data synthesis Two reviewers (NL-V and AL-V) independently compiled the titles and abstracts of the previously selected articles and entered them into an Excel spreadsheet, eliminating studies that did not refer to the research question posed. To determine the concordance between reviewers, Cohen's kappa index (κ) [32] was calculated and discrepancies between the two, regarding the eligibility of the studies, were reviewed and discussed by a third reviewer (BM de S). Finally, the selected articles were obtained for reading, review, data extraction and inclusion. The bibliographic references of the included studies were also reviewed as an additional source of potential studies.

Subgroup analysis Two meta-analyses were performed: the first according to the parameters or biomarkers investigated in the selected studies; the second according to the follow-up periods: short-term, 2- and 3-weeks follow-up.

Sensitivity analysis Risk of Bias according to the Cochrane Risk of Bias Tool (RoB2).

Language restriction Languages other than English.

Country(ies) involved India and Egypt.

Keywords anti-oxidant, lycopene, periodontal disease, gingivitis, periodontitis, meta-analysis.

Contributions of each author

Author 1 - Nansi López-Valverde - Conceptualization, methodology, formal analysis and writing—review and editing.
Email: nlovalher@usal.es

Author 2 - Antonio López-Valverde - Conceptualization, writing—original draft preparation.
Email: alopezvalverde@usal.es
Author 3 - Juan Manuel Aragoneses - Data curation.
Email: jaraglam@uax.es
Author 4 - Bruno Macedo de Sousa - Investigation.
Email: bsousa@fmed.uc.pt
Author 5 - José Antonio Blanco Rueda - Validation and supervision.
Email: jablancor@usal.es