

# INPLASY

## Effectiveness of hyaluronic acid in the treatment of peri-implant diseases: Results of a meta-analysis

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### ADMINISTRATIVE INFORMATION

**Support** - None.

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

**Conflicts of interest** - None declared.

**INPLASY registration number:** INPLASY2024100050

**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 October 2024 and was last updated on 11 October 2024.

### INTRODUCTION

**Review question / Objective** Is Hyaluronic Acid (HA) treatment effective as a sole or adjuvant therapy for the treatment of peri-implantitis?. Evaluate the efficacy of HA in the treatment of peri-implant diseases.

**Condition being studied** The term peri-implantitis describes an inflammatory response to an infection induced by the accumulation of bacterial plaque on the surface of the implant biomaterial, which leads to a loss of the supporting bone.

### METHODS

**Search strategy** Two reviewers (NL-V, AL-V) independently searched PubMed/Medline, Embase, Cochrane Central, Dentistry & Oral Sciences Source and Web of Science (WOS) databases until August 2024. Two reviewers (NL-V, AL-V) independently searched PubMed/Medline, Embase, Cochrane Central, Dentistry & Oral

Sciences Source databases and the Web of Science (WOS) until August 2024 using the terms Medical Subject Headings (MeSH): Peri-Implantitis\* / diagnosis OR Peri-Implantitis\* / AND Dental Implants\* AND Dental Plaque\* AND Hyaluronic Acid / therapeutic use\* AND Humans\*. In addition, a manual search and queries in the gray literature were performed; the bibliographic references of the included studies were also consulted to obtain the most information.

**Participant or population** Adult subjects with peri-implantitis.

**Intervention** HA treatment.

**Comparator** Conventional treatment or no treatment.

**Study designs to be included** Randomized Controlled Trials (RCTs).

**Eligibility criteria** The original research studies were selected according to the following inclusion criteria: (i) randomized clinical trials (single or double-blind) that included in the study more than 10 subjects  $\geq$  18 years of age; (ii) with peri-implant pathologies; (iii) that provided data on clinical parameters indicative of peri-implant disease; (iv) with statistical methods that included means and standard deviation, together with units with which to quantify mediator levels; (v) published in English. We excluded studies that did not follow all the criteria defined above, with a lack of data demonstrating peri-implant disease, experimental studies in animals or in vitro, clinical cases or case series, literature reviews and irrelevant studies such as editorials, contributions to congresses, historical reviews...).

**Information sources** PubMed/Medline, Embase, Cochrane Central, Dentistry & Oral Sciences Source and Web of Science (WOS) databases until August 2024. Two reviewers (NL-V, AL-V) independently searched PubMed/Medline, Embase, Cochrane Central, Dentistry & Oral Sciences Source databases and the Web of Science (WOS) until August 2024.

**Main outcome(s)** The electronic search found a total of 32 results of which 8 full-text publications were evaluated and 5 were excluded based on a priori criteria.

The PD, AL and MBL variables analyzed in the three included studies were used for the meta-analysis. A meta-analysis of the pooled studies and individual studies was performed for each of the variables analyzed. All were homogeneous ( $I^2=0\%$ ). The meta-analyses for the variables MBL and PD, as well as the overall effect showed a trend toward intervention; the meta-analysis for the AL variable was the only one that did not show this trend. No analysis of adverse effects was performed due to lack of data.

**Quality assessment / Risk of bias analysis** Risk of bias assessment is one of the pillars of evidence-based medicine; therefore, two reviewers (NL-V and AL-V) independently analyzed the quality of the included studies according to the Cochrane Risk of Bias tool. Two of the included studies [15,16] met the domains. The study by Rakašević et al had the highest number of biases, especially in the domains "Assignment concealment", "Blinding of participants and staff", and "Blinding of outcome data".

**Strategy of data synthesis** Data obtained from the selection of RCTs were analyzed using Review Manager software (RevMan Software. Version

5.4.1; The Cochrane Collaboration, Copenhagen, Denmark; 2020). A meta-analysis of pooled studies and a subgroup analysis was performed for each of the variables assessing peri-implantitis. All were based on mean difference (MD) and standard deviation (SD) for estimating continuous data and for evaluating categorical data, 95% confidence intervals (CI). Heterogeneity was considered unimportant with  $I^2= 0-30\%$ ; moderate,  $I^2= 40-50\%$ ; substantial  $I^2= 60-75\%$  and considerable  $I^2\geq 75\%$ . The threshold for statistical significance was set at  $p < 0.05$ . Due to the homogeneity of the results, a fixed-effects meta-analysis was performed.

**Subgroup analysis** The PD, AL and MBL variables analyzed in the three included studies were used for the meta-analysis.

**Sensitivity analysis** No analysis of adverse effects was performed due to lack of data.

**Country(ies) involved** Spain.

**Keywords** hyaluronic acid, dental implants, peri-implantitis, clinical trial, meta-analysis.

#### **Contributions of each author**

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