INPLASY PROTOCOL

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None declared.

Efficacy of metronidazole on peri-implantitis: A systematic review and meta-analysis of randomized studies

López-Valverde, N[1]; López-Valverde, A[2]; Blanco-Rueda, JA[3].

Review question / Objective: **In patients with peri-implantitis, is adjuvant local or systemic treatment with metronidazole effective on signs of inflammation and bone destruction?**
Eligibility criteria: **Inclusion criteria: a) RCTs (single or double-blind) performed in patients with peri-implantitis defined as bleeding and/or suppuration on peri-implant probing (≥ 4 mm).b) Studies comparing the efficacy of local/systemic metronidazole adjuvant therapy vs. single surgical or non-surgical treatmentc) Articles published in English.Exclusion criteria: a) Less than five patients per treatment group.b) Lack of clinical data on bone destruction.c) Case series or clinical casesd) Undefined cases and non-relevant studies.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 07 January 2023 and was last updated on 07 January 2023 (registration number INPLASY202310015).

INTRODUCTION

Review question / Objective: **In patients with peri-implantitis, is adjuvant local or systemic treatment with metronidazole effective on signs of inflammation and bone destruction?**

Rationale: **Peri-implant diseases (mucositis and peri-implantitis) are considered pathological conditions associated with biofilm that affect osseointegrated dental implants. These pathologies require a clear definition and differentiation of a state of peri-implant health, so that clinicians can establish an adequate treatment, it being generally accepted that mucositis is an inflammation of the soft tissues adjacent to the implant, with reversible character and peri-implantitis is a progressive and**

irreversible form, characterized by the loss of bone tissue and which decreases osseointegration. Surgical and non-surgical treatments, based on the scientific evidence of periodontal treatments, aim to control infection and reduce the bacterial load, having demonstrated the ineffectiveness of surgical treatment alone [9,10]; however, the benefits of local or systemic antibacterials, used as adjuvants, have been demonstrated, and it has become a routine practice to administer antibiotics locally in the treatment of peri-implantitis. The non-surgical treatment of advanced lesions of peri-implantitis with systemic metronidazole reduced the probing depth, although some investigations have indicated that the effect of adjuvant antibiotics in the non-surgical treatment of peri-implantitis could be influenced by the severity of the disease.

Condition being studied: Peri-implantitis around dental implants results in an irreversible infectious pathological condition that terminates implant survival and leads to implant failure.

METHODS

Search strategy: Four electronic databases were searched for relevant articles published in the last 10 years up to December 2022: MEDLINE (through PubMed), WOS, Embase and The Cochrane Library. The search filter "Randomized Controlled Trial" was applied. The electronic search was complemented with a manual search in the following journals: Clinical Im-plant Dentistry and Related Research; Clinical Oral Implants Research; International Journal of Oral and Maxillofacial Implants; Journal of Clinical Periodontology; Journal of Periodontology.

Participant or population: Four electronic databases were searched for relevant articles published in the last 10 years up to December 2022: MEDLINE (through PubMed), WOS, Embase and The Cochrane Library. The search filter "Randomized Controlled Trial" was applied. The electronic search was complemented with a manual search in the following journals: Clinical Im-plant Dentistry and Related Research; Clinical Oral Implants Research; International Journal of Oral and Maxillofacial Implants; Journal of Clinical Periodontology; Journal of Periodontology.

Intervention: Surgical or non-surgical treatment of peri-implantitis.

Comparator: Patients not receiving adjuvant treatment with metronidazole.

Study designs to be included: Randomized Controlled Trials.

Eligibility criteria: Inclusion criteria: a) RCTs (single or double-blind) performed in patients with peri-implantitis defined as bleeding and/or suppuration on peri-implant probing (≥ 4 mm).b) Studies comparing the efficacy of local/systemic metronidazole adjuvant therapy vs. single surgical or non-surgical treatmentc) Articles published in English.Exclusion criteria: a) Less than five patients per treatment group.b) Lack of clinical data on bone destruction.c) Case series or clinical casesd) Undefined cases and non-relevant studies.

Information sources: MEDLINE (through PubMed), WOS, Embase and The Cochrane Library.

Main outcome(s): Inflammation and bone destruction.

Additional outcome(s): PPD probing pocket depth CAL Clinical attachment level BoP Bleeding on probing Plaque Score Supuration Score Bleeding Score Bone Level.

Quality assessment / Risk of bias analysis: Two reviewers (NL-V and AL-V) independently assessed the quality of each RCT according to the Cochrane Risk of Bias Tool (RoB2). Five domains of bias (randomization process, deviations from intended interventions, missing outcome data, outcome measurement, and selection of reported outcomes) were assessed. The Cochrane Hand-book for Systematic Reviews of Interventions was used. The

rating "high" indicated a high risk of bias, "low" indicated a low risk of bias, and "some doubt" indicated the presence of bias due to lack of information or uncertainty about the potential for bias. Studies were classified as low or high risk of bias or of concern. Any discrepancies in the assessment of RoB2 were discussed between the two reviewers to reach agreement.

Strategy of data synthesis: Meta-analysis was performed using RevMan (Review Manager Software. Version 5.4.1; The Cochrane Collaboration, 2020). Given the homogeneity of the studies, a fixed-effects model was used; mean difference (MD) and standard deviation (SD) were used to assess the continuous variable (bone loss) with a 95% confidence interval (CI).

Subgroup analysis: Group 1.PPD probing pocket depth; Group 2.CAL Clinical attachment level; Group 3.BoP Bleeding on probing; Group 4.Plaque Score; Group 5.Supuration Score; Group 6.Bleeding Score Bone Level.

Sensitivity analysis: No significant statistical differences were found between the groups.

Language restriction: Only articles published in English.

Country(ies) involved: Spain.

Keywords: Dental implants, Peri-implantitis, Anti-Bacterial Agents/ therapeutic use, Metronidazole, Humans.

Contributions of each author:

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