INPLASY PROTOCOL

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None declared.

Role in the osseointegration of titanium dental implants, of bioactive surfaces based on biomolecules: A systematic review and meta-analysis of in vivo studies

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Review question / Objective: **Does the bioactive surface of titanium dental implants, based on biomolecules, influence osseointegration?. The aim of our study was to evaluate the role and efficacy of bioactive surfaces in osseointegration. Our review study limited the research interest to titanium dental implants coated with a biomolecule, i.e., an organic molecule produced by a living organism.**
Condition being studied: **In recent years, much attention has been paid to topographical modifications of dental implant surfaces, as well as to their coating with biologically active substances.a bioactive surface is one capable of achieving faster and higher quality osseointegration, shortening waiting times and solving situations of poor bone quality. Molecules that can be applied for bioactive purposes include bioceramics, ions and biomolecules. Collagen and bone morphogenetic protein have been suggested as bone stimulating agents. Biofunctionalization of the implant surface with a biomimetic active peptide has also been shown to result in a significant increase in bone-to-implant ratios and an increase in peri-implant bone density.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 June 2022 and was last updated on 17 June 2022 (registration number INPLASY202260076).

INTRODUCTION

Review question / Objective: **Does the bioactive surface of titanium dental implants, based on biomolecules, influence osseointegration?. The aim of our study was to evaluate the role and efficacy of bioactive surfaces in osseointegration. Our review study limited the research interest to titanium dental implants coated with a biomolecule, i.e., an organic molecule produced by a living organism.**

Rationale: **The aim of our study was to evaluate the role and efficacy of bioactive surfaces, on osseointegration.**

Condition being studied: In recent years, much attention has been paid to topographical modifications of dental implant surfaces, as well as to their coating with biologically active substances.a bioactive surface is one capable of achieving faster and higher quality osseointegration, shortening waiting times and solving situations of poor bone quality. Molecules that can be applied for bioactive purposes include bioceramics, ions and biomolecules. Collagen and bone morphogenetic protein have been suggested as bone stimulating agents. Biofunctionalization of the implant surface with a biomimetic active peptide has also been shown to result in a significant increase in bone-to-implant ratios and an increase in peri-implant bone density.

METHODS

Search strategy: The electronic databases PubMed/MEDLINE, WOS and EMBASE were searched until May 2022, with the terms Medical Subject Headings (MeSH): "titanium dental implants", "surface properties", "bioactive surface modifications", "biomolecules", "BMP", "antibac-terial agent", "peptide", "collagen", "grown factor", in combination with "osseointegra-tion", "bone apposition", "osteogenic", "osteogenesis", "new bone formation", "bone to implant contact", "bone regeneration" and "in vivo studies". The Boolean operators AND/OR were used to refine the search. In addition, relevant studies in the gray literature and reference lists of included studies were also examined (cross-referenced).

Participant or population: Subjects received endosseous implantation.

Intervention: Implants with incorporated bioactive surfaces based on biomolecules.

Comparator: Implants with conventional etched surfaces (SLA type).

Study designs to be included: Preclinical studies in unmodified experimental animal models.

Eligibility criteria: a) Studies regarding Ti implant surfaces coated with biomolecules; b) Studies reporting evaluation of the effect of biomolecular coatings on bone formation or osseointegration; c) Studies published in English.

Information sources: PudMed, EMBASE, Web Of Science.

Main outcome(s): Three categories of biomolecular coatings have been evaluated in this review: (1) peptides, (2) BMPs and (3) extracellular matrix The initial electronic search yielded 10,697 references. After eliminating duplicates and irrelevant articles based on their title and abstracts, 84 articles were selected, of which, after eliminating those that did not meet inclusion criteria (in vitro studies, systematic reviews, modified animals...), 26 full texts were selected.

Quality assessment / Risk of bias analysis: The included studies were evaluated according to the ARRIVE (Animal Research: Re-porting of In Vivo Experiments) guidelines, which include a total of 23 items. Each item was evaluated by reviewers N.L.-V. and A.L.-V. who attributed scores of 0 (not reported) or 1 (reported) by performing a complete count of all included studies. The SYRCLE risk of bias tool (an adapted version of the Cochrane RoB tool with specific biases in animal studies) was used to assess the methodology of the scientific evidence in all selected studies.

Strategy of data synthesis: Studies that made no reference to the research question were removed and the titles and abstracts of the articles selected were obtained and entered in an Excel spreadsheet. Two reviewers (N.L.-V. and A.L.-V.) selected the titles and abstracts independently. Discrepancies in terms of study inclusion were discussed between the two mentioned re-viewers until consensus was reached. Subsequently, full texts of the selected studies were obtained for their review and inclusion.

Subgroup analysis: Peptides, BMPs and Components of the extracellular matrix. The meta-analysis was performed using RevMan software [Review Manager (RevMan) (Computer program). Version 5.4.1, The Cochrane Collaboration, 2020].

Sensitivity analysis: Not applicable.

Country(ies) involved: Spain.

Keywords: Titanium dental implants, bioactive surface modification, biomolecule, osseointegration, in vivo.

Contributions of each author:

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