

INPLASY PROTOCOL

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Conflicts of interest:
None declared.

Systematic review of studies evaluating the microbiome of periimplantitis using next generation sequencing techniques

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Review question / Objective: This systematic review aims to summarize and critically analyse the methodology and findings of studies which have utilized sequencing techniques to elucidate the microbial profiles of peri-implantitis.

Condition being studied: Peri-implantitis is defined as an infection of the peri-implant tissues accompanied by suppuration and clinically significant progressing crestal bone loss after the adaptive phase, leading to decreased osseointegration and pocket formation.

Eligibility criteria: Original studies investigating the microbiome of peri-implant tissues through next-generation DNA sequencing methods will be included. Culture-based study, conference papers, review articles, studies regarding peri-implantitis associated with other systematic factors (smoking, diabetes mellitus, etc.), articles that examine only specific microorganisms will be excluded from this systematic review. Non-English language articles and research conducted on non-human specimens will be excluded.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 29 December 2022 and was last updated on 29 December 2022 (registration number INPLASY2022120111).

INTRODUCTION

Review question / Objective: This systematic review aims to summarize and critically analyse the methodology and findings of studies which have utilized sequencing techniques to elucidate the microbial profiles of peri-implantitis.

Rationale: Dental implants exhibit high success rates of upto 97 % and above. However, contributory factors related to occlusal overloading and peri-implant tissue infection have been associated with implant failure. Peri-implantitis is defined as an infection of the peri-implant tissues

accompanied by suppuration and clinically significant progressing crestal bone loss after the adaptive phase, leading to decreased osseointegration and pocket formation. Biofilm removal and control with instruments such as Gracey curettes, ultrasonic scalers and air powder abrasive devices are employed with questionable success in the treatment of peri-implantitis since mechanical debridement also comes with its challenges especially at the apically facing thread surfaces as demonstrated by Steiger-Ronay et al. Antimicrobials are also ineffective if mechanical debridement was inadequately performed as mentioned previously. To date, the treatment of peri-implantitis is similar to the periodontitis. The prognosis of this condition is uncertain and hence determining the fundamental cause is important for preventive strategies and also targeted approaches. It is evident that peri-implantitis has a microbial cause, but the exact interaction or mechanism is not clearly known. Owing to the fact that many of the initial studies evaluating the microbiome were based on culture-based techniques, more recent next generation sequencing techniques may give us an insight on a more targeted approach on peri-implantitis treatment which in turn can improve the prognosis of this condition. This systematic review aims to summarize and critically analyse the methodology and findings of studies which have utilized sequencing techniques to elucidate the microbial profiles of peri-implantitis. Owing to the fact that many of the initial studies evaluating the microbiome were based on culture-based techniques, more recent next generation sequencing techniques may give us an insight on a more targeted approach on peri-implantitis treatment which in turn can improve the prognosis of this condition.

Condition being studied: Peri-implantitis is defined as an infection of the peri-implant tissues accompanied by suppuration and clinically significant progressing crestal bone loss after the adaptive phase, leading to decreased osseointegration and pocket formation.

METHODS

Search strategy:

Database Search terms

Medline 1 Peri-implantiti\$

2 (Peri adj2 Implantiti\$

3 Peri-implant\$ adj2 inflam\$

4 Peri-implant\$ adj2 infect\$

5 Peri-implant\$ adj2 disease\$

6 exp Peri-Implantitis/ or exp Dental Implants/ or exp Dental Implantation, Endosseous/

7 peri-implant adj2 mucositi\$

8 peri adj2 implant adj2 mucositi\$

9 periimplant adj2 mucositi\$

10 periimplant\$ adj2 mucos\$

11 exp sequence analysis/ or exp sequence analysis, dna/ or exp sequence analysis, rna/ or exp rna-seq/

12 exp RNA, Ribosomal, 16S/

13 exp Microbiota/

14 exp Bacteria/

15 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10

16 11 or 12 or 13 or 14

17 15 and 16

18 Limit 17 to English and Humans

Cochrane 1 peri-implantiti*

2 periimplantiti*

3 (Peri-Implantitis):ti,ab,kw

4 Peri-implant* NEAR/2 inflam*

5 Peri-implant* NEAR/2 infect*

6 peri-implant muco*sitis

7 peri-implant NEAR/2 disease*

8 peri-implant infect*

9 MeSH descriptor: [Peri-Implantitis] explode all trees

10 dental implant*

11 dental implant, endosseous

12 endosseous dental implant*

13 periimplant* NEAR/2 mucos*

14 MeSH descriptor: [Sequence Analysis, DNA] explode all trees

15 MeSH descriptor: [Sequence Analysis] explode all trees

16 MeSH descriptor: [Sequence Analysis, RNA] explode all trees

17 MeSH descriptor: [RNA-Seq] explode all trees

18 MeSH descriptor: [RNA, Ribosomal, 16S] explode all trees

19 MeSH descriptor: [Microbiota] explode all trees

20 MeSH descriptor: [Bacteria] explode all trees
 21 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #13
 22 #10 or #11 or #12
 23 #14 or #15 or #16 or #17 or #18 or #19 or #20
 24 #21 and #22 and #23
 Scopus 1 peri-implant*
 2 peri W/2 implant*
 3 peri-implant* W/2 inflam*
 4 peri-implant* W/2 infect*
 5 peri-implant* W/2 disease*
 6 peri-implant W/2 mucositi*
 7 peri W/2 implant W/2 mucositi*
 8 periimplant W/2 mucositi*
 9 periimplant* W/2 mucos*
 10 dental AND implants
 11 dental AND implantation AND endosseous
 12 sequence AND analysis
 13 sequence AND analysis AND dna
 14 sequence AND analysis AND rna
 15 rna-seq
 16 rna AND ribosomal AND 16s
 17 microbiota
 18 bacteria
 19 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
 20 10 or 11
 21 12 or 13 or 14 or 15 or 16
 22 17 or 18
 23 19 and 20 and 21 and 22.

Participant or population: Human beings enrolled in studies evaluating the microbiome of periimplantitis using next generation sequencing techniques will be eligible for this review, with no exclusions based on ethnicity or age.”

Intervention: Culture independent next generation sequencing analysis of oral microbiome in periimplantitis.

Comparator: Culture independent next generation sequencing analysis of oral microbiome in healthy implants.

Study designs to be included: Observational and case-control studies

Eligibility criteria: Original studies investigating the microbiome of peri-implant tissues through next-generation

DNA sequencing methods will be included. Culture-based study, conference papers, review articles, studies regarding peri-implantitis associated with other systematic factors (smoking, diabetes mellitus, etc.), articles that examine only specific microorganisms will be excluded from this systematic review. Non-English language articles and research conducted on non-human specimens will be excluded.

Information sources: Cochrane, Medline, and Scopus databases.

Main outcome(s): Microbial diversity and relative abundances of various microorganisms.

Additional outcome(s): Correlation with Demographic data; Correlation with severity of disease; Correlation with risk factors.

Data management: A systematic literature search will be performed on the Cochrane, Medline, and Scopus databases using specific search keywords to identify articles on peri-implantitis and oral cavity microbiome without date limitations. The search strategy will involve a combination of the following key terms: peri-implantitis, inflammation, disease, infection, consequence, sequence analysis, RNA, 16S, metagenomics, metagenome, microbiota and bacteria. The keywords will be combined using Boolean operators “AND” and “OR” in the strategic search. This systematic review will follow the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria. The database searches will be conducted, and removal of duplicates from all three databases will be performed to filter the total number of articles retrieved. Two authors will independently screen through the articles by titles and abstracts. Original studies investigating the microbiome of peri-implant tissues through next-generation DNA sequencing methods will be included. Culture-based study, conference papers, review articles, studies regarding peri-implantitis associated with other systematic factors (smoking, diabetes mellitus, etc.), articles that

examine only specific microorganisms will be excluded from this systematic review. Non-English language articles and research conducted on non-human specimens will be excluded.

Quality assessment / Risk of bias analysis: The Newcastle-Ottawa Scale (NOS) will be used to assess the quality of the non-randomized studies.

Strategy of data synthesis: Study group will consist of all culture independent studies utilizing next generation sequencing techniques on microbiome associated with periimplantitis which are heterogeneous and there is no uniformity in reporting of the data hence no quantitative synthesis will be carried out.

Subgroup analysis: None planned.

Sensitivity analysis: None planned.

Language restriction: Only English articles will be included.

Country(ies) involved: United Arab Emirates, Malaysia.

Other relevant information: None.

Keywords: periimplantitis; dental implants; oral microbiome; microbiome.

Dissemination plans: Planned to be published in a Scopus indexed journal.

Contributions of each author:

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