Which non-surgical treatment protocol should I use as first-line intervention against peri-implantitis?

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Summary

Systematic review conclusion: All combinations of non-surgical approaches for treating peri-implantitis showed small but more significant probing pocket depth reduction than debridement only. There is insufficient evidence to rate any particular non-surgical treatment for peri-implantitis as providing significantly better performance than debridement alone.

Critical appraisal conclusion: Removal of biofilm by means of mechanical or automatic debridement and reducing bacterial load with adjunctive use of antimicrobial agents, without altering the implant surface, remains the standard of care for first-line intervention to any non-surgical treatment approach for peri-implantitis. At this stage of time the efficacy and validity of mechanical or automatic debridement methods for removing biofilm as well as adjunctive antimicrobial therapies remain unknown and needs to be tested by properly executed RCTs.

Implications for clinical practice: Currently there is no gold standard non-surgical treatment protocol. Clinicians, however, should be committed to monitoring and maintaining peri-implant health through continuous assessment and the provision of individualized supportive care. Patient motivation and proper oral hygiene practices to limit infection is very important.

Clinical question

“In patients with peri-implantitis, what is the clinical effect of other non-surgical approaches in comparison to sub-gingival scaling in terms of clinical attachment level and pocket depth changes compared?”

Review methods

Methodology

The reviewers conducted the systematic review of the literature according to the PRISMA\textsuperscript{1} and AMSTAR\textsuperscript{2} guidelines. The network meta-analysis was conducted in accordance with the guidelines for good research practices for indirect treatment comparisons.\textsuperscript{3}

Search strategy and study selection

Two independent reviewers searched the following electronic databases: [MEDLINE-Pubmed, SCOPUS, CINAHL, DARE, Biosis Preview and Web of Knowledge, up to and including 1 January 2014 to identify articles that met the inclusion criteria. In addition they searched for grey literature (IADR meetings, clinical trials.gov,}
controlledtrials.com, Pro-Quest Dissertation Abstracts and Thesis database and OpenGrey (http://www.opengrey.eu) for potential studies and clinical trials in progress. They also conducted a manual search of relevant journals from January 2000 to January 2014. No language restrictions were used. The two independent reviewers assessed the full-text of potential articles for inclusion into the study. Disagreements on inclusion of a study were resolved by discussion between the reviewers until consensus was achieved. They also screened the reference lists of included randomized controlled trials (RCTs) for relevant studies. The investigators recorded all studies that were rejected as well as the reason for exclusion.

Eligibility and exclusion criteria
The reviewers searched for RCTs in humans and non-surgical approaches for treating peri-implantitis. RCTs without any intervention or with treatment outcomes other than clinical attachment level (CAL) and probing pocket depth (PPD) changes were excluded. All other study designs, animal, and in-vitro studies were excluded. Studies investigating surgical approaches and those with duplicated data were also excluded.

Outcome measures and data extraction
The reviewers used two endpoints to assess the clinical effect of non-surgical peri-implantitis therapies: CAL and PPD. Two independent reviewers extracted the data from the included studies. Data was double-checked and any disagreement on data extraction was resolved by discussion between reviewers until consensus was achieved. They contacted the authors of the original studies for clarification of dubious data and request for unpublished data.

Data analysis
Network meta-analysis (NMA) was conducted using the Bayesian random-effects hierarchical model that incorporates information from both direct and indirect comparisons of multiple therapies in a single analysis. Standard meta-analysis of direct pair-wise comparisons were also performed and compared to results from the NMA. To be valid, interventions in a NMA should be connected. The NMA based on CAL was not connected, and therefore its assessment was not feasible. Therefore, only results in PPD changes were reported.

Studies with split-mouth design were separated from those with parallel group design in order to take account of potential correlation between treatment effects of treatment groups with split-mouth RCT's. The reviewers also made adjustments for studies that reported results from site level data analysis by calculating appropriate standard errors using the number of patients. Consistency amongst the network was statistically investigated. They also used a comparison-adjusted funnel plot to assess whether smaller studies produced larger treatment effects. The treatments were ordered by defining the comparisons of an active treatment versus placebo (debridement) only.

Risk of bias of the included RCT's was assessed according to the Cochrane Collaboration risk of bias assessment tool. Four reviewers were submitted to a training phase prior to the risk of bias assessment. The overall quality of the evidence within the pair-wise meta-analysis was graded using the GRADE approach.

Main results
The search process yielded 11 RCT's studies eligible for the NMA. Ten of the RCT's had a parallel group design and one study used a split-mouth design. The NMA compared the PPD between 8 different treatments namely: (i) debridement + chlorhexidine, (ii) photodynamic therapy, (iii) debridement and antibiotics, (iv) air abrasive system, (v) Vector ultrasonic system, (vi) debridement and periochip, (vii) Er:YAG laser monotherapy, and (viii) debridement alone (control). Overall, the examined combinations of therapeutic approaches generated greater PPD reduction than isolated debridement (control) alone. The differences between the combinations however, were very small. The reviewers ascribed the small differences in outcomes between therapies to heterogeneity amongst RCT's. The results from the NMA indicated that debridement in conjunction with antibiotics achieved the greatest additional PPD reduction in comparison to debridement only (0.490 mm 95% Credible Intervals [CrI]: -0.647 to 1.252). The second greatest additional PPD reduction was provided by the combination of debridement and periochip (0.400 mm 95% CrI: -0.843 to 1.629) more PPD reduction than debridement only. Debridement and antibiotics achieved greater PPD reduction (0.262 mm 95% CrI: -1.260 to 0.771) than debridement combined with a chlorhexidine gel. Large CrI indicated considerable uncertainty. Results from the NMA were in general comparable to those from the pair-wise meta-analysis. The network funnel plot showed only small study bias. No inconsistency was found within the network. In general there was a low to moderate risk of bias across all included studies. Three studies were considered to be at
high risk of bias, because one of the authors was working for a company supporting the respective study. Seven studies were industry supported. Overall, the quality of the evidence was considered very low by the GRADE assessment. The main reasons for grading the evidence as very low were the risk of bias limitations and imprecision within the included studies. A statistically significant heterogeneity was found amongst the RCT’s (p=0.046; I² = 46.1%).

**Conclusion**

The authors of this review concluded that all combinations of non-surgical therapies for treating peri-implantitis generated small but more significant PPD reduction than debridement alone. However, they also stated that the results should be interpreted with caution due to the large credit intervals. They also pointed out that currently available evidence does not support the valuation that any particular non-surgical treatment for peri-implantitis performs better than debridement alone.

**Are the results valid?**

The methodological rigor of this review was excellent and in a class of its own. However, the methodological quality of the individual RCTs included in this review had several basic limitations and weaknesses that affected the quality of the evidence presented. Overall, there was marked variability and inconsistencies between the studies for all outcomes measured. This is likely due to differences in the sample population characteristics, definition of peri-implantitis, characteristics of the interventions used, and inconsistencies with measurement of primary and secondary outcomes.

Various risk factors were excluded from the study including smoking, poor oral hygiene, untreated periodontal disease, and diabetes that could modify both initial outcome of treatment as well as the long-term outcome. Some of the studies were lacking information on the presence or absence of clinical inflammation (bleeding or suppuration on probing) in the inclusion criteria and therefore had to be discarded as an outcome measure in the meta-analysis. Consequently the only clinical endpoint used in this meta-analysis was PPD. This raises some concern because reduction of PPD might not indicate that therapies will be effective in the long-term neither is there any proof of evidence that reduction of PPD after non-surgical therapy will reduce implant failure.

Overall, there was a lack of uniformity in the assessed treatment regimens. Some interventions simultaneously involved both mechanical and chemical treatment of implant surfaces in order to remove bacterial plaque, whilst other therapies were based on single or repeated application.

Another potential limitation of the present meta-analysis is the short follow-up (up to 12 months) as this hinders more definitive conclusions about the efficacy of therapies. Whilst clinical healing could be expected to be complete by 3 months following cause related therapy (i.e removal of the...
biofilm), detectable changes in radiographic marginal bone levels may not be apparent at this time. Long-term RCT’s remain desirable. The number of studies included in the review were relatively insufficient, potentially leading to fragile probabilities. Adding on a study to the meta-analysis could tip the probability scale in any direction.

Most domains presented a low risk of bias. However, one domain (allocation concealment) was considered a high or unclear risk of bias in 9 of 11 RCTs assessed. Estimates of treatment effects may be inflated when allocation concealment is not preserved. Additionally, three of the RCTs included in the meta-analysis were considered at high risk of reporting bias because authors involved in the studies were working for the companies supporting the study at the time of the study and the findings from these studies suggest more positive or favourable results for therapies supported by industry.

The high level of variability, lack of consistency, and risk of bias, does not lend support to the validity of the results. However, the results of the NMA were consistent to those from pair-wise meta-analysis, thus supporting the validity of the results. Additionally, the comparison-adjusted funnel did not support biases towards larger effects in smaller trials.

Overall, the weaknesses of the study were greater than its strengths, thus questioning the validity of the results.

What were the key findings?
All the combinations of therapeutic approaches generated greater PPD reduction compared to using debridement alone. The differences between the combinations however ranged between small and considerable uncertainty, and therefore may not be clinically relevant, thus indicating that any decision-making regarding choices for best treatment approach should be done with caution.

The Vector ultrasonic system had the greatest probability to be ranked as the best non-surgical therapeutic approach for peri-implantitis. However, two other approaches, debridement with periochip and photodynamic therapy, presented with similar probabilities. Although ranking of therapies are helpful in practical decision-making, caution should be exercised due to sparse evidence and limitations in the included studies.

How are the results of this review applicable in clinical practice?
Treating peri-implantitis effectively through a non-surgical approach has great significance to the patient because this could mean saving or losing an implant. A non-surgical approach as opposed to a surgical approach also means less discomfort, less morbidity and reduced cost. Post-operative complications and early implant failures are important patient outcomes because of health, inconvenience and cost implications thereof. As a general rule, antibiotic prophylaxis is always indicated when there is an important risk of infection, either because of the characteristics of the surgical procedure (i.e. type and duration of surgery), because of the patient’s local or systemic infection risk (i.e. diabetes, immunodeficiency’s, inflammatory arthropathies), or for patients with post-bacteraemia focal infection risk factors (i.e. infectious endocarditis, infection of joint prostheses).

Most of the individual studies had specific exclusion criteria, including patients who smoked, patients with full mouth plaque scores or full mouth bleeding scores above 20%, pregnant or lactating women, patients who had taken systemic antibiotics in recent months prior to treatment, patients with implants with < 2mm keratinized mucosa or no keratinized mucosa. Consequently, the results reported should be interpreted with caution and may not apply to all patients in the practice situation. Availability and accessibility to the technologies assessed in this review may also be limited due to high cost of equipment and skills training required.

Clinical resolution
Clinicians involved with dental implant treatment must have a comprehensive understanding of the need for ongoing maintenance and peri-implant health, peri-implant disease, the assessment thereof, and correct diagnosis and early interception of disease, as well as appropriate skills and tools for managing these complications.

Non-surgical peri-implantitis therapy as first line treatment plays a pivotal role in the treatment of peri-implant disease. Removal of biofilm by means of mechanical or automatic debridement, and reducing bacterial load to levels compatible with peri-implant health by means of adjunctive use of antimicrobial agents without altering the implant surface, remains the standard of care for first-line intervention to any non-surgical treatment approach for peri-implantitis. At this stage of time the efficacy and validity of mechanical or automatic debridement protocols for removing biofilm as well as adjunctive antimicrobial therapies for reducing bacterial load remain unknown and needs to be tested by properly executed head-to-head RCT’s.
Disclosure
Dr Johan Hartshorne is trained in clinical epidemiology, biostatistics, research methodology and critical appraisal of research evidence. This critical appraisal is not intended to, and do not, express, imply or summarize standards of care, but rather provide a concise reference point for dentists to aid in understanding and applying research evidence from referenced early view or pre-published articles in top ranking scientific publications and to facilitate clinically sound decisions as guided by their clinical judgement and by patient needs.

References