Peri-implant diseases
This evidence summary aims to locate and summarise evidence on how peri-implant mucositis and peri-implantitis should be diagnosed and treated. It does not include detailed descriptions of the studies cited nor does it include information that was not presented in the literature.

The Curious about website encourages dental professionals to raise issues where a review of the available evidence would provide a useful resource for other dental professionals.

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Key findings

- Diagnosis of disease can be carried out using probing parameters and radiographic assessment.
- Overall there is no reliable evidence to suggest which intervention could be the most effective for treating either peri-implant mucositis or peri-implantitis.
- Some treatment protocols may improve peri-implant diseases but none conclusively appear to be more effective than another.
- There is weak evidence that antibacterial mouthrinses are effective in reducing plaque and marginal bleeding around implants though guidelines do not recommend its use.

Review question

How should peri-implant mucositis and peri-implantitis be diagnosed and treated?

Aims

To identify the most effective methods for diagnosing peri-implantitis and peri-implant mucositis and the most effective interventions for treating peri-implantitis and peri-implant mucositis.

Note: To improve readability the term mucositis will be used throughout this summary but will refer solely to dental implant related mucositis. Mucositis in other situations, for example as a complication of cancer treatment, is not covered.

The case for action

Implants

Dental implants have revolutionised dental rehabilitation, prosthetic dentistry and maxillary reconstruction. They are reported to be functionally stable with long-term success rates. Consequently, their use is increasing. Estimates suggest that, at the turn of the millennium in the United States, over two million dental implants were provided annually. By 2020 this could double and be accompanied by a high incidence of peri-implantitis.

Mucositis and Peri-implantitis

There is evidence that poor oral hygiene, a history of periodontitis and cigarette smoking are risk indicators for peri-implant disease. Further factors with a suggested association include alcohol consumption, diabetes, hepatitis and specific IL-1 genotypes. Infection associated with implants is different from infection associated with natural teeth. For example tissues around implants are more prone to plaque-associated infections and tissue destruction than their natural counterparts and tissue surrounding an implant is affected by factors such as the type and shape of the implant. Peri-implant disease has been categorised into mucositis and peri-implantitis. Estimates (2013) indicate a high frequency of disease but arguments have been put forward for the under and over estimation of both mucositis and peri-implantitis due to, for example, the reversible nature of mucositis and the lack of a standard definition of peri-implantitis. In basic terms, mucositis can be likened to gingivitis with peri-implantitis corresponding to adult periodontitis.

Mucositis

Peri-implant mucositis is described as inflammation of the peri-implant mucosa without signs of supporting bone loss. The condition is bacteria-induced and reversible with early intervention and removal of etiology. Typical signs are reddening, swelling and bleeding on periodontal probing. Estimates (2013) of the frequency of mucositis in general and in high risk populations is 63.4 per cent (participant-based) and 30.7 per cent when the implant is used as a unit of analysis.

Peri-implantitis

Peri-implantitis is a progressive inflammatory disease of the hard and soft tissues surrounding an implant caused by an infection, which is accompanied by bone resorption, decreased osseointegration and increased pocket formation beyond normal biologic remodelling. Participant-based estimates (2013) for peri-implantitis give a frequency of 18.8 per cent with this figure falling to 9.6 per cent when the unit of analysis is the implant.

Diagnosis and treatment

Diagnostic measures for peri-implant diseases need to be sensitive enough to detect the early signs of infection to prevent lasting damage. Various criteria have been identified to diagnose and monitor for peri-implant diseases, including:

- Probing parameters - for example detection of bleeding on probing, periodontal probing depth and suppuration
- Radiographic assessment to detect loss of supporting bone, once tissue homeostasis has been established

1 IL-1 is a key regulator of the inflammatory response.
• Microbial analysis - for example of peri-implant crevicular fluid or saliva to monitor the subgingival flora.

As bleeding on probing is frequently seen at implants with and without ‘progressive’ bone loss, it cannot be used alone for the detection of peri-implantitis. A pocket of 6 mm, accompanied by other signs and/or symptoms such as bleeding and pain, has been suggested to indicate peri-implant disease though this depth is not universally accepted and other sources state alternatives such as ≥ 5 mm. Checking occlusion and the integrity of the implant is important in identifying biomechanical complications as biological and biomechanical complications can occur together and will affect the approach to treatment.

Most treatment options have been adapted from treating periodontal disease and are aimed at removing the etiological factors, for example, controlling infection or removing overstress and preventing disease progression. The successful treatment of peri-implant mucositis combining debridement (surgical and non-surgical) and chemical plaque control or antimicrobial treatment have been documented, however, long-term data to support these treatment protocols are limited. Treatment measures include:

• Surface decontamination
• Antimicrobial treatment
• Laser therapy
• Surgical treatment

Options to tackle biomechanical complications include retightening or replacing implant components or the use of an occlusal splint.

The evidence

Current guidance (SDCEP) supports the use of probing parameters and radiographic assessment for identifying peri-implant inflammation and infection and peri-implantitis. Figure one covers the steps for identifying and treating mucositis and peri-implantitis.

Overall there is no reliable evidence to suggest which intervention could be the most effective for treating either mucositis or peri-implantitis. Cochrane reviews for each disorder were not able to reach a conclusion. Subsequently published randomised controlled trials (RCT) provided no evidence to amend this. While some treatments did have significant effects when compared to baseline, none were conclusively more effective than another.

Diagnosis

No systematic reviews or RCTs were located covering the diagnosis of peri-implant diseases. However guidance on implantitis noted that the BPE is not suitable for the screening of dental implants due to factors such as tissue surrounding implants being less resistant to probing and the presence of excess residual cement. A marked increase in probing depth and the presence of suppuration and bleeding suggested peri-implant inflammation and infection and progressive bone loss suggested peri-implantitis. Gentle probing pressure was recommended for examining peri-implant tissues and, if probing depth was recorded, it should be measured from a fixed landmark, for example, the implant shoulder. There was no evidence that metal probes are detrimental to the tissues around the superstructure or implant.

Treatment

Mucositis

Systematic review

There is weak evidence that antibacterial mouthrinses are effective in reducing plaque and marginal bleeding around implants. Positive results were seen in two studies involving both self and professionally-administered antimicrobial strategies (respectively):

• Antisptic mouthwashes: Listerine versus placebo (five per cent hydroalcohol mouthrinse). Statistically significantly less plaque and marginal bleeding were found in the Listerine group, at three months, though this group had statistically significantly higher mean pocket probing depths (PPD) scores. No significant differences were found for probing ‘attachment’ levels (PAL).

• Subgingival irrigation: chlorhexidine irrigation versus chlorhexidine mouthwash. Participants using chlorhexidine irrigation had statistically significantly lower mean plaque scores than the group using chlorhexidine mouthwash and a lower marginal bleeding index at three months.

Of the further four strategies covered in the systematic review no overall significant differences were seen between the intervention and control groups. These involved the following comparisons (length of follow up is given in parenthesis):

Self-administered interventions:
• Sonic versus manual toothbrushing (24 weeks)
• Triclosan versus sodium fluoride dentifrice (six months)

Professionally administered interventions:
• Mechanical debridement plus minocycline or chlorhexidine gel (12 months)
• Mechanical debridement with titanium curettes or with an ultrasonic device (six months)

Randomised controlled trials^{30-32}

Randomised controlled trials published since the systematic review examined professionally administered interventions. All studies compared an intervention of interest to debridement with no significant added benefit being seen for any intervention except for the use of Azithromax®.

Reduced mean PPD and bleeding scores were seen at six months in those taking systemic Azithromax® for four days over those who did not receive Azithromax®. However the authors suggest that the improvement could be due to improved oral hygiene.

Interventions showing no significant benefit between the treatment investigated and debridement were:

• Adjunctive chlorhexidine gel (0.5 per cent) with non-surgical mechanical debridement (three months)
• Adjunctive Glycine powder air-polishing (GPAP) to oral hygiene instruction and non-surgical debridement (three months)

Guidance^{27}

Published guidance covering the treatment of mucositis acknowledges the incomplete evidence base and that removal of plaque and calculus deposits and re-establishing effective personal oral hygiene are likely to be important elements of effective treatment. The guidance recommends supra-mucosal debridement, cleaning the abutment and use of the Oral Hygiene TIPPS behaviour change strategy to address inadequate oral hygiene. Oral Hygiene TIPPS is an intervention strategy that aims to make patients more confident in performing effective plaque removal and helps plan how and when patients will look after their teeth and gums. Mouthwash use or irrigation is not recommended.

Peri-implantitis

Systematic review^{29}

Twelve treatment strategies were evaluated but the available evidence did not determine the most effective way to treat peri-implantitis. There were indications that, locally-applied antibiotics (8.5 per cent doxycycline hyclate) or augmentation with an animal-derived bone substitute (Bio-Oss™) significantly decreased PAL and PPD. Most of the trials that tested more complex and expensive therapies did not show any statistically or clinically significant advantages over deep mechanical cleaning.

Of the twelve strategies for treating peri-implantitis, positive changes were seen with the following two interventions:

Non-surgical intervention:
• Manual debridement and subgingival chlorhexidine with or without local antibiotics saw statistically significant differences for changes in PAL and PPD in favour of the group treated with antibiotics (8.5 per cent doxycycline hyclate) after 18 weeks.

Surgical intervention:
• The comparison of two bone grafting materials that are applied directly to the bone, a nanocrystalline hydroxyapatite synthetic material (Ostim™) and a bovine-derived xenograft (Bio-Oss™), together with a resorbable collagen barrier (Bio-Gide™) to treat peri-implant infrabony defects deeper than 3 mm saw a statistically significant difference for PAL and PPD changes in favour of the Bio-Oss™ group at four years. However three patients were withdrawn from the study due to severe pus formation and no statistically significant differences for changes in marginal soft tissue recession (REC) were seen.

No significant overall differences were seen with the following interventions:

Non-surgical interventions:
• Local antibiotics (Metronidazole gel 25 per cent) versus ultrasonic debridement (12 weeks)
• Er:YAG laser versus manual debridement with chlorhexidine subgingival application (six months and one year)
• Er:YAG laser versus air-abrasive device (Perio-Flow®) (six months)

Surgical intervention:
• Oral amoxicillin 50mg/kg for eight days followed by resective surgery, metronidazole (Elyzol 25 per cent) and tetracycline hydrochloride with or without smoothing of the implant surface (implantoplasty). (Two years)

Adjunctive treatment to surgical intervention:
• Photodynamic therapy with mechanical cleaning (four months)
• Local drug delivery (minocycline) or photodynamic therapy (phenothiazine Chloride) with mechanical debridement (six and twelve months)

Randomised controlled trials

Clinical trials published since the systematic review was written examined a further three interventions:

• Photodynamic therapy (toluidine blue) with mechanical cleaning (four months)
• Local drug delivery (minocycline) or photodynamic therapy (phenothiazine Chloride) with mechanical debridement (six and twelve months)

3 Photodynamic therapy (in this instance) involves applying photosensitive dyes to periodontal pockets and activating the dye with light of a specific wavelength to kill periodontal pathogens.
• Matrix chips (MatrixC) or chlorhexidine chips (PerioC) with debridement (six months)\textsuperscript{(36)}

Of these further interventions, adjunctive local minocycline delivery, photodynamic therapy, matrix chips (MatrixC) and chlorhexidine chips (PerioC) had significant effects on some clinical parameters over debridement but there was no difference between treatment groups.

**Guidance**\textsuperscript{(27)}

Guidance published by the SDCEP acknowledges the incomplete evidence base for treating peri-implantitis and states that re-establishing effective self-performed oral hygiene and professional removal of supra- and sub-mucosal plaque and calculus deposits and excess residual cement are likely to be important components of treatment. The guidance suggests that if radiographic examination of the implant, detects clinically significant progressing crestal bone loss the patient should be referred back to the clinician who placed the implant. If this is not possible recommended treatment is described in Figure one. A follow-up appointment should be arranged after one – two months to assess the outcome of treatment. If there is no improvement or if acute pain and infection are present, advice should be sought from secondary care. If the inflammation has settled and the situation is stable a radiographic follow-up at six – 12 months should be arranged.

**Complications, adverse effects and side effects**

For mucositis there was insufficient data to quantify adverse effects. Two effects relating to patient preferences, were less changes in patient taste perception for an amine fluoride/stannous fluoride mouthrinse versus a chlorhexidine mouthrinse and less pain with the use of 35 per cent phosphoric acid than titanium curettes.\textsuperscript{(28)} With peri-implantitis complications were reported.\textsuperscript{(29,33)} These included recurrence of peri-implantitis (of up to 100 per cent), perforation of the buccal keratinised mucosa, slight pigmentation of the peri-implant soft tissues, exposed barriers and minor spontaneously resolving, post-operative swelling and wound dehiscence.\textsuperscript{(29,33)}

**Discussion**

Diagnostic measures in common use, probing parameters and radiographic assessment, are supported by available guidance and are easier to employ in general practice that microbial analysis. There are indications that the efficacy of measures recommended by the guidance to treat peri-implantitis is dependent on the clinical ability of the clinician.\textsuperscript{(33)} As no particular treatment method was found to be more effective in treating mucositis or peri-implantitis it has been suggested that the more patient friendly intervention(s) should be used.\textsuperscript{(28)} Ease of maintenance should also be considered since it can play an important role in patient compliance.
Methods

Search strategy

Separate searches were run to cover mucositis and peri-implantitis. Key terms, both free text and controlled vocabulary, for each disease were combined with search terms covering diagnosis, treatment and management. Ovid Expert Searches for observational studies, randomised controlled trials, economic studies and systematic reviews and the Cochrane Highly Sensitive Search Strategy for RCTs were employed for MEDLINE and the Cochrane Oral Health Group’s search filter for isolating RCTs for EMBASE.

A Cochrane review covering the treatment of mucositis current until 2010 was located and used as a starting point for the evidence base for mucositis treatment. A Cochrane review covering the treatment of peri-implantitis current until 2012 was also located and used as a starting point for the evidence base for peri-implantitis treatment. Systematic reviews published prior to this were located but due to the high esteem in which Cochrane reviews are held and that the earlier systematic reviews did not reach alternative conclusions they were not included.

The databases searched were:
- The Cochrane Oral Health Group’s Trials Register
- The Cochrane Central Register of Controlled Trials (CENTRAL)
- MEDLINE via Ovid
- EMBASE via Ovid

No language restrictions were applied. Search dates were limited to publication post 2012 for peri-implantitis treatment and 2010 to cover mucositis treatment. Studies covering mucositis relating to chemo or radiotherapy were excluded. No date limits were applied to searches covering diagnosis. Grey literature was searched based on the Canadian Agency for Drugs and Technologies in Health practical search tool Grey matters. Searches were carried out between February and April 2015. For peri-implant disease treatment studies were included if they met the following criteria:

- Randomised controlled trials
- Evaluated interventions to treat either mucositis or peri-implantitis (including parallel group and split-mouth designs)
- Participants had at least one dental implant affected by either mucositis or peri-implantitis
- Employed any non-surgical or surgical procedure including the use of local or systemic therapeutic agents as well as any other interventions aimed at the recovery of peri-implant oral health
- Types of outcome measures:
  - Implant failure as defined by the Cochrane review
  - Radiographic marginal bone level change on intraoral radiographs taken with a parallel technique
  - Complications and side effects
  - Recurrence of mucositis or peri-implantitis
  - Changes in PAL, PPD or REC
  - Aesthetics evaluated by patients
  - Aesthetics evaluated by dentists
  - Cost (treatment time plus material costs)

Results

From over 600 search results ten publications, two systematic reviews, six subsequently published RCTs and one guidance document, were found that met the inclusion criteria for this summary. Two studies were rejected at the last sift due to the analysis unit not being the patient and a further study was rejected as the analysis unit was unclear and the authors did not reply to correspondence. All studies were parallel group studies.

Only low quality evidence was located. The included RCTs had few subjects and (for the majority) short follow-up periods, varying from 12 weeks to four years, and although overall the risk of bias of the studies was either low or unclear only single trials were available for each outcome. Most studies provided sample size calculations or stated the number of participants needed per group to detect a difference of a specific size, for example, 1 mm difference in bone level, but not all planned sample sizes were met. Some deviations from protocols were reported and some patients were lost to follow up. In a number of studies the proportion of subjects in each group with confounding factors, for example a history of treated periodontitis, was significantly different. One study was included though the implant was the study unit as only patients with one implant were included in the study.

4 A parallel group study is commonly used to compare two treatments. Subject allocation is usually achieved by randomisation with the same number of subjects not being required in each group. The design is commonly used in randomised controlled trials with statistical analysis often involving a simple t-test of the between group difference in the outcome, which is usually a mean or a proportion.
References


32. Ji YJ, Tang ZH, Wang R, Cao J, Cao CF, Jin LJ. Effect of glycine powder air-polishing as an adjunct in the


