

Clinical efficacy of antibiotics in the treatment of peri-implantitis

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Objective: The aim of the present study was to review the pertinent literature with reference to the clinical efficacy of antibiotics in the treatment of peri-implantitis. **Methods:** To address the focused question ‘Are locally and systemically delivered antibiotics useful in the treatment of peri-implantitis?’ PubMed/Medline and Google-scholar databases were explored from 1992 until February 2013 using a combination of the following keywords: ‘antibiotic,’ ‘dental implant,’ ‘inflammation,’ ‘peri-implantitis’ and ‘treatment’. Letters to the editor, case-reports and unpublished data were excluded. **Results:** Ten studies were included. In six studies, peri-implantitis was treated using a non-surgical approach (scaling and root planing), whereas in four studies, a surgical approach was adopted for treating peri-implantitis. In three studies systemic antibiotics were administered and in six studies locally delivered antibiotics were used for treatment. One study used the oral route for antibiotic delivery. In three studies, minocycline hydrochloride was locally delivered as an adjunctive therapy to non-surgical mechanical debridement of infected sites. Nine studies reported that traditional peri-implantitis treatment with adjunct antibiotic therapy reduces gingival bleeding, suppuration and peri-implant pocket depth. In one study, despite surgical debridement of infected sites and systemic antibiotic cover, nearly 40% of the implants failed to regain stability. There was no placebo or control group in eight out of the nine studies included. **Conclusion:** The significance of adjunctive antibiotic therapy in the treatment of peri-implantitis remains debatable.

Key words: Antibiotic, dental implant, inflammation, peri-implantitis, treatment

INTRODUCTION

It is well-known that dental implants can osseointegrate and remain functionally stable in healthy as well as medically compromised individuals^{1–14}; however, the risk of complications occurring following implant placement cannot be disregarded^{13,14}. Risk factors associated with peri-implant complications include inadequate primary stability at the time of implant placement, occlusal trauma, fractured components, pain, local and systemic infections, neuropathy and tobacco smoking^{15–17}. Peri-implantitis (PI) is an inflammatory condition characterised by loss of supporting bone in the tissues surrounding the implant¹⁸. In general, the frequency of PI has been reported to be 5–8% for various implant systems¹⁹. Clinical signs

of PI include gingival bleeding, suppuration, increased pocket depth (PD) and implant mobility; whereas alveolar bone loss can be observed on radiographs^{18,20,21}. In addition, studies have also shown a similarity in bacterial flora associated with PI and periodontitis^{8,22–24}.

Various treatment regimes for PI have been proposed in the literature. These include plaque control regimens, mechanical debridement of the affected areas, irrigation with antiseptic agents [such as chlorhexidine (CHX), saline and 10% hydrogen peroxide], surgical flap access into infected peri-implant tissues and laser therapy^{8,9,25,26}.

As it is known that bacteria can transfer from periodontally involved teeth to an implant, and that the microbes associated with PI resemble those of

periodontal disease^{22,25}, it is hypothesised that local or systemic delivery of antibiotics with traditional PI treatment regimes eliminates periodontopathogenic bacteria to a greater extent compared with when these treatment regimes are performed alone. This may in turn facilitate healing of PI sites. As locally and/or systemically delivered antibiotics apparently play essential roles in the treatment of PI, it is pertinent to investigate the type of antibiotic, dosage and duration of use that would be most effective for treating PI.

The aim of the present review was to assess the clinical efficacy of antibiotics in the treatment of PI.

METHODS

Focused question

The focused question addressed was: ‘What is the clinical efficacy of locally and systemically delivered antibiotics in the treatment of PI?’

Inclusion criteria

The selection protocol encompassed the following: (1) original studies; (2) clinical studies; (3) hand searching of the reference lists of potentially relevant original and review studies; (4) intervention (use of locally and systemically delivered antibiotics in the treatment of PI); and (5) studies published only in the English language (*Figure 1*).

Exclusion criteria

The exclusion criteria encompassed the following: (1) experimental studies; (2) letters to the editor; (3) his-

toric reviews; and (4) unpublished data (*Figure 1*). Any disagreement among the authors was resolved via discussion.

Search methods

As a first step, the authors searched the National Library of Medicine, Washington, DC (MEDLINE–PubMed) and Google Scholar databases for appropriate articles addressing the focus question (as stated above). These databases were explored from 1992 up to and including February 2013 using the following key indexing terms in different combinations: ‘antibiotic’, ‘dental implant’, ‘inflammation’, ‘peri-implantitis’ and ‘treatment’.

In the second step, reference lists of original and review studies that were found to be relevant in the first step were hand-searched. Titles of research articles containing words suggesting the use of antibiotics as adjuncts to PI therapy were also sought. After final selection, studies that fulfilled the selection criteria were processed for data extraction.

Data extraction and management

The initial search yielded 75 articles. Scrutiny of the titles and abstracts abridged the number of studies to 10^{1–10}. Sixty-five studies that did not abide by the inclusion criteria were excluded (see Appendix A). As a limited number of original clinical studies addressed our focused question, the pattern of the present systematic review was customised to primarily summarise the pertinent data.

RESULTS

Characteristics of studies included

All studies^{1–10} were performed at universities or health-care centres. The numbers of patients included in these studies ranged from 9 to 281 individuals. These individuals were aged between 25 years and 79 years. The total numbers of dental implants inserted in the study participants ranged between 9 and 193 titanium implants. Three studies^{4,6,7} were randomised clinical trials, two studies^{2,5} had a prospective cohort design, two studies^{8,10} were prospective follow-ups, two^{1,9} studies were case series and one study² had a retrospective design (*Table 1*).

In six studies^{4–7,9,10}, PI was treated using a non-surgical approach (scaling and root planing), whereas in four studies^{1–3,8} a surgical approach (open flap debridement) was adopted. In three studies^{2,8,10} systemic antibiotics were administered to the study subjects, whereas six studies^{1,4–7,9} used locally delivered antibiotics for the treatment of PI. One study² used

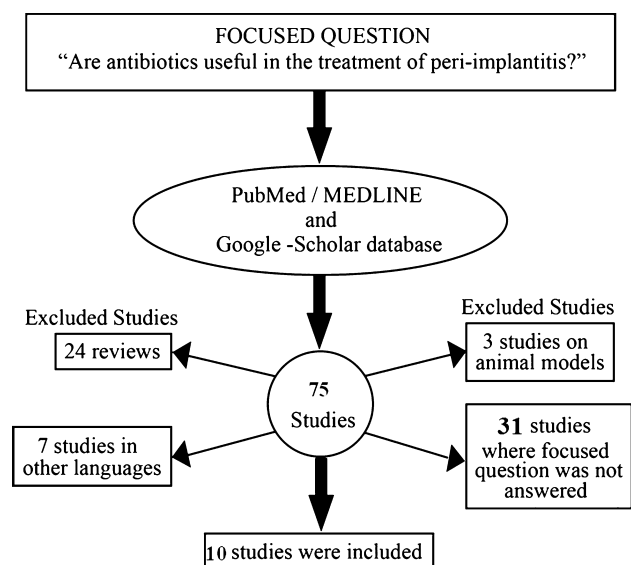


Figure 1. Study selection protocol.

Table 1 Clinical studies on the effect of antibiotic therapy on the treatment of peri-implantitis (PI)

Author/s <i>et al.</i> (Year)	Study design	Subjects/number of implants	Treatment protocol	Antibiotic/s used	Route of antibiotic delivery	Control/placebo group? (Yes/No)	Follow-up	Main results
AlGhamdi AS ¹	Case series	80/193	Open flap debridement and implant surface cleaning with hand instruments	Tetracycline solution + doxycycline powder	Local	No	~30 months	Open flap debridement with adjunct antibiotic therapy caused significant reduction in probing depth and suppuration at PI sites
Heitz-Mayfield <i>et al.</i> ²	Prospective cohort study	24/36	Open flap debridement, implant surface cleaning with hand instruments and saline irrigation	Amoxicillin + metronidazole	Systemic	No	12 months	Open flap debridement with adjunct antibiotic therapy caused significant reduction in probing depth and suppuration at PI sites
Charalampakis <i>et al.</i> ³	Retrospective	281/NA	228 patients (83.2%) were treated surgically (open flap debridement, implant surface cleaning) 46 patients (16.8%) were treated non-surgically (mechanical debridement via curettes).	Amoxicillin + metronidazole (~50% cases) Metronidazole (~20% cases) Ciprofloxacin (~11% cases) Others (~19% cases)	Oral	No	1–6 years	Bone plasty with adjunct antibiotic therapy antibiotics during surgery was significantly associated with arrested PI lesions.
Renvert <i>et al.</i> ⁴	Single-masked, randomised, two-arm clinical trial	25/31	Non-surgical (scaling and root planing)	Minocycline hydrochloride	Local	No	12 months	Mechanical treatment of PI with minocycline hydrochloride as an adjunct demonstrated reduction in probing depth
Salvi <i>et al.</i> ⁵	Open-label case cohort study	25/31	Mechanical debridement with curettes	Minocycline hydrochloride	Local	No	12 months	Mechanical treatment of PI with minocycline hydrochloride as an adjunct demonstrated reduction in probing depth
Renvert <i>et al.</i> ⁶	Randomised clinical trial	32/NA	Non-surgical mechanical debridement with curettes and CHX wash	Minocycline hydrochloride	Local	No	12 months	Mechanical treatment of PI with minocycline hydrochloride as an adjunct demonstrated reduction in probing depth
Büchler <i>et al.</i> ⁷	Randomised clinical trial	28/48	Non-surgical mechanical debridement with curettes	Doxycycline	Local	Yes	4.5 months	Probing attached levels were significantly higher in PI cases treated with non-surgical debridement + doxycycline than those treated with non-surgical debridement alone
Leonhardt <i>et al.</i> ⁸	Prospective follow-up	9/44	Open flap debridement and disinfection with 10% hydrogen peroxide	Part 1: clindamycin Part 2: amoxicillin + metronidazole Part 3: tetracycline Part 4: tetracycline Part 5: amoxicillin + metronidazole Part 6: ciprofloxacin Part 7: sulfonamide + trimethoprim Part 8: metronidazole Part 9: ciprofloxacin	Systemic	No	5 years	Despite surgical debridement and antibiotic therapy, seven implants were lost. In 58% cases, surgical treatment with adjunct antibiotic therapy was successful for treating PI

Table 1 Continued

Author/s <i>et al.</i> (Year)	Study design	Subjects/number of implants	Treatment protocol	Antibiotic/s used	Route of antibiotic delivery	Control/placebo group? (Yes/No)	Follow-up	Main results
Mombelli <i>et al.</i> ⁹	Case series	25/30	Local debridement and irrigation with 0.2% CHX	Tetracycline HCl-containing fibres	Local	No	12 months	Local treatment of PI with tetracycline HCl-containing fibres as an adjunct demonstrated reduction in probing depth and bleeding
Mombelli & Lang ¹⁰	Prospective follow-up	9/9	Local debridement and irrigation with 0.5% CHX	Ornidazole (1 g daily for 10 days)	Systemic	No	12 months	Local treatment of PI with ornidazole as an adjunct demonstrated reduction in probing depth and bleeding

CHX, chlorhexidine.

the oral route for antibiotic delivery. In three studies, minocycline hydrochloride was locally delivered as an adjunctive therapy to non-surgical mechanical debridement of infected sites⁴⁻⁶. Nine studies^{1-7,9,10} reported that traditional PI treatment with adjunct antibiotic therapy reduced gingival bleeding, suppuration and peri-implant pocket depth. In one study⁸, despite surgical debridement of infected sites and systemic antibiotic cover, nearly 40% of the implants failed to regain stability. There was no placebo or control group in nine studies^{1-6,8-10}. These results are shown in *Table 1*.

DISCUSSION

From the studies¹⁻¹⁰ included in the present systemic review, it is postulated that antibiotics, when used as adjuncts to conventional PI treatment regimes, promote healing of inflamed peri-implant tissues. Although mechanical debridement and disinfection of implant surfaces (using curettes and CHX, respectively) removes the oral biofilm and periopathogenic microbes to some extent, it is tempting to speculate that an absolute extermination of the oral biofilm is difficult to accomplish because of variations in surface characteristics and the morphology of various implant systems. This may be a logical foundation for using locally delivered and systemic antibiotics as adjuncts to conventional PI treatment regimes. Nevertheless, there is no scientific justification in this regard because none of the clinical studies¹⁻¹⁰ included in the present review used a control group (that is, treatment of PI without local or systemic antibiotics). The study by Leonhardt *et al.*⁸ reported 5-year results following the treatment of PI. In this study⁸, the PI lesions were surgically exposed, affected implants were cleaned with an antiseptic agent and systemic antibiotics were administered. The results showed that, despite the surgical and antimicrobial treatment regimen applied, additional loss of supporting bone was found in nearly 40% of the advanced PI lesions. Thus the clinical efficacy of antibiotics as adjuncts to conventional PI therapy is rather dubious. There is an urgent need for double-blinded placebo-controlled randomised clinical trials to demonstrate the efficacy of locally delivered and systemically delivered antibiotics in the treatment of PI.

It is notable that the type of antibiotic, route of administration, dosage and duration of use varied among studies. For example, in the studies by Renvert and colleagues^{4,6} and Salvi *et al.*⁵ local delivery of 1 mg of minocycline hydrochloride, when used as an adjunct to mechanical debridement of implant sites, was reported to reduce inflammation, whereas Büchter *et al.*⁷ showed that local delivery of doxycycline as an adjunct is effective in the treatment of PI.

Heitz-Mayfield *et al.*² reported that systemic administration of a combination of amoxicillin and metronidazole promotes the healing of inflamed peri-implant tissues following surgical curettage whereas Mombelli & Lang¹⁰, reported that mechanical debridement of PI lesions, pocket irrigation with chlorhexidine and adjunctive systemic administration of 1000 mg ornidazole resulted in improved clinical conditions. In this context, the criteria for selecting the type and dosage of an antibiotic for the treatment of PI are yet to be established.

In conclusion, our focused question ‘What is the clinical efficacy of locally and systemically delivered antibiotics in the treatment of PI?’ remains unanswered.

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Conflict of interest

None declared.

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A APPENDIX

List of studies excluded. Reason for exclusion is shown in parenthesis after the reference.

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