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study

Non-surgical treatment of peri-implantitis: does adjunctive systemic metronidazole help patients?

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Background

Peri-implantitis is a pathological condition around implants, characterised by inflammation of the peri-implant mucosa and progressive loss of bone. A prevalence of peri-implantitis of 18.5% at patient level and 12.8% at implant level has been reported (Dreyer et al., 2018). Risk factors for peri-implantitis are poor oral hygiene, a history of periodontitis, and tobacco smoking. Diabetes mellitus, alcohol consumption, and genetic traits may also have a negative impact.

The microbiota associated with peri-implantitis are characterised by a mixed anaerobic infection. Their composition is comparable to that of periodontitis lesions around teeth.

At present, there is no universally accepted standard of care for the treatment of peri-implant diseases. Non-surgical therapy alone does not seem to be effective in a significant proportion of cases. Although published case series have indicated promising additional benefits when using systemic antibiotics as an adjunct to non-surgical peri-implantitis therapy, no randomised clinical trials have been conducted to assess the effects of systemic metronidazole as an adjunct to the non-surgical treatment of peri-implantitis.

Aim

The aim of the present study was to evaluate the clinical, radiographic, and microbiological outcomes after non-surgical treatment of peri-implantitis with adjunctive systemic metronidazole or a placebo.

Materials & methods

- This triple-blind, randomised, placebo-controlled clinical trial included patients requiring non-surgical treatment of peri-implantitis.
- Exclusion criteria were allergy to metronidazole, treatment history of bisphosphonates, pregnancy or breast-feeding, antibiotic treatment in the previous three months, and contraindicated systemic conditions.
- Thirty-two subjects with 62 implants were randomly assigned into two groups to receive either a mechanical non-surgical instrumentation session and systemic metronidazole (test) or placebo (control).
- Before baseline examination, patients were instructed in proper oral hygiene (full-mouth plaque score; FMPS ≤20%) and supragingival debridement was performed.
- Both groups received a single session of non-surgical instrumentation under local anaesthesia. The implant-supported restorations were removed whenever possible and mechanical instrumentation was performed by an ultrasonic device with a stainless-steel tip followed by removal of granulation tissue with stainless-steel curettes. After irrigation with 0.12% chlorhexidine digluconate, the restorations were reinserted onto the implants.
- Immediately after the treatment session, all patients received 500mg metronidazole (test) or placebo tablets (control) three times per day for seven days.
- At the first-week post-treatment visit, patients were asked to return any medication not taken and to report adverse events.
- The following parameters were recorded: pocket probing depth (PPD), recession, clinical attachment level (CAL), bleeding on probing (BoP), FMPS and full-mouth bleeding score (FMBS), marginal bone-level changes on periapical radiographs, and microbiological changes at the deepest peri-implant pocket.
- Success criteria were defined as: PPD ≤5mm without BoP or <5mm irrespective of BoP and no further bone loss between baseline and one year.
- Re-evaluation was performed after three, six, and 12 months following treatment.

Table: Mean microbiological outcomes for baseline, 3, 6, and 12 months

	Treatment group	Baseline positive (%)/>10^6(%)	3 months positive (%)/>10^6(%)	6 months positive (%)/>10^6(%)	12 months positive (%)/>10^6(%)
Aa	Test	0/16 (0%)	0/16 (0%)	0/14 (0%)	0/15 (0%)
	Control	0/16 (0%)	0/16 (0%)	1/14 (7%)	1/16 (6%)
	p value	.7	.7	.5	.3
Pg	Test	15/16 (94%)	5/12 (42%)*	3/14 (21%)*	4/15 (27%)*
	Control	9/16 (56%)	6/15 (40%)	6/14 (43%)	7/16 (44%)
	p value	.01	.6	.4	.3
Tf	Test	14/16 (86%)	4/12 (33%)*	4/14 (29%)*	5/15 (33%)*
	Control	14/16 (86%)	6/15 (40%)*	8/14 (57%)	13/16 (81%)
	p value	.7	.7	.3	.001
Fn	Test	15/16 (94%)	9/12 (75%)	13/14 (93%)	11/15 (73%)
	Control	16/16 (100%)	13/15 (87%)	14/14 (100%)	16/16 (100%)
	p value	.3	.2	.3	.06
Cr	Test	13/16 (81%)	6/12 (46%)*	4/14 (28%)*	3/15 (2%)*
	Control	11/16 (69%)	9/15 (60%)	6/14 (43%)	16/16 (100%)
	p value	.3	.3	.3	.04

Abbreviations: Aa, *Aggregatibacter actinomycetemcomitans*; Cr, *Campylobacter rectus*; Fn, *Fusobacterium nucleatum*; Pg, *Porphyromonas gingivalis*; Tf, *Tannerella forsythia*.
*p value <.05 for intra-group comparisons.

Results

- Thirty-two patients completed the study (16 in the test group and 16 in control) although three patients (two in the test group and one in control) missed the three-month visit because of mobility restrictions related to the Covid-19 pandemic.
- At the one-week follow-up visit, six subjects (38%) in the test group and five subjects in the control group (31%) reported adverse events (gastrointestinal disorder, headache, metallic taste, and oral-tissue alterations). Fifteen subjects (94%) in the test group and 14 subjects (88%) in the control group completed the seven-day course of adjunctive systemic medication as prescribed.
- After 12 months, the test treatment resulted in statistically significantly greater PPD reduction (2.53 vs. 1.02mm), CAL gain (2.14 vs. 0.53mm) and radiographic bone gain (2.33 vs.1.13mm) compared with the control treatment.
- A division into moderately deep (5-6mm) and deep (>6mm) PPD categories yielded statistically significant differences favouring the test group in all variables except recession, after three and six months at moderately deep sites.
- Microbiological findings showed a greater decrease in the detection of *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Campylobacter rectus* in the test group compared with the control group.
- Treatment success after 12 months amounted to 56.3% in the test group and 25% in the control group. No implants were lost during the study.

Limitations

- The potential influence of the inclusion of more favourable bony-defect configurations may have affected the clinical and radiographic outcomes.
- Detailed information about the surface characteristics of the treated implants is missing. Because of surface characteristics, decontamination of implants with non-modified (machined) surfaces might be more effective compared with that of implants with modified (micro-rough) surfaces.
- Adjunctive antibiotics may not be indicated in the management of initial stages of peri-implantitis as clinical success may be achieved with non-surgical therapy alone. In advanced cases of peri-implantitis, additional surgical therapy may be indicated irrespective of the use of adjunctive antibiotics.
- The long-term effects of the adjunctive delivery of systemic antibiotics in the non-surgical management of peri-implantitis remain to be determined.

Conclusions & impact

- Improvements in clinical, radiographic, and microbiologic outcome parameters were observed in both treatment modalities. However, the outcomes with the adjunctive use of systemic metronidazole were more pronounced after 12 months.
- After 12 months, treatment success was achieved in more patients and implants in subjects receiving adjunctive systemic metronidazole.
- Because of the increase in antibiotic resistance, adjunctive delivery of systemic metronidazole for the non-surgical management of peri-implantitis should be carefully considered in daily practice on a case-by-case basis.

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