Persson GR, Salvi GE, Heitz-Mayfield LJA et al. Antimicrobial therapy using a local drug delivery system (Arestin) in the treatment of peri-implantitis I: microbiological outcomes. Clin Oral Imp Res 2006; 17: 386-393. (35 ref.)

Purpose: To assess, in cases with peri-implantitis, the anti-bacterial effects of the adjunct local administration of minocycline (Arestin) microspheres over a 12-month period.

Materials and Methods: Patients were screened for the presence of one osseo-integrated titanium implant with at least 2 mm radiographic alveolar bone loss around the implant between the time of implant placement to the time point of study enrollment. Patients who had been prescribed local or systemic antibiotics and/or anti-inflammatory drugs for at least 6 months or longer, who were allergic to tetracycline, and/or who required antibiotic prophylaxis, were excluded from this study. Eventually, twenty-five (12 females, 13 males; age range: 35-75 years) systemically, nonpregnant adult subjects with evidence of peri-implantitis were selected for this clinical study. Informed consent was obtained from all subjects. The study protocol was approved by the university's Ethics Committee.

At the initial visit, subjects underwent oral hygiene instructions, mechanical debridement, prophylaxis with a rubber cup, and topical application of 0.12% chlorhexidine. Next, clinical baseline measurements were collected to assess the probing depths, presence of bleeding upon probing, plaque index, and gingival recession. In addition, microbiological baseline samples were obtained at the implant site with the deepest probing depth using a sterile standard curette (1 implant/site.) Samples were then analyzed by the checkerboard DNA-DNA hybridization technique as developed by Socransky (1994). Subsequently, all selected implant sites received Arestin (1 mg minocycline). Subjects were instructed to refrain from toothbrushing for 12 hours and to avoid interproximal cleaning devices for 10 days. Subjects returned for clinical and microbiological assessments at days 10, 30, 60, 90, 180, 270, and 360. If deemed necessary, additional Arestin was administered at day 180 and/or day 360.

Findings and Conclusions: Throughout the 360-day period, implants could be classified into three groups: 1) implants that did not require rescue treatment (additional Arestin administration); 2) those that were rescued treated with additional Arestin; and 3) those that were lost from the study due to persistent active peri-implantitis after day 180. Only the first 2 groups were considered as successful treatment since the implants lasted throughout the 360 day period; the third group, on the other hand, was defined as implant failures.

At baseline, the DNA-DNA hybridization method failed to detect any differences in total bacterial DNA load (TBL), specific microbial counts, and bacterial loads by complexes between the three separate groups. Similarly, when subjects returned at day 180 for clinical and microbiological reassessments, no differences in TBL, specific microbial counts and bacterial loads by complexes were noted between the groups

Microbiological analysis of the successfully treated implants demonstrated that Arestin was able to maintain its effects up until day 180. This was evident by statistically significant reductions in TBL, *T. denticola*, *T. forsynthia*, and *P. gingivalis* from day 0-180 only. However, the effects of Arestin failed to last for the entire 360-day period. This was evident by the fact that significant reductions in TBL, *T. denticola*, *T. forsynthia*, and *P. gingivalis* were neither maintained, from the previous time frame, nor noted from day 270 to day 360.

By the end of the experimental period, successfully treated implants treated with Arestin demonstrated statistically significant reductions in *A. actinomycetemcomitans* levels only. Microbiological analysis of the implant failures failed to demonstrate any correlation between the baseline microflora present at failing implants and the predictable clinical outcomes. Likewise, no association could be found between the baseline microflora present at successful implants and the predictable clinical outcomes.

In all, implants that were diagnosed with peri-implantitis were successfully controlled by Arestin in 48% of subjects for 360 days, while 32% of the subjects demonstrated failure resulting in implant loss. Therefore, further studies are required to assess the predictive value of defined microbiota in combination with local antibiotic therapy.

Trejo PM, Bonaventura G, Weng D, Caffesse RG. Effect of mechanical and antiseptic therapy on peri-implant mucositis: and experimental study in monkeys. Clin Oral Impl Res. 17, 2006;294-304. (45 refs.)

Purpose: To evaluate clinically and histologically the effect of mechanical therapy with or without antiseptic therapy on peri-implant mucositis lesions in monkeys.

Materials and Methods: The sample size of the study included 9 cynomolgus monkeys, in which the mandibular second premolar and 1st and 2nd molars were extracted in order to allow for fixture placement. After 4 months of healing, full thickness mucoperiosteal flaps were reflected in the edentulous areas and 2 ITI implants (solid screw implants 3.3 mm X 8 mm) were placed in both mesial and distal positions with at least 3 mm distance between the implants and the adjacent teeth. A total of 35 implants were placed and oral hygiene procedures (meticulous brushing and application of 0.12% chlorhexidine to the tissues) were employed in order to maintain a clinically healthy peri-implant mucosa. After 90 days of healing, a baseline examination was completed. The following clinical parameters were assessed: 1) modified plaque index (mPII); 2) gingival index (GI); 3) pocket depth (PD); 4) clinical attachment level (CAL); 5) recession (REC); and 6) bleeding on probing (BOP). REC, CAL, and PD were assessed using a plastic periodontal probe. Peri-implant lesions were created by cessation of plaque control procedures and the use of silk ligatures in order to promote plaque development circumferential the peri-implant mucosa. After induction of mucositis, each monkey was randomly assigned to one of the following 3 groups: 1) group A: mechanical cleansing group consisting of plaque removal with acrylic scalers and rubber cups; 2) group B: mechanical cleansing with the addition of antiseptic therapy consisting of local irrigation with 0.12% chlorhexidine and a local application of 0.2% chlorhexidine gel; and 3) group C: control group receiving neither mechanical nor antiseptic therapy. The procedures in groups A and B were performed for a period of 60 days. After peri-implant mucositis treatment and reestablishment of the plaque control regimen for a 2 month time period, clinical measurements were taken, and the monkeys were sacrificed and prepared for histological analysis. All histologic measurements were made under a light microscope and included the following: 1) the supra- or sub-mucosal position of the mucosal margin (MM) in relation to the implant shoulder; 2) the bone level in relation to the implant shoulder; 3) the soft tissue height from the mucosal margin to the first bone-to-implant contact; 4) the position of the peri-implant sulcus; 5) the connective tissue adaptation as determined by the distance from the apical termination of the junctional epithelium to the first bone-to-implant contact. Also measured histologically were the volume fractions of the mucosal tissues occupied by inflammatory cells, epithelial cells, vascular structures, and areas of connective tissue infiltration along the implant surface. The data collected were subjected to statistical analyses to assess the effect of mechanical therapy alone versus the effect of mechanical therapy with antiseptic therapy in the treatment of peri-implant mucositis.

Findings:
PD: The mean PD values after induction of peri-implant mucositis for the control, mechanical, and mechanical and antiseptic groups demonstrated a significant increased from baseline measurements of 1.78 mm, 2 mm, and 2.1 mm to 3.46 mm, 3.51 mm, and 3.7 mm, respectively. After 2 months of treatment, the mean PD values for groups A, B, and C were 1.68 mm, 2.1 mm, and 2.57 mm, respectively. The resultant reductions in PD at the end of the study period demonstrated that both treatment groups were statistically different from the control group; however, there was no significant difference between the treatment groups.
CAL: The mean CAL values after induction of peri-implant mucositis for the control, mechanical, and mechanical and antiseptic groups became worse from the baseline measurements of 2.64 mm, 2.97 mm and 3.09 mm to 3.96 mm, 3.81 mm, and 4.11 mm at mucositis, respectively. After 2 months of treatment, the mean CAL values improved to 2.63 mm and 2.59 mm for treatment groups A and B, respectively. The resultant gains in attachment at the end of the study period were 1.18 mm, 1.52 mm, and 0.83 mm for groups A, B, and C, respectively. Both the treatment groups demonstrated a statistical difference from the control group; however, the ANOVA test did not detect a significant difference between the treatment groups, while the *t*-test demonstrated that group B had a statistically greater gain in CAL than group A.

REC: The mean REC values after induction of peri-implant mucositis for groups C, A, and B were reduced from baseline measurements of -0.86 mm, -0.97 mm, and -0.99 mm to -0.49 mm, -0.3 mm, and -0.38 mm, respectively. All 3 values were found to be statistically different from baseline. After 2 months, group C demonstrated a mean REC of -0.55 mm and the mean REC values for the groups A and B increased to -0.95 mm and -0.48 mm, respectively. The increases in REC values at the end of the study were 0.65 mm, 0.1 mm, and 0.06 mm, respectively for groups A, B, and C. The greatest REC change was seen in group A (mechanical treatment alone).

PII and GI: No significant differences were demonstrated between the mPII and GI values between the treatment groups; however, both treatment group values differed from that of the control group. After the induction of mucositis in all 3 groups, the majority of sites harbored a plaque score of 2. After treatment, 83.3% of the group A sites and 93.1% of the group B sites had a plaque score of 0. In contrast, group C demonstrated only 1.5% of the sites with a plaque score of 0. All 3 groups demonstrated severely inflamed gingiva (GI=3) when mucositis was induced. After treatment, groups A and B demonstrated excellent gingival conditions. A GI score of 0 was seen in 76.4% of sites treated mechanically and in 73.6% of sites treated with combination therapy. In the control group, only 6% of the sites demonstrated a GI score of 0.

Histometric results: The total height from the MM to the first bone-to-implant contact was roughly equal for the groups A (2.93 mm), B (3.01 mm), and C (2.98 mm). The height of the pocket/junctional epithelium was 2.12 mm and 2.1 mm for the treatment groups which was roughly the same for the control group (2.25 mm). The height of the connective tissue was demonstrated to have varied by less than 0.2 mm between the groups.

Morphometric results: The control group demonstrated the greatest percentage of inflammatory cells and vascular changes. The total infiltrated connective tissue amounted to 57.4%. The infiltrated connective tissue demonstrated in groups A and B amounted to 26.9% and 34.2%, respectively. The proportion of epithelial cells examined in the control group was statistically lower than the proportion of epithelial cells found in both treatment groups.

Conclusions: Induced peri-implant mucositis lesions with pocket depths of 3-4 mm responded favorably to mechanical therapy, regardless of the use of chlorhexidine. Both treatment groups resulted in significant improvements in peri-implant parameters, and gingival health surrounding the peri-implant mucosa. Although the mechanical plus chlorhexidine group demonstrated a greater gain in attachment with less recession than the implants treated by mechanical treatment alone (i.e. 1.52 mm vs. 1.18 mm and 0.1 mm vs. 0.65 mm), these differences did not translate into a clinical benefit. Histologically, both treatment modalities resulted in minimal inflammation compatible with health of the peri-implant mucosa.

Trejo DM, Bonaventura G, Weng D et al. Effect of mechanical and antiseptic therapy on peri-implant mucositis: An experimental study in monkeys. Clin Oral Impl. Res 2006; 294-304.

Purpose: To evaluate clinically and histologically the effect of mechanical therapy with with or without the use of adjunctive antiseptic therapy on peri-implant mucositis lesions.

Materials and Methods: Nine cynomolgus monkeys were used for this study. Two ITI implants were placed into each side of the mandible, after 90 days of healing, peri-implant lesions were induced by placing silk ligatures for 1 week, allow plaque accumulation for 2-weeks and then ligatures were placed again for additional 3-weeks. At the end of the plaque accumulation period and induction of mucosistis, the ligatures were removed and a second clinical examination was performed, when the monkeys were randomly assigned to one of the following groups: Group A (Mechanical cleansing without antiseptic therapy), Group B (Mechanical cleansing with CHX 0.12% irrigation and CHX 0.2% gel application or Group C (Neither mechanical or antiseptic therapy was administrated). The maintenance protocol was as follows: for Group A (Toothbrushing 4X week with water for 60 days), Group B (Mechanical debridement plus toothbrushing 4Xweek with CHX, and application of PlakOut gel each time for 60 days and Group C (None). At the end of the maintenance the animals were sacrificed and histological evaluation made.

Findings and Conclusions: Mean PD values at mucositis were 3.5, 3.7 and 3.4mm and CAL were 3.8, 4.1 and 3.9 mm for groups A, B and C respectively. Anova mean changes in PD and CAL after treatment were not statistically significant between groups. Only a P value of 0.01 was observed between the control and the treatment group. Data obtain from the T-test, showed no statistical significant between groups A and B for PD reduction but was significant for CAL ($P<0.03$). It was observed that Group A showed more recession and less differences in CAL gain than Group B. Histopathological evaluation revealed no statistical significant differences between treatment groups for any linear measurement. The inflammation level was observed to the more significant in the Group C than Group A and/or B. ($P<0.01$). The treatment groups showed the same level of low inflammation after 2 months of treatment. The results of this study reveals that the mechanical therapy with or without the combination of antiseptic therapy, showed to harvest lower inflammation compatible with health and the mechanical effect alone is sufficient to achieve clinical and histologic resolution of the lesions.

Render S, Lessem J, Dahlen G, et al. Topical minocycline microspheres versus topical chlorhexidine gel as an adjunct to mechanical debridement of incipient peri-implant infections: a randomized clinical trial. J Clin Periodontol 2006;33:362-269. (32 refs.)

Purpose: To study the clinical and microbiological results during a period of 12 months after application of Arestin as an adjunct to mechanical treatment of peri-implant infections compared with an adjunctive treatment using 1% CHX gel application.

Materials and Methods: 32 patients, 41-75 years of age, participated in the study. Inclusion criteria were 1) the presence of bone loss limited to ≤ 3 threads around Branemark implants, 2) one or more peri-implant sites with PD≥4mm, 3) the presence of anaerobic bacteria, and one or more of the following species: P. gingivalis, P. intermedia, P. nicgrescens, T. forsythensis, A. actinomycetemcomitans, or T. denticola. Full-mouth (FMX) plaque score, FMX bleeding score, local plaque score, PD, bleeding on microbial sampling, and BOP were measured at baseline. Subgingival microbial sampling was also performed from the deepest site. Supra- and subgingival calculus and plaque was removed from implant surfaces. Patients were randomly assigned to minocycline or CHX treatment. At days 10, 30, 60, 90, 180, 270, and 360, local plaque scores, PD, and BOP were recorded. Microbial samples were obtained at days 10, 30, 90, 180, and 360. Microbial samples were processed and culture analysis was performed.

Findings: 2 patients with the CHX group were excluded because of use of systemic antibiotics. The mean PD for the 4 surfaces of implants at screening was 3.9mm for both the CHX and minocycline groups. At 12 months, the PD remained the same for CHX groups, while the depth was reduced to 3.6mm for the minocycline group. PD for the deepest sites at screening averaged 5.1mm for the CHX group and 5.0mm for the minocycline group. At 12 months, the corresponding depths were 4.9mm and 4.4mm, respectively. The reduction of PDs from baseline was significantly greater for the minocycline group. Also, the reductions of bleeding on probing/microbial sampling scores from baseline were significantly greater for the minocycline group than for the CHX group after 1, 2, 3, and 6 months. The microbial analysis revealed similar longitudinal effects of the 2 antimicrobial agents. The mean bacterial values were the highest at baseline and gradually decreased during the experimental period. No statistical significance was obtained between the 2 antimicrobials for any bacteria and at any time point.

Conclusions: The use of a local antibiotic as an adjunct to mechanical treatment of incipient peri-implantitis lesions demonstrated improvements in probing depths that were sustained over 12 months.