Spontaneous progression of peri-implantitis at different types of implants. An experimental study in dogs. I: clinical and radiographic observations

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Abstract
Aim: The aim of the present study was to analyze tissue reactions to plaque formation following ligature removal at commercially available implants exposed to experimental peri-implantitis.

Material and methods: Six Labrador dogs about 1 year old were used. All mandibular premolars and the three anterior premolars in both sides of the maxilla were extracted. After 3 months four implants representing four different implant systems with different surface characteristics – implant group A (turned), B (TiOblast), C (sandblasted acid-etched; SLA) and D (TiUnite) – were placed in a randomized order in the right side of the mandible. Three months after implant installation experimental peri-implantitis was initiated by placement of ligatures in a submarginal position and plaque accumulation. At week 12, when about 40–50% of the supporting bone was lost, the ligatures were removed. During the subsequent 24-week period plaque accumulation continued. Radiographic and clinical examinations were performed during the ‘active breakdown’ period (plaque accumulation and ligatures) and the plaque accumulation period after ligature removal. The experiment was terminated at week 36.

Results: The bone loss that took place during the ‘active breakdown’ period varied between 3.5 and 4.6 mm. The additional bone loss that occurred during the plaque accumulation period after ligature removal was 1.84 (A), 1.72 (B), 1.55 (C) and 2.78 mm (D).

Conclusion: Spontaneous progression of experimentally induced peri-implantitis occurred at implants with different geometry and surface characteristics. Progression was most pronounced at implants of type D (TiUnite surface).

Peri-implantitis is a common biological complication in implant therapy (Berglundh et al. 2002; Fransson et al. 2005, 2008; Roos-Jansäker et al. 2006a). The clinical and radiographic features of this condition include bleeding on probing and loss of supporting marginal bone. While clinical studies may identify certain individuals who are at risk for peri-implantitis, such as periodontitis susceptible subjects (Hardt et al. 2002; Karoussis et al. 2003; Roos-Jansäker et al. 2006b), experimental studies provide information on histopathological characteristics of the lesions in peri-implantitis. Thus, in experiments in dogs and monkeys [Lindhe et al. 1992; Schou et al. 1993; Marinello et al. 1995; Gotfredsen et al. 2002; Lang et al. 2003] a ligature model was used to induce peri-implantitis. The placement of ligatures around the neck portion of the implants together with plaque accumulation resulted in the formation
of inflammatory lesions in the peri-implant tissues and loss of supporting bone.

A new experimental peri-implantitis model was described by Zitzmann et al. (2004). They examined tissue reactions during a 12-month period after ligature removal in experimental peri-implantitis. It was observed that bone loss did not only occur during the ‘active’ ligature period but also during the period of continuing plaque formation after the removal of ligatures. Although the amount of additional bone loss that took place during the 12-month period differed between implants and animals, the findings by Zitzmann et al. (2004) demonstrated that spontaneous progression of peri-implantitis may occur also after the removal of ligatures. This model of ‘spontaneous progression in experimental peri-implantitis’ was subsequently applied by Berglundh et al. (2007). They placed custom-made implants with different surface roughness in the mandible of beagle dogs. Experimental peri-implantitis was induced by ligature placement and plaque accumulation and the ligatures were removed when about 40% of the height of the supporting bone was lost. During the subsequent 5-month period of continuous plaque formation additional bone loss occurred at implants with a rough surface, while no further progression was observed at implants with a smooth surface. Berglundh et al. (2007) suggested that progression of peri-implantitis, if left untreated, is more pronounced at implants with a rough surface than at implants with a smooth surface. In this context it should be noted that the implants in the study by Berglundh et al. (2007) had either a polished or roughened sand-blasted acid-etched [SLA] surface, i.e. surface characteristics that were markedly different from those present at commercially available implants. The aim of the present study was therefore to analyze tissue reactions to plaque formation following ligature removal at commercially available implants exposed to experimental peri-implantitis.

Material and methods

Animals

The study protocol was approved by the regional Ethics Committee for Animal Research, Göteborg, Sweden. Six Labrador dogs about 1 year old were used. The outline of the experiment is presented in Fig. 1. During all surgical procedures general anaesthesia was induced with intravenously injected Propofol (10 mg/ml, 0.6 ml/kg) and sustained with \( N_2O:O_2 \) (1:1.5–2) and Isoflurane employing endotracheal intubation.

Surgery

All mandibular premolars and the three anterior premolars in both sides of the maxilla were extracted. After 3 months mucoperiosteal flaps were elevated in the right side of the mandible. Four implants representing four different implant systems with different surface characteristics [implant group A, B, C, D; Table 1] were placed in a randomized order. The implants in group A, B and D were provided with healing abutments, while a healing cap was placed on the implants in group C. The flaps were adjusted and sutured around the neck portion of the implants. Radiographs were obtained after implant placement using a customized film holder (Hawe Super Bite, Hawe Neos Dental, Bioggio, Switzerland). The radiographs were analyzed using an Olympus SZH10 stereo microscope (Tokyo, Japan) and digital images were obtained using a Leica DFC280 camera [Wetzlar, Germany]. Different landmarks were identified for each implant type. The abutment fixture junction was used as a reference point for implant categories A, B and D, while at the implants of type C the most apical point of the abutment screw was identified. The vertical distance between the landmark and the marginal bone level was assessed at the mesial and distal aspects of each implant using a Leica QWin software (Leica Imaging Systems Ltd., Cambridge, UK). Double assessments were made by two examiners with a 2-month interval.

The sutures were removed after 2 weeks and a plaque control program including daily cleaning of implants and teeth was initiated.

Experimental peri-implantitis

Three months after implant installation experimental peri-implantitis was initiated [Baseline; Fig. 1]. Thus, the oral hygiene procedures were abandoned, cotton ligatures were placed in a submarginal position around the neck portion of the implants [Lindhe et al. 1992] and a new set of

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<th>Table 1. Characteristics of implant types</th>
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Fig. 1. Outline of the study: Ligatures were placed at week 0 (Lig. +) and removed 12 weeks later (Lig. –). Radiographs (X) were obtained at weeks 0, 3, 6, 9, 12, 18, 26 and 36.
radiographs was obtained. The ligatures were replaced at week 3, 6, and 9. At week 12, when about 40–50% of the supporting bone was lost, the ligatures were removed. During the subsequent 24-week period plaque accumulation continued. Radiographic and clinical examinations were performed at weeks 3, 6, 9, and 12 of the period of plaque accumulation and ligatures (‘active breakdown’ period) and at weeks 18, 26 and 36 of the plaque accumulation period after ligature removal. At week 36 the dogs were euthanized with a lethal dose of Sodium-Pentothal® (Hospira Enterprices B.V, Hoofddorp, the Netherlands) and perfused through the carotid arteries with a fixative consisting of a mixture of 5% glutaraldehyde and 4% formaldehyde buffered to a pH of 7.2 (Karnovsky 1965). The mandibles were retrieved and stored in the fixative.

Data analysis
Mean values for all variables were calculated for each implant in each animal. Differences were analyzed using analysis of variance (ANOVA) and the Student–Newman–Keuls test. The null hypothesis was rejected at $P < 0.05$.

Results
Healing after implant placement was uneventful at all implant sites. Plaque formation during experimental peri-implantitis resulted in overt signs of inflammation in the peri-implant mucosa of all implants (Fig. 2). During the period of plaque formation after ligature removal one implant of type A and one implant of type D were lost. The implant of group A was lost on week 26 and the implant of group D was lost week 35 of the experiment.

Radiographs from the different implant sites at ligature placement (baseline), ligature removal (week 12) and biopsy (week 36) are presented in Fig. 3. The results from the radiographic measurements are reported in Table 2. For the two implants that were lost during the experiment, the radiographic bone loss was judged to encompass the entire intra-osseous portion of the lost implants of type A and D on week 26 and 35, respectively.

During the 3 months of the ligature period of ‘active breakdown’ the mean bone loss was 3.53 mm for the implants in group A, 4.19 mm for the group B implants, 4.68 mm for the implants in group C and 3.58 mm for the group D implants (Table 2). The additional bone loss that occurred during the plaque accumulation period after ligature removal, i.e. between week 12 and 36, was 1.84 mm for implants in group A, 1.72 mm for implants in group B, 1.55 mm for the category C implants and 2.78 mm for the implants in group D (Fig. 4 and Table 2). The difference between the group C implants and the implants in group D was statistically significant.

The results from the reproducibility assessments of the radiographic measurements are reported in Tables 3 and 4. The intra-examiner evaluation revealed small differences between the two assessments. The variance and standard deviation (SD) were 0.09 and 0.29 for examiner 1 and 0.04 and 0.21 mm for examiner 2, respectively. The inter-examiner variance and SD were 0.05 and 0.23, respectively.

Discussion
In the present study tissue reactions that occurred following ligature removal at implants subjected to experimental peri-implantitis were analyzed. The different types of implants included in the experiment, which differed with regards to geometry and surface characteristics, exhibited
The new experimental model of ‘spontaneous progression of peri-implantitis’ described by Zitzmann et al. [2004] and Berglundh et al. [2007] was applied in the present experiment. Thus, the ligatures were initially forced into a position apical to the mucosal margin and a ‘pocket’ between the implant and the mucosa was thereby created. As previously demonstrated [Lindhe et al. 1992], the mechanical trauma produced by the ligatures together with plaque accumulation resulted in the establishment of large inflammatory lesions in the adjacent peri-implant tissues and substantial bone loss. When about 30–40% of bone loss had occurred in the present experiment the ligatures were removed and, hence, during the subsequent 6-month period of continuing plaque formation no mechanical trauma remained in the ‘pocket area’ of the different types of implants. The additional loss of supporting bone that occurred during this 6-month period was therefore regarded as a result of ‘spontaneous’ progression of the peri-implantitis lesions. In the study by Berglundh et al. [2007] referred to above, tissue reactions at custom-made implants with either polished or roughened SLA surfaces were examined. It was reported that spontaneous progression of peri-implantitis was more pronounced at the implants with the rough surface than at the implants with the smooth surface. The difference in surface roughness, as expressed in Sa values [Wennerberg & Albrektsson 2000], between the implant types in the study by Berglundh et al. [2007], however, was in relative terms large. Thus, the Sa values were 0.35 μm for the polished implants and 2.29 μm for the roughened SLA implants.

In the present study commercially available implants were used. The surface roughness, expressed in Sa values, varied between 1.0 and 2.0 μm for the implants of type B (TiOblast), C (SLA) and D (TiUnite) and between 0.5 and 1.0 μm for the implant type A (turned) [Albrektsson & Wennerberg 2004]. Despite the comparably small differences in surface roughness between the four implants types in the present study, spontaneous progression of experimental peri-implantitis was most pronounced at implant type D. The reason for this difference is not fully understood but may be related to other characteristics of the implant surface modifications than presented in Sa values.

Comparisons between different types of implants in experimental peri-implantitis were reported previously. Thus, Tillmanns et al. [1998] examined ligature-induced peri-implantitis at hydroxy-apatite (HA)-coated, titanium-plasma-sprayed (TPS) and turned implants in dogs. It was reported that no clinical, radiographic or microbiological differences were found between the implant types at 3 and 6 months after subgingival placement of cotton ligatures. Zechner et al. [2004] placed custom-made one-piece and two-piece implants with TPS surfaces in dogs. Experimental peri-implantitis was induced by double ligatures that were comprised of polyester sutures and thin stainless steel wires. The ligatures were placed at the level with or slightly below the mucosal margin and plaque was allowed to form on the implants during a 4-month period. The results from the radiographic and histological evaluations revealed that marked bone loss had occurred around the implants with ligatures. The findings reported by Tillmanns et al. [1998] and Zechner et al. [2004] are consistent with observations made in the present study and in previous experiments [Zitzmann et al. 2004; Berglundh et al. 2007] and demonstrate that spontaneous progression of peri-implantitis with additional loss of supporting bone. Progression was more pronounced at implants with a TiUnite surface than at implants with a Turned, SLA or a TiOblast surface.

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the amount of tissue destruction and bone loss that occur during a phase of ‘active breakdown’ depends on the presence and position of the ligature around the implant rather than the surface characteristics of the implant.

Experimental peri-implantitis at implants with different surfaces was also examined in a study by Shibli et al. [2003] and Martins et al. [2004]. They placed ligatures in a submarginal position around implants with either a HA-coated, dual-etched, TPS or a turned surface. New ligatures were placed in a further apical position after 20 and 40 days. It was reported that no differences were found regarding clinical, radiographic and microbiological characteristics between the different implant types after 60 days of ‘active’ breakdown. Martins et al. [2003] analyzed the same experimental material presented by Shibli et al. [2003] and Martins et al. [2004]. Thus, following the 60 days of ligature-induced breakdown at the four different types of implants all ligatures were removed. During the subsequent 12-month period supragingival plaque control was performed by daily scrubbing with 0.12% chlorhexidine and scaling of abutments once per month. No subgingival instrumentation was performed. The authors reported that marginal bone loss occurred also during the 12-month period after ligature removal and varied between 0.60 and 0.74 mm. The finding that progression of experimentally induced peri-implantitis took place after the removal of ligatures is in agreement with data presented in the current experiment. Although the period following ligature removal in the present study was shorter than in the experiment by Martins et al. [2003] (6 vs. 12 months) the amount of ‘spontaneous progression’ was considerably larger in the current trial. Thus, the additional bone loss that took place following ligature removal at implants A, B, C and D of the present material varied between 1.15 and 2.78 mm and was about two to four times larger than that reported by Martins et al. [2005]. The difference in spontaneous progression of peri-implantitis between the two studies may be explained by the fact that supragingival plaque control was performed after ligature removal in the study by Martins et al. [2005], while in the present experiment no plaque control procedures were applied during the corresponding period. Another explanation to the differences in marginal bone loss after ligature removal between the studies may be related to the bone level measurements at implants that were lost during the spontaneous progression period. Thus, in the study by Martins et al. [2005] 17 out of 36 implants were lost during the 12-month ‘chronic phase’. Implant loss occurred among all the different implant types but was most pronounced in the group of HA-coated implants (six out of nine). The lost implants in the study by Martins et al. [2005] may have been excluded from the bone level measurements. In the present study, however, only one implant from group A (turned) and one implant from group D (TiUnite) were lost during the spontaneous progression period. At these implants marginal bone loss was judged to encompass the entire implant length.

The accuracy of the radiographic measurements was evaluated in the present study. Thus, the intra-examiner and inter-examiner variations that were calculated from the double assessments were small and in line with data presented by Gröndahl et al. [1998]. They described inter- and intra-observer variability in radiographic bone level assessments at 172 implants. It was reported that the total inter-observer variation was about 0.14 mm with the intra-observer variation as its largest component (0.08 mm).

In summary, the current study demonstrated that spontaneous progression of experimentally induced peri-implantitis occurred at implants with different geometry and surface characteristics. Progression was most pronounced at implants of type D (TiUnite surface).

References


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