Bisphosphonate-coated titanium screws as dental implants in patients
Per Aspenberg*1, Jahanmehr Abtahi, Pentti Tengvall.
Orthopaedics, Linköping, Sweden
Per.Aspenberg@inr.liu.se

Background: Dental implants in the jaws bones carry very high loads. They normally need to osseointegrate for several months before an abutment can be connected and load-bearing can start. Shortening of this time, or even immediate load-bearing, would be a clinical advantage. As the implants are available for mechanical measurements (see methods) during the osseointegration process, they can serve to study implant fixation in humans in general. Most dental implant manufacturers have focused on implant surface to improve bone-to-implant contact, by e.g. blasting, acid etching or chemical modification.

Bisphosphonates act specifically on osteoclasts and inhibit resorption. They are used in many clinical settings, including prevention of osteoporosis, Paget’s disease and osteolysis associated with bone metastases. In the response to trauma, bone formation and resorption are not coupled. Thus, inhibition of resorption leads to more bone formed. They normally need to osseointegrate for several months before an abutment can be connected and load-bearing can start. Shortening of this time, or even immediate load-bearing, would be a clinical advantage. As the implants are available for mechanical measurements (see methods) during the osseointegration process, they can serve to study implant fixation in humans in general. Most dental implant manufacturers have focused on implant surface to improve bone-to-implant contact, by e.g. blasting, acid etching or chemical modification.

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Several animal studies have been published concerning improvement in mechanical fixation of screw-shaped implants by coating the surface with bisphosphonates. Bisphosphonate-coated dental implants in dog mandibles have shown increased bone density and bone formation (1). After several series of animal experiments in our laboratory (2), we tested bisphosphonate-coated dental implants in edentulous patients.

Methods: Five consecutive edentulous patients (mean age 66 years, non smokers) were included in this study. Brånemark implants, MK III Ti Unite 3,75 mm in diameter were used. Each patient received 6 control implants and 1 bisphosphonate-coated implant. The control implants were placed in position 13-23 according to the available bone height and ridge width, and were considered as sufficient for the clinical needs. Thereafter, the bisphosphonate-coated implant was placed in the premolar or molar region, minimum 5-6 mm distal to the last regular implant. The coated implants were 10 mm long. The other implants varied between 11.5 and 13 mm. The coating procedure was performed exactly as described (2). Briefly, a crosslinked layer of fibrinogen was covalently bound to the metal, and then small amounts of pamidronate and ibandronate were bound and adsorbed to the fibrinogen (implants so treated get a stronger bond to the fibrinogen). These preliminary findings warrant a randomised study.

The implants were evaluated with a resonance frequency analyser, type “Ostell” (Integration Diagnostics, Savedalen, Sweden). This was done peroperatively at insertion and at abutment connection after 6 months. The implant stability quotient (ISQ) was recorded. A change in the ISQ value is considered to reflect a change in implant stability (3). Measurements were repeated three times for each implant, with the transducer oriented perpendicular to the long axis of the implant. The mean of these measurements was recorded.

At abutment connection two of the bisphosphonate coated implants were removed en bloc and prepared for undemineralized histology.

This is a pilot study, but post-hoc, we tested the hypothesis that the mechanical fixation (increase in ISQ value) would be better for the bisphosphonate coated implants (see results).

Results: No complications were seen with the coated implants. Histology showed osseointegration. A total 105 radiographs (210 implant sites) were taken. Small changes occurred during the healing period in the marginal level bone loss, never exceeding 1 mm. No significant differences were found for this variable. The ISQ values for all implants ranged from 47 to 82, with a mean for all implants of 62 at insertion and 64 at abutment connection. ISQ-values for bisphosphonate-coated implants ranged from 51 to 76, with a mean ISQ of 58 at insertion and 69 at abutment connection. In all five patients, the bisphosphonate-coated implants had the largest increase in ISQ values, although in one there was a tie (Figure 1). The probability for this occurring by random is (1/7)^5 = 1/16,807. With correction for the tie it is still less than 0.01.

Discussion: Resonance Frequency Analysis (RFA) is a useful instrument for noninvasive monitoring of implant stability in vivo. The reported ISQ levels for successfully integrated implants range from 57 to 82, with a mean ISQ of 69 after 1 year of loading (4).

The ISQ values reflect several aspects of fixation. The most important is thought to be the height of the implant extending out of the bone. Probably, the quality of the fixation in the marginal bone is also important. The change over time is thought to reflect the quality of the fixation better than the absolute values (3). We therefore chose to look primarily at this variable.

The higher increase in ISQ for the bisphosphonate coated implants could indicate that the coating had improved the fixation in the same way as in animal models. However, as the study was not blinded, other explanations are possible. Because the site used was less favourable for bridge fixation, there is little experience in the interpretation of ISQ values from this region. It is possible that a larger increase would be a normal phenomenon here.

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