

Locally Delivered Alendronic Acid Enhances Bone Formation Around Porous Titanium Implants

+Pura, J; Lim, LZ; Bobyn, JD; Bobyn, KM; Tanzer, M
+McGill University, Montreal, Quebec, Canada

Introduction:

Fixation of orthopaedic implants by bone ingrowth has been shown to reliably result in stable and lasting fixation. However, results are less successful in challenging scenarios such as revision surgery, trauma and tumor reconstruction. One approach to enhancing biologic fixation is to utilize bisphosphonates, which partially suppress the resorptive phase of bone remodeling, thereby tipping the balance toward a net increase in bone formation. The systemic effects of the drug can be eliminated by locally delivering the drug directly from the implant to the surrounding bone. The bisphosphonate, alendronic acid (AA) is of particular interest as this drug has a long history of clinical use. The purpose of this study was to determine the effect of locally delivered AA on the biologic fixation of porous titanium implants using a canine femoral implant model and three different drug doses. Specifically, we looked at the effect of varying doses of AA on bone ingrowth, bone apposition, and peri-implant bone formation around porous coated canine implants.

Materials and Methods:

Cylindrical implants (9 mm in diameter, 90 mm in length) were fabricated with a solid titanium core and an outer random porous structure using a metal laser sintering technique (provided by Pipeline Biomedical). The porous layer had an average porosity of 65% and mean pore size of 400 μm . All implants had a thin (15 μm) plasma-sprayed coating of hydroxyapatite (HA) to permit binding of the AA to the implant. Alendronic acid (AA) in aqueous solution was evenly applied onto the surface of each implant in a drop-wise fashion. Three AA doses were used: 0.5 mg, 1.5 mg and 4.5 mg. The implants were specifically formulated to reproducibly produce a biphasic elution of AA within and around the outer porous structure. The implants were dried, sterilized, and surgically inserted within the femoral intramedullary canal of 15 large (35 - 45 kg) adult mongrel dogs using a procedure like an open intramedullary nailing (approved by institutional ethics board). In each case, one femur received the AA-dosed implant while the contralateral femur received an identical implant without AA (control). The femora were harvested at 12-weeks and radiographed before being embedded in acrylic for undecalcified histology. Thin section histology enabled quantification of peri-implant bone formation, bone apposition and bone ingrowth using backscattered scanning electron microscopy (BSEM). Statistical comparisons between control/AA-dosed implants and between the varying dosed implants were made using paired and unpaired student's t tests, with $p < 0.05$.

Results:

Contact images consistently revealed more bone surrounding and in contact with the porous implants dosed with AA compared with controls. Quantification of BSEM

images demonstrated that the peri-implant bone was greater for all doses of the AA loaded implants as compared to controls. Peri-implant bone in the AA loaded implants was 42.1% ($p=0.18$), 96.5% ($p=0.04$) and 125.9% ($p=0.04$) greater than that in controls for the 0.5 mg, 1.5 mg and 4.5 mg doses respectively. All doses of AA resulted in increased bone apposition, but the greatest effect was seen in the 1.5 mg dose ($p=0.05$). Apposition was 42.3% greater in the 0.5 mg implants ($p=0.15$), 73.2% greater in the 1.5 mg implants and 40.8% greater in the 4.5 mg implants ($p=0.15$) than their corresponding controls. The amount of bone ingrowth was found to be similar to the control implants in the 0.5 mg and 4.5 mg implants, but 31.1% greater in the 1.5 mg implants ($p=0.03$).

Discussion:

This study demonstrated the feasibility of enhancing bone formation around and within porous coated implants by controlled, localized elution of the bisphosphonate, alendronic acid. The porous titanium implants that were loaded with AA were associated with a greater amount of bone formation around and apposed to the porous implants at 12 weeks. The 1.5 mg AA dosage was associated with enhanced bone formation, both in and around the porous implant. The additional net bone resulting from AA elution, including the abundant supportive bone around the implant would effectively increase mechanical fixation. The positive effect with implant delivered AA at clinically significant time points indicates that local AA is a suitable adjunct therapy for challenging arthroplasty cases. Alendronic acid, with its short half-life and long history of safety, could be the preferred drug candidate for bisphosphonate loaded implants.