Introduction

Since the addition of hydroxyapatite (HA) coatings, fixation of uncremented implants has improved and their survival has increased. In spite of the positive clinical results, Vogely et al. showed in a rabbit infection model that HA-coated implants have a higher susceptibility for infection compared to uncoated titanium implants.

Local antibiotic delivery from the bone cement has proven its protective effect against infection for cemented implants. However, until now, strategies for local antibiotic delivery from uncremented implants have received little attention. This is related to the high temperatures used in applying HA, but also due to the low porosity of many implants, thereby reducing the potential antibiotic load. By using a porous, titanium foam implant with a biomimetic HA coating (PeriApatite), the antibiotic load can be improved such that adequate local concentrations are reached postoperatively. Previous research showed that it readily and completely releases both gentamycin and tobramycin'. It is hypothesized that by applying antibiotics to the PA-coated titanium foam implant, either the infection susceptibility or even the recurrence of infection in case of a revision procedure can be reduced.

In this study we investigated in an animal infection model, the efficacy of adding tobramycin to a PA-coated titanium foam implant in preventing implant related Staphylococcus infection; this in comparison to both PA-coated and uncoated implants.

Materials and Methods

We received approval for this study from the Animal Care and Use Committee of the Utrecht University. A total of 54 female NZW rabbits (mean weight 2970 gr) received a rod-shaped PeriApatite-coated (PA), uncoated (Ti) or Tobramycin-PeriApatite-coated (PA-Tobra) titanium foam implant (Ø 4.5mm, length 1.2cm) in the medullary canal of their proximal left tibiae (Figure 1). Each group was divided in 3 subgroups (n=6), which were contaminated with 3 different concentrations of S.aureus. All rabbits had a follow-up of 28 days.

Figure 1. Left: PA-coated implant; Right: infected tibia after 28 days, implant in situ.

Surgery: Surgery was performed under inhalation anesthesia and aseptic conditions. With a medial parapatellar incision, the knee was opened and anterior to the ACL the tibial canal was entered. By drilling, an opening of 4,5mm was created. Subsequently, the canal was rinsed with 10ml PBS using a tissue grinder. Serial 10-fold dilutions were made and plated on blood agar plates. After an overnight incubation at 37°C the number of viable bacteria were counted. For each sample the number of viable bacteria per gram of bone was calculated (CFU/gr).

Statistical analysis: Results are reported as mean±SEM. For the outcome infection (yes or no) we used logistic regression analysis. For other outcomes we used a two-way ANOVA. P<0.05 was considered significant.

Results

One rabbit (PA, 10E+04 CFU) died after 6 days because of septicemia. Because of the short follow-up, this rabbit was excluded from the analysis. All other rabbits recovered well from surgery. After 7 days, the ESR and WBC showed a significant increase for both the PA and Ti group compared to the PA-Tobra group (p<0.002), in which the ESR and WBC remained normal. The ESR and WBC returned to normal in the subsequent weeks. Weight loss after 28 days for the PA, Ti and PA-Tobra groups was 188±66, 161±51 and 6±16 grams respectively (p=0.008).

Based on the bacteriological cultures of bone samples 10 of 17 rabbits (59%) in the PA group and 12 of 18 rabbits (67%) in the Ti group were considered infected after 28 days. In the PA-Tobra group 2 of 18 rabbits (11%) were infected, which was a significant reduction (p=0.001) compared to both other groups. None of the control tibiae showed bacterial growth. The actual number of CFU’s cultured was also significantly less in the PA-Tobra group compared to both other groups (p=0.003) (Figure 2). No significant differences were observed between the PA and Ti-group.

Discussion

Although it did not prevent infection in all rabbits, the addition of tobramycin to the PA-coated implants significantly reduced the infection susceptibility, compared to both PA-coated and uncoated implants. Apart from reducing the number of infections, it also significantly reduced the number of bacteria found in infected cases. The difference in infection susceptibility between HA-coated and uncoated implants, which was reported previously, was not confirmed in this study.

We can conclude, that the application of tobramycin to PA-coated titanium foam implants appears to be an easy and effective local antibiotic strategy for uncremented implants in the prevention of Staphylococcal infections. Its efficacy against other microorganisms and in case of a revision remains a topic for further research.

References