GENTAMICIN-COATING OF CEMENTLESS PROSTHESES LEADS TO IMPROVEMENT OF INFECTION PROPHYLAXIS IN RABBITS

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Introduction
Infections remain a critical issue in total joint arthroplasty. Addition of antibiotics to bone cement was shown to significantly improve antimicrobial prophylaxis in cemented joint arthroplasty. In cementless joint arthroplasty a comparable local antibiotic has not been possible yet. The aim of the current study was to investigate the antimicrobial effect of two different combined gentamicin-hydroxyapatite coatings for cementless prostheses in a rabbit infection model.

Materials and Methods
The coating consists of a 5µm thin HA layer over which further coatings, e.g. gentamicin, RGD-layers, and combined gentamicin-RGD-layers can be applied. HA coating process is done by an electrochemical followed by inkjet process for gentamicin coating both at 37 °C. The study protocol was approved by the local animal care committee. Staphylococcus aureus with a dose of 10^7 CFUs was inoculated into the intramedullary canal of the tibia of 30 rabbits followed by the implantation of standard hydroxyapatite (HA) K-wires, K-wires coated with a gentamicin-hydroxyapatite combination, and coated with a RGD-gentamicin-hydroxyapatite combination in 10 rabbits, respectively. The animals were sacrificed after 28 days and X-ray, histological and microbiological methods by agar plating and DNA-pulse field gel electrophoresis were carried out on the bone and on the removed K-wire itself to detect infection. Statistical analysis was done using a two sided Chi-square-test. p- values < 0.05 were considered to be statistically significant.

Results
Two animals in the control and one animal in the HA-gentamicin group died of acute diarrhea on post-operative day 2 which was not related to surgery or potential K-wire associated infection. Infection rates were 88% (8 of 9 animals) for the standard HA, 0% (0 of 9 animals) for the HA-gentamicin and 0% (0 of 10 animals) for the HA-RGD-gentamicin group. There was a highly statistically significant reduction of infection rates by both gentamicin-coating types compared to standard HA-coating (p < 0.001). There was excellent correlation between the agar plating findings for the K-wire on one side and for the bone samples on the other side. In all cases when there was positive culture growth on the agar plates of the rolled out K-wires there was also positive growth of the corresponding bone samples from the same animals showing that viable bacteria in this model of implant-related infections are found both on the K-wire itself and on the surrounding host bone.

Discussion
HA coating is brought by plasma spraying technology onto the surface of the implant, making additional incorporation of other biologic active molecules - e.g. antibiotics - impossible due to the high processing temperatures. This is the main reason why antibiotic coating of cementless prostheses has not been introduced in clinical practice yet. There are several studies reporting on the in vitro release kinetics for vancomycin, tobramycin and for several other antibiotics from HA-coated titanium implants coated by a “biomimetic” process with temperatures of 37 °C. However, there are no published data on in vivo antimicrobial efficacy of these coatings in animal infection models.

In summary, the reported HA-gentamicin and HA-RGD-gentamicin coating showed a highly significant reduction in infection rates in a rabbit model with S. aureus without any infection in 19 animals of both gentamicin groups. Histology showed good new bone formation towards the implant indicating good bone ingrowth of the implant despite gentamicin coating. Comparable data have never been shown in another in vivo study before. The used rabbit infection model is suitable and reliable for such purposes. This gentamicin coating technology promises a new way in the prophylaxis of prosthetic infections in cementless joint arthroplasty for the future.