ABSTRACT INTRODUCTION: Patients with open fractures clearly show a high risk of infection (5-33%) due to bacterial contamination and soft tissue damage. The gram positive bacteria, Staphylococcus aureus and S. epidermidis, are the major causative agents of the bone disease osteomyelitis. Systemic application for treatment of osteomyelitis has been known for years, however, pathologic changes in bone and its surrounding tissues as well as particular attributes of Staphylococci, like switching the phenotype to the so called “small colony variants” (SCV), are complicating a sufficient antibiotic treatment. Antibiotic coated implants appear to be a promising tool to reduce these problems by stabilizing the fracture and treating infections without multiple following operations through high local concentration and continuous release of antibiotics at the side of infection. Aim of this study was to evaluate the development and time course of an osteomyelitis with or without local gentamicin administration by gentamicin coated implants in a rat infection model.

METHODS: All experiments were approved by the Animal Experimentation Ethics Committee of Muenster, Germany (Reg. No. 50.0835.1.0). 96 three-month-old Sprague Dawley rats were used for study purposes. Surgery of the left hind leg was performed as described elsewhere [1]. Animals were divided into three groups: without any implant (group I), receiving an uncoated (group II) or receiving a gentamicin coated implant (Group III). After opening the intramedulary cavity animals were infected by application of PBS containing S. aureus (ATCC 49230) with a concentration of 10^5 CFU (colony forming units) / 20µl. Group II and III obtained an uncoated or gentamicin coated 0.8 mm titanium Kirschner-wire respectively. Furthermore each group was divided into four different life spans (each with eight animals). After 3, 7, 14 and 28 days, animals were sacrificed, left tibiae were dissected under sterile conditions, cryogenic grinded and surrounding tissues as well as particular attributes of Staphylococci, like switching the phenotype to the so called “small colony variants” (SCV), are complicating a sufficient antibiotic treatment. Antibiotic coated implants appear to be a promising tool to reduce these problems by stabilizing the fracture and treating infections without multiple following operations through high local concentration and continuous release of antibiotics at the side of infection. Aim of this study was to evaluate the development and time course of an osteomyelitis with or without local gentamicin administration by gentamicin coated implants in a rat infection model.

RESULTS SECTION: Neither in cardiac blood nor in the kidneys any bacterial growth was found. Local infection was defined as bacterial growth out of bone meal and/or of roll over cultures of explanted K-wires, however the latter were superior. Only in group I, receiving no implant, infection was solely determined from bone meal. In this group S. aureus was seen in four of 32 animals (12.5 %). By contrast, the overall infection rate of animals received an uncoated implant (group II) was approximately 96.8 %. However, bacterial growth determined from bone meal showed a slight, non significant decrease in progression of time (Fig. 1). The comparison of microbiological signs of infection of animals treated with uncoated versus coated implants (Fig. 2) could show, gentamicin coated implants avoided infection up to 84.4 %. Adjusted with the overall infection rate of 96.8 % the protection rate drops to 83.9 %. Bacteria of the remaining five infected animals receiving a gentamicin K-wire were still sensitive for gentamicin. On species level, bacteria of all groups grown from bone meal or roll over cultures were positively tested for S. aureus. As shown in pulsfied electrophoresis for randomised samples, tested bacteria possessed clonal identity to the inoculated strain ATCC 49230. Independently of retention, neither S. aureus grown in presence of gentamicin nor randomised samples collected from the other groups were identified as SCVs.

DISCUSSION: Due to absent bacterial growth in both kidneys and cardiac blood, hemagogenic spreading of the induced infection was excluded and a local infection of the left tibia was approved.

Furthermore it could be shown, 10^5 CFU S. aureus were insufficiently to induce infections without implants, whereas equal concentrations S. aureus associated with uncoated K-wires achieved infection rates of approximately 97 %. Since animals of group I received no implants, infection could not determined by roll over cultures, which seemed to be more sensitive than bacterial count, so infection rate might be higher than indicated in here.

In progression of time, the infection rate of animals receiving uncoated implants was nearly consistent (Fig. 2), whereas bacterial count was slightly decreased (Fig. 1), suggesting infections became chronic. In contrast, gentamicin coated implants were able to avoid infection in approximately 84 %. Therefore antibiotic coated implants seem to be highly effective in prevention of osteomyelitis without induction of gentamicin resistance or induction of SCV phenotype.

REFERENCES:

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