12 Best Papers

[O114] INFECTED BONE TISSUE DECREASES THE PENETRATION OF CEFUROXIME

Mikkel Tøttrup[1], Mats Bue[1], Janne Koch [2], **Louise Kruse Jensen**[3], Pelle Hanberg[1], Bent Aalbæk[3], Kurt Fuursted[4], Henrik Elvang Jensen[3], Kjeld Søballe[1]

[1]Aarhus University Hospital, Department of Orthopaedic Surgery, Aarhus, Denmark
[2]Leo Pharma, Ballerup, Denmark
[3]University of Copenhagen, Department of Veterinary Disease Biology, Frederiksberg C, Denmark
[4]Statens Serum Institut, København S, Denmark

Aim: A reason for treatment failure, in cases of periprosthetic bone infections and osteomyelitis, may be incomplete or heterogeneous tissue distribution of antimicrobials to the affected bone. Decreased bioavailability has been demonstrated in healthy bones but never in pathological bone tissue. Therefore, the aim was to obtain pharmacokinetic parameters of cefuroxime in infected bone tissue by means of microdialysis in a porcine model of implant associated osteomyelitis

Method: An implant cavity of 4 mm in diameter was drilled 25 mm into the right tibial bone of ten pigs (30 kg/BW). Subsequently, a small steel implant (K-wire 2 x 2 mm) and 10^4 CFU of *Staphylococcus aureus* was inserted and injected into the implant cavity. Five days after inoculation, two additional drill holes of 2 x 25 mm were drilled into the trabecular bone tissue adjacent to the implant cavity and into the left uninfected tibia. After intravenous administration of 1500 mg of cefuroxime, the concentration was measured in plasma and in the three tibial drill holes for 8 hours. All measurements were performed with microdialysis. Post mortem, the presence of bone infection was assessed by computed tomography (CT) scans and cultures of swabs.

Results: Destruction of bone tissue was seen on CT scans around all implant cavities but not in the adjacent trabecular bone tissue of the right leg or in the left leg. All swabs from the implant cavity and 8/10 swabs from the adjacent trabecular tissue were positive for ***S. aureus***. Conversely, all swabs from the left tibia were negative. The area under the concentration-time curves differed significantly, with the lowest found in the implant cavity ($P<0.001$). Although not significant, cefuroxime penetration into the adjacent bone tissue was incomplete.

Conclusions: This is the first study to show, by microdialysis, that the destructive bone processes associated with implant associated osteomyelitis significantly impair cefuroxime penetration. Our results support the clinical conception of fast diagnosis and initiation of antibiotic treatment if surgery is to be avoided. It is of crucial importance to know the exact level of antibiotics, which actually reaches a pathological bone focus in order to obtain more targeted and effective antibiotic treatments of bone infections.

References: Effects of implant associated osteomyelitis on cefuroxime bone pharmacokinetics – assessment in a porcine model. JBJS 2016; 98: 63-69.