PLGA Encapsulating Antibiotic Loaded Titanium Prosthesis in Osteomyelitis Prevention in Rats

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ABSTRACT INTRODUCTION:
Implant-related infection is a catastrophic complication in orthopedic surgery as it may result in poor functional outcome, chronic osteomyelitis, prosthesis failure or even sepsis and death. Various local antibiotic delivery systems have been attempted, such as antibiotic-loaded bone cements, but the amount and rate of antibiotic release from bone cement is still not satisfactory.

Our previous in vitro results using double layers of poly(lactic-co-glycolic acid) (PLGA) encapsulations on antibiotic-coat-titanium discs had extended antibiotic releasing time without burst release up to 10 days. The purpose of this study continued our previous study to further test the efficacy of PLGA encapsulating antibiotic titanium pin in rats in preventing osteomyelitis.

METHODS:
Osteomyelitis rat model
36 male 12 weeks old Sprague-Dawley rats (Laboratory Animal Center, NCKU, Taiwan) were used in this study. The study and animal care protocols were approved by the Institutional Animal Care and Use Committee (IACUC) of the Laboratory Animal Center at National Cheng Kung University (Reg. No. 99208). This osteomyelitis model was built by injecting 10^7 CFU/0.5ml of Staphylococcus aureus of the bacterial suspension and implant materials into the bone marrow cavity through 18 G needle at hip joint. (Fig 1) A rat osteomyelitis model was confirmed by x-ray, micro-CT and histological staining. A 0.7 mm titanium pin was encapsulated with double layer PLGA/cefuroxime mixture for in vivo implantation. The rats were divided into S. aureus osteomyelitis (S.A.), titanium pin in osteomyelitis (SA+Ti), and PLGA encapsulating antibiotic titanium pin in osteomyelitis groups. The data were evaluated on postoperative 1, 4, and 7 weeks.

RESULTS:
The osteomyelitis in femur cannel was still persisting at postoperative 7th week from x-ray images. (Fig 3) The width ratio at P1, no significant differences were found in 1 and 4 weeks in all three groups; however, SA+PLGA/Cef group had significant reduction in width ratio. (Fig 4) The width ratio at P2, SA+PLGA/Cef group had significantly reduced in both 4 and 7 weeks after surgery. (Fig 4) Histology also revealed S.A+PLGA/cef group had less bone damage and less infection than S.A+Ti group. (Fig 5)

DISCUSSION:
The rat osteomyelitis model was established by directly injecting 10^8 CFU/0.5ml of Staphylococcus aureus into femur canal and confirmed by x-ray images. The implantation of pin into intramedullary canal of rat was feasible with low mortality which was similar to the implantation of hip prosthesis in human. The osteomyelitis rat was persisting in infection up to 7 weeks in pure titanium pin implantation group, which was confirmed by femoral shaft width ratio and pathology analysis. However, in PLGA/cefuroxime encapsulation group, the infection was significantly relieved.

SIGNIFICANCE:
This study successfully established osteomyelitis rat model and the anti-infection performance of double layer PLGA/ cefuroxime group was better than titanium pin group. The study provides a constructing concept of implant infection prevention in orthopedic surgeries.

REFERENCES: