HIGH DOSE, COMMON ANTIBIOTICS INHIBIT CELLULAR PROLIFERATION

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INTRODUCTION: Methylmethacrylate cement (PMMA) is widely used in joint replacement surgery as a depot of delivery for antibiotics. PMMA impregnated with antibiotics is currently used commonly for prevention and treatment of periprosthetic infection. Several studies investigating the in vitro elution rates of the common antibiotics mixed in PMMA or calcium sulfate, have demonstrated a marked variability in elution depending on the volume, exchange rate, and the physical environment. Although elution of antibiotics from PMMA usually shows potent bactericidal effects, the antibiotic concentration can reach intermittent systemic toxicity and prolonged local effects. The main objective of this study was to investigate whether local doses of various antibiotics theoretically released from PMMA had any effect on local cell populations. The study investigated the influence of various concentrations of three commonly used antibiotics, namely vancomycin, ciprofloxacin, and tobramycin on preosteoblast and prechondrocyte cells. The findings of this study have pertinent clinical relevance as osteoblast and chondrocyte proliferation are critical for the process of osseointegration of press fit components and fracture healing. These results are crucial for determining the optimal antibiotic composition of bone cement that would provide an ideal balance between the microbicidal effects and the host cellular toxicity.

RESULTS: The effect of Oflox on cellular morphology of MLO-A5 osteocyte-like cells and N1511 prechondrocyte-like cells was first studied. Osteocytes cultured with increasing dosages of Oflox showed a drastic change in morphology (Fig. 1), and cell numbers, as well as increased cytotoxicity with increased antibiotic dosages. By the MTT assays, MLO-A5 pre-osteocytes (A) and N1511 pre-chondrocytes (B) show increased cytotoxicity with increased antibiotic dosages.

DISCUSSION: This study highlights a few important findings. High local concentration of Cipro, and to a lesser extent Vanco and Tobra were seen to have detrimental effects on osteoblastic and chondrocytic cellular proliferation. Further, the morphology of these cells appeared to be influenced by the presence of antibiotics even at lower concentrations. Further studies are needed to determine the optimal concentration of antibiotics being impregnated into PMMA so that effective infection treatment can be achieved without imparting local cellular toxicity.

ACKNOWLEDGEMENTS: We gratefully acknowledge the Department of Defense DAMD-17-03-1-0713, and NCI R25 CA48010. Presented results are not the statement or policy of the funding agencies.