[O98] HYDROGEL IMPREGNATION OF BONE CHIPS ALLOWS PROLONGED CEFAZOLIN RELEASE

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Aim: To prevent infections after orthopedic surgery, intravenous antibiotics are administered perioperatively. Cefazolin is widely used as the prophylactic antibiotic of choice. Systemic antibiotic therapy may however be less effective in longstanding surgery where bone allografts are used. Bone chips have been shown to be an effective carrier for certain types of antibiotics and may provide the necessary local antibiotic levels for prophylaxis. To be efficient a prolonged release is required. In contrast to vancomycin with proven efficient prolonged release from Osteomycin, this has not been described for cefazolin. We developed a protocol to bind cefazolin to bone chips by means of a hydrogel composed of proteins naturally present in the human body.

Method: Three types of bone chips were evaluated: fresh frozen, decellularized frozen and decellularized lyophilized. Bone chips were incubated with 20 mg/ml cefazolin or treated with liquid hydrogel containing either 1 mg/ml fibrin or 1 mg/ml collagen and 20 mg/ml cefazolin. The cefazolin hydrogel was distributed in the porous structure by short vacuum treatment. Bone chips with cefazolin but without hydrogel were either incubated for 20 min- 4h or also treated with vacuum. Cefazolin elution of bone chips was carried out in fetal bovine serum and analyzed by Ultra Performance Liquid Chromatography – Diode Array Detection.

Results: Soaking of bone chips without hydrogel resulted in a quick release of cefazolin, which was limited to 4 hours. When vacuum was applied elution of >1 µg/ml cefazolin was measured for up to 36 hours. Combination with collagen hydrogel resulted in a higher cefazolin concentration released at 24 hours (3.9 vs 0.3 µg/ml), but not in a prolonged release. However, combination of decellularized frozen bone chips with fibrin hydrogel resulted in an initial release of 533 µg/ml followed by a gradual decline reaching the minimal inhibitory concentration for S. aureus at 72 hours (1.7 µg/ml), while not measurable anymore after 92 hours.

Conclusions: Processed bone chips with hydrogel-cefazolin showed a markedly prolonged cefazolin release. When combined with a fibrin hydrogel, high initial peak levels of cefazolin were obtained, followed by a decreasing release over the following three days. This elution profile seems desirable, with high initial levels to maximize anti-bacterial action and low levels for a limited time to stimulate osteogenesis. Further preclinical studies are warranted to show effectiveness of hydrogel-cefazolin impregnated bone chips.