IL-1 Receptor Antagonist Rescue Chondrocytes from Cellular Death Following Intraarticular Fractures in a Porcine Pilon Fracture Model

Tyler J Thorne, Dillon Christopher O'Neill[1], Eleanor Sato, Joseph Featherall, Lillia Steffenson[2], Willie Dong, Graham John Dekeyser, Aaron L Olsen, Justin Haller[2]
[1]Orthopedics, [2]University of Utah

INTRODUCTION:

We investigated 1) the percentage of chondrocytes undergoing apoptosis or necrosis on both the tibial plafond and talus at 24 and 48 hours following high-energy pilon fractures and 2) if an IL-1 receptor antagonist (IL-1Ra) can rescue chondrocytes from cellular death.

METHODS:

Of 14 porcine hindlimbs, 4 hindlimbs were used as controls, 5 were used as fracture models and 5 underwent fracture with treatment of 150 ng/ml of IL-1Ra. For each limb, 2 chondral samples were taken from the tibial plafond and the talus, within 5mm of the fracture. Samples were processed at 24 hours or 48 hours with Hoechst 33342 as a counter stain, FAM FLICA Caspase-1 probe for apoptosis, and 7-aminoactinomycin D (7-AAD) for necrosis (Figures 1-3). Confocal microscopy and subsequent cell counting were performed. Data was analyzed via ANOVA with Tukey post-hoc test.

RESULTS:

All control samples had chondrocyte survival rates >94%, necrosis rates <5%, and apoptotic rates <2%. All fracture models had significantly lower chondrocyte survival rates than the controls, while all treatment groups had greater survival rates than the fracture models (Table 1). At 48 hours both the talus and plafond fracture groups had the lowest chondrocyte survival rates 23%(SD 0.09) and 27%(SD 0.12) which was significantly lower than the 24-hour fracture groups 51%(SD 0.03) and 53%(SD 0.24). The treatment group had significantly increased survival rates, with talus and plafond fracture group survival rates at 24 hours ((0.80%(SD 0.12); 0.82%(SD 0.06)), and 48 hours ((0.77%(SD 0.06); (0.71%(SD 0.05)). At 24-hours, chondrocyte death was driven by necrosis (39-45%), while apoptosis increased from 4-7% at 24 hours to 15-18% at 48 hours (Figures 4-6).

DISCUSSION AND CONCLUSION:

Following pilon fractures, IL-1Ra increased chondrocyte survival rates by 42.9-44.3% and 89.8-108% at 24 and 48 hours, respectively. Early chondrocyte death is driven by necrosis, with apoptosis increasing by a factor of three at 48 hours.