

Local Administration of Clodronate, Simvastatin, and Hydroxyapatite in an Immature Piglet Model of Femoral Head Osteonecrosis for Legg-Calve Perthes Disease: A Pilot Study

Emil Varas, Joseph Panos, Christopher Nagelli, Kishore Rajendran, Paola Rullan Oliver, Harry Kwang-Woo Kim, Todd A Milbrandt, Emmanouil Grigoriou

INTRODUCTION: Legg-Calve-Perthes Disease (LCPD) accounts for >10% of hip arthroplasties performed annually and lacks an effective clinical treatment. The ischemic event results in necrotic debris and triggers an inflammatory response. Previous animal-model studies show that treatment with clodronate and simvastatin restore near anatomic shape of the femoral head. Preliminary studies have also shown that hydroxyapatite particles can enhance the compressive modulus without compromising injectability. We hypothesized that the addition of hydroxyapatite would aid in prevention of femoral head collapse.

METHODS: A validated piglet model of femoral head avascular necrosis was used, using one hip as control and inducing infarcts in the other. Treatment groups received an injectable simvastatin and clodronate, or the same treatment with hydroxyapatite. After three weeks, the femoral heads were harvested and scanned using a Micro-CT to study morphological changes. The femoral heads were segmented, and the femoral head bone volume (FHBV) was assessed.

RESULTS: Ten heads were assessed (five controls, five treated). The average FHBV for the controls was 1.97cm³ (range: 1.62 cm³ - 2.25 cm³). The hips treated with simvastatin and clodronate had an FHBV of 0.71 cm³ (range: 0.56 cm³ - 0.85 cm³), accounting for a 64% decrease compared to controls. Treatment with clodronate, simvastatin, and hydroxyapatite yielded an average volume of 1.19 cm³ (range: 0.63 cm³ - 2.33 cm³), a 39% reduction compared to controls. Despite a slightly higher volume in the hydroxyapatite group, both treatment groups had markedly decreased femoral head volume when compared to controls, while the hydroxyapatite group had better preservation of the epiphyseal contour.

DISCUSSION AND CONCLUSION: While a combination of simvastatin and clodronate, even when combined with hydroxyapatite, may provide some protective effects, it does not prevent femoral head collapse. Further femoral heads have already been treated and harvested and are undergoing analysis. Our study reveals preliminary findings of our experimental investigation of different combinations of local pharmacological agents on an immature piglet model.