Parthenolide Reduces Empty Lacunae And Osteoclastic Bone Surface Resorption Induced By Polyethylene Particles In A Murine Calvarial Model Of Peri-Implant Osteolysis

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INTRODUCTION:

Particle-induced osteolysis is a major cause of aseptic loosening and subsequent implant failure following total joint arthroplasty. Studies have shown excessive osteoclast bone resorption induced by particles is responsible for peri-prosthetic loosening. Parthenolide (PAR) significantly inhibits osteoclastogenesis *in vitro* [1]. *In vivo* and *in vitro* studies have demonstrated the effect of PAR blocking NF-κβ in lipopolysaccharide (LPS)-induced osteolysis mice [2] and synovial cells derived from RA patients [3]. The study aimed to determine the effects of PAR on bone volume (BV) and bone surface resorption as assessed by live-animal microcomputed tomography (μCT) and possible osteocyte death as indicated by empty lacunae histologically in polyethylene (PE) particle-induced calvarial osteolysis in mice.

MATERIALS & METHODS:

24 mice were scanned by μCT to determine baseline BV and calvarial bone surface features 7 days prior to the administration of particles. At day 0, PE at 2×10^8 particles/mL were implanted over the calvariae. 1mg/kg/day PAR was injected subcutaneously at days 0, 4, 7 and 10. Following sacrifice at day 14, μCT scanning was repeated. BV and surface resorption were assessed over a rectangular region of interest on the mouse calvariae. Quantification of surface bone resorption (resorption pit analysis) was performed on the three-dimensional (3D) μCT images using ImageJ. Serum was collected for CTX-1 and Osteoclast Associated Receptor (OSCAR) levels by ELISA. Statistical significance (p<0.05) between two groups was determined by student *t*-tests.

RESULTS:

μCT analysis demonstrated BV was increased overtime in all mice consistent with normal growth. The 3D images at day 14 showed pits on the calvariae of mice with PE. When compared to the control, PE significantly decreased BV (p=0.0368), increased surface bone resorption area (p=0.0022), and increased the percentage of empty lacunae (p=0.0043). Interestingly, PAR significantly reduced the resorption surface area (p=0.0022) and the percentage of empty osteocyte lacunae (p=0.0087) in the PE-calvariae, but it did not affect BV, serum CTX-1 or OSCAR levels.

DISCUSSIONS:

For the first time we have used μCT analysis to show that PAR treatment significantly reduces pit formation on the surfaces of the calvariae in the PE-induced osteolysis. However, this PAR treatment did not significantly inhibit PE-induced loss of bone volume.

CONCLUSION:

The ability of PAR to inhibit PE-induced surface bone erosion may better reflect the *in vivo* situation, where bone resorption occurs on the surface at the bone-implant interface and may also be related to the role of osteocytes in this pathology.

REFERENCES:

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