**Introduction**

Spinal fusion in the management of spinal disorders is a common procedure with more than 550,000 annual procedures in the US alone. Posterolateral fusion (PLF) is the most common type of lumbar spine fusion. The success rate ranges from 65-95% and therefore research has focused on increasing the rate and avoidance of donor site pain. Bone graft extenders, enhancers and substitutes have been extensively studied. Even though demineralized bone matrixes and growth factors are available for clinical use, there are FDA restrictions and the need for extensive research in enhancement of spinal fusion persists.

EPO is best known for its erythropoietic function and is intensively investigated in the survival of the cardiac muscle after myocardial infarct and neurons after trauma. Previous unrelated studies demonstrated EPO’s capability to induce angiogenesis and to promote endochondral ossification. Both of these processes are essential for new bone formation in spinal fusion. Thus, it seems of major interest to investigate the effect of EPO on early bone formation in PLF.

Our hypothesis was, that EPO improves the outcome of PLF. Bone healing increases either due to an indirect effect via angiogenesis and improved nutrition or direct effects through receptor enhanced survival and differentiation of bone generating cells.

Our objective was to determine the efficacy of EPO as an autograft enhancer and document its systemic effect in PLF rabbit model.

**Methods**

**Study design**

Twenty-two skeletally mature, male New Zealand white rabbits (3.5-4.5 kg) underwent uninstrumented PLF (L5-L6) as previously described. Autologous bone was harvested from the iliac crest bilaterally and consisted of 2 g per side. Eleven rabbits each were assigned to treatment and control group. This decision was based on power calculation (alpha = 0.05; power = 0.8; miredif = 0.2; sd = 0.25): 

\[ n = \frac{(1.96+0.842) \times (0.2^2/0.25^2)}{0.5^2} = 10.05. \]

Treatment consisted of s.c. injections of 250 IU/kg/day Epoetin beta (NeoRecormon, Roche, Denmark). The control group received saline injections of equal volume. The injections started 2 days preoperatively and continued until 17 days postoperatively. Injections were given without removing the animals from their cages.

The study was approved by the Danish Institutional Animal Care and Use Committee.

**Outcome measurements**

Blood samples were taken 3 days preoperatively and 2, 4 and 6 weeks postoperatively. Hemoglobin (Hgb), hematocrit (Hct), platelets (Plt) and white blood cells (Wbc) were measured to monitor EPO’s systemic effect. The recombinant human EPO (rhEPO) concentration was measured at the same time points using EPO ELISA kit (Roche Diagnostics, Denmark). CT scan (0.6 mm thick, non overlapping) was performed 6 weeks postoperatively. Only CT scans showing clear uni- or bilateral fusion were considered fused. The volume of the fusion mass was analyzed as previously described. All animals were killed after CT, and the lumbar spine removed.

The arthrodesed and adjacent segments were evaluated for motion with a manual flexion-extension movement in the sagittal plane. Only complete absence of motion was deemed as fused. Signs of infection were recorded. The spines were frozen in liquid nitrogen and an antero-posterior x-ray was taken (45 kV, 90 cm tube-plate distance). The spines were cut in the midsagittal plane and embedded in methylmethacrylate for μCT and histological evaluation. Two blinded observers performed mp, x-ray and CT analyses.

**Statistics**

Fusion mass volume and blood samples were analyzed by unpaired t-test and fusion rates by Fischer’s exact test. Results were considered significant at p<0.05. All means are shown ± standard deviation.