Insulin-mimetic Local Therapeutic Adjuncts for Enhancing Spinal Fusion in a rat model

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Introduction: Spinal fusion is a common treatment for many spinal disorders, and agents that can improve fusion rates and decrease time until fusion can help limit morbidity associated with pseudoarthrosis. Previous studies have found that insulin and insulin-like growth factor treatment can stimulate fracture healing in diabetic and normal animal models[1,2]. Our laboratory has previously demonstrated the ability of local insulin to enhance posterolateral fusion in a rat model[3]. Several metals, such as vanadium and zinc have been shown to exert insulin-mimetic effects in isolated cells, tissues and diabetic animal models[4,5]. The effects of vanadium have also been studied during fracture healing. When given systemically, vanadium increased bone mineral content and biomechanical strength in a femur fracture model of diabetic rats[6-8]. Also, local administration by introducing an intramedullary organic vanadium salt has been shown to enhance chondrogenesis and angiogenesis within 7-10 days post fracture, which increased mechanical strength at 4 weeks post-fracture[2]. We hypothesized that local administration of insulin-mimetic agents, zinc or vanadium, would enhance spinal fusion in a rat model.

Methods: 50 Sprague-Dawley Rats weighing approximately 500g underwent L4-L5 posterolateral intertransverse lumbar fusion. After decortication and application of approximately 0.3g of autograft per sided, one of five pellets were added to each fusion site: a low dose Vanadium Calcium Sulfate pellet (0.75 mg/kg), a high does Vanadium Calcium Sulfate pellet (1.5mg/kg), a low dose Zinc Calcium Sulfate pellet (0.5 mg/kg), a high dose Zinc Calcium Sulfate pellet (1.0 mg/kg), or a control of micro-recrystalized palmitic acid pellet. Systemic blood glucose levels were measured at 24 hours postoperatively. Animals were sacrificed at 8 weeks and analyzed qualitatively by two blinded independent observers with manual palpation and radiographic scoring, and quantitatively by microCT analysis.

Results: Compared with controls, the high dose zinc group demonstrated a significantly higher manual palpation grade (p=.008), radiographic score (p=0.05), and bone formation on microCT (172.7mm3 vs. 126.7mm3 for controls) (p<0.01). The low dose zinc trended towards significantly higher manual palpation (p=0.055), and radiographic scores (p=0.066) and had significantly more bone formed on microCT (172.9mm3) (p<0.01) compared with controls. The high dose vanadium had significantly higher manual palpation scores (p=0.002) and bone formation on MicroCT (170.8mm3) (p<0.01), and no difference in radiographic scores (p=0.270). Low dose vanadium had significantly more bone on microCT (172.9mm3) (p<0.05), trended towards higher scores on manual palpation (p=0.072) and had no difference on radiographic scores (p=0.807).

Discussion: Local insulin-mimetic agents applied to the fusion bed in a rat posterolateral lumbar fusion model appear to improve fusion rates. Previous studies have demonstrated the benefits of local insulin application in the same model, and it appears that zinc and vanadium have similar effects.

Significance: This is the first study to demonstrate that the application of an insulin-mimetic agent to the fusion bed increases rates of successful fusion.

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