Use of an antifibrotic agent improves the effect of platelet-rich plasma on muscle healing after injury


Basic science findings that could profoundly affect the treatment of a very common sports injury - Kelly Cunningham MD


Abstract

BACKGROUND: Muscle contusions are a common type of muscle injury and are frequently encountered in athletes and military personnel. Although these injuries are capable of healing in most instances, incomplete functional recovery often occurs because of the development of fibrosis in the muscle. We hypothesized that a combination of platelet-rich plasma (PRP) injection and oral administration of losartan (an antifibrotic agent) could enhance muscle healing by stimulating muscle regeneration and angiogenesis and by preventing fibrosis in contusion-injured skeletal muscle.

METHODS: Contusion injuries were created in the tibialis anterior muscles of mice. Two treatments were tested, alone and in combination: 20 μL of PRP injected into the contusion site one day after injury, and 10 mg/kg/day of losartan administered beginning three days after injury and continuing until the end point of the experiment. Muscle regeneration and fibrosis development were evaluated by histological analysis, and functional recovery was measured by physiological testing.

RESULTS: Muscle regeneration and muscle function were significantly promoted in the combined PRP + losartan treatment group compared with the other groups. Combined PRP + losartan treatment significantly decreased the expression of phosphorylated Smad2/3 and the development of fibrosis compared with PRP treatment alone, and it increased vascular endothelial growth factor (VEGF) expression and the number of CD31-positive structures compared with losartan treatment alone. Follistatin, a positive regulator of muscle growth, was expressed at a higher level in the PRP + losartan group compared with the other groups.

CONCLUSIONS: PRP + losartan combinatorial therapy improved overall skeletal muscle healing after muscle contusion injury by enhancing angiogenesis and follistatin expression and by reducing the expression of phosphorylated Smad2/3 and the development of fibrosis. These results suggest that blocking the expression of transforming growth factor (TGF)-β1 with losartan improves the effect of PRP therapy on muscle healing after a contusion injury.

CLINICAL RELEVANCE: These findings could contribute to the development of biological treatments that aid in the healing of skeletal muscle after injury.

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