Improving Recovery Following Recurrent Hamstring Injury Using an Angiotensin II Receptor Blocker: Two Case Studies

†Stem Cell Research Center, Children’s Hospital of Pittsburgh, Pittsburgh, PA
*Department of Orthopaedic Surgery, University of Pittsburgh, Pittsburgh, PA

INTRODUCTION
Hamstring muscle injuries are common in young competitive athletes. A recent study on National Football League training camp injuries reports hamstring injuries were the most common among muscle strain as well as the most severe. Recurrence is common, secondary to the pressure to return to play prior to complete healing of the injury, with a higher re-injury rate than any other type of injuries. Although muscles can undergo regeneration after injury, the healing process is slow and often culminates in incomplete functional recovery and formation of fibrosis.

A growing understanding of the cellular and molecular events that commonly occur during fibrosis in various tissues, including skeletal muscle, has provided a strong foundation for the development of effective therapies to prevent fibrosis and improve tissue healing. Because TGF-β1 plays such a crucial role in tissue fibrosis, particularly in skeletal muscle, it warrants attention as a key target for anti-fibrotic applications. Of the agents to block TGF-β1, Losartan potassium, a non-peptide molecule that works as an angiotensin II receptor blocker, is particularly attractive for clinical application as it is FDA approved and has minimal side effects. In a murine model, we have found that angiotensin receptor blocker-treated mice exhibited a histological, dose-dependent improvement in muscle regeneration and a significant reduction in fibrous tissue formation within the area of injury.

Given that Losartan has already been used clinically with an extremely safe side effect profile, we have conducted two case studies in young college athletes that sustained recurrent hamstring injuries and whose recoveries were safely improved with Losartan. This is an off-label use of Losartan (i.e.: the FDA has not approved labeling for the described purpose). Here we report the results obtained.

METHODS
Both subjects were submitted to the same protocol that is herein described: after obtaining the subjects’ informed consent for treatment, both subjects were started on a 30-day treatment course of Losartan at the manufacturer’s recommended oral dose of 50 mg per day. Both subjects were healthy and had none of the contra-indications for the use of Losartan. In addition to the medication, they underwent a routine rehabilitation program that gradually progressed to eccentric strengthening. The subjects reported no side effects while they were taking the study medication and remained normotensive throughout.

They were initially evaluated by clinical examination and were subsequently evaluated every 7 days with serial measurements (with a hand-held dynamometer - Lafayette Instrument Inc) of hamstring flexibility and strength as well as their blood pressure. Prior to the start of the medication the subjects were submitted to a magnetic resonance imaging (1.5T; GE-Sigma, Waukesha, WI, USA). After a period of 11 weeks the subjects underwent an isokinetic test (Biodex II) to better evaluate muscle strength compared to the non-injured side.

RESULTS

- Subjects

Subject #1: male, 21 years old, college athlete (football punter). He presented 10 days after an acute onset of “searing” pain in his left posterior thigh when he was kicking with his left leg. He referred a similar injury 5 weeks prior to the present injury.

Subject #2: male, 22 years old, college athlete (Ultimate Frisbee). He presented 4 days after an acute onset of pain in his left posterior thigh while he was sprinting. He referred two previous hamstring injuries (2 and 7 months prior to the present injury).

- MRI results (at time of injury)

Subject #1: Acute Grade 2 hamstring strain was observed with a partial thickness tear of the biceps femoris at the proximal myotendinous junction with surrounding edema without an associated avulsion fracture or hematoma.

Subject #2: Grade 2 strain with partial thickness tear of the left biceps femoris at the mid aspect, extends approximately 6 cm in the craniocaudal dimension.

- Hamstring flexibility and strength

Subject #1: By the third week after the injury, no deficit was evident in hamstring flexibility. By the ninth week, the isometric hamstring strength measurements at 30 and 90 degrees of knee flexion were 92 and 84% than the uninjured side respectively (Fig.1).

Subject #2: Also, by the third week after the injury, no deficit was evident in hamstring flexibility. By the ninth week, the injured side had a higher isometric hamstring strength measurement at 30 and 90 degrees of knee flexion. They were 132% and 110% than the uninjured side respectively (Fig.1).

- Isokinetic testing results

Subject #1: Eleven weeks after the injury, an isokinetic test of the hamstrings was performed showing an essentially normal result. Peak hamstring torque, on the uninjured side, was 96% of the injured side at 60 degrees per second and 107% of the injured side at 180 degrees per second.

Subject #2: Thirteen weeks after the injury, an isokinetic test of the hamstrings was performed showing an essentially normal result. Peak hamstring torque of the injured side was 96.3% compared to the uninjured side at 60 degrees per second and 97.3% of the uninjured side at 180 degrees per second.

DISCUSSION / CONCLUSION
We have described use of Losartan, which is an FDA-approved angiotensin II receptor blocker, to treat two healthy collegiate athletes with a grade 2 biceps femoris injury. The patients tolerated the course of Losartan well with no hypotension or any other side effects. Additionally, the patients demonstrated recovery of normal flexibility and strength compared to the contra-lateral leg. Both subjects were ready for return to sports in 9 to 11 weeks after injury.

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