INTRODUCTION

The administration of non-steroidal anti-inflammatory drugs (NSAID’s) is a common prescriptive therapy for acute and overuse tendon injuries. Although this class of drugs is known to inhibit the formation of inflammatory mediators, the primary therapeutic mechanisms have yet to be isolated. It has been hypothesized that NSAID’s may also possess additional beneficial mechanisms beyond the suppression of systemic inflammatory responses. This study utilizes a cultured tendon explant model to characterize the biomechanical effects of NSAID administration, in conjunction with daily rehabilitative loading, following a controlled compressive midsubstance tissue injury.

METHODS

Flexor digitorum profundus tendon specimens were sterilely isolated from the middle digit of White Leghorn chicken feet (48 day old). All tendon explants were clamped in serpentine grips, cultured in standard medium supplemented with antibiotics, and allowed to recover for 48 hours following isolation and handling.

Immediately following this recovery period, all samples were subjected to a calibrated 20 lb. (~4.0 MPa), 10 second, midsubstance compressive crimping injury (Minns and Muckle, 1982). At this time point, the specimens were divided into two treatment groups; one receiving daily rehabilitatory regimens (2 hrs., 0.25 - 3 MPa cyclical load at 0.5 Hz) and the other remaining in a continuous non-loaded condition. Tendons subjected to daily rehabilitation underwent treatment within a tissue loading device receiving waveforms produced via a pneumatic servo-valve.

The rehabilitation treatment group was further divided into two subsets (n=7/group): controls and Celebrex treated (5 µM). The non-loaded treatment group was divided into three subsets (n=7/group): controls, Celebrex treated (5 µM), and Piroxicam treated (5 µM). Media was supplemented with 2 µM arachidonic acid for 48 hrs. following crimping, with daily samples recovered during this time period being analyzed in duplicate for inflammatory mediators, prostaglandin E2 and nitric oxide, by ELISA and colorimetric assays. Following this period of arachidonic acid supplementation, media was replaced every 48 hours.

Tissue culture strain measurements were performed using video dimensional analysis of midsubstance suture markers immediately following injury, on day 8, and on day 14. Histological specimens were divided into 10mm segments and incubated with MTT for 4 hours to evaluate cell viability by colorimetric assay. Mechanical properties of the tendon specimens were evaluated by tensile failure tests utilizing cryogrips in
conjunction with video strain analysis of midsubstance suture markers.

RESULTS

In tests of nonviable tendons, the immediate effect of crimping was found to cause a significantly (P<0.05) higher strain at the failure load relative to uncrimped controls. Loaded Celebrex samples indicated a significantly lower strain at the immediate post-injury time point relative to the loaded controls. Collectively, all crimped samples revealed a significant increase in strain from the time point of injury through day 14. Non-loaded controls and Celebrex samples displayed significantly higher values in failure stress (Figure 1) and elastic modulus, relative to non-loaded Piroxicam specimens. MTT assays showed significantly higher cellular viability in compressed tissues relative to uninjured tissues, presumably due to cell proliferation. Specimens receiving NSAID treatment displayed significantly lower PGE\textsubscript{2} concentrations relative to controls.

Biomechanical failure data revealed no effects due to the daily rehabilitation loading, in contrast to earlier studies indicating decreases in mechanical properties due to stress deprivation (Hannafin et al, 1995). Failure data did reveal adverse drug treatment effects due to the NSAID Piroxicam, and displayed no changes resulting from Celebrex treatments. This data contradicts previous in vivo ligament studies (Elder et al, 2001; Dahners et al, 1988), indicating a need for further studies characterizing the effects of NSAID treatments on soft tissue injuries.

NSAID treatment was effective, in both loaded and non-loaded conditions, in inhibiting the production of the inflammatory mediator PGE\textsubscript{2}, as seen in the significant decreases in concentration immediately following the compression injury.

REFERENCES


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