Enhanced Flexor Tendon Healing Through Sustained Delivery of PDGF-BB

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INTRODUCTION: Prior studies have reported a high incidence of failure in the early period following flexor tendon repair [e.g., 1]. Adhesion formation between the repaired tendon and the digital sheath and repair site gapping can lead to loss of finger function and risk for tendon rupture. The delivery of growth factors during tendon healing can lead to improvements in the properties of the healing tissue [2]. The growth factor PDGF-BB has been shown to stimulate cell proliferation and matrix synthesis in vivo and in vitro [2, 3]. The goal of the current study was to determine the effect of PDGF-BB on intrasynovial flexor tendon healing. We hypothesized that sustained delivery of PDGF-BB would promote cell proliferation and collagen synthesis leading to improved biomechanical properties of the repair.

METHODS: Delivery system: A delivery system (DS) was used that provides for sustained growth factor administration by immobilizing high affinity heparin-binding growth factors, protecting them from degradation during the early intervals following delivery [4]. PDGF-BB release in the presence or absence of cells was examined in vitro using ELISAs. Animal model: To determine the effect of PDGF-BB on tendon healing in vivo, fibrin matrices loaded with 500ng (1.25µg/mL) PDGF-BB were implanted between repaired flexor tendon stumps of 28 dogs (“PDGF” group) [5]. The adjacent flexor tendon in each dog was injured and repaired and received either fibrin matrices without growth factor (“DS Control” group) and or no additional treatment (“Repair Only Control” group). Uninjured normal tendons were also used for some assays. Animals were sacrificed 7, 14, or 42 days after surgical repair. Biochemistry: Total DNA was determined as described previously (N=4 for 7 and 14 days, N=8 for 42 days) [3]. Reducible and stable non-reducible collagen crosslinks were quantified by cation-exchange and reversed-phase HPLC, respectively, as described previously (N=4 for 7 and 14 days, N=8 for 42 days) [3]. Biomechanics: Tendons were tested for range of motion (N=4 for 7 and 14 days, N=8 for 42 days) and in uniaxial tension (N=8 for 42 days) [6]. Functional properties (i.e., range of motion) were assessed using a motion analysis system (PC Reflex, Qualysys). Rotation of the proximal interphalangeal (PIP) joint, rotation of the distal interphalangeal (DIP) joint, and linear excursion of the flexor tendon were calculated. After range of motion testing, tendon specimens were pulled in uniaxial tension until failure (8500R; Instron Corp) [6]. A 1N preload was applied and the tendon was loaded at a rate of 0.375 mm/s until failure. Strain was measured at the repair site using a motion analysis system (PC-Reflex). From the force-elongation curves we determined maximum load, repair-site stiffness, repair site rigidity, and repair-site strain at 20N force.

RESULTS: Delivery system: Sustained release of PDGF-BB from fibrin matrices was achieved in vitro in the presence of cells (i.e., active release; Fig. 1) and in the absence of cells (i.e., passive release).

Biochemistry: DNA concentration in the repaired tendons was significantly elevated levels of DHLNL. PDGF treated tendons had a lower concentration of DHLNL than untreated repaired tendons at 42 days (Fig. 2). Biomechanics: PIP joint rotation and flexor tendon excursion were significantly higher in the PDGF-BB treated tendons compared to the repair alone tendons at 42 days (Fig. 3). Results for the delivery system control were similar to those for the repair only control, suggesting that the improvements in range of motion in the PDGF group were due to the growth factor and not due to the delivery system. There were no significant differences in tensile properties when comparing PDGF-BB to repair alone tendons (Table 1).

DISCUSSION: PDGF-BB enhanced flexor tendon healing:
1- The delivery system provided sustained release of PDGF-BB.
2- PDGF-BB accelerated the cell proliferation phase of healing, as evidenced by early increases in DNA.
3- Return to normal functional properties (i.e., range of motion and tendon excursion) was accelerated. Improved motion may have been due to the early restoration of the repaired tendon’s gliding surface. Improved motion was due to the PDGF-BB treatment, not due to the fibrin/heparin delivery system.
4- Tensile properties were not significantly improved with PDGF-BB treatment. The failure to achieve improvements in ultimate load, stiffness, and strain in the experimental group may have been due to sub-optimal PDGF-BB dosage or sub-optimal release kinetics.

ACKNOWLEDGMENTS: NIH R01 5R01AR033097.


Paper No. 233 • 55th Annual Meeting of the Orthopaedic Research Society