IMPROVED ENDOGENOUS INTRASYNOVIAL FLEXOR TENDON HEALING INDUCED BY MONOFILAMENT NYLON COATED WITH BASIC FIBROBLAST GROWTH FACTOR.

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Purpose: We have developed a monofilament nylon thread coated with basic fibroblast growth factor (bFGF) to deliver bFGF in the repaired tendon and to facilitate endogenous tendon healing. We investigated the usefulness of this thread on tendon repair model in vivo.

Methods: We employed the early active flexion exercise model using the flexor digitorum profundus of the rabbit’s hind limb. The tendons were repaired by end to end suture according to the modified method of Kessler (Y2), or interlace suture according to the method of Pulvertaft (Figure 4). The bioactive thread was soaked in bFGF solution (H-group: 2000μg/ml: total 15μg within repaired tendon tissue, or L-group: 400μg/ml: total 3μg). Basic FGF was released during 1 week (1w-group) or 3 weeks (3w-group). Four groups with bFGF (H-1w, H-3w, L-1w, L-3w) and a control group (the coated thread without bFGF) were compared at 1, 3 and 6 weeks after surgery. All sutured sites were examined macroscopically to confirm that the gaps were less than 3 mm, and microscopically after hematoxylin-eosin staining, in situ hybridization and immunohistochemistry. Ultimate load and rigidity of the repaired tendons were also evaluated. The experimental study was approved by the Institutional Animal Care and Use Committee of the School of Medicine. At the end of the experiments, all animals were killed with an overdose of sodium pentobarbital. Statistical analyses: Chi-square analysis, ANOVA with post hoc analysis and Student’s t-test were used for statistical analysis.

Results: Tendon repair by end to end suture according to the Y2 method: Increased cellular infiltration and proliferation of fibroblasts and inflammatory cells were observed in the L-groups but not in H-groups (Figure 1). The expression of bFGF mRNA and protein increased in the tendon in accordance with the higher cellular density due to proliferation and infiltration at the repaired site. Endogenous bFGF expression seemed to be enhanced by exogenous bFGF. The epitenon but not the endotenon showed a vigorous response to the coated thread in vivo. Mechanical strengths increased significantly in the L-1w group at 3 weeks after surgery by 35% (ultimate load as shown in Figure 2). However, there was no significant increase in strength at 1 and 6 weeks, or in the other groups. Tendon repair by interlace suture: The positive contribution of this bFGF containing thread was more clearly observed in this situation. Epitenocyte proliferation was vigorous, and early reparative changes were enhanced by bFGF (Figure 3).

Discussion: Cellular infiltration and proliferation from epitenon layer lead to degradation and remodeling of tendon fibers at the tendon-repaired site, which are important to strengthen the repaired tendon at an early stage. The present results showed that exogenous bFGF enhanced tendon repair and a clear difference was observed at 3 weeks compared with the control group. The appropriate dosage (400μg/ml) and duration of release (1w) was determined. This system showed excellent efficacy in a condition of interlace suture such as free tendon graft or tendon transfer, in clinical practice (Figure 4).

Figure 1. Photomicrograph showing a longitudinal slice of the repaired tendon (Y2 method) at 3w after surgery. Note the increased thickness of the epitenocytes layer and cell density at the repaired site, which were extremely enhanced in the L-1 groups (B), not in the H-3 groups (C) and H-1 groups (D). A (a): control group; B (b): L-1 group; C (c): H-3 group; D (d): H-1 group. a, b, c, d: high magnification showing the connecting site.

Figure 2. Ultimate load of the repaired tendon at 3 and 6 w after surgery. At 3 weeks, the ultimate load of the L-1 group was significantly higher by 35% as compared to the control at 3 weeks after surgery.

Figure 3. Photomicrograph showing a longitudinal slice of the repaired tendon (Pulvertaft method) at 3w after surgery. Note the increased thickness of the epitenocytes layer and cell density at the interlacing site, which were extremely enhanced in the L-1 groups (B, b), not in the control groups (A, a).

Figure 4. This bFGF releasing system stimulated epitenon layer, and showed excellent efficacy in a condition of interlace suture such as free-tendon graft or tendon transfer, in clinical practice.