Molecular Elucidation of the Mechanism of Action of Steroids in Trigger Finger

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INTRODUCTION:

Trigger finger is one of the most common hand disorders treated by orthopedic surgeons. A lifetime risk estimated at 2.6% in the general population and 4% to 10% in patients with diabetes. Conservative treatment of trigger finger is a variety of options, but most common treatments is steroid injection. However, there are no reports evaluating the antifibrotic and anti-inflammatory effects of steroid injections on tendon sheath. Therefore, we aimed to investigate the antifibrotic, and anti-inflammatory effects of steroid injection at the molecular levels in the context of trigger finger tendon sheath.

METHODS:

The molecular genetic procedures conducted in this study were approved by the ethics committee of our institution. We collected tendon sheath fibroblasts from patients with trigger finger at the time of A1 pulley release surgery. Inclusion criteria are the clinical diagnosis of trigger finger on the index, middle, and ring fingers. Eventually, 10 patients (5 men and 5 women; mean age 67.5 ± 6.4 years) were enrolled. Harvested cells (3×10^5/well) were seeded into 6-well dishes and incubated overnight. The medium was replaced with fresh medium with 250, 500, or 1,000 μg/mL of triamcinolone acetonide (TA) or without TA (control) and incubated for 24 hours. Antifibrotic and anti-inflammatory effects were assessed via the measurement of the messenger RNA (mRNA) levels of the collagen type I alpha 1, 2, and 3 chains (Col1A1, Col1A2, and Col3A1), transforming growth factor-β1 (TGF-β1), connective tissue growth factor (CTGF), α smooth muscle actin (αSMA), IL-6, cyclooxygenase-2 (COX-2), and nuclear factor-kappa B (NF-κB) genes. Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) was used as reference. Gene expression was assessed 3 and 7 days after the injection of TA (1000 mg/mL) using the patients enrolled in this molecular study. Collected cells (3×10^5/well) were seeded into 6-well dishes and cultured overnight. The medium was replaced with fresh medium containing 1,000 μg/mL TA or no TA (control). After 1, 3, and 7 days, after picrosirius red staining, absorbance was measured at 540 nm according to the CellQuanti protocol. Differences in fibrosis- and inflammation-related gene expression, and in the Quantitative protein evaluation using picrosirius red staining were assessed using the Mann-Whitney U test. Results were considered significant at a p value of <0.05. Statistical analysis was performed using SPSS Statistics for Windows.

RESULTS:

Incubation with TA for 1 day significantly downregulated the expression of fibrosis-related genes Col1A1 and Col1A2 (p <0.01) and upregulated the expression of TGF-β1, CTGF, and αSMA (p <0.01) (Figure1). The expression of Col1A1, Col1A2, Col3A1, and αSMA was significantly downregulated (p <0.01), whereas that of TGF-β1 was significantly upregulated (p <0.05) in cells incubated with TA for 3 days. The expression of Col1A1, Col1A2, Col3A1, CTGF, and αSMA was significantly downregulated (p <0.01) in cells incubated with TA for 7 days (Figure2). The expression of inflammation-related genes NF-κB was significantly upregulated after incubation with TA for 1 and 3 day (p <0.01), that of COX-2 was significantly upregulated after incubation with TA for 3 and 7days (p <0.01), and that of IL-6 was significantly upregulated after incubation with TA for 1, 3 and 7days (p <0.05). Upon quantitative evaluation using picrosirius red staining, cell incubation for 1, 3 and 7 days with TA led to the percentage of fibroblast cells was found to be significantly less than in the control group (p <0.05) (Figure3).

DISCUSSION:

It was suggested that the antifibrotic effect may be mainly involved as the expression of the effect on the tendon sheath in patients with trigger finger. The effectiveness of physical therapy for trigger finger has also been reported, and improving the flexibility of the tendon sheath is considered important for the conservative treatment of trigger finger. On the contrary, the results of this study did not suggest an anti-inflammatory effect. It was suggested that the tenderness in the A1 pulley was not due to inflammation, but could be due to other causes.

SIGNIFICANCE:

This study is the first molecular evaluation of steroid effects on trigger finger. Continued research may lead to the elucidation of the mechanism of trigger finger onset.