The Effects of Hypertonic Dextrose Injection on the Subsynovial Connective Tissue in the Carpal Tunnel: A Novel Animal Model of Carpal Tunnel Syndrome

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Introduction: Idiopathic carpal tunnel syndrome (CTS) is a common chronic pressure induced neuropathy of the median nerve. The cause of the pressure elevation is unknown, but it is known to be associated with non-inflammatory fibrosis and thickening of the subsynovial connective tissue (SSCT). Some investigators have suggested that the SSCT fibrosis might be a cause of the neuropathy, but thus far there have been no animal models to study this possibility.

Prolotherapy is an alternative medical treatment in which irritants are injected to induce fibrosis as a way to cure various enthesopathies. The most common irritant used clinically is hypertonic dextrose. The purpose of this study was to investigate the effects of hypertonic dextrose injection on the SSCT in a rabbit model, specifically to see if the changes induce fibrosis similar to that seen in patients with CTS, and to see if such changes were associated with changes in median nerve function.

Materials and Methods: Surgical procedure

The experimental protocol was reviewed and approved by our Institutional Animal Care and Use Committee. Thirty-two New Zealand white rabbits weighing 4.0–4.5 kg were used. Following the induction of anesthesia, one fore paw was randomly selected to inject 0.1 ml of 10% dextrose solution (Hospira inc., IL) into the SSCT under direct vision, using a small incision. The contralateral paw was injected with a similar amount of 0.9% saline solution as a control. After the injection, the rabbits were allowed full cage activity. After 12 weeks of observation, the rabbits were sacrificed for the following evaluations.

Electrophysiological analysis (n=12)

Electromyography (EMG) was performed, recording from the thenar muscle with stimulation of the median nerve 3.0cm proximal to the recording point. Stimulation was carried out until a supramaximal response was visualized on the monitor. For each animal, identical recordings were done on the contralateral nerve as control. Recording was performed before injection and 12 weeks after injection, immediately prior to sacrifice.

Mechanical properties (n=12)

After sacrificing the animals, the fore paw was harvested with the carpal tunnel intact. The specimen was mounted in a custom fixture. The fixture was mounted on a custom-made microtester, which was composed of a linear servo motor (MX 80 Daedal, Irwin, PA) and a load cell accurate to 0.01N (MDB-5, Transducer Techniques, Temecula CA). The middle digit FDS tendon was exposed and the proximal end was connected with 5-0 Vicryl suture to a load cell. The middle digit FDS tendon was then sharply cut 5 mm distal to the distal edge of the carpal tunnel. Under displacement control, the middle finger FDS tendon was moved through the carpal tunnel at a rate of 0.5 mm/s. The ultimate tensile load and the energy absorption were measured to estimate the shear force within the SSCT.

Histological analysis (n=8)

Tissue for histology was formalin fixed and paraffin embedded. Five μm sections were made and stained with standard Hematoxylin and Eosin. Specimens were evaluated qualitatively for cellularity, neovascularization, fibrosis, and inflammation.

Statistical Analysis

Student’s t test was used for analyzing differences. The results were expressed as mean ± standard error of the mean (SEM). Significant differences were defined by P<0.05.

Results: Electrophysiological analysis

The mean distal latency was 1.9 ± 0.4 ms in the dextrose group, and 1.6 ± 0.3 ms in the saline group (Fig 1, P<0.05). The mean amplitude was 1.2 ± 0.6 mV in the dextrose group and 1.7 ± 0.6 mV in the saline group (not significant).

Mechanical property test

Three animals were excluded because of tissue preparation failure. The mean maximum force was 961.7 ± 448.8 mN in the dextrose group, and 704.2 ± 307.6 mN in the saline group (not significant). The mean energy absorption was 6.48 ± 3.19 mJ in the dextrose group, and 4.08 ± 1.85 mJ in the saline group (Fig 2, P<0.05).

Histological analysis

The dextrose group showed thickening of the collagen bundles and vascular proliferation within the SSCT (Fig 3-A). The saline group did not show any detectable change (Fig 3-B).

Discussion: This study assessed the biological effect of hypertonic dextrose injection on the rabbit carpal tunnel SSCT. We demonstrated that injection of 10% dextrose induced delay of median nerve conduction and SSCT fibrosis. These are consistent with the findings in CTS patients. These results suggest that hypertonic dextrose injection may be useful in the development of a novel animal model of carpal tunnel syndrome. We plan to investigate this further by assessing effects over time and with differing concentrations of dextrose.

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