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Journal of Orthopaedic Research 23 (2005) 218–223

Journal of Orthopaedic Research

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Carpal tunnel pressure alters median nerve function in a dose-dependent manner: a rabbit model for carpal tunnel syndrome

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Abstract

Background: An in vivo animal model for carpal tunnel syndrome (CTS) is presented which allows for graded application of pressure to the median nerve within the carpal canal. We hypothesized that such pressure would cause electrophysiologic changes in the median nerve in a dose-related manner, with NCS/EMG changes consistent with CTS in humans.

Methods: In 40 New Zealand white rabbits, ranging from 2 to 2.5 kg, angioplasty catheters were placed in the carpal tunnel in the forepaws and pressures ranging from 50 to 80 mm Hg applied to one side while the contralateral side served as the control and remained uninflated. Pressure was applied until a 15% increase in distal motor latency was obtained for 2 consecutive weeks by nerve conduction studies.

Results: All the experimental limbs exhibited a 15% increase in distal motor latency. None of the control limbs showed a significant increase in distal motor latency. In the experimental animals the 15% delay was achieved in approximately 4–5 weeks in the 50–70 mm Hg groups and in approximately 1 week in the 80 mm Hg group.

Conclusion: This new animal model for CTS demonstrates a direct cause and effect relationship between carpal tunnel pressure and median nerve dysfunction. We anticipate that this in vivo model with clinically relevant outcomes will facilitate identification of injury mechanisms, and will serve as a basis for future development of novel interventions and treatments.

Keywords: Carpal tunnel syndrome; Animal model; Peripheral nerve morphology; Nerve compression; Nerve conduction study

Introduction

Carpal tunnel syndrome (CTS) is a significant cause of disability in the adult population with a population prevalence of approximately 3% [1]. The symptoms of CTS are typical of a peripheral neuropathy: pain, paresthesia and hypesthesia in the nerve's distribution with eventual loss of both sensory and motor function over time if there is sufficient severity to cause axonal dropout. While CTS has been linked to a variety of clinical entities and diseases [3,8,16], the majority of clinical cases are of idiopathic origin.

The objective diagnosis of CTS is typically based on a nerve conduction study—electromyogram (NCS/EMG) demonstrating median nerve dysfunction localized to the wrist. An increase in sensory and motor latencies are generally the first NCS observed abnormalities, followed by decreased nerve conduction velocity. Usually the amplitude of the compound motor action potential also decreases. Thenar muscle denervation, demonstrated by fibrillation potentials and positive sharp waves on EMG, can result if the compression is severe.

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doi:10.1016/j.orthres.2004.05.014

The clinical presentation of CTS, however, does not always mirror the above pattern. Some patients have significant pain, without NCS/EMG data to support their diagnosis of CTS, whereas other patients never have significant pain, and only seek medical attention when their painless neuropathy is so severe that there is complete atrophy of the thenar intrinsic muscles. For the latter patients, the NCS/EMG studies demonstrate features such as unobtainable sensory and motor conduction with clear denervation patterns upon needle EMG insertion.

CTS is hypothesized to be the direct result of increased pressure within the carpal canal—a confined anatomic space which is bounded by the carpal bones on the dorsal side, the trapezium on the radial side, the hook of the hamate on the ulnar side, and the transverse carpal ligament on the palmar side [4–6,9,12,14,19]. Numerous epidemiological studies support the etiologic role of nerve compression by demonstrating that repetitive and forceful gripping are major risk factors for the development of CTS [1,7,15,20,23]. In addition, increased tunnel pressure has been measured in patients who have CTS compared to normal controls. Moreover, in normal patients, increased pressure within the canal occurs when the provocative clinical maneuvers for diagnosing CTS are performed [5,18].

Human CTS studies have been limited by the inability to longitudinally evaluate multiple time points to elucidate injury/inflammation/repair events. An animal model can overcome these limitations by providing an opportunity to control tunnel pressure while monitoring the effects on nerve function and morphology. We have chosen the rabbit because the size of its forepaw allows for surgical manipulation, and because of its historical significance as a model system in which peripheral nerve compression has been studied.

The purpose of this study was to develop and validate a model for CTS in the rabbit. We hypothesized that elevated pressure to the median nerve within the rabbit carpal tunnel (Fig. 1A and B) would cause median neuropathy based on electrophysiologic changes, and that the exposure duration required to cause median neuropathy would have an inverse relationship to the pressure magnitude. We present our study incorporating a novel technique for pressurizing the median nerve within the carpal canal.

Materials and methods

Animals/study summary

Forty New Zealand white rabbits, ranging from 2 to 2.5 kg were utilized for this study. All animals were cared for and all experiments were performed according to the regulations of University of California, San Francisco, and the protocol was approved by the Committee on Animal Research (CAR).

They were randomly assigned to one of four groups consisting of 10 animals each. In each group a distinct pressure (50, 60, 70, and 80 mm Hg) was applied to the median nerve at the carpal canal via an inflatable angioplasty balloon catheter (OMG 4.0R-18-80-2-2.0; Cook, Co., Bloomington, IN, USA) (Fig. 1C). A deflated catheter was inserted into the contralateral carpal tunnel to serve as a control. The balloon pressure inside the carpal tunnel was measured at the time of surgery, at daily intervals during the first 7 days, and at weekly intervals until the animals were sacrificed. Nerve conduction studies were performed at weekly intervals under general anesthesia. The animals were sacrificed when delayed latency of the median nerve (defined as greater than 15% change in conduction velocity) was noted on 2 consecutive weeks. At no time did any of the animals exhibit any signs of significant pain or discomfort in terms of ambulation or the ability to feed, and all were able to maintain their weights.

Surgical procedure

To insert the catheters, an incision centered over the carpal tunnel was made on the volar portion of the forepaw extending from the midpaw to the elbow. The flexor retinaculum extending to the transverse carpal ligament was exposed. The median nerve was then isolated for a length of approximately 3 cm proximal and approximately 1 cm distal to the transverse carpal ligament. A subcutaneous tunnel was made from the proximal end of the incision on the forepaw to the scruff of the rabbit's neck. A subcutaneous pocket was formed at the dorsal midline over C_2–C_8 by reflecting the fascia for a diameter of approximately 5 cm. The distal tip of the angiocatheter with guide wire in place was then pulled from the incision on the rabbit's back to the forepaw and placed deep to the transverse carpal ligament, overlying the median nerve. The distal tip of the balloon angiocatheter was anchored in position by tying the tip with 4-0 suture and fixing the knot with cyanoacrylate glue. This tip was then held in position by tying the remaining suture to the intercarpal ligaments distal to the transverse carpal ligament. The forepaw was then put through a passive range of motion at the wrist, elbow and shoulder to ensure that the catheter remained in place throughout the entire range of motion, and that there was enough slack to prevent displacement and dislodging with forepaw motion. The integrity of the balloon was confirmed by inflation with sterile normal saline. The forepaw incision was then closed. The remaining portion of the catheter was coiled in a loose loop and tied loosely together with 4-0 silk suture to prevent the catheter from kinking.

The neck incision was closed with the proximal portion of the catheter protruding approximately 10 cm. A three-way stopcock was attached to the proximal balloon port and the external transducer [PROPAQ (model 104, software version 6.0)] was connected to the stopcock. The remaining proximal portion of the catheter was then secured in the jacket pockets.

The rabbit was then turned to the opposite prone lateral position to expose the contra-lateral forelimb. A similar incision was made on this paw with the distal portion of a similar balloon catheter tip placed in the same position as the operational catheter. The same anchoring technique was used to position the control catheter.

Initial balloon inflation

The intraluminal balloon pressure was measured using the PROPAQ by attaching a 3-way stopcock to the balloon catheter port, then attaching the PROPAQ and a variable plunger syringe to the second port. Previous pilot studies demonstrated that the pressure measured inside the catheter was equivalent to the pressure outside the catheter, when a second catheter was used solely to monitor pressure created between the inflated balloon and the surrounding tissues. Initially, the PROPAC was calibrated to the intraluminal balloon pressure, which was zero Incremental addition of sterile normal saline to the balloon was performed via the variable plunger syringe until the desired pressure was reached (50, 60, 70 or 80 mm Hg). The stopcock was then closed and kept attached to the balloon catheter port, and the PROPAC and variable plunger syringe removed.