



Original Article

Effects of deep heating provided by therapeutic ultrasound on demyelinating nerves

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Abstract. [Purpose] Physiotherapeutic heating agents are classified into two groups: superficial-heating agents and deep-heating agents. Therapeutic ultrasound is a deep-heating agent used to treat various musculoskeletal disorders. Numerous studies have attempted to determine the impact of ultrasound on healthy nerve conduction parameters. However, the instantaneous effects of deep heating via ultrasound on demyelinating nerves do not appear to have been described previously. The present study aimed to assess and compare the impact of ultrasound on demyelinating nerve and healthy nerve conduction parameters. [Subjects and Methods] Carpal tunnel syndrome was used as a focal demyelination model. Thirty-two hands of 25 participants with carpal tunnel syndrome were enrolled in the study. Ultrasound parameters were 3.3 MHz, 1.0 W/cm², 8 minutes, and continuous wave. Electrodiagnostic studies were performed initially, at the midpoint (4th min), and immediately after (8th min) ultrasound application. [Results] Reduced motor conduction velocity was found in demyelinating nerves at the 4th and 8th minutes. Ulnar nerve onset latency was significantly prolonged in the 8th minute recording, compared to the initial value. There were no significant differences in relative velocity and latency changes between demyelinating and normal nerves. [Conclusion] Deep heating via ultrasound may inversely affect conduction velocity in demyelinating nerves.

Key words: Demyelination, Electrodiagnosis, Ultrasonic therapy

(This article was submitted Dec. 7, 2015, and was accepted Jan. 8, 2016)

INTRODUCTION

The impact of heat on nerve conduction was initially described by Hodgkin and Katz in 1949¹⁾. Changes in sodium and potassium channel activation are primarily responsible for heat-related nerve conduction changes^{1, 2)}. With increasing temperature, voltage-gated sodium channel activation and deactivation becomes increasingly rapid, and channels remain open for a shorter duration. Depending on the decreasing ion passage, the action potential amplitude diminishes and conduction velocity (CV) accelerates²⁾. These differences that were defined at a single-fiber level were found to be similar in an in vivo environment³⁾. In healthy nerve fibers, heating has been reported to increase both the sensory and motor nerve CV^{4, 5)}. In demyelinating diseases, nerve conduction blocks are observed with increasing body temperature^{6, 7)}. With respect to focal demyelinating conditions, superficial heating has been reported to increase nerve CV^{5, 8–10)}.

Heating modalities are mostly categorized as superficial and deep heating agents. Superficial heating modalities primarily increase the temperature of the skin and superficial subcutaneous tissues. In contrast, deep heating modalities change the temperature of deeper tissues to a depth of approximately 5 cm¹¹⁾. Therapeutic ultrasound (US) is a deep-heating agent used to treat various musculoskeletal disorders^{12–14)}. The biophysical effects of US on tissues occur through 2 mechanisms: (1) thermal effects acquired with continuous application, and (2) non-thermal effects acquired from pulse application¹⁵⁾. In addition, the depth of penetration increases with increasing US frequency¹¹⁾.

Studies have reported contradicting results concerning the effects of deep heating produced by US on healthy nerve

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conduction parameters. With respect to motor nerve CVs, continuous US was found to depend on intensity. Zankel and Farmer reported decreased ulnar motor nerve CVs with sonation intensities of 1 to 2 W/cm², but increased velocities at other intensities^{16, 17}). Madsen reported decreased CVs after sonation at 0.88 and 1.28 W/cm², but increased CVs with sonation at 1.92 W/cm²¹⁸). On the other hand, Kramer¹⁹) observed increased motor CVs with all 5 tested sonation intensities in a range of 0.5–2.5 W/cm². Regarding sensory conduction velocities, US application is generally associated with decreased sensory latencies and increased CVs in healthy nerves^{20, 21}). However, not all studies support this effect. Recently, Burnham et al. reported no significant change in healthy nerve conduction parameters after US application⁵).

Carpal tunnel syndrome (CTS), the most common neuropathy, is caused by entrapment of the median nerve under the flexor retinaculum. Prolonged pressure on the nerve leads to focal demyelination. Patients usually present with paresthesias, pain, and numbness or a tingling sensation in the fingers innervated by the median nerve. Initial treatment of this condition is conservative, and includes splinting, exercises, medication, and physical therapy modalities. In a previous study, continuous US therapy at different intensities was applied to the palmar carpal tunnel area during 10 sessions. The researchers observed a decreased motor nerve conduction velocity and increased motor distal latency in median nerve conduction. The authors therefore suggested that continuous US should not be recommended for the treatment of carpal tunnel syndrome because of possible adverse effects on nerve conduction parameters due to overheating²²). This negative effect of US on demyelinating nerve conduction must be considered, and therefore the biophysical effects of US should be assessed to confirm this result.

Previous reports do not appear to have described the instantaneous effects of deep heating on demyelinating nerves. However, such information would be important to the clarification of the effects of deep-heating modalities such as US on diseased nerves. Therefore, the authors aimed to analyze and compare instantaneous changes after deep heating in demyelinating and healthy nerves in the present study.

SUBJECTS AND METHODS

This study was designed as a cross-sectional controlled trial (Fig. 1). The effects of deep heating on motor and sensory nerve conduction studies were analyzed immediately before, at the midpoint, and immediately after the application of therapeutic US. The study was conducted in compliance with the principles of the Declaration of Helsinki. The study protocol was approved by the local ethical committee (dated 20.06.2012, no. 69), and patients provided written informed consent to participate.

Before all applications, the room temperature was recorded. Patients were left to rest to allow their skin temperature to adapt to room temperature. The skin surface temperature on the palm was measured before, at the midpoint, and at the end of the US application using an infrared skin thermometer (Medisana AG, Neuss, Germany). The infrared skin thermometer was reported to be highly reliable and valid for the purposes of an electrodiagnostic laboratory²³). The probe head of the thermometer was placed on the skin surface of the palm, and the temperature was recorded in °C.

A total of 32 hands of 25 subjects (mean age: 51.6 ± 9.5 years) were recruited for the study. Eligible subjects were identified among patients referred to our electrodiagnostic laboratory with symptoms and diagnoses of CTS²⁴). A sample size of 19 would achieve 92% power for the detection of a mean difference in pre-treatment and post-treatment sensory velocities of 1.9 m/s with an estimated standard deviation of 2.4 m/s, and a significance level (alpha) of 0.05 using a 2-sided paired t-test²⁵). Patients were excluded if they had diseases that would affect nerve conduction, such as polyneuropathy, cervical radiculopathy, rheumatic diseases, or traumatic nerve injury. Patients were also excluded if they had contraindications to US application and/or were administered a corticosteroid injection in the last 6 months.

Nerve conduction studies were conducted using a Nihon Kohden Neuropack-S1 electromyogram device (Tokyo, Japan). Motor conduction studies were conducted using low- and high-frequency amplifier settings at 5 and 10 kHz, respectively. The amplifier settings for sensory conduction studies were 2 kHz for the low and 20 kHz for the high frequency. The sensitivity and sweep velocity were respectively set at 20 microvolts (μV)/division and 2 msec/division for sensory studies and 5 millivolts/division and 2 msec/division for motor conduction studies. Median motor nerve conduction parameters were recorded from the abductor pollicis brevis muscle, and ulnar motor nerve conduction parameters were recorded from the adductor digiti minimi muscle using superficial electrodes (orthodromic). The nerve was first stimulated from 7 cm proximal to the recorded muscle. A second stimulation was applied from the antecubital fossa for the median nerve, and from the cubital tunnel for the ulnar nerve. Onset latency and nerve CV were recorded. Median sensory nerve conduction studies were recorded from the 2nd finger, and ulnar sensory nerve conduction studies were recorded from the 5th finger using a ring electrode (antidromic). Peak latencies and CVs of the sensory action potential were recorded. Median versus ulnar sensory conduction comparison studies were recorded from the 4th finger, and the peak latency of the sensory response was recorded. All stimulation and recording points were marked on the skin. Electrodiagnostic studies were repeated from the same marked points at the midpoint (4th min) and end (8th min) of US application.

US applications were performed using an Intellect Mobile Combo US Unit (Chattanooga, TN, USA). Each subject was exposed to continuous-wave US treatment with a sonation intensity of 1.0 W/cm² and frequency of 3.3 MHz. A 0.5-cm² US head was used. A circular application technique with a soundhead movement speed of approximately 3 cm/second was used. The treatment area was 4 cm × 2.5 cm, expanding from 1-cm distal to 2.5-cm proximal of the wrist crease, including the median and ulnar nerve traces. The size of the radiated area with respect to the diameter of the US head was within the

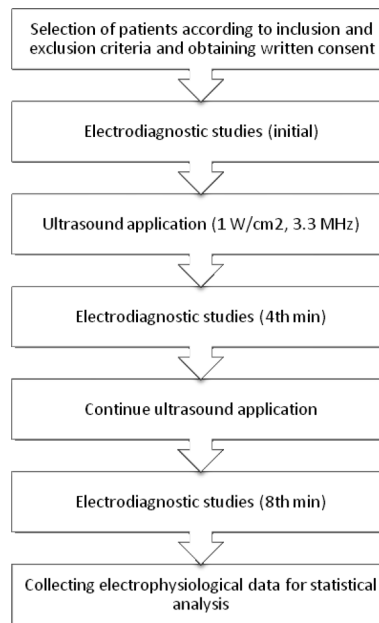


Fig. 1. Study design

Table 1. Changes in skin surface temperature

	Before application	4th minute	8th minute
Temperature (°C)	36.8 (36.5–37.0)	36.8 (36.5–37.1)	36.7 (36.5–37.2)

Absolute change values are presented as medians (25–75 percentiles)

recommended limits¹⁸). The transmission gel was brought to room temperature before treatment.

The Kolmogorov-Smirnov test was used to assess the normality of numeric variables. For numeric variables that were normally distributed, comparisons between 2 groups were made using the independent sample t-test, and results are expressed as means \pm standard deviations. For the scores and numeric variables that were non-normally distributed, comparisons between 2 groups were made using the Wilcoxon t-test or Friedman test, and results are expressed as medians (25th–75th percentiles). P values <0.05 were considered statistically significant.

RESULTS

The mean room temperature throughout the study was 26.9 ± 1.2 °C. There were no statistically significant differences between skin surface temperature measurements before US application and at the 4th and 8th minutes ($p > 0.05$; Table 1).

Table 2 summarizes the median values of changes in motor and sensory latencies and nerve CVs recorded from median and ulnar nerves before and at the 4th and 8th minutes of US application. Regarding motor studies, the CVs of demyelinating median nerves exhibited significant decreases at the 4th and 8th minutes. In addition, a significant prolongation in the healthy ulnar nerve onset latency was identified at the 8th minute when compared to the initial value. There were no significant differences in the before- and after-US values for median motor latency, median sensory latency and CV, ulnar motor CV, ulnar sensory latency and CV, and median-ulnar 4th finger peak latency.

Relative changes in electrophysiological parameters obtained from demyelinating and normal nerves at the 4th and 8th minutes of US application are compared in Table 3. There were no significant differences between demyelinating and normal nerves in terms of velocity and latency changes due to deep-heat application.

DISCUSSION

The main question addressed in this study was whether the application of deep heating would differently affect demyelinating and normal nerves. Previous studies of healthy nerves observed inconsistent effects of US. Some of these reports^{16–18}) suggested that the CVs of healthy motor nerves decreased at sonation intensities of approximately 1 W/cm^2 , except for 1 study²⁵) that observed an increased CV. In addition, previous research indicated an association between sonation and in-

Table 2. Summary of changes in nerve conduction parameters with deep heating

	Initial	4th minute	8th minute
Median nerve			
Motor			
Latency (msec)	4.61 (4.26–4.95)	4.58 (4.32–5.19)	4.66 (4.09–5.14)
CV (m/s)	53.95 (50.60–56.55)*	52.15 (50.15–54.75)	52.60 (50.85–54.75)
Sensory			
Latency (msec)	4.03 (3.33–4.61)	4.03 (3.39–4.5)	4.05 (3.42–4.64)
CV (m/s)	37.0 (33.5–45.0)	36.0 (33.5–43.1)	36.9 (33.3–41.3)
Ulnar nerve			
Motor			
Latency (msec)	2.60 (2.46–2.88)**	2.64 (2.54–2.95)	2.77 (2.54–3.03)
CV (m/s)	62.65 (59.55–5.60)	60.60 (58.15–63.85)	61.40 (57.65–64.10)
Sensory			
Latency (msec)	2.40 (2.34–2.67)	2.43 (2.31–2.58)	2.48 (2.31–2.59)
CV (m/s)	56.35 (51.55–59.20)	56.50 (52.00–59.10)	56.45 (51.90–59.55)
Med-Uln 4P			
APLD (msec)	1.20 (0.92–2.30)	1.18 (1.00–2.34)	1.13 (0.98–2.26)

Absolute change values are median (25th–75th percentiles). CV: conduction velocity; Med-Uln 4P: median and ulnar nerve sensory conduction study to the fourth digit; APLD: absolute peak latency difference

*The first measurement differs significantly from the 4th and 8th minute measurements ($p < 0.05$)

**The first measurement differs significantly from the 8th minute measurement ($p < 0.05$)

Table 3. Comparison of changes in demyelinated and normal nerves with deep heating

	Median Nerve	Ulnar Nerve
ML1-ML2	-0.05 (0.28)	-0.06 (0.21)
ML1-ML3	-0.01 (-0.23–0.21)	-0.08 (-0.31–0.02)
MCV1-MCV2	1.25 (0.00–4.77)	1.30 (-1.22–2.60)
MCV1-MCV3	0.91 (3.77)	1.57 (3.55)
SL1-SL2	-0.03 (-0.10–0.08)	0.01 (-0.07–0.07)
SL1-SL3	0.00 (-0.10–0.10)	-0.01 (-0.05–0.11)
SCV1-SCV2	0.14 (1.99)	0.30 (4.67)
SCV1-SCV3	0.55 (-0.60–1.72)	0.25 (-4.37–3.20)

Absolute change values are shown as means (standard deviations) or medians (25th–75th percentiles) as indicated. 1: initial value; 2: value at 4th minute; 3: value at 8th minute; ML: motor latency; MCV: motor conduction velocity; SL: sensory peak latency; SCV: sensory conduction velocity

creased sensory nerve CVs in healthy nerves^{19, 21, 25}). In the present study, a statistically significant deceleration was observed with deep heating in both in demyelinating and healthy nerve motor CVs, but not in sensory CVs.

Previously, reduced healthy nerve motor conduction speed following US radiation has been attributed to micromassage action¹⁶) or a mechanical effect¹⁷) of US. Todnem et al. reported that motor CVs increased non-linearly with increasing skin temperature²⁶). This non-linear relationship between body temperature and nerve CVs might also explain the results of the present study. The authors of that earlier study also surmised that a decreased motor CV might be related to the cooling effect of the transmission gel. According to a report by Kramer et al., intensities above 1.5 W/cm² were necessary to exceed the cooling effect of the transmission gel²⁵). In the present study, the sonation intensity was 1.0 W/cm², or below the lower limit determined by Kramer et al²⁵). The present study was conducted at a frequency of 3.3 MHz. However, previous work has demonstrated temperature elevation in deeper tissue layers at a continuous US application of 1 MHz²⁷). Additionally, the effective radiating area and output power of US devices from different manufactures may differ, resulting in different degrees of tissue heating^{28, 29}). Consequently, these variables differed between studies and increased the difficulty of drawing a precise conclusion.

The median and ulnar nerves, which have similar structures and anatomical locations, respond similarly to temperature

changes^{30, 31}). In the present study, healthy ulnar nerves in the arms affected by CTS comprised the control group and were compared with demyelinating median nerves. Use of the ipsilateral ulnar nerves as the control group enabled the elimination of potential biases such as deep tissue temperature differences or the amount of US radiation. As nerve conduction studies can be affected by many other parameters, such as height, age, sex, tissue temperature, and room temperature, the simultaneous comparison of healthy control and demyelinated nerves in the same arm is a strength of this study.

CTS is the most common of all demyelinating nerve disorders. Deep heating via US is often used for CTS treatment. Several studies have evaluated the cumulative effect of US treatment in patients with CTS^{18, 32, 33}). In the first study, US pulsed mode 1:4 US was applied at 1 MHz and 1.0 W/cm² for 15 minutes and 20 sessions, and significant improvements were observed in motor distal latency and sensory nerve conduction³²). In another study, improvements in motor latencies and amplitudes of were observed in patients with CTS after 15 sessions of US³³). In contrast, another study found no significant difference in nerve conduction after 10 sessions of US with changing dosages, but identified a mild increase in motor latencies and deceleration of motor CVs with US applications at 1.5 W/cm² and 0.8 W/cm²²²). These studies focused on the effectiveness of US with consecutive applications. In contrast, the present study focused on the immediate biophysiological results of deep heating from US.

Subcutaneous temperature measurement was not performed in this study, and this omission could be perceived as a limitation. However, previous reports described a significant correlation between intramuscular and skin surface temperatures, and skin surface temperature measurement is more reliable and reflective of the subcutaneous tissue temperature close to the nerve^{23, 30}). Therefore, in the present study used skin surface temperatures measured with an infrared thermometer, rather than subcutaneous tissue temperatures.

The present study revealed a significant reduction in the demyelinating motor nerve CV, but not the sensory nerve CV, after deep heating. This finding could raise questions about the effectiveness of deep heating for diseased peripheral nerves. However, the present study only obtained results using continuous US at 3.3 MHz and 1W/cm², with application times of 4 and 8 minutes. In the future, similar studies involving different US parameters will enable researchers to obtain a wider variety of results.

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