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● *Original Contribution*

ELECTROPHYSIOLOGICAL AND FUNCTIONAL EFFECTS OF SHOCK WAVES ON THE SCIATIC NERVE OF RATS

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Abstract—Extracorporeal shockwave therapy (ESWT) has been applied in lithotripsy and treatments of musculoskeletal disorders over the past decade, but its effects on peripheral nerves remain unclear. This study investigated the short-term effects of shockwaves on the sciatic nerve of rats. The nerves were surgically exposed and then stimulated with shockwaves at three intensities. We evaluated the motor nerve conduction velocity (MNCV) of treated sciatic nerves before, immediately after (day 0) and at 1, 4, 7 and 14 d after shockwave treatment. Two functional tests—the sciatic functional index and the withdrawal reflex latency—were evaluated before and at 1, 4, 7 and 14 d after shockwave application. The rats were sacrificed on days 0, 1, 4, 7 and 14 for morphologic observation. The degassed treatment group received high-intensity shockwave treatment using degassed normal saline as the contact medium, and MNCV was measured before and on days 0, 1, 4, 7 and 14. The sham group received the same procedure as the treatment groups (*i.e.*, the surgical operation to expose the sciatic nerve) but with no shockwave treatment. The control group received no surgical operation or shockwave treatment. The results showed moderate decrease in the MNCV after shockwave treatment and damage to the myelin sheath of large-diameter myelinated fibers. The effect was largest (reduction to 60.9% of baseline MNCV) and of longest duration (7 to 14 d) in the high-intensity group. There were no significant changes in functional tests. These results indicated that direct application of shockwaves can induce reversible segmental demyelination in large-diameter fibers, with the electrophysiological changes being positively correlated with the intensity of the shockwaves. (E-mail: jjluh@ntu.edu.tw)

Key Words: **Peripheral nerve, Extracorporeal shockwave therapy, Sciatic functional index, Withdrawal reflex latency, Motor nerve conduction velocity.**

INTRODUCTION

Shockwaves are characterized by high positive pressures (~100 MPa) and negative pressures (5 to 10 MPa), a rapid rise time (30 to 120 ns) and a short pulse duration (5 μs) (Sturtevant 1996). They were first used in lithotripsy to treat kidney stones (Chaussy et al. 1982) and subsequently to treat musculoskeletal disorders (Loew et al. 1995; Rompe et al. 1996a, 1996b).

The effects of extracorporeal shockwave therapy (ESWT) on bone, cartilage, connective tissue and vessels have been studied in human and rabbits, with the aim of understanding mechanisms that underlie treatments for musculoskeletal disorders (Durst et al. 2002; Wang et al. 2003). The effects of ESWT on peripheral nerves have also been reported recently. Applying ESWT to normal rat skin can induce degeneration of intracutaneous nerve fibers, with this effect reversing within two weeks (Ohtori et al. 2001; Takahashi et al. 2006). It was postulated that this effect is responsible for the immediate pain relief after ESWT. However, the myelin sheath can be damaged histologically by ESWT in horses and dogs (Bolt et al. 2004; Wang et al. 2002), and further functional damage induced by such histologic changes would challenge the safety of ESWT. The range of clinical indications has widened, with ESWT being applied to different body regions. However, the possibility of dam-

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age to the nerve remains unknown because the nerves cannot be seen from the body surface. If damage to peripheral nerves does occur, it is not known whether these changes are long lasting, cause functional damage or relate to the intensity of ESWT.

The purpose of this study was to evaluate the short-term effects of shockwaves on the electrophysiological, histologic and functional properties of mixed peripheral nerves. We hypothesized that shockwaves could induce reversible segmental demyelination of peripheral nerves, with this effect being correlated with the shockwave intensity.

MATERIALS AND METHODS

Experimental animals

All procedures were approved by the Laboratory Animal Center of National Taiwan University College of Medicine. All the animals had free access to food and water during the study. Eighty-four adult male Wistar rats weighing 359 ± 62*g* (mean ± SE) were used in this study. Sixty-six animals were randomized into three different-intensity treatment groups. Seven rats in each group were evaluated with motor nerve conduction velocity (MNCV) before and immediately after (day 0) and at 1, 4, 7 and 14 d after shockwave application. Three rats were chosen in each group to be sacrificed at 0, 1, 4, 7 and 14 d after shockwave application, respectively, for observing morphologic changes. The functional activity was assessed before and at 1, 4, 7 and 14 d after treatment in all rats. Moreover, three rats were assigned to a degassed treatment group and were treated with high-intensity shockwaves, with degassed normal saline used as the contact medium. The MNCV studies were performed before and at 0, 1, 4, 7 and 14 d after treatment in the rats. Twelve rats in a sham group received the same experimental procedure but without the application of shockwaves. Rats were sacrificed at 0, 1, 4, 7 and 14 d after treatment to observe morphologic changes of the sciatic nerve. Three rats in the control group received no surgical operation or shockwave treatment, with only their functional activity being assessed.

Shockwave treatment

Piezoelectrically-generated shockwaves (Piezoson 100, Richard Wolf, Knittlingen, Germany) were applied to the surgically-exposed sciatic nerve with a handheld applicator to ensure the precision of the shockwave treatment and the consistency of nerve conduction measurements. All animals were given vedaprofen (0.5 mg/kg) as an oral analgesic before surgery. The entire procedure was performed under aseptic conditions. The animals were anesthetized with chloral hydrate (400 mg/kg, IP), and an IM injection of enrofloxacin (5 mg/kg) was given as an antimicrobial agent. After the hair was removed from it, the right lateral thigh of the animal was prepared aseptically using iodine and 70% alcohol. The skin was then cut, and subcutaneous tissue and muscles were separated to expose at least 5 cm of the sciatic nerve in the sciatic notch. Shockwave treatment was applied to the exposed sciatic nerve 3 cm distal to the sciatic notch, with sterile saline warmed to 38°C as the contact medium in the three different-intensity treatment groups, and 38°C degassed sterile saline was used in the degassed treatment group. Each animal received 2,000 pulses of 4-Hz shockwaves at a high, moderate or low intensity, corresponding to an energy flux density of 0.49, 0.19 or 0.08 mJ/mm^2, respectively. The sciatic nerve was examined for discoloration, swelling, edema, hematoma and bleeding immediately after the shockwave treatment was completed.

Motor nerve conduction studies

MNCV was investigated under general anesthesia using a computerized neurodiagnostic system (VikingQuest, Nicolet Biomedical, Madison, WI, USA) before and at 0, 1, 4, 7 and 14 d after shockwave treatment in all four treatment groups. The MNCV was also measured in the sham group on days 0, 1, 4, 7 and 14. The sciatic nerve was stimulated at a supramaximal voltage using monopolar needle electrodes. The proximal stimulating site was proximal to the shockwave treatment site and 1 cm distal to the sciatic notch, and the distal stimulation site was 5 cm distal to the sciatic notch. The stimulating needle electrodes were fixed to a spatula to minimize variability of the conduction distance (Fig. 1a). Square-wave pulses of 500-μs duration were delivered at 1 Hz. The detected signals were amplified and band-pass–filtered between 1 Hz and 10 kHz. The proximal latency (L_p) and distal latency (L_d) of the evoked muscle action potentials were recorded from the first intrinsic foot muscles with monopolar needle electrodes. A ground electrode was positioned on the tail of the rat (Fig. 1b). After the MNCV measurements, the skin and muscles were sutured. Finally, the distance (D) between the proximal and distal stimulation sites was measured with digital calipers (resolution of 0.01 mm; United Precision Machine, Shenzhen, China), and the MNCV was calculated according to the following equation:

$$\text{MNCV} = D/(L_p - L_d). \quad (1)$$

The computed MNCV was normalized to the baseline MNCV in the same animal.