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Effect of Extracorporeal Shock Wave Therapy on Denervation Atrophy and Function Caused by Sciatic Nerve Injury

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Abstract. [Purpose] The present study examined the effects of treatment using extracorporeal shock wave therapy (ESWT) on the muscle weight and function of the hind limb in sciatic nerve injury. [Subjects] Forty rats with sciatic nerve crushing injury were randomly divided into two groups: an ESWT group (n=20), and a control group (n=20). [Methods] The ESWT group received extracorporeal shock wave treatment, and the control group did not receive any treatment after injury. Experimental animals were measured for muscle weight on an electronic scale and were tested for function on a sciatic functional index (SFI). [Results] All groups showed significant increases in the weights of the left soleus and gastrocnemius muscles, and decreases in the weights of the right soleus and gastrocnemius muscles ($p<0.05$). Comparison of SFI scores and muscle weights between the groups showed significant differences in SFI scores, and the right soleus and gastrocnemius muscles ($p<0.05$) [Conclusion] Exercise programs that use ESWT can be said to be effective at improving the function of the sciatic nerve and preventing the denervation atrophy.

Key words: ESWT, Sciatic nerve, Peripheral nerve

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INTRODUCTION

Neurological damage from external injury or trauma occurs more often in the peripheral nervous system than in the central nervous system. Neurological damage to the peripheral nervous system may result in severe physiological, morphological, cytological, or functional impairments, such as loss of motor function of the muscles that are controlled by the damaged neurons[1)].

Similarly, a decrease in protein synthesis may cause denervation atrophy[2)], and inhibition of sensory neurons may cause dysesthetic sensation[3)]. Damage to the sensory and motor neurons may lead to functional disorders[4)].

There are two major types of treatment for peripheral nerve damage: invasive and non-invasive. Methods of invasive treatment include injection and surgery, and non-invasive treatments include electrical stimulation, exercise, aquatic therapy, and medication[5, 6)].

Extracorporeal shock wave therapy (ESWT), a non-invasive treatment, relieves the pain of peripheral nerve damage and promotes local arterial remodeling and cellular regeneration. It is also known as an effective treatment for enhancing muscle strength and decreasing muscle tone. Murata et al. examined the pain-relieving effect of extracorporeal shock wave treatment, and reported that ESWT activates axonal regeneration, which stimulates reinnervation and promotes amelioration of desensitization[7)]. Bolt et al., in their study of the functional and morphological effects of shock wave treatment on palmar digital nerve damage, reported that pain relief caused by changes in peripheral pain perception exerted a positive effect on peripheral nerve regeneration[8)]. However, research into the effects of ESWT on muscular atrophy and function of sciatic nerve damage is currently inadequate. Therefore, we studied the effects of ESWT on the inhibition of neurological muscular atrophy and functional improvement following sciatic nerve damage.

SUBJECTS AND METHODS

Subjects

This study used 40 eight-week-old Sprague-Dawley male rats weighing between 250 g and 300 g. Sciatic nerve crushing injury was induced in all the animals, which were then randomly divided into two groups: an experimental group (n=20) that received extracorporeal shock wave treatment, and a control group (n=20) that did not receive any treatment.

The experimental group received the first treatment immediately after the nerve crushing damage and, starting on the next day, received three treatments per week for two weeks (total of six treatments). All surgical procedures and experimental protocols followed Daegu University's guidelines and were approved by the Institution of Animal Care

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Table 1. Comparison of SFI scores and muscle weights between pre-test and post-test for each group (Mean ± SD)

		Pre-test	Post-test
ESWT group (n=20)	SFI*	–71.61 ± 16.44	–54.81 ± 2.16
	Rt. soleus*	124.73 ± 15.49	82.25 ± 15.21
	Rt. gastrocnemius*	1,966.27 ± 142.92	1,698.83 ± 243.40
	Lt. soleus*	126.56 ± 12.42	140.89 ± 25.35
	Lt. gastrocnemius*	1,982.78 ± 154.97	2,114.67 ± 233.26
Control group (n=20)	SFI	–77.45 ± 13.21	–72.98 ± 4.21
	Rt. soleus*	128.56 ± 10.14	52.54 ± 18.97
	Rt. gastrocnemius*	1,936.73 ± 205.00	1,152.67 ± 65.92
	Lt. soleus*	128.78 ± 10.14	154.73 ± 5.07
	Lt. gastrocnemius*	2,028.63 ± 179.21	2,262.84 ± 60.85

*p<0.05, ESWT=extracorporeal shock wave therapy, SFI=sciatic functional index

and Use Committee (IACUC).

Methods

For general anesthesia, Zoletil (Virbac, Korea) and Rompun (Bayer, Korea) were mixed at 1:1 ratio and injected into the abdomen of the rats at a dose of 2 ml/kg. To induce artificial sciatic nerve damage, the region between the right thigh and knee joint was shaved and incised (2 cm long). Following the incision, the sciatic nerve was removed from the surrounding muscles, and the region about 7 cm away from the ankle joint, just before the point where the tibial nerve and peroneal nerve separate, was compressed for 30 seconds under three steps of pressure with hemostatic forceps[9].

Extracorporeal shockwave treatment (ESWT) was applied using an ESWT machine (HAEMIL, Soltar, Korea) with low intensity output with a PAD5 applied to the sciatic nerve damage area. ESWT was applied at a frequency of 3 Hz and energy flux density of 0.09 mJ/mm^2, 300 times.

All measurements were made on the first and the 14th day after the sciatic nerve damage. To determine the changes in denervation muscular atrophy of peripheral nerves, soleus muscles from both ends and the gastrocnemius muscle were excised and washed with saline water, and the muscles were weighed using a microbalance (BL-320H, Shimadzu, Switzerland).

To discover the effect of sciatic nerve damage on functional change, the sciatic functional index (SFI) was measured. Both hind feet of the mice were painted with black ink, and the mice were allowed to walk through a dark room (50 × 8 × 10 cm) so that their footprints could be tracked.

Analysis of the footprints consisted of measuring the length between the heel and third toe (print length, PL), the length between the first and fifth toes (toe spread, TS), and the length between the second and fourth toes (intermediary toe spread, IT). These measurements were used to calculate SFI. The value of SFI of a normal rat is usually around 0, whereas that of a rat with severe injury is close to −100.

The paired t-test was used to compare the treatment effects in each group. The independent t-test was used to compare the groups. The data were processed using SPSS for Windows Version 20.0, and a significance level (α) of 0.05.

RESULTS

The ESWT group showed significant increases in the weights of the left soleus and gastrocnemius, muscles and decreases in the weights of the right soleus and gastrocnemius muscles ($p<0.05$). The ESWT group also showed a significant difference in SFI scores ($p<0.05$) (Table 1).

The control group showed significant increases in the weights of the left soleus and gastrocnemius muscles ($p<0.05$), and the weights of right soleus and gastrocnemius muscles showed significant decreases ($p<0.05$). However, the SFI scores of control group did not show a significant difference.

Comparison of SFI scores and muscle weights between the groups showed significant differences in SFI scores, and right soleus and gastrocnemius muscle weights ($p<0.05$) (Table 2).

DISCUSSION

Peripheral nerves recover very slowly after an injury, and recovery is often incomplete[10]. Damage to peripheral nerves locally or generally decreases motor, sensory, and voluntary control of the denervated region, peripheral nerve damage also cause loss of motor function and diminishes functional activity and overall quality of life[11].

The region that is under the control of the damaged nerves experiences dysesthetic sensation, which, with time, may also cause collateral damage to the spinal ganglion, anterior horn, or posterior horn of the spinal cord[12]. Peripheral nerve damage also affects the microvessels, impeding nutrients from reaching the neurons, and causes malfunction in signal transduction and muscle degeneration. Denervated muscle atrophy leads to decrease in protein synthesis and increase in protein degradation, and it may occur as a result of peripheral nerve damage, in which neurons lose control of the surrounding muscles[13].

Muscle atrophy caused by post-peripheral nerve injury denervation causes greater damage than muscle atrophy

Table 2. Comparison of SFI scores and muscle weights between the groups (Mean ± SD)

	ESWT group (n=20)	Control group (n=20)
SFI*	–16.80 ± 16.05	–4.47 ± 12.12
Rt. soleus*	42.27 ± 23.96	76.56 ± 22.30
Rt. gastrocnemius*	552.74 ± 213.68	784.54 ± 186.50
Lt. soleus	–14.72 ± 23.24	–26.84 ± 14.04
Lt. gastrocnemius	–216.61 ± 374.22	–234.57 ± 139.43

*p<0.05, ESWT=extracorporeal shock wave therapy, SFI=sciatic functional index

caused by casting, tenotomy, or bed rest[14]. Sunderland[15], in a study of muscle atrophy resulting from crush injury administered to rats, reported that the weight of the gastrocnemius and soleus muscles and the cross-sectional areas of muscle fibers decreased significantly with time. Sakakima et al. found that, after two weeks of nerve injury, the affected side showed the highest degree of muscle atrophy[16].

In the present study, the ESWT group showed significant increases in muscle weights due to the excessive use of the left soleus and gastrocnemius muscles ($p<0.05$). However, the weight of the right soleus and gastrocnemius muscles showed significant decreases in weight due to denervation atrophy ($p<0.05$). In other words, ESWT did not completely prevent muscle atrophy. The control group also showed significant differences in the weights of all muscles ($p<0.05$). The control group showed significant increases in muscle weights due to excessive use of left soleus and gastrocnemius muscles ($p<0.05$). When comparing the degree of atrophy between the groups, we found that the right soleus and the gastrocnemius showed significant differences ($p<0.05$). This result indicates that ESWT reduced the level of muscle atrophy by counteracting the changes that occurred from inhibition of muscle contraction and decrease of protein synthesis.

Since peripheral nerve damage reduces the control of the motor and sensory functions of the corresponding muscles, overall functional activity also reduces. If adequate treatment is not provided immediately after an injury, functional disorders may occur, even after the regeneration of peripheral nerves[17]. Symptoms that may follow sciatic nerve damage include reduction of joint movement, imbalance of postural alignment, and compensation of movement[18]. Previous studies have found that the gait of rats show decreases in knee joint and ankle joint movements and in stride and step lengths, resulting in an overall decrease in functional activity[19].

Murata et al. observed the effect of extracorporeal shockwave treatment on peripheral nerve damage, and reported that the shockwave promotes reinnervation and amelioration of desensitization by activating axonal regeneration[7]. In present study, the ESWT group showed a significant increase in SFI score after the treatment and there was also a significant difference between the groups ($p<0.05$). These results indicate that ESWT stimulates regeneration and reordering of the nerves, which in turn activates the conjunction of muscle and neurons, and increases functional activity. Our study was conducted in a short time with a small number of subjects. In further studies, we hope to discover the effects of extracorporeal shockwave treatment on peripheral nerve damage in various regions of the body.

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