Int J Clin Exp Med 2019;12(5):5836-5843
www.ijcem.com /ISSN:1940-5901/IJCEM0089733

Original Article

Efficacy of acupoint injections of Shenfu, combined with mecobalamin tablets, for treatment of the neck type of cervical spondylopathy and its effect on serum creatine kinase and lactate dehydrogenase levels

Jiwen Dong[1], Weimin Hao[2]

[1]*Sports Human Body Teaching and Research Section, Physical Education College, Shanghai Normal University, Shanghai City, China;* [2]*Department of Epidemiology, School of Public Health, Shanghai Medical College, Fudan University, Shanghai City, China*

Received December 12, 2018; Accepted January 11, 2019; Epub May 15, 2019; Published May 30, 2019

Abstract: Objective: The aim of this study was to investigate the efficacy of acupoint injections of Shenfu combined with mecobalamin tablets for treatment of the neck type of cervical spondylopathy, examining its effects on serum creatine kinase (CK) and lactate dehydrogenase (LDH) levels. Methods: A total of 150 patients with the neck type of cervical spondylopathy were enrolled as subjects and randomly divided into the observation group (n=75) and control group (n=75). Based on routine treatment, patients in the observation group were treated with acupoint injections of Shenfu combined with mecobalamin tablets. A total of 6 main and adjunct acupuncture points (Main acupoint: Jiaji acupoint; Adjunct acupuncture points: Tianzong, Jianjing, Shousan Li, Hegu, Quchi, Ashi acupoint) were selected. Each acupoint was injected with 0.8-1 mL of Shenfu injection, once a day for 1 month, as well as mecobalamin tablets, 0.5 mg each time, 3 times per day for 1 month. Patients in the control group were treated with methylcobalamin tablets and point injections of normal saline. The dosage and course of mecobalamin tablets and normal saline, together with the acupoint position, were the same as those in the observation group. Efficacy, visual analogue scale scores (VAS), neck pain questionnaires (NPQ), Japanese Orthopedic Association (JOA) scores, spinal functional improvement, and CK and LDH levels were compared between the two groups. Results: The total effective rate of treatment in the observation group (97.33%) was significantly higher than that in the control group (81.33%). Differences were statistically significant (P=0.002). VAS and NPQ scores in the observation group were significantly lower than those in the control group, after treatment (P<0.001). JOA scores in the observation group were significantly higher than those in the control group, after 6 months of treatment (P<0.001). The excellent and good rate of spinal cord function improvement in the observation group was significantly higher than that in the control group, after 6 months of treatment (94.67% vs 84.00%, P=0.034). Levels of CK and LDH in the observation group were significantly lower than those in the control group (P<0.001). Conclusion: Acupoint injections of Shenfu combined with mecobalamin tablets can effectively relieve cervical pain symptoms of the neck type of cervical spondylopathy, reduce levels of CK and LDH, and promote the recovery of cervical muscle injuries and spinal cord nerve function. Therefore, its efficacy is significantly better than that of mecobalamin tablets alone.

Keywords: Shenfu injections, neck type of cervical spondylopathy, acupoint injection, creatine kinase, lactate dehydrogenase

Introduction

With a change in work and lifestyles, incidence of cervical spondylopathy has increased year by year, with a tendency toward a younger age [1]. The neck type of cervical spondylopathy, also known as local cervical spondylopathy, is one of the common orthopedic diseases in clinic. It is mainly characterized by posterior neck pain, shoulder and back pain, and abnormal sensations, such as soreness, distention and numbness. These are often accompanied by a series of clinical syndromes, including corresponding tenderness points and neck stiffness [2]. It seriously affects the stability, flexibility, and frequency of the cervical vertebrae, severe-

ly restricting cervical movement and directly threatening the quality of life of patients [3]. At present, the pathogenesis of the neck type of cervical spondylopathy remains unclear. However, some studies have shown that abnormalities of cervical muscle tissue plays an important role in the process of cervical spondylopathy [4, 5]. Muscle damage can lead to changes in enzyme activity associated with skeletal muscle. It has been reported that serum creatine kinase (CK) and lactate dehydrogenase (LDH) levels in patients with myogenic pain of the neck and shoulder are significantly higher than those in normal subjects [6]. Therefore, they can effectively intervene with the cervical muscle group to slow down and prevent cervical degeneration, reducing occurrence of cervical spondylopathy [7].

Trophic nerves and microcirculation improvements are the main treatments for the neck type of cervical spondylopathy. Mecobalamin tablets, with vitamin B12 as the prosthetic group, are also commonly used drugs. However, some patients have not received good efficacy after application [8]. Shenfu injections, mainly composed of ginsenoside and aconitine, have been widely used in various diseases. They can improve immune function, directly inactivate antioxidant free radicals, improve blood circulation, and provide anti-oxidation effects [9, 10]. Moreover, the acupoint injection not only plays the role of acupuncture, but also achieves the dual role of activating blood circulation and dredging collaterals [11]. It has been reported that acupoint injections of angelica sinensis have achieved good results in the treatment of cervical spondylopathy [12, 13]. However, there are few reports on the efficacy of Shenfu injections, combined with mecobalamin tablets, in the treatment of the neck type of cervical spondylopathy with improvements of cervical muscle damage. In this study, the efficacy of Shenfu injections, combined with mecobalamin tablets, for treatment of the neck type of cervical spondylopathy was examined, as well as its effects on serum CK and LDH levels. The aim of this study was to provide a basis for clinical evaluation.

Materials and methods

Subjects

A total of 150 patients with the neck type of cervical spondylopathy, diagnosed by the Orthopedic Department, were selected and divided into the observation group (n=75) and control group (n=75), according to random number table. Patients in the observation group were treated with acupoint injections of Shenfu, combined with mecobalamin tablets. Patients in the control group were treated with acupoint injections of normal saline combined with mecobalamin tablets.

Inclusion criteria: Patients were over 18 years old and met the diagnostic criteria for the neck type of cervical spondylopathy; Clinical manifestations were limited cervical movement, neck or occipital pain, rigidity of the cervical muscles, and corresponding tenderness; Patients with segmental changes in cervical physiological radians at the corresponding lesions detected by imaging examination; Patients with complete clinical data and active cooperation with this study [14].

Exclusion criteria: Patients with severe liver and kidney insufficiency and cardiovascular and cerebrovascular diseases; Patients with hypertension, diabetes mellitus, and allergies to acupoint injections of Shenfu and mecobalamin tablets; Patients with coagulation disorders; Patients with mental diseases. The current study was approved by the Ethics Committee of Shanghai Normal University. All patients and families provided informed consent.

Treatment methods

Selected patients were divided into the observation group and control group, according to a random number table, with 75 patients in each group. Both groups of patients were given routine basic treatment, including health education, proper neck exercises, and hot compresses. Based on routine treatment, patients in the observation group were treated with acupoint injections of Shenfu (Ya'an Sanjiu Pharmaceutical Co., Ltd.), combined with mecobalamin tablets (Eisai Co., Ltd., Japan). The tablets were taken orally, half an hour before meals, 0.5 mg each time, 3 times per day. A total of 6 main and adjunct acupuncture points (Main acupoint: Jiaji point; Adjunct acupuncture points: Tianzong, Jianjing, Shousan Li, Hegu, Quchi, Ashi acupoint) were selected. Injection sites of the acupoints were fully exposed and sterilized with 75% alcohol. A syringe with 5 mL of Shenfu was quickly punctured into the selected acupoints, while needle depth was controlled at

Table 1. Comparison of general data

Group	Observation group (n=75)	Control group (n=75)	t/χ^2	P
Gender (male/female)	45/30	47/28	0.112	0.737
Age (year)	47.8±12.6	50.2±12.8	1.157	0.249
Body mass index (kg/m^2)	23.7±1.3	24.0±1.5	1.309	0.193
Course of disease (day)	4.4±1.5	4.6±2.0	0.693	0.490
Lesion segment			0.385	0.535
Single interval	13	16		
Multiple interval	13	16		
Hypertension (case)	14	17	0.366	0.545
Diabetes mellitus (case)	16	12	0.703	0.402
Analgesia therapy (case)	20	23	0.293	0.588

0.5-1.5 cm. The drug was injected slowly after no blood was withdrawn. The dosage was controlled at 0.8-1 mL at each acupoint, once a day. Based on routine treatment, patients in the control group were treated with methylcobalamin tablets and point injections of normal saline. Dosages and course of mecobalamin tablets were the same as those in the observation group. Injections of normal saline took the place of the Shenfu injections. The position, dosages, and course were the same as those in the observation group. The duration of treatment was 1 month for both groups.

Outcome measures

Comparison of efficacy between the two groups included: (Cure) Complete disappearance of upper limb radiating pain, numbness, and neck stretch, along with unlimited neck movement, negative results of brachial plexus traction test, and compression test of intervertebral foramen; (Effective) Disappearance of upper limb radiating pain, numbness, and neck stretch, along with recovery of neck movement; (Ineffective) No improvement or aggravation of upper limb radiating pain, numbness, and neck stretch [15]. Total effective rate = (cure number + effective number)/total number *100%.

Comparison of visual analogue scale (VAS) and neck pain questionnaire (NPQ) scores between the two groups: Cervical pain was evaluated by VAS and NPQ scores. VAS scores ranged from 0 to 10, with 0 for painless and 10 for severe pain. Higher scores indicate more severe pain. NPQ was used to measure the feelings of patients concerning pain degrees, effects on sleep, nocturnal acmesthesia or numbness, duration of symptoms, effects on carrying objects, on reading and watching TV, on work and housework, on social activities, and driving. The total score was 36, with higher scores indicating greater effects on the patients.

Comparison of cervical and spinal cord function between the two groups: Cervical and spinal cord function of the patients was evaluated by Japanese Orthopedic Association (JOA) [16]. The total score of JOA was 17, 4 for upper limb function, 4 for lower limb function, 6 for acmesthesia, and 3 for bladder function. Patients were assessed with JOA scores before treatment and 6 months after treatment. Improvement rate of spinal cord function = ((postoperative JOA score - preoperative JOA score))/((17 - preoperative JOA score)) *100%. Improvement rate of spinal cord function: <25%, poor; 25%-50%, normal; 50%-75%, good; >75%, excellent. Good and excellent rate = (excellent number + good number)/total number *100%.

Comparison of serum CK and LAH levels between the two groups: A total of 5 mL of venous blood was extracted from the cubital veins of the patients before and after treatment. It was centrifuged at 2,500 r/min for 10 minutes. Next, upper serum was collected and stored at -20°C/for preservation. Levels of serum CK and LDH were measured by the enzyme kinetics method with an automatic biochemical analyzer (Hitachi 7170).

Adverse reactions, including nausea, vomiting, infections, allergic reactions, acupuncture syncope, and broken needles, were compared between the two groups.

Statistical methods

All data were analyzed with SPSS 20.0 software. Measurement data are expressed as mean ± standard deviation. Comparisons between the two groups were performed by independent-sample t-test. Comparisons before and after treatment between the two groups were performed by paired t-test. Count data are expressed as rates and were compared by Chi-squared test. P<0.05 indicates statistical significance.

Table 2. Comparison of efficacy

Group	Observation group (n=75)	Control group (n=75)	χ^2	P
Cure	26	15		
Effective	47	46		
Ineffective	2	14		
Total effective rate (%)	97.33	81.33	10.070	0.002

Table 3. Comparison of VAS and NPQ scores before and after treatment

Group	Observation group (n=75)	Control group (n=75)	t/χ^2	P
VAS scores				
Before treatment	4.2±0.8	4.3±1.0	0.676	0.500
After treatment	2.1±0.4	3.4±0.6	15.610	<0.001
t	20.330	6.683		
P	<0.001	<0.001		
NPQ scores	28.6±6.2	29.1±6.5	0.482	0.631
Before treatment	9.8±3.7	15.3±4.6	8.068	<0.001
After treatment	22.550	15.010		
t	<0.001	<0.001		
P	20.33	6.683		

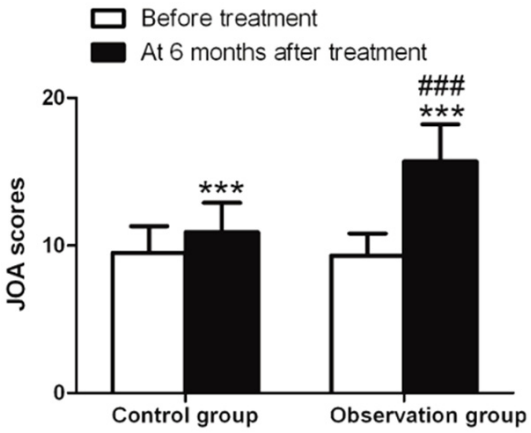

Figure 1. Comparison of JOA scores before treatment and 6 months after treatment between the two groups. Compared with the same group before treatment, ***P<0.001; compared with the control group, ###P<0.001.

Results

Comparison of general data

There were no statistically significant differences in age, gender, body mass index, course of disease, and lesion segments between the two groups (P>0.05). Thus, they were comparable. See **Table 1**.

Comparison of efficacy

In the control group, the cure number was 15, the effective number was 46, and the total effective rate was 81.33%. In the observation group, the cure number was 26, the effective number was 47, and the total effective rate was 97.33%. There were significant differences in total effective rates between the two groups (χ^2=10.070, P=0.002). See **Table 2**.

Comparison of VAS and NPQ scores

There were no significant difference in VAS and NPQ scores between the two groups before treatment (P>0.05). The VAS and NPQ scores in the two groups after treatment were significantly lower than those before treatment. Differences were statistically significant (all P<0.001). The VAS and NPQ scores in the observation group were significantly lower than those in the control group after treatment. Differences were statistically significant (both P<0.001). See **Table 3**.

Comparison of cervical and spinal cord function

There were no significant differences in JOA scores between the two groups before treatment. JOA scores in the two groups after 6 months of treatment were significantly higher than those before treatment. Differences were statistically significant (P<0.001). JOA scores in the observation group was significantly higher than those in the control group after 6 months of treatment (P<0.001). See **Figure 1**. After 6 months of treatment, the excellent and good rate of spinal cord function improvement in the observation group was 84.00% (63/75), while that in the control group was 94.67% (71/75). There were significant differences in the excellent and good rate of spinal cord function improvement between the two groups (χ^2=4.478, P=0.034). See **Table 4**.

Table 4. Comparison of cervical and spinal cord function

Group	Observation group (n=75)	Control group (n=75)	χ^2	P
Excellent	48	43		
Good	23	20		
Normal	3	8		
Poor	1	4		
Excellent and good rate (%)	94.67	84	4.478	0.034

Comparison of CK and LDH levels

There were no significant differences in levels of CK and LDH between the two groups before treatment. CK and LDH levels of patients in the two groups after treatment were significantly lower than those before treatment, with statistically significant differences (all P<0.001). CK and LDH levels in the observation group were significantly lower than those in the control group after treatment. Differences were statistically significant (both P<0.001). See **Figure 2**.

Comparison of adverse reactions

There were no adverse reactions, such as nausea, vomiting, infection, allergic reactions, acupuncture syncope, and broken needles, during treatment for both groups.

Discussion

In recent years, incidence of cervical spondylopathy has increased. It has become more prevalent among a younger age group. The neck type of cervical spondylopathy is the earliest phenotype. Besides cervical symptoms, it mainly manifests as straightened, disappeared, or recurved cervical physiological curvature on imaging examinations. If not treated in time, the spinal cord may be softened or necrotic. Even with corresponding treatment, patient recovery remains poor. Some studies have shown that retrogression, trauma, inflammatory injuries, or alloplasia of cervical vertebra are important factors leading to the development of the neck type of cervical spondylopathy [17]. At present, most scholars believe that cervical curvature straightening caused by cervical muscle imbalances accounts for much of the pathogenesis of the neck type of cervical spondylopathy [18]. From the perspective of Traditional Chinese Medicine, cervical spondylopathy belongs to the category of “stiff neck”, “Bi syndrome”, “neck and shoulder pain”, “vertigo”, and so forth. This indicates that muscle tissue plays an important role in the occurrence and development of cervical spondylopathy [19]. Results of the current study show that neck pain (VAS scores and NPQ scores) of patients in the control group, after treatment with mecobalamin tablets, was significantly lower than that before treatment. JOA scores were significantly higher than those before treatment. The excellent and good rate was 84.00% after 6 months of follow-up. Results suggest that mecobalamin tablets can relieve the symptoms of patients with the neck type of cervical spondylopathy. However, 16.00% of the patients still had poor results, suggesting that this may be related to severity of spinal cord compression and failure to completely improve local blood supply.

From the perspective of Traditional Chinese Medicine, the main treatment principles of the neck type of cervical spondylopathy are tonifying qi and activating blood, clearing meridians and dredging collaterals. Shenfu injections, a pure Chinese medicine extract preparation, is mainly the extract of radix aconiti lateralis preparata and red ginseng. It has the effects of invigorating qi for relieving desertion and reviving yang for resuscitation [20]. Studies have shown that it can reduce peripheral resistance, raise blood pressure, increase coronary blood flow, and improve myocardial oxygen tolerance [21]. Further studies have shown that Shenfu injections can improve tissue microcirculation, blood supply, and oxygen supply. They can also antagonize spinal cord ischemia-reperfusion injuries [22, 23]. In this study, Shenfu injections were directly injected into the diseased site by acupoint injections. In this process, acupuncture could dredge the qi and blood of governor vessels and bladder meridian, allowing the drug to play the greatest role of activating blood. Thus, the combined application of mecobalamin tablets could nourish the cervical nerves and promote the recovery of neural function. Results of this study showed that, compared with the control group, Shenfu injections combined with mecobalamin tablets could significantly reduce VAS and NPQ scores, which illustrates that symptoms of neck pain were reduced. This treatment increased JOA

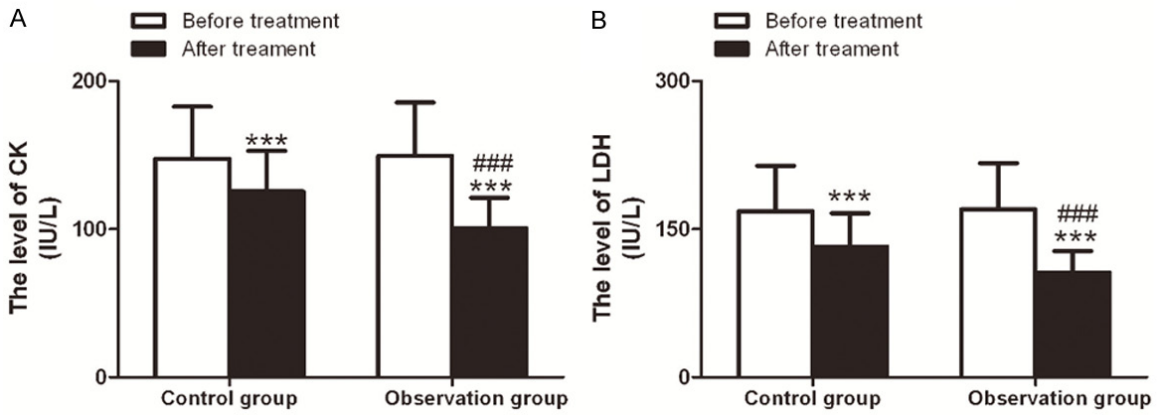

Figure 2. Comparison of CK and LDH of the two groups before and after treatment. A: CK, creatine kinase; B: LDH, lactate dehydrogenase. Compared with the same group before treatment, ***P<0.001; compared with the control group, ###P<0.001.

scores, indicating that the spinal cord function of patients was improved. Moreover, there were no adverse reactions during treatment. Results indicate that Shenfu injections, combined with mecobalamin tablets, are effective in the treatment of the neck type of cervical spondylopathy and are beneficial to the recovery of spinal cord nerve function, with good safety.

Studies have shown that, as one of the key enzymes of energy metabolism in muscle cells, creatine kinase (CK) contains four isozymes, most of which are found in skeletal muscle cells [24]. If the muscle tissue is damaged, membrane permeability will increase and CK will be released into the blood in large quantities. It follows that this change in CK levels is one of the sensitive indicators for evaluation of muscle loss, adaptation, and recovery [25]. Moreover, studies have shown a high correlation between muscle soreness and serum CK levels [26]. Lactate dehydrogenase (LDH), one of the key enzymes in the process of glycogen anaerobic glycolysis, contains five isozymes. It distributes in different tissue cells and forms a specific zymogram, which is most abundant in skeletal muscle. If the muscle tissue is damaged, its contained LDH will be released into the blood, resulting in a change in enzyme levels. Thus, the detection of LDH is helpful in the diagnosis of the damaged site [27]. It has been reported that anaerobic energy metabolism and LDH levels increase when skeletal muscles are damaged [28]. Results of the present study show that levels of CK and LDH, in the two groups after treatment, were significantly lower than those before treatment. Levels of CK and LDH in the observation group were significantly lower than those in the control group, after treatment, suggesting an increased permeability of skeletal muscle cell membrane in patients with the neck type of cervical spondylopathy and an accumulation of released CK and LDH in the blood. Compared with mecobalamin tablets alone, CK and LDH levels of patients treated with acupoint injections of Shenfu, combined with mecobalamin tablets, were significantly decreased. Additionally, muscle injuries were better repaired.

In summary, acupoint injections of Shenfu, combined with mecobalamin tablets, are effective for treatment of the neck type of cervical spondylopathy. This treatment can significantly reduce cervical pain of patients and promote the recovery of spinal cord nerve function. It can also significantly decrease levels of CK and LDH and promote the recovery of damaged cervical skeletal muscles, providing an experimental basis for treatment of the neck type of cervical spondylopathy. There were some limitations to the current study, however. The sample size was too small and this was a single-center study, lacking long-term follow-up results.

Disclosure of conflict of interest

None.

Address correspondence to: Jiwen Dong, Sports Human Body Teaching and Research Section, Physical Education College, Shanghai Normal University, No. 100 Guilin Road, Xuhui District, Shanghai City 20-

0234, China. Tel: +86-021-64322311; E-mail: dongjiwen13dw@163.com

References

[1] Naito K, Yamagata T, Ohata K and Takami T. Management of the patient with cervical cord compression but no evidence of myelopathy: what should we do? Neurosurg Clin N Am 2018; 29: 145-152.

[2] Koyanagi I. Options of management of the patient with mild degenerative cervical myelopathy. Neurosurg Clin N Am 2018; 29: 139-144.

[3] Bakhsheshian J, Mehta VA and Liu JC. Current diagnosis and management of cervical spondylotic myelopathy. Global Spine J 2017; 7: 572-586.

[4] Evans LT and Lollis SS. Dynamic compression of the spinal cord by paraspinal muscles following cervical laminectomy: diagnosis using flexion-extension MRI. Case Rep Radiol 2015; 2015: 275623.

[5] Mitsutake T, Sakamoto M, Chyuda Y, Oka S, Hirata H, Matsuo T, Oishi T and Horikawa E. Greater cervical muscle fat infiltration evaluated by magnetic resonance imaging is associated with poor postural stability in patients with cervical spondylotic radiculopathy. Spine 2016; 41: E8-14.

[6] Louthrenoo W, Weerayutwattana N, Lertprasertsuke N and Sukitawut W. Serum muscle enzymes, muscle pathology and clinical muscle weakness: correlation in Thai patients with polymyositis/dermatomyositis. J Med Assoc Thai 2002; 85: 26-32.

[7] Tamai K, Romanu J, Grisdela P, Paholpak P, Zheng P, Nakamura H, Buser Z and Wang JC. Small C7-T1 lordotic angle and muscle degeneration at C7 level were independent radiological characteristics of patients with cervical imbalance: a propensity score-matched analysis. Spine J 2018; 18: 1505-1512.

[8] Cui ML, Kong XL and Wang JG. Clinical efficacy of pishen bingbu recipe in patients with sympathetic cervical spondylosis and its impact on heart rate variability. Zhongguo Zhong Xi Yi Jie He Za Zhi 2008; 28: 1034-1037.

[9] Zhang N, Liu J, Qiu Z, Ye Y, Zhang J and Lou T. Shenfu injection for improving cellular immunity and clinical outcome in patients with sepsis or septic shock. Am J Emerg Med 2017; 35: 1-6.

[10] Lv SJ, Lai DP, Wei X, Yan Q and Xia JM. The protective effect of Shenfu injection against elderly severe pneumonia. Eur J Trauma Emerg Surg 2017; 43: 711-715.

[11] Zhang Y, Wang C and Guo Y. Of clinical reseach on cervical spondylosis treated with acupoint injection in recent five years. Zhongguo Zhen Jiu 2012; 32: 477-479.

[12] Li K, Wei D and Li JK. Acupuncture plus acupoint-injection for treatment of cervical spondylosis of vertebroarterial type. J Tradit Chin Med 2008; 28: 243-244.

[13] Terayama H, Yamazaki H, Kanazawa T, Suyama K, Tanaka O, Sawada M, Ito M, Ito K, Akamatsu T, Masuda R, Suzuki T, Sakabe K. Multi-acupuncture point injections and their anatomical study in relation to neck and shoulder pain syndrome (so-called katakori) in Japan. PLoS One 2015; 10: e0129006.

[14] Li SY, Suyou L, Chen J, Maiwulanjiang M, Liu JH, Shan Z, Wang CY, Fan SW and Zhao FD. Comparison of modic changes in the lumbar and cervical spine, in 3167 patients with and without spinal pain. PLoS One 2014; 9: e114-993.

[15] Liu LA, Zhang S, Wang H and Tang LX. Acupuncture combined with moxibustion plaster for nerve-root type cervical spondylosis. Zhongguo Zhen Jiu 2016; 36: 139-143.

[16] Omori M, Shibuya S, Nakajima T, Endoh T, Suzuki S, Irie S, Ariyasu R, Unenaka S, Sano H, Igarashi K, Ichimura S and Ohki Y. Hand dexterity impairment in patients with cervical myelopathy: a new quantitative assessment using a natural prehension movement. Behav Neurol 2018; 2018: 5138234.

[17] Kong L, Tian W, Cao P, Wang H, Zhang B and Shen Y. Predictive factors associated with neck pain in patients with cervical disc degeneration: a cross-sectional study focusing on modic changes. Medicine (Baltimore) 2017; 96: e8447.

[18] Steilen D, Hauser R, Woldin B, Sawyer S. Chronic neck pain: making the connection between capsular ligament laxity and cervical instability. Open Orthop J 2014; 8:326-345.

[19] Lin JH, Chiu TTW and Hu J. Chinese manipulation for mechanical neck pain: a systematic review. Clin Rehabil 2012; 26: 963-973.

[20] Wang YY, Li YY, Li L, Yang DL, Zhou K and Li YH. Protective effects of Shenfu injection against myocardial ischemia-reperfusion injury via activation of eNOS in rats. Biol Pharm Bull 2018; 41: 1406-1413.

[21] Li YH, Yu B, Duan ZZ, Akinyi OM, Yu JH, Zhou K, Zhang Y and Gao XM. The coronary dilation effect of ShenFu injection was mediated through NO. PLoS One 2014; 9: e92415.

[22] Zhang H, Wan Z, Yan X, Wang DG, Leng Y, Liu Y, Zhang Y, Zhang H and Han X. Protective effect of Shenfu injection preconditioning on lung ischemia-reperfusion injury. Exp Ther Med 2016; 12: 1663-1670.

[23] Yang LJ, Wang J, Tian ZF and Yuan YF. Shenfu injection attenuates neonatal hypoxic-ischemic brain damage in rat. Neurol Sci 2013; 34: 1571-1574.

[24] Stajer V, Vranes M and Ostojic SM. Correlation between biomarkers of creatine metabolism

and serum indicators of peripheral muscle fatigue during exhaustive exercise in active men. Res Sports Med 2018; 1-8.

[25] Zhao X, Bi C and Yang Z. Studies on the creatine kinase MM isoforms of normal and duchenne muscular dystrophic patients. Chin Med J (Engl) 1998; 111: 75-77.

[26] Clifford T, Bell O, West DJ, Howatson G and Stevenson EJ. The effects of beetroot juice supplementation on indices of muscle damage following eccentric exercise. Eur J Appl Physiol 2016; 116: 353-362.

[27] Wang L, Shan Y, Chen L, Lin B, Xiong X, Lin L and Jin L. Colchicine protects rat skeletal muscle from ischemia/reperfusion injury by suppressing oxidative stress and inflammation. Iran J Basic Med Sci 2016; 19: 670-675.

[28] Ozkan H, Ekinci S, Uysal B, Akyildiz F, Turkkan S, Ersen O, Koca K and Seven MM. Evaluation and comparison of the effect of hypothermia and ozone on ischemia-reperfusion injury of skeletal muscle in rats. J Surg Res 2015; 196: 313-319.