Int J Clin Exp Med 2021;14(2):1331-1337
www.ijcem.com /ISSN:1940-5901/IJCEM0122447

Original Article

Clinical efficacies of electroacupuncture combined with epalrestat and α-lipoic acid in patients with diabetic peripheral neuropathy and its effects on nerve conduction velocity and oxidative stress

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Received September 15, 2020; Accepted October 12, 2020; Epub February 15, 2021; Published February 28, 2021

Abstract: Objective: To investigate the clinical efficacies of electroacupuncture (EAP) combined with epalrestat and α-lipoic acid (α-LA) in patients with diabetic peripheral neuropathy (DPN) and its effects on nerve conduction velocity and oxidative stress (OS). Methods: A prospective study was conducted on 138 patients with DPN, who were divided into the control group (treated with epalrestat + α-LA, n = 69) and observation group (treated with EAP + epalrestat + α-LA, n = 69). Clinical efficacy was observed 14 days after treatment. Nerve conduction function, Visual Analogue Scale score and OS factors were measured in both groups. Results: The total effective rate in the observation group was significantly higher than that in the control group (P = 0.036). After treatment, motor nerve conduction velocity and sensory nerve conduction velocity of the median nerve and common peroneal nerve in both groups were significantly improved compared with those before treatment, and the improvement in the observation group was significantly better than that in the control group (all P < 0.05). There were opposite trends in the neurological function score and degree of neuralgia (all P < 0.05). After treatment, malonaldehyde and superoxide dismutase in the two groups were significantly decreased and increased respectively compared with those before treatment (both P < 0.05), and the improvement of the two indicators in the observation group was significantly better than that in the control group (P < 0.001). Conclusion: EAP combined with epalrestat and α-LA in the treatment of DPN can improve clinical efficacy, promote nerve repair and improve the state of OS, which is worthy of clinical application.

Keywords: Electroacupuncture, diabetic peripheral neuropathy, clinical efficacy, neurological function, oxidative stress

Introduction

Diabetes mellitus (DM) is a metabolic disease characterized by elevated blood glucose. With the development of modern society and increased processing of the diet, the incidence of DM is increasing annually [1, 2]. DM is mainly caused by increased blood glucose, wherefrom the body changes under the influence of long-term hyperglycemia, resulting in multiple complications [3]. Diabetic peripheral neuropathy (DPN) is the most common complication of DM, with an incidence of 30% [4, 5]. The early symptoms of DPN are not obvious; with the progression of this disease, limb disorders, and pain or loss of sensory function may occur [6]. Its pathogenesis is mainly related to the occurrence of oxidative stress (OS) and the promotion of the secretion of inflammatory factors *in vivo* under the effect of hyperglycemia [7]. Therefore, the treatment of DPN mainly focuses on symptom improvement based on the patient's glycemic control. Epalrestat is an aldose reductase inhibitor, which can effectively reduce endothelial cell function damage [8]. Besides, α-lipoic acid (α-LA) is an antioxidant that can improve the state of OS [9]. Clinically, the combined application of the two drugs has a certain effect on DPN, but there are some patients still have poor effects or no obvious improvement of symptoms [10]. In recent years, it has been found that the application of electroacupuncture (EAP) in the treatment of DPN has achieved certain clinical results [11]. There

is currently no observation on the efficacy of EAP combined with epalrestat and α-LA in the treatment of DPN. Thus, this study explored the therapeutic effects and mechanism of EAP combined with epalrestat and α-LA in the treatment of DPN.

Materials and methods

Clinical information

A total of 138 patients admitted to the Department of Endocrinology of The Second Affiliated Hospital of Hainan Medical University from January 2017 to June 2019 were selected for a prospective study. Those patients were divided into a control group (treated with epalrestat + α-LA, n = 69) and an observation group (treated with EAP + epalrestat + α-LA, n = 69) according to a random number grouping method. The study was approved by the Hospital Ethics Committee of The Second Affiliated Hospital of Hainan Medical University, and all the included patients or their family members signed the consent form.

Inclusion criteria and exclusion criteria

The included patients, aged 18-76 years old, were in line with DM and DPN standards [12]. Additionally, patients with severe cardiac, renal, pulmonary dysfunction, other neuropathy and malignant tumors were excluded. Patients who were allergic to drugs were also excluded.

Methods

Control group: Patients were required to increase their vegetable intake, and reduced alcohol and simple sugar intake. Overweight or obese patients (body mass index > 25) were encouraged to lose weight and increase daily activity (moderate activity for at least 20 min a day). On the basis of blood glucose control, 50 mg of oral epalrestat (Yangtze River Pharmaceutical Group, China) was added, three times a day before meals. Moreover, patients were treated with intravenous drip infusion of α-LA injection (Jiangsu Shenlong Pharmaceutical Co., Ltd., China; 12 mL: 300 mg) and 0.9% normal saline (Double-Crane Pharmaceutical Co., Ltd., China; 100 mL) for 30 min once per day, lasting for 14 days.

Observation group: The same treatment was given in the observation group. Besides, EAP was performed. The patients were treated with EAP at Ganshu, Pishu, Shenshu, Zusanli, Quchi, Neiguan, Yanglingquan, Taixi and Taichong on both sides. The procedure of acupuncture was as follows. The patients were kept sitting position, the acupuncture points were routinely disinfected, and disposable sterile acupuncture needles (0.3 mm×40 mm; Suzhou Acupuncture Goods Co., Ltd., China) were used for acupuncture treatment. Ganshu: Oblique insertion 0.5-0.8 Cun; Pishu: straight insertion 0.5-1.0 Cun; Shenshu: straight insertion 0.5-1.0 Cun; Zusanli: straight insertion 1.0-1.5 Cun; Quchi: straight insertion 1.0-1.5 Cun; Neiguan: straight insertion 0.5-1.0 Cun; Yanglingquan: straight insertion 1.0-1.5 Cun; Taixi: straight insertion 0.5-1.5 Cun; Taichong: straight insertion 0.5-1.0 Cun. After inserting the needle into each point, the needle was lifted, inserted and twisted in order to make the acupuncture point produce needing sensation. The procedure of EAP was as follows. After getting needing sensation produced by acupuncture, the single-side Quchi-Neiguan and Yanglingquan-Taichong were set as the EAP point. And 6805-D electroacupuncture apparatus (Shantou Medical Equipment Factory Co., Ltd., China) was used for electric stimulation with disperse-dense wave (4 Hz of disperse wave, 20 Hz of dense wave, and 6 s of disperse-dense cycle). The intensity of electrical stimulation was set according to the patient's tolerance and EAP was conducted for 30 min/time, once a day, lasting for 14 days.

Outcome measures

Primary outcome measures: (1) Electromyograph was adopted to measure motor nerve conduction velocity (MNCV) and sensory nerve conduction velocity (SNCV) of the median nerve and common peroneal nerve before treatment and 14 days after treatment [12]. (2) Toronto clinical scoring system (TCSS) was used to measure neurological function, with the highest score of 19 points. A higher score indicated more sever neurological injury [13]. (3) Visual Analogue Scale (VAS) was used to record the scores of neuralgia before treatment and 14 days after treatment [14]. (4) After 14 days of treatment, the efficacy was evaluated according to the diagnostic criteria of clinical efficacy of DPN, which was divided into markedly effective, effective and ineffective [12]. The total effective rate = Number of cases of (markedly effective + effective)/total number of cases * 100%.

Table 1. Comparison of general information and baseline data (x ± SD)

Item	Observation group (n = 68)	Control group (n = 69)	χ^2/t	P
Gender (male/female)	43/25	39/30	0.642	0.423
Age (year)	61.3 ± 7.4	62.1 ± 8.3	0.595	0.553
Couse of DM (year)	10.4 ± 4.2	10.9 ± 4.9	0.641	0.523
Body mass index (kg/m^2)	24.92 ± 3.45	24.78 ± 4.16	0.214	0.831
Glycosylated hemoglobin (%)	5.9 ± 0.6	6.0 ± 0.7	0.897	0.371
Complication (n)				
Hyperlipidemia			0.190	0.663
Yes	38	36		
No	30	33		
Hypertension			0.005	0.994
Yes	39	40		
No	29	29		
Coronary heart disease			0.397	0.528
Yes	25	29		
No	43	40		
Obesity			0.084	0.772
Yes	24	26		
No	44	43		
Cerebral infarction			0.351	0.554
Yes	32	29		
No	36	40		
Hyperuricemia			0.615	0.433
Yes	25	21		
No	43	48		

Note: DM: Diabetes mellitus.

Secondary outcome measures: After admission, 5 mL of venous blood was taken at 8am in a fasting condition before and after treatment. Serum enzyme-linked immunosorbent assay was adopted to determine malonaldehyde (MDA; ml058112-1, Shanghai Enzyme-linked Biotechnology Co., Ltd., China) and superoxide dismutase (SOD; ml063052-1, Shanghai Enzyme-linked Biotechnology Co., Ltd., China).

Statistical analysis

SPSS 17.0 software was used for statistical analysis. The measurement data in line with a normal distribution were expressed by mean ± standard deviation (x ± sd), and those in line with homogeneity of variance were tested by t test. Paired t test was used for intra-group comparison, and independent t test was adopted for comparison between groups; and were expressed as t. Count data were expressed as n/%; the comparison was performed by Pearson Chi-square test and expressed as χ^2. $P < 0.05$ indicated a statistically significant difference.

Results

Comparison of general information and baseline data

During the treatment, one patient in the observation group withdrew from the study due to sudden myocardial infarction. There was no difference in general information and baseline data between the two groups (all $P > 0.05$), as shown in **Table 1**.

Comparisons of nerve conduction velocity (NCV), neurological function score and degree of neuralgia

After treatment, MNCV and SNCV of the two groups were significantly improved compared with those before treatment, and the improvement of the observation group was significantly better than that of the control group ($P < 0.001$). See **Table 2**. There were opposite trends in the neurological function score and degree of neuralgia (both $P < 0.001$), as shown in **Tables 3**, **4**.

Table 2. Comparison of nerve conduction velocity (x ± SD, cm/s)

Item	Median nerve		Common peroneal nerve	
	MNCV	SNCV	MNCV	SNCV
Before treatment				
Observation group (n = 68)	37.35 ± 2.17	35.12 ± 2.09	39.87 ± 1.97	37.96 ± 2.07
Control group (n = 69)	37.86 ± 2.29	34.99 ± 2.12	40.13 ± 2.07	38.05 ± 2.21
After treatment				
Observation group (n = 68)	43.62 ± 2.17***,###	45.87 ± 2.89***,###	48.74 ± 2.96***,###	45.97 ± 2.93***,###
Control group (n = 69)	40.26 ± 2.03***	41.97 ± 2.41***	43.78 ± 2.56***	42.23 ± 2.56***

Note: Compared within group before and after treatment, ***P < 0.001; compared with control group after treatment, ###P < 0.001. MNCV: motor nerve conduction velocity; SNCV: sensory nerve conduction velocity.

Table 3. Comparison of neurological function score (x ± SD, score)

Item	Observation group (n = 68)	Control group (n = 69)	t	P
Before treatment	11.34 ± 2.43	11.45 ± 2.29	0.273	0.786
After treatment	6.76 ± 1.55	8.05 ± 1.69	4.654	< 0.001
t	13.101	9.923		
P	< 0.001	< 0.001		

Table 4. Comparison of degree of neuralgia (x ± SD, score)

Item	Observation group (n = 68)	Control group (n = 69)	t	P
Before treatment	5.32 ± 1.44	5.46 ± 1.52	0.553	0.581
After treatment	1.53 ± 0.73	2.34 ± 1.03	5.304	< 0.001
t	19.362	14.110		
P	< 0.001	< 0.001		

Table 5. Comparison of clinical efficacy (n, %)

Item	Markedly effective	Effective	Ineffective	Total effective rate (%)
Observation group (n = 68)	35 (51.47)	29 (42.65)	4 (5.88)	64 (94.12)
Control group (n = 69)	27 (39.13)	30 (43.48)	12 (17.39)	57 (82.61)
χ^2				4.398
P				0.036

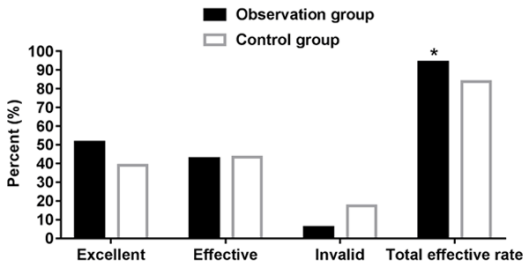

Figure 1. Comparison of clinical efficacy. Compared with control group, *P < 0.05.

Comparison of clinical efficacy

The total effective rate in the observation group was significantly higher than that in the control group (94.12% vs 82.61%, P < 0.05). See **Table 5** and **Figure 1**.

Comparisons of MDA and OS factors

After treatment, MDA and SOD in the two groups were significantly decreased and increased respectively compared with those before treatment (both P < 0.05), and the improvement of the two indicators in the observation group was significantly better than that in the control group (P < 0.001). See **Table 6**.

Discussion

With the continuous increase in the number of DM patients, the number of DPN patients is

Table 6. Comparison of MDA and OS factors (x ± SD)

Item	Before treatment		After treatment	
	Observation group (n = 68)	Control group (n = 69)	Observation group (n = 68)	Control group (n = 69)
MDA (mg/L)	23.68 ± 2.82	23.89 ± 3.46	7.76 ± 2.26$^{***,\#\#\#}$	13.67 ± 2.32***
SOD (ng/L)	121.15 ± 5.16	124.76 ± 5.48	206.08 ± 1.27$^{***,\#\#\#}$	188.32 ± 1.35***

Note: Compared within group before and after treatment, $^{***}P < 0.001$; compared with control group after treatment, $^{\#\#\#}P < 0.001$. OS: oxidative stress; MDA: malonaldehyde; SOD: superoxide dismutase.

also increasing [15]. DPN, the most common complication of DM, can impact a variety of nerves such as motor, sensory and autonomic nerves. Its impact on nerves is manifested as sensory disorders of the limb and motor disorders of the muscle, seriously affecting the life quality of patients [16]. NCV is the gold standard for the diagnosis of DPN. Patients will have pain during the long-term detection of NCV, thus the neurological function score is also used to evaluate the degree of neuropathy. A study has reported that the application of EAP in the treatment of sciatic nerve injury can improve the sciatic nerve function and make it recover faster thermal sense and touch [17]. Another study has indicated that the application of EAP can promote the recovery of nerve conduction function in patients with DPN; after acupuncture, the conduction of nerve velocity is increased and the growth of microvessels at the nerve injury site is promoted, so as to improve the state of nerve ischemia and hypoxia [18]. Research has proved that a significant curative effect depends on the selection of acupuncture and moxibustion sites for the treatment of DPN in the lesioned area [19]. After DPN modeled rats were treated with EAP, it was found that apoptosis of the sciatic nerve was reduced, which alleviated sciatic nerve injury [20]. In this study, it was also shown that the improvement of nerve function and the recovery of nerve conduction function in the observation group were better than those in the control group, which was related to the promotion of nerve repair by EAP. Severe pain occurs in patients with DPN due to hyperalgesia and hypersensitivity caused by neuropathy [21, 22]. Previous studies have shown that the application of EPA can improve chronic neuralgia and effectively relieve pain caused by DPN [23, 24]. A study has reported that low-frequency EPA has a better effect on the pain caused by DPN than high-frequency treatment. In this study, the pain caused by DPN was significantly alleviated in the observation group, which was consistent with the above research results. The judgment of clinical efficacy of DPN is mainly reflected by the improvement of nerve function and the reduction of pain symptoms. The above two indicators were improved in the observation group, suggesting that the neurological recovery of observation group is superior to that of the control group.

During the development of DM, free radicals may be increased while antioxidant capacity may be weakened through non-enzymatic glycosylation of protein, self-oxidation of glucose, activation of protein kinase, glycosylation of antioxidant enzymes and improvement of polyol pathway activity, which may lead to OS. OS refers to a stress state in which the body generates a large number of mitochondrial reactive oxygen species after being stimulated, leading to a decrease in antioxidant capacity. Once OS occurs in DPN patients, the progression of diabetes will be promoted by the sensitivity reduction of peripheral tissues to insulin and the damage to islet β cells [9]. Particularly, SOD and MDA are both important indicators to measure OS [25]. SOD, mainly distributed in cells and body fluids, is an important scavenger of reactive oxygen species, which functions in maintaining the balance of oxidation and antioxidation. It can protect cells from damage by breaking down hydrogen peroxide and lipid peroxide, as well as preventing lipid peroxidation. MDA, a product of lipid peroxidation, is also regarded as a risk factor of DPN. It is the material basis of cell membrane damage, whose content reflects the severity of lipid peroxidation in vivo and the cell damage [25]. CRP is an acute phase protein synthesized by liver cells. When the body is stimulated by inflammation, CRP level changes rapidly, which can well reflect the degree of inflammation [26]. TNF-α and IL-6 are important inflammatory indicators

in the inflammatory response, which are closely related to blood coagulation and vascular endothelial injury [27, 28]. Research has reported that the occurrence of DPN is closely associated with the production of inflammatory factors under the state of OS [29, 30]. Under the action of inflammatory factors, neuropathy can be aggravated and disease progression can be promoted [31, 32]. This study showed that EAP for the treatment of DPN can effectively reduce the level of inflammatory factors [33]. Another study indicated that EAP might inhibit inflammatory factors by inhibiting the release of TNF-α by macrophages [34]. What's more, acupuncture can effectively regulate the NF-κB signaling pathway and reduce neuronal apoptosis to achieve an anti-inflammatory effect [35]. In this study, it was also found that the level of oxidation factors in the observation group was improved significantly, and the improvement of OS state was conducive to the recovery of nerve function, which might be related to the above mechanism of action.

However, there are still limitations in this study. With a small sample size and short follow-up time, we are aware that a multicenter randomized controlled study with larger sample size and long follow-up time are needed, and the mechanism of acupuncture improving DPN remains to be explored in the future.

In summary, EAP combined with epalrestat and α-LA in the treatment of DPN can promote nerve repair and improve the state of OS, which is worthy of clinical application.

Disclosure of conflict of interest

None.

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References

[1] Kuo CL, Lu CL, Chang YH and Li CY. Population-based cohort study on dementia risk in patients with type 1 diabetes mellitus. Neuroepidemiology 2018; 50: 57-62.

[2] Gong JJ, Du XY, Li ZK, Li XH, Guo M, Lu J, Wang Y, Chen ZW and Li CL. Differential expression of genes identified by suppression subtractive hybridization in liver and adipose tissue of gerbils with diabetes. PLoS One 2018; 13: e0191212.

[3] Li PW, Zhang C, Gao P, Chen XW, Ma B, Yu DH, Song YX and Wang ZN. Metformin use and its effect on gastric cancer in patients with type 2 diabetes: a systematic review of observational studies. Oncol Lett 2018; 15: 1191-1199.

[4] Pareja-Ríos A, Ruiz-de la Fuente-Rodríguez P, Bonaque-González S, López-Gálvez M, Lozano-López V and Romero-Aroca P. Intravitreal dexamethasone implants for diabetic macular edema. Int J Ophthalmol 2018; 11: 77-82.

[5] Baeriswyl M, Taffé P, Kirkham KR, Bathory I, Rancati V, Crevoisier X, Cherix S and Albrecht E. Comparison of peripheral nerve blockade characteristics between non-diabetic patients and patients suffering from diabetic neuropathy: a prospective cohort study. Anaesthesia 2018; 73: 1110-1117.

[6] Iqbal Z, Azmi S, Yadav R, Ferdousi M, Kumar M, Cuthbertson DJ, Lim J, Malik RA and Alam U. Diabetic peripheral neuropathy: epidemiology, diagnosis, and pharmacotherapy. Clin Ther 2018; 40: 828-849.

[7] Bansal R and Singh R. Exploring the potential of natural and synthetic neuroprotective steroids against neurodegenerative disorders: a literature review. Med Res Rev 2018; 38: 1126-1158.

[8] Zhang NJ, Jiang L, Zhou ZB and Chai YM. Case-control study on locking plates fixation for the treatment of Neer 3-and 4-part proximal humerus fractures. Zhongguo Gu Shang 2014; 27: 38-40.

[9] Ghelani H, Razmovski-Naumovski V, Pragada RR and Nammi S. (R)-α-Lipoic acid inhibits fructose-induced myoglobin fructation and the formation of advanced glycation end products (AGEs) in vitro. BMC Complement Altern Med 2018; 18: 13.

[10] Restivo DA, Casabona A, Frittitta L, Belfiore A, Le Moli R, Gullo D and Vigneri R. Efficacy of botulinum toxin a for treating cramps in diabetic neuropathy. Ann Neurol 2018; 84: 674-682.

[11] He XF, Wei JJ, Shou SY, Fang JQ and Jiang YL. Effects of electroacupuncture at 2 and 100 Hz on rat type 2 diabetic neuropathic pain and hyperalgesia-related protein expression in the dorsal root ganglion. J Zhejiang Univ Sci B 2017; 18: 239-248.

[12] Abuzinadah AR, Kluding P, Wright D, D Silva L, Ryals J, Hendry B, Jawdat O, Herbelin L, McVey AL, Barohn RJ, Dimachkie MM and Pasnoor M. Less is more in diabetic neuropathy diagnosis: comparison of quantitative sudomotor axon

reflex and skin biopsy. J Clin Neuromuscul Dis 2017; 19: 5-11.
[13] Bril V and Perkins BA. Validation of the Toronto Clinical Scoring System for diabetic polyneuropathy. Diabetes Care 2002; 25: 2048-2052.
[14] Dahlstrand U, Sandblom G, Nordin P, Wollert S and Gunnarsson U. Chronic pain after femoral hernia repair: a cross-sectional study. Ann Surg 2011; 254: 1017-1021.
[15] Degu H, Wondimagegnehu A, Yifru YM and Belachew A. Is health related quality of life influenced by diabetic neuropathic pain among type II diabetes mellitus patients in Ethiopia? PLoS One 2019; 14: e0211449.
[16] Rojas DR, Kuner R and Agarwal N. Metabolomic signature of type 1 diabetes-induced sensory loss and nerve damage in diabetic neuropathy. J Mol Med (Berl) 2019; 97: 845-854.
[17] Zhang MX, Zhang Y, Bian YH, Fu H, Xu Y and Guo Y. Effect of long-term electroacupuncture stimulation on recovery of sensorimotor function after peripheral nerve anastomosis. Acupunct Med 2018; 36: 170-175.
[18] Zhang X and Liu ZS. Literature study on characteristics of acupuncture and moxibustion in improvement of diabetic peripheral neuropathy. World Chin Med 2017; 12: 176-179.
[19] Dimitrova A, Murchison C and Oken B. The case for local needling in successful randomized controlled trials of peripheral neuropathy: a follow-up systematic review. Med Acupunct 2018; 30: 179-191.
[20] Pan H, Huang HP, Zhang LY, Ma SQ, Yang HM and Wang HF. "Adjusting internal organs and dredging channel" electroacupuncture treatment prevents the development of diabetic peripheral neuropathy by downregulating glucose-related protein 78 (GRP78) and caspase-12 in streptozotocin-diabetic rats. J Diabetes 2019; 11: 928-937.
[21] Candrilli SD, Davis KL, Kan HJ, Lucero MA and Rousculp MD. Prevalence and the associated burden of illness of symptoms of diabetic peripheral neuropathy and diabetic retinopathy. J Diabetes Complications 2007; 21: 306-314.
[22] Gonçalves NP, Vægter CB, Andersen H, Østergaard L, Calcutt NA and Jensen TS. Schwann cell interactions with axons and microvessels in diabetic neuropathy. Nat Rev Neurol 2017; 13: 135-147.
[23] Zhou YF, Ying XM, He XF, Shou SY, Wei JJ, Tai ZX, Shao XM, Liang Y, Fang F, Fang JQ and Jiang YL. Suppressing PKC-dependent membrane P2X3 receptor upregulation in dorsal root ganglia mediated electroacupuncture analgesia in rat painful diabetic neuropathy. Purinergic Signal 2018; 14: 359-369.
[24] Garrow AP, Xing M, Vere J, Verrall B, Wang LF and Jude EB. Role of acupuncture in the management of diabetic painful neuropathy (DPN): a pilot RCT. Acupunct Med 2014; 32: 242-249.
[25] Song MS, Ryu PD and Lee SY. Kv3.4 is modulated by HIF-1α to protect SH-SY5Y cells against oxidative stress-induced neural cell death. Sci Rep 2017; 7: 2075.
[26] Wei P, Han B, Zhang WJ, Bai J, Jiang CY, Qiu CR, Zhang Q, Fu Q and Yang XJ. Effect of ticagrelor on the serum level of hs-CRP, ESM-1 and short-term prognosis of patients with acute STEMI. Exp Ther Med 2017; 13: 604-608.
[27] Qin LZ, Li W, Huang Y, Lu F, Li SJ, Yang HQ and Zhang JW. PTX3 expression in the plasma of elderly ACI patients and its relationship with severity and prognosis of the disease. Eur Rev Med Pharmacol Sci 2016; 20: 4112-4118.
[28] Yan QH, Wang X, Zha M, Yu MS, Sheng MX and Yu JY. The RhoA/ROCK signaling pathway affects the development of diabetic nephropathy resulting from the epithelial to mesenchymal transition. Int J Clin Exp Pathol 2018; 11: 4296-4304.
[29] Cao J, An W, Reeves AG and Lippert AR. A chemiluminescent probe for cellular peroxynitrite using a self-immolative oxidative decarbonylation reaction. Chem Sci 2018; 9: 2552-2558.
[30] Chen J, Liu WJ, Yi H, Hu XL, Peng LY and Yang FR. MicroRNA-155 mimics ameliorates nerve conduction velocities and suppresses hyperglycemia-induced pro-inflammatory genes in diabetic peripheral neuropathic mice. Am J Transl Res 2019; 11: 3905-3918.
[31] Mu ZP, Wang YG, Li CQ, Lv WS, Wang B, Jing ZH, Song XJ, Lun Y, Qiu MY and Ma XL. Association between tumor necrosis factor-α and diabetic peripheral neuropathy in patients with type 2 diabetes: a meta-analysis. Mol Neurobiol 2017; 54: 983-996.
[32] Xia J and Sun RL. Association between interleukin-6 rs1800795 polymorphism and the decreased risk of type 2 diabetes mellitus: an updated meta-analysis. Int J Clin Exp Med 2019; 12: 86-97.
[33] Gim GT, Lee JH, Park E, Sung YH, Kim CJ, Hwang WW, Chu JP and Min BI. Electroacupuncture attenuates mechanical and warm allodynia through suppression of spinal glial activation in a rat model of neuropathic pain. Brain Res Bull 2011; 86: 403-411.
[34] Liaw JJ and Peplow PV. Effect of electroacupuncture on inflammation in the obese zucker fatty rat model of metabolic syndrome. J Acupunct Meridian Stud 2016; 9: 73-79.
[35] Shu Q, Chen L, He WJ, Zhou HJ and Liang FX. A review of inflammatory signaling pathway regulated by acupuncture. World J Acupunct Moxibustion 2016; 26: 63-69.