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Influences of Tongdu Tiaoshen acupuncture therapy on neurological function, inflammatory factors and carotid atherosclerotic plaques in patients diagnosed with atherosclerotic cerebral infarction

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Abstract

Background

To assess the influences of Tongdu Tiaoshen acupuncture therapy on neurological function, inflammatory factors along with carotid atherosclerotic plaques in patients suffered from atherosclerotic cerebral infarction (CI).

Methods

One hundred and thirty-four patients diagnosed with atherosclerotic CI in our hospital from January 2022 to December 2024 were selected and divided into a study group (n=67) and a control group (n=67). The control group accepted oral atorvastatin calcium tablets. The study group accepted oral atorvastatin calcium tablets plus Tongdu Tiaoshen acupuncture therapy.

Results

Compared with the control group, the study group had lower NIHSS and mRS scores after one month of therapy ($P<0.01$). The results also showed reduced levels of IL-6, TNF-α and CRP, lower S-100β and NSE levels, higher BI scores, and improved sleep quality as indicated by lower PSQI scores (all $P<0.01$; for example, the between-group differences at one month for NIHSS, IL-6, BI and PSQI were 2.69 points (95% CI: 2.03-3.34), 3.18 units (95% CI: 2.50-3.86), 10.75 points (95% CI: 8.29-13.21) and 2.14 points (95% CI: 1.89-2.39), respectively).

Conclusion

Tongdu Tiaoshen acupuncture adjunctive to atorvastatin may improve vascular, neurological, inflammatory, and functional outcomes in atherosclerotic cerebral infarction, possibly via reductions in serum S-100β and NSE.

Keywords: atherosclerotic cerebral infarction, Tongdu Tiaoshen acupuncture therapy, neurological function, carotid atherosclerotic plaques, inflammatory response

Introduction

Cerebral infarction (CI) is a cerebrovascular disease caused by insufficient blood supply to the brain due to ischemia, vascular obstruction or narrowing[1]. It has a high incidence rate, a high disability rate as well as a high mortality rate, and has emerged as one of the primary "killers" threatening human health[2]. In China, approximately two million people are newly diagnosed with CI each year, among whom about 1.5 million die and only 6.5 million survive. It has caused significant economic pressure and mental burden on the country and society[3].

The formation of atherosclerotic plaques is a common cause of CI[4]. Currently, it is believed that atherosclerosis (AS) is a long-term and chronic inflammatory pathological process, and atherosclerotic plaques can accumulate in the arteries and form the basis for the occurrence of CI[5]. Evidence-based medical research has confirmed that dyslipidemia and inflammatory responses are significant factors contributing to the instability of atherosclerotic plaques. Statins mainly have effects such as regulating blood lipids, anti-inflammation and anti-atherosclerosis. Currently, one of the most commonly applied statin drugs in clinical practice for AS is atorvastatin[6]. It has powerful effects in improving blood lipids, reducing inflammatory responses, and alleviating oxidative stress, and has become the first-line medication for primary and secondary prevention of CI[7]. However, when atorvastatin is used alone in the treatment of AS, it also has certain limitations[8]. For instance, the lipid-lowering responses of different patients to atorvastatin vary. For some patients, even when using the maximum tolerated dose, their low-density lipoprotein cholesterol (LDL-C) levels still fail to reach the target value[9]. Besides, long-term utilization of atorvastatin may elevate the risk of adverse reactions, such as abnormal liver function and new-onset diabetes[10]. With the widespread application of traditional Chinese medicine (TCM) in clinical treatment of diseases, the combined use of Chinese and Western medicines for the treatment of CI has become a new treatment direction[11].

Acupuncture, as a part of TCM, originated in China over 2,000 years ago. It is a minimally invasive treatment method that can regulate the body's condition, has unique therapeutic effects, is easy to operate, and has few adverse reactions[12]. It has been reported that in China, acupuncture has been widely applied in CI treatment for a long time[13]. Basic research has indicated that acupuncture stimulation activates the relevant areas of the brain in CI patients, adjusts the sensory-motor network of the ipsilateral hemisphere, enhances the collaboration of the bilateral sensory-motor networks,

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regulates cerebral blood circulation and metabolism[14], while laboratory studies have shown that acupuncture can alleviate glutamate-mediated excitatory toxicity, regulate inflammatory responses, promote the generation of vascular cells and glial astrocytes, ultimately reduce brain cell damage and promote neural recovery[15]. Animal experiments have demonstrated that acupuncture can treat CI by improving microcirculation, increasing cerebral blood flow, enhancing cerebral metabolism, resisting free radical damage and lipid peroxidation reactions, reducing the toxicity of excitatory amino acids, and inhibiting cell apoptosis[16]. Clinical studies have also shown that acupuncture, as an important adjunctive treatment method, can further elevate the effectiveness of conventional treatment for CI[17].

Tongdu Tiaoshen acupuncture therapy, as a representative form of acupuncture therapy, is guided by the theories of traditional Chinese meridian and collateral theory and Chinese theory of consciousness[18]. It emphasizes the function of acupuncture in regulating consciousness, aiming to achieve the effect of treating both the body and the spirit simultaneously[19]. The governor meridian is the sea of Yang meridians, governing the Qi of all Yang meridians throughout the body and having close connections with the brain and other organs[20]. By acupuncturing the governor meridian and related acupoints, one can regulate the functions of the nervous system, balance Yin and Yang, unblock meridians, enhance Yang Qi, improve brain function, and regulate the functions of internal organs[21]. A previous study has indicated that the Tongdu Tiaoshen acupuncture therapy is effective in relieving the clinical symptoms of CI patients[22]. However, the effects of Tongdu Tiaoshen acupuncture therapy on neurological function, inflammatory factors as well as carotid atherosclerotic plaques in atherosclerotic CI patients remain unclear.

In this study, we aimed to assess the influences of Tongdu Tiaoshen acupuncture therapy on neurological function, inflammatory factors as well as carotid atherosclerotic plaques in patients suffered from atherosclerotic CI.

Material and Methods

Materials

One hundred and thirty-four patients diagnosed with atherosclerotic cerebral infarction (CI) in our hospital from January 2022 to December 2024 were enrolled. Eligible patients were randomly assigned in a 1:1 ratio to the control group (n = 67) or the study group (n = 67) using a computer-generated randomization sequence prepared by an independent statistician. Allocation codes were placed in sequentially numbered, sealed, opaque envelopes that were opened by the treating acupuncturist after patient enrollment.

Inclusion criteria: (1) All participants met the diagnostic criteria stipulated in the 2018 Chinese Guidelines for the Diagnosis and Treatment of Acute Ischemic Stroke; (2) The patient was diagnosed with atherosclerotic CI based on cranial CT or MRI scans and magnetic resonance angiography (MRA); (3) At the time of admission, the patient had not received thrombolytic, anticoagulant, or other treatments. Exclusion criteria: (1) Malignant tumors; (2) Other severe organ failure; (3) Mental disorders; (4) Contraindications for acupuncture treatment. This study was conducted with the informed consent of the patients, and was approved by the Medical Ethics Committees of our hospital.

Methods

Patients in both groups accepted symptomatic treatments such as oxygen inhalation, blood pressure reduction, control of blood sugar, anticoagulation, and nerve nutrition support.

The control group received symptomatic treatment along with oral atorvastatin calcium tablets. In addition to this regimen, the study group also received Tongdu Tiaoshen acupuncture therapy. The patient was placed in a prone position. The following acupoints were selected: Yamen (GV15), Baihui (GV20), Dazhu (BL11), Zhiyang (GV9), Mingmen (GV4), Shenzhu (GV12), cervical Jiaji (EX-B2, C1–C7), lumbar Yangguan (GV3), and Fengfu (GV16). Disposable sterile needles with specifications of 0.25 mm × 25 mm and 0.30 mm × 40 mm were used. Routine disinfection was performed with 75% ethanol. Acupuncture was conducted in accordance with relevant standards. After getting the Qi of acupuncture, the needle was kept in place. Acupuncture was performed once every 10 minutes, with the needle remaining in place for 40 minutes.

Both groups received treatment for a period of 1 month. Neurological function, carotid ultrasound, serum biomarkers, BI and PSQI scores were assessed by investigators who were blinded to group allocation, and statistical analyses were performed using de-identified group labels.

Observation indicators

(1) Five mL of fasting elbow venous blood was collected from patients and then centrifuged. Using an automatic biochemical analyzer (manufactured by Beckman Coulter Biotech (Suzhou) Co., Ltd.), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C) along with LDL-C were measured. (2) Using the Mindray ultrasound instrument (manufactured by Mindray Biomedical Corporation), the intima-media thickness (IMT) of the common carotid artery and plaque area were measured (3) Utilizing the National Institute of Health Stroke Scale (NIHSS) and the Modified Rankin Scale (mRS), patients' neurological function was assessed 23, 24. The score ranges of the NIHSS scale and the mRS scale were 0 to 42 points and 0 to 6 points respectively. The lower the score, the better neurological function. (4) Five mL of fasting elbow venous blood was collected from patients and then centrifuged. The levels of interleukin-6 (IL-6), tumor Necrosis Factor-α (TNF-α) along with C-reactive protein (CRP) were determined by enzyme-linked immunosorbent assay. (5) Five mL of fasting elbow venous blood was collected from patients and then centrifuged. The levels of serum S-100 calcium-binding protein β (S-100β) protein and neuron-specific enolase (NSE) were determined by enzyme-linked immunosorbent assay. (6) Using the Barthel Index (BI) 25, patients' ability to perform daily activities was assessed. The BI score ranged from 0 to 100, with a higher score indicating better daily living ability. (7) Using the Pittsburgh Sleep Quality Index (PSQI) 26, patients' sleep quality was assessed. The PSQI scale consisted of 7 dimensions, with a total score ranging from 0 to 21. The sleep quality was inversely proportional to the score of the scale. (8) Incidence of adverse reactions including gastrointestinal reactions, drug-induced liver and kidney damage, muscle pain was recorded.

Statistical analysis

GraphPad Prism 10.0 statistical software was employed for analyzing the data.

Table 1 Baseline data in both groups

Items	Control group (n=67)	Study group (n=67)	χ^2/t	P
Gender			0.12	0.72
Male	37 (55.22)	35 (52.24)		
Female	30 (44.78)	32 (47.76)		
Age (years)	64.40±8.03	64.56±8.13	0.11	0.90
Hypertension			0.03	0.86
Yes	36 (53.73)	37 (55.22)		
No	31 (46.27)	30 (44.78)		
Diabetes			0.12	0.71
Yes	25 (37.31)	23 (34.33)		
No	42 (62.69)	44 (65.67)		
Hyperlipemia			0.21	0.64
Yes	10 (14.93)	12 (17.91)		
No	57 (85.07)	55 (82.09)		
Smoking			0.20	0.65
Yes	11 (16.42)	13 (19.40)		
No	56 (83.58)	54 (80.60)		
Drinking			0.07	0.78
Yes	7 (10.45)	8 (11.94)		
No	60 (89.55)	59 (88.06)		

Table 2 Incidence of adverse reactions in both groups

Groups	Cases	Gastrointestinal reactions	Drug-induced liver and kidney damage	Muscle pain	Total incidence rate
Control group	67	2 (2.99)	2 (2.99)	2 (2.99)	6 (8.97)
Study group	67	2 (2.99)	1 (1.49)	1 (1.49)	4 (5.97)
χ^2					0.43
P					0.51

The measurement data were exhibited by mean ± standard deviation (x±s), and t-test was conducted for comparison. The counting data were exhibited as number and rate (%), and χ2 test was applied for comparison. P<0.05 was considered as statistically significant.

Results

Baseline data in both groups

As revealed in Table 1, the baseline data between the two groups showed no significant differences (P>0.05), implying the baseline data were comparable.

Blood lipid level in both groups

Prior to therapy, TC, TG, LDL-C and HDL-C levels manifested no difference between 2 groups (P>0.05). Following one month of therapy, TC, TG and LDL-C levels were diminished while HDL-C level was elevated in both groups (all P<0.01). In contrast to the control group, the study group had lower TC, TG and LDL-C levels as well as higher HDL-C level following one month of therapy (all P<0.01; between-group differences at one month for TC, TG, LDL-C and HDL-C were 0.47 mmol/L [95% CI 0.14-0.80], 0.28 mmol/L [95% CI: 0.15-0.41], 0.45 mmol/L [95% CI: 0.26-0.64] and 0.16 mmol/L [95% CI: 0.06-0.26], respectively; Figure 1).

IMT of the common carotid artery and plaque area in both groups

Prior to therapy, IMT of the common carotid artery and plaque area manifested no difference between 2 groups (P>0.05). Baseline IMT of the common carotid artery was 1.68 ± 0.20 mm in the control group (95% CI: 1.63 to 1.72) and 1.69 ± 0.24 mm in the study group (95% CI: 1.63 to 1.74), and baseline plaque area was 0.99 ± 0.29 mm² vs 0.99 ± 0.30 mm² (95% CI: 0.92 to 1.05 vs 0.91 to 1.06), with a mean between-group difference of 0.00 mm² (95% CI: -0.10 to 0.10)). Following one month of therapy, IMT of the common carotid artery and plaque area were diminished in both groups (P<0.01). In contrast to the control group, the study group had lower IMT of the common carotid artery and plaque area following one month of therapy (P<0.01; at one month, the study group exhibited a lower IMT of the common carotid artery than the control group by 0.22 mm (95% CI: 0.17 to 0.27) and a smaller plaque area by 0.26 mm² (95% CI: 0.20 to 0.32); Figure 2).

Neurological function in both groups

Prior to therapy, NIHSS score and mRS score manifested no difference between 2 groups (P>0.05). Following one month of therapy, NIHSS score and mRS score were diminished in both groups (P<0.01). In contrast to the control group, the study group had lower NIHSS score and mRS score following one month of therapy (P<0.01; at one month, NIHSS scores were 8.85 ± 2.05 in the control group (95% CI 8.36 to 9.33) and 6.16 ± 1.81 in the study group (95% CI 5.73 to 6.59), indicating a lower NIHSS score in the study group by 2.69 points (95% CI 2.03 to 3.34); mRS scores were 1.52 ± 0.38 vs 1.20 ± 0.23 (95% CI 1.43 to 1.62 vs 1.14 to 1.25), corresponding to a lower mRS score in the study group by 0.33 points (95% CI 0.22 to 0.44). The mean reductions in NIHSS from baseline were 7.49 points (95% CI 6.73 to 8.25) in the control group and 10.17 points (95% CI 9.40 to 10.93) in the study group, corresponding to an additional NIHSS improvement of 2.68 points (95% CI 1.59 to 3.76) in the study group; Figure 3).

Inflammatory response in both groups

Prior to therapy, IL-6, TNF-α and CRP levels manifested no difference between 2 groups (P>0.05; for example, baseline IL-6 levels were 17.54 ± 2.25 in the control group and 17.59 ± 2.57 in the study group, with a mean between-group difference of −0.05 units (95% CI −0.88 to 0.78)). Following one month of therapy, IL-6, TNF-α and CRP levels were diminished in both groups (P<0.01). In contrast to the control group, the study group had lower IL-6, TNF-α and CRP levels following one month of therapy (P<0.01; at one month, IL-6, TNF-α and CRP levels in the control vs study groups were 9.85 ± 2.08 vs 6.67 ± 1.87, 14.57 ± 4.15 vs 9.17 ± 2.54 and 7.26 ± 1.56 vs 5.19 ± 1.09, with between-group

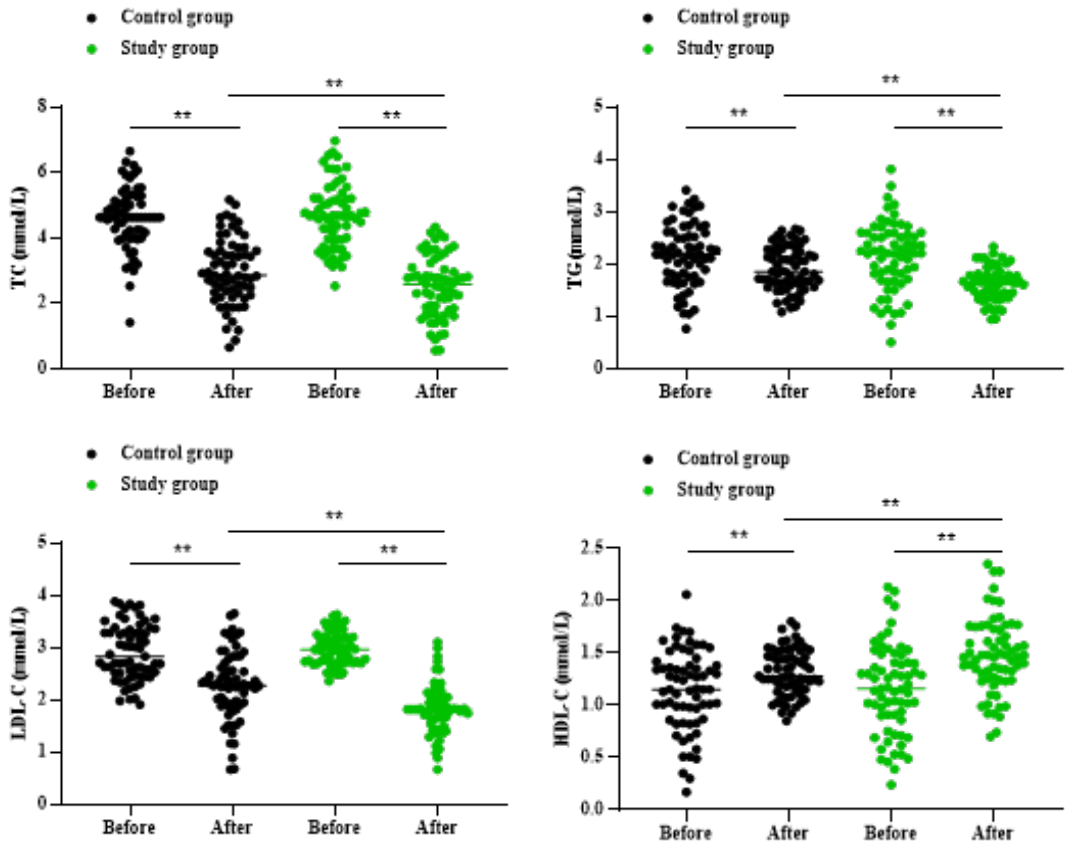

Figure 1 Blood lipid level in both groups. **P<0.01.

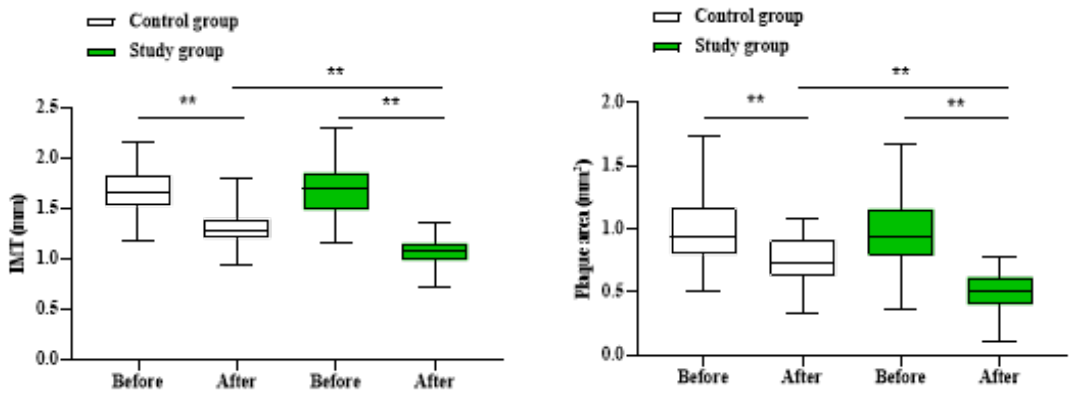

Figure 2 IMT of the common carotid artery and plaque area in both groups. **P<0.01.

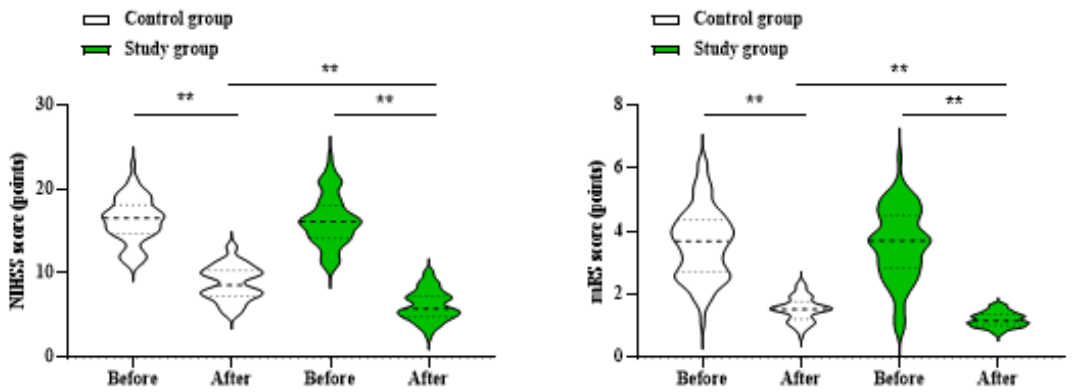

Figure 3 Neurological function in both groups. **P<0.01.

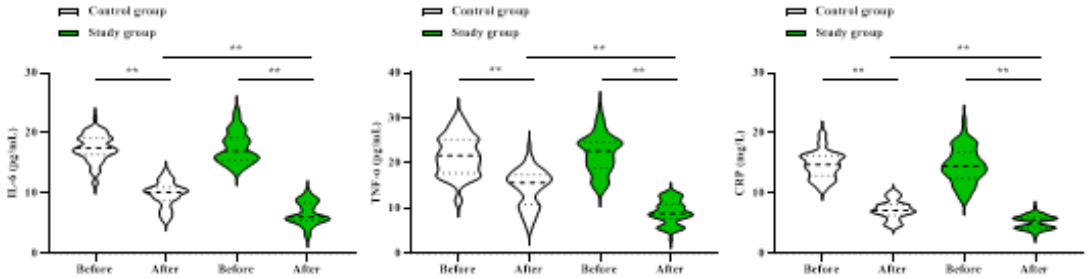

Figure 4 Inflammatory response in both groups. **P<0.01.

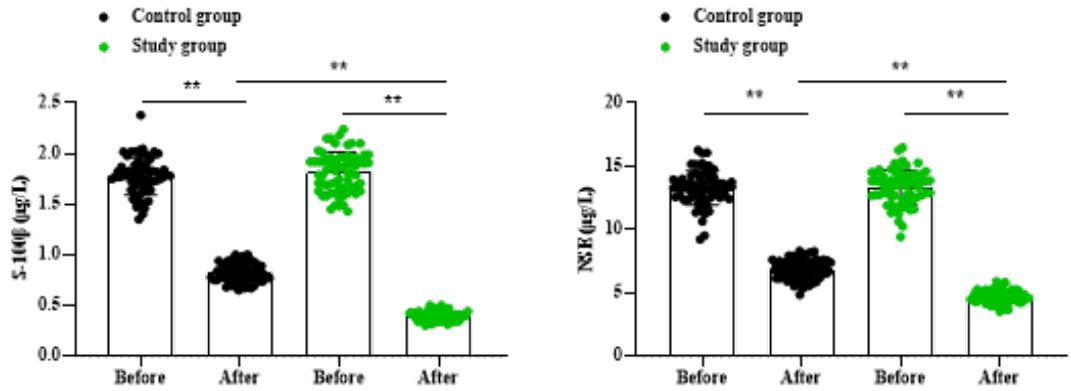

Figure 5 Serum S-100α and NSE levels in both groups. **P<0.01.

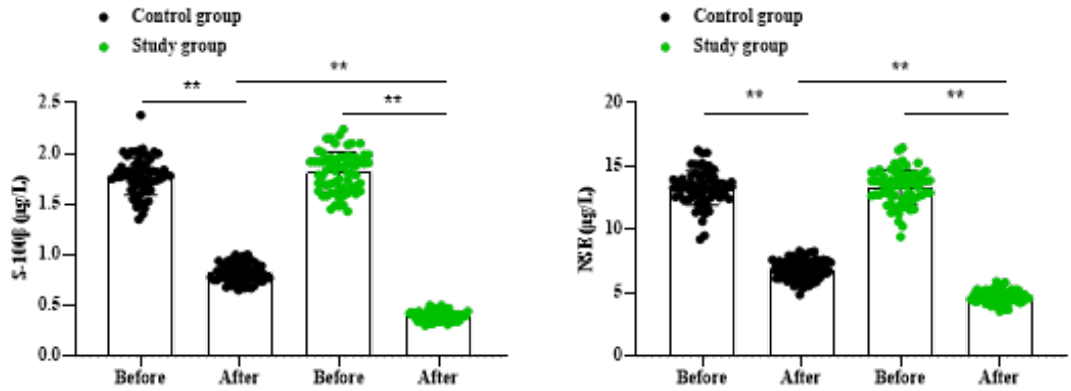

Figure 6 Daily living ability in both groups. **P<0.01.

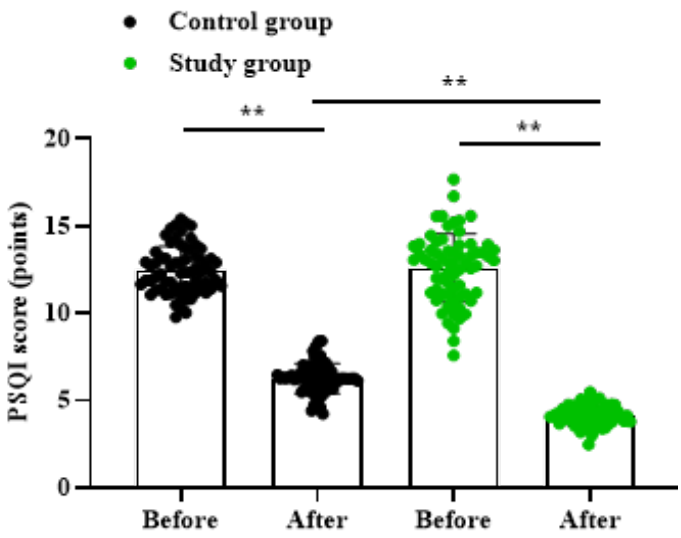

Figure 7 Sleep quality in both groups. **P<0.01.

differences of 3.18 units (95% CI 2.50 to 3.86), 5.40 units (95% CI 4.22 to 6.59) and 2.06 units (95% CI 1.60 to 2.52), respectively; Figure 4).

Serum S-100β and NSE levels in both groups

Prior to therapy, S-100β and NSE levels manifested no difference between 2 groups (P>0.05). Following one month of therapy, S-100β and NSE levels were diminished in both groups (P<0.01). In contrast to the control group, the study group had lower S-100β and NSE levels following one month of therapy (P<0.01; at one month, S-100β levels in the control vs study groups were 0.82 ± 0.09 vs 0.40 ± 0.05, and NSE levels were 6.85 ± 0.79 vs 4.68 ± 0.51, with between-group differences of 0.43 (95% CI 0.40 to 0.45) and 2.17 (95% CI 1.94 to 2.40), respectively; Figure 5).

Daily living ability in both groups

Prior to therapy, BI score manifested no difference between 2 groups (P>0.05). Following one month of therapy, BI score was elevated in both groups (P<0.01). In contrast to the control group, the study group had higher BI score following one month of therapy (P<0.01; at one month, BI scores in the control vs study groups were 65.82 ± 6.89 vs 76.56 ± 7.58, with a between-group difference of 10.75 (95% CI 8.29 to 13.21); Figure 6).

Sleep quality in both groups

Prior to therapy, PSQI score manifested no difference between 2 groups (P>0.05). Following one month of therapy, PSQI score was declined in both groups (P<0.01).

In contrast to the control group, the study group had lower PSQI score following one month of therapy (P<0.01; at one month, PSQI scores in the control vs study groups were 6.25 ± 0.85 vs 4.12 ± 0.58, with a between-group difference of 2.14 points (95% CI 1.89 to 2.39); Figure 7).

Incidence of adverse reactions in both groups

As revealed in Table 2, the incidence of adverse reactions between 2 groups showed no significant difference (P>0.05).

Discussion

CI falls under the category of "stroke" in TCM[27]. According to TCM, the brain is closely related to the functions of internal organs[28]. The governor meridian can command all the Yang meridians, connect internal organs, regulate Yin and Yang, control the brain's blood vessels, and is closely related to the brain and spinal cord[29]. The Tongdu Tiaoshen acupuncture therapy was proposed by Professor Zhang[30]. This therapy holds that the lesion is in the brain, and the treatment should start with the governor meridian. "Tongdu" refers to dredging the governor meridian and related collateral meridians to ensure the normal circulation of Qi and blood, and nourish the spirit[31]. "Tiaoshen" means adjusting the brain function[32]. The Tongdu Tiaoshen acupuncture therapy can promote the normal operation of the brain[33].

Excessive levels of blood lipids are the main factor contributing to the formation of AS[34]. Active lipid-lowering treatment can reduce the formation of infarction lesions[35]. LDL-C, HDL-C, TC and TG are all commonly used indicators for assessing lipid levels[36]. Among them, TC refers to the total amount of lipoproteins containing all types of cholesterol in the blood[37]. TG mainly participate in the energy metabolism within the human body and generate heat energy. Excessive TG levels in the blood can cause the blood to become thick, allowing lipids to deposit on the inner walls of blood vessels. Over time, these deposits gradually form AS[38]. LDL-C, one of the types of cholesterol, is called "bad cholesterol" because it is more likely to deposit on the inner walls of blood vessels, leading to AS. LDL-C is the main factor contributing to AS[39]. Because HDL-C can transport cholesterol from the blood vessels to the liver for decomposition and metabolism, it can reduce the deposition of cholesterol on the inner walls of blood vessels, thereby playing a role in preventing AS[40]. Therefore, it is also called "good cholesterol". In our study, the results indicated that compared to the control group, the study group had lower TC, TG and LDL-C levels as well as higher HDL-C level following one month of therapy. All these results suggested that Tongdu Tiaoshen acupuncture therapy could lower blood lipid level of patients with atherosclerotic CI. Consistent with our finding, Han et al. suggested that acupuncture method for consciousness-restoring resuscitation could modulate metabolic disorder of lipids in the patient of CI with hyperlipidemia[41].

Our study also manifested that in contrast to the control group, the study group had lower IMT of the common carotid artery and plaque area following one month of therapy, suggesting that Tongdu Tiaoshen acupuncture therapy could reduce the IMT of the common carotid artery and plaque area of patients with atherosclerotic CI. Similarly, Huang et al performed a randomized controlled clinical trial to prove that acupuncture could diminish the thickness and volume of carotid plaque and improve the stability of plaque in patients suffered from carotid AS[42].

Another important finding of our paper was that compared to the control group, the study group had lower NIHSS score and mRS score following one month of therapy, implying that Tongdu Tiaoshen acupuncture therapy could improve the neurological function of patients suffered from atherosclerotic CI. Likewise, Tsai et al. conduced a double-blinded randomized controlled trial to indicate that acupuncture improved the neurological function of patients suffered from acute ischemic stroke[43].

The inflammatory response runs through the entire pathological process of CI. Many reports have indicated that when inflammatory cells gather at the site of CI, they will secrete a large amount of inflammatory factors, inducing the generation of oxygen free radicals, which aggravates the oxidative stress response of the body, thereby damaging the vascular endothelial cells and brain tissue, and further worsening the degree of neurological functional impairment in patients[44]. TNF-α, IL-6, and CRP are commonly used indicators for clinical assessment of inflammatory responses. Among them, TNF-α is an important inflammatory mediator within atherosclerotic plaques. It promotes the generation of neurotoxic substances such as nitric oxide and excitatory amino acids, and can induce the aggregation and infiltration of white blood cells, thereby exacerbating local inflammatory responses and further aggravating brain damage[45]. IL-6 is an inflammatory cytokine with dual functions of immune regulation and chemotaxis. It can induce the aggregation of neutrophils, generate reactive oxygen metabolites, and damage tissue cells[46]. It has been reported that during the development of CI, the body's inflammatory and immune response processes will release a large amount of IL-6, and IL-6 will stimulate the production of other inflammatory mediators, triggering an inflammatory cascade reaction and exacerbating brain damage[47]. CRP is an acute-phase response protein synthesized by the liver. Its expression is related to the occurrence and development of CI[48]. During the development of atherosclerotic CI, the increase in CRP expression will activate the body's complement system, promote the release of monocytes, stimulate the generation of plasminogen inhibitor in arterial endothelial cells, and may subsequently damage the vascular endothelial cells, aggravate brain injury, as well as affect the prognosis of patients[49]. In our study, the results suggested that in contrast to the control group, the study group had lower IL-6, TNF-α along with CRP levels following one month of therapy, implying that Tongdu Tiaoshen acupuncture therapy could reduce the inflammatory response of patients with atherosclerotic CI. In line with our findings, Chen et al. implemented a systematic review and meta-analysis to indicate that acupuncture could diminish TNF-α, IL-6 along with CRP levels in CI patients[50].

Serum S-100β is a biochemical marker for brain nerve injury, which has a regulatory effect on the growth of neurons and axons. It not only can reflect the neurological deficits of patients with CI, but also is related to sleep disorders and cognitive functions of these patients[51]. The serum NSE level is the dimeric form of enolase within brain cells. In patients with CI, the serum NSE level significantly increases after the occurrence of CI, and the increase in this level is positively related to the area of CI and the degree of neurological impairment[52]. The results of our study indicated that in contrast to the control group, the study group had lower S-100β and NSE levels, higher BI score and lower PSQI score following one month of therapy, suggesting that Tongdu Tiaoshen acupuncture therapy may improve the daily living ability and sleep quality via regulating the levels of

brain nerve damage markers in patients with atherosclerotic CI. Additionally, our study indicated that the incidence of adverse reactions between 2 groups showed no difference, showing the safety of Tongdu Tiaoshen acupuncture therapy.

Conclusion

Our study demonstrates that Tongdu Tiaoshen acupuncture therapy can lower blood lipid level, diminish carotid atherosclerotic plaques, improve neurological function, reduce inflammatory response, improve daily living ability and sleep quality of patients with atherosclerotic CI, and may be related to the reduction of serum S-100β and NSE levels. However, the specific mechanism of action remains to be further studied.

Conflict of interest

The authors declare no financial or personal relationships that could influence this work.

Funding

None.

Author contributions

Chijie Yang and Yinyin Zhang contributed equally to this work, including conceptualization, methodology, data curation, and original draft preparation. Yanying Yang* (corresponding author) supervised the study, provided critical revisions, and approved the final manuscript.

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