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Original Article

Effect of acupuncture on sleep quality and neurological function in stroke patients with sleep apnea syndrome

Peng Zhang, Lingsu Cheng, Qian Tian, Guang Chen, Chao Chen, Junfeng Xu

Department of Acupuncture, First Teaching Hospital of Tianjin University of Traditional Chinese Medicine, National Clinical Research Center for Chinese Medicine Acupuncture and Moxibustion, Tianjin, China

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Abstract: Objective: To investigate the effect of acupuncture on sleep quality and neurological function in stroke patients with sleep apnea syndrome (SAS). Methods: In this prospective study, a total of 88 stroke patients with SAS were randomized into two groups: observation group (44 cases; patients received the western medicine treatment combined with acupuncture) and control group (44 cases; patients were given western medicine treatment only). All patients in both groups were treated for three weeks. The clinical efficacy, sleep quality, apnea-hypopnea index (AHI), cognitive function, neuron-specific enolase (NSE) and S100 calcium binding protein β (S100β) levels before and after treatment were compared between patients in the two groups. Results: Compared with those before treatment, the sleep latency, sleep duration, sleep efficiency and minimal oxygen saturation (SaO_{2min}) increased, while the longest apnea time and AHI decreased in both groups after treatment. More significant changes were found in the observation group (all $P<0.05$). After treatment, the overall effective rate in the observation group was higher than that in the control group ($P<0.05$); serum levels of NSE and S100β in both groups were lower than those before treatment, and the levels of the observation group were lower than those of the control group (all $P<0.05$); Montreal Cognitive Assessment (MoCA) scores in both groups were higher than those before treatment, and scores of the observation group were higher than those of the control group (all $P<0.05$). Conclusion: Western medicine treatment combined with acupuncture can significantly relieve the clinical symptoms of stroke patients with SAS and improve sleep quality and neurological function. Therefore, it is worthy of clinical application.

Keywords: Stroke, sleep apnea syndrome, acupuncture, sleep quality, neurological function

Introduction

Stroke is a major disease leading to disability and death in Chinese people, especially in the elderly [1]. Sleep apnea syndrome (SAS) is a disease of recurrent apnea during sleep caused by airway stenosis and obstruction of the upper respiratory tract, which is mostly accompanied by snoring during sleep and daytime sleepiness. With the development of the disease, it can cause hypoxemia and hypercapnia. In some severe cases, it may lead to respiratory and circulatory failure, resulting in the death of patients [2]. Elderly stroke patients are more likely to develop SAS, which influence not only the sleep quality, but also their neurological function [3].

Western medicine treatment can relieve nocturnal airway obstruction, apnea and other symptoms to a certain extent. Surgical treatment, one of the typical western medicine treatments, produces serious damage to the body, while drug treatment causes significant adverse reactions [4]. According to Traditional Chinese Medicine (TCM), SAS is classified into “drowsiness” and “snoring”. Stroke patients have obstructed airways and inhibited lung-qi, which can cause respiratory dysfunction and apnea. From the TCM theory, the repeated collapse of the pharynx during sleep is the main cause of the occurrence of SAS [5]. Acupuncture can improve recurrent pharyngeal collapse through specific acupoint stimulation, which relieves clinical symptoms in patients with SAS [6]. However, there has been no study investigating the effect of acupuncture on neurological function in stroke patients with SAS. This study aims to investigate the effect of acupuncture on sleep quality and neurological function in stroke patients with SAS.

Materials and methods

General information

In this prospective study, a total of 88 stroke patients with SAS treated in our hospital from February 2019 to January 2020 were randomized into an observation group and a control group, each with 44 cases.

Inclusion criteria: Patients aged from 45 to 70 years; patients who met the diagnostic criteria of stroke and SAS in "Chinese acute ischemic stroke diagnosis and treatment guidelines 2014" and "Guidelines for the diagnosis and treatment of obstructive sleep apnea hypopnea syndrome (2011 Revision)" [7, 8]. Patients who signed informed consent. Exclusion criteria: Patients with severe cognitive impairment or Alzheimer's disease; patients with brain tumors; patients who could not bear acupuncture treatment; patients who were unable to finish the laboratory biochemical examination; patients with chronic insomnia. This study was approved by the ethics committee of our hospital.

Methods

The control group was treated with western medicine, such as edaravone injection (Batch number: 190626, Shandong Luoxin Pharmaceutical Group Co., Ltd., China), Xueshuantong injection (Batch number: 190808, Livzon (Group) Limin Pharmaceutical Factory, China), aspirin enteric-coated tablets (Batch number: 191029, Shanghai Xinyi Bailuda Pharmaceutical Co., Ltd., China), deproteinized calf blood extract for injection (Batch number: 190420, Wuhan Humanwell Pharmaceutical Co., Ltd., China). Treatment lasted for 3 weeks. Acupuncture treatment was added to the patients in observation group apart from the western medicine treatment in the control group. Lianquan point, the main point in this treatment, was punctured by a disposable filiform needle (diameter: 0.3 mm, length: 50 mm) in depth about 50 mm to the direction of the tongue base. Twisting and reinforcing method was applied to manipulate the needle so that it was well settled and retained for 30 min when the patient felt slight numbness and distension of the throat. Another disposable filiform needle was used to slowly puncture into the place about 20 mm near the Lianquan point with the depth about 20 mm. The needle was retained for 30 min as well. A pulse electrotherapy instrument (KWD-808, Shenzhen Senta Times Technology Co., Ltd., China) was connected to the patient with the frequency set at 2 Hz and the current intensity was manipulated catering to the patient's tolerance. The whole treatment was performed for 3 weeks with 30 min/time, once a day before bedtime.

Outcome measures

Main outcome measures: sleep quality of patients was evaluated by Polysomnography (SOMNlab2, Weinmann Medical Technology, Germany) before and after treatment. The sleep latency, sleep duration, the longest apnea and sleep efficiency were recorded and compared between the two groups [9]. Apnea-hypopnea index (AHI) and the minimal oxygen saturation (SaO_{2min}) of patients was also measured and compared between the two groups before and after treatment by the Polysomnography [9]. Clinical efficacy was evaluated according to AHI and clinical symptoms, which could be divided into five dimensions: cured, markedly effective, effective and ineffective [10]. Cured referred to the cases as snoring and apnea and other clinical symptoms basically disappeared with AHI <5 times/h and SaO_{2min} >90%. Significantly effective referred to the cases as clinical symptoms were significantly alleviated with AHI <20 times/h or at least 50% less than that before treatment. Effective referred to those as clinical symptoms were alleviated and AHI was 25%-50% less than that before treatment. Ineffective referred to those as clinical symptoms and AHI did not meet the above criteria. The overall effective rate = (cured cases + markedly effective cases + effective cases)/total cases ×100%.

Secondary outcome measures: neurological function: about 5 mL of venous blood was drawn before and after treatment, which was centrifuged after coagulation. The serum was isolated to detect serum levels of neuron-specific enolase (NSE) and S100 calcium binding protein β (S100β) by enzyme-linked immunosorbent assay (ELISA). NSE is mainly present in neuroendocrine cells and neurons in the brain. S100β is the most active molecule in the S100 protein family and is specifically present in cen-

Table 1. Comparison of general information of patients between the two groups (n, $\bar{x}$ ± sd)

Index	Observation group (n=44)	Control group (n=44)	χ^2/t	P
Gender (n)			1.137	0.286
Male	24	19		
Female	20	25		
Age (years)	56.8±5.3	57.4±6.4	0.479	0.633
BMI (kg/m^2)	23.43±3.22	23.20±3.19	0.337	0.737
Diseases (n)			1.640	0.200
Cerebral hemorrhage	24	18		
Cerebral infarction	20	26		
Underlying diseases (n)			0.886	0.642
Hypertension	26	21		
Hyperlipidemia	13	15		
Diabetes	8	10		
Smoking history (n)			0.463	0.496
Yes	16	13		
No	28	31		
Drinking history (n)			0.210	0.647
Yes	13	15		
No	31	29		

Note: BMI: body mass index.

tral glial cells and glial cells of other types. Therefore, by checking the cerebrospinal fluid or serum levels of both proteins, the neurological changes after brain tissue damage in patients could be reflected [11]. Montreal Cognitive Assessment (MoCA) was used to assess the cognitive function of patients before and after treatment, with a total score of 30 points. The score is positively correlated with the cognitive function [12].

Statistical analysis

SPSS 20.0 was utilized for statistical analysis of data. Count data were expressed as n (%), and χ^2 test was performed for comparison between groups; measurement data in line with the normal distribution were represented as $\bar{x}$ ± sd. Paired t test was implemented for comparison before and after intervention in the same group; independent samples t test was carried out for comparison between groups. P<0.05 was considered statistically significant.

Result

Comparison of general information of patients between the two groups

There was no statistically significant difference in the general information between the two groups (P>0.05), so the general data were comparable. See **Table 1** for details.

Comparison of sleep quality of patients between the two groups

Compared with those before treatment, the sleep latency, sleep duration and sleep efficiency of patients in both groups increased after treatment, while the longest apnea time was shortened. There were more significant changes in the observation group (all P<0.05). See **Table 2** for details.

Comparison of AHI and SaO_{2min} of patients between the two groups before and after treatment

After treatment, AHI decreased and SaO_{2min} increased in both groups. More significant changes were found in the observation group (all P<0.05). See **Table 3** for details.

Comparison of clinical efficacy between the two groups before and after treatment

The overall effective rate after treatment in the observation group was higher than that in the control group (P<0.05), as shown in **Table 4**.

Comparison of serum levels of NSE and S100β between the two groups before and after treatment

After treatment, the serum levels of NSE and S100β in both groups were lower than those before treatment, and both protein levels of the observation group were lower than those of the control group (all P<0.05). See **Table 5** for details.

Comparison of MoCA scores between the two groups before and after treatment

After treatment, the MoCA scores of the two groups were higher than those before treatment, and the scores of the observation group were higher than those of the control group (all P<0.05). See **Table 6** and **Figure 1** for details.

Table 2. Comparison of sleep quality of patients between the two groups ($\bar{x}$ ± sd)

Groups	Sleep latency (min)	Sleep duration (min)	The longest apnea time (s)	Sleep efficacy (%)
Observation group (n=44)				
Before treatment	26.53±6.55	324.48±30.58	70.07±8.84	83.38±4.85
After treatment	40.05±6.06$^{*,\#}$	440.09±39.96$^{*,\#}$	47.70±7.90$^{*,\#}$	90.09±5.49$^{*,\#}$
Control group (n=44)				
Before treatment	25.89±5.84	322.95±35.64	69.80±7.96	83.10±5.55
After treatment	35.59±5.48*	370.95±37.50*	53.33±6.60*	85.98±5.83*

Note: Compared with that before treatment, $^{*}P<0.05$; compared with the control group after treatment, $^{\#}P<0.05$.

Table 3. Comparison of AHI and SaO_{2min} of patients between the two groups before and after treatment ($\bar{x}$ ± sd)

Groups	AHI (times/h)	SaO_{2min} (%)
Observation group (n=44)		
Before treatment	18.49±4.30	86.69±4.44
After treatment	6.09±1.92$^{*,\#}$	94.48±4.93$^{*,\#}$
Control group (n=44)		
Before treatment	18.98±4.88	87.04±5.29
After treatment	13.59±4.30*	90.13±4.30*

Note: Compared with that before treatment, $^{*}P<0.05$; compared with the control group after treatment, $^{\#}P<0.05$. AHI: Apnea-hyponea index; SaO_{2min}: minimal oxygen saturation.

Discussion

Central nervous system dysfunction in stroke patients can cause the weakness or even loss of throat muscle tone and stiffness of throat muscle, thus resulting in the occurrence of SAS, which is also the main reason why the incidence of SAS in stroke patients is higher than that of ordinary people [13]. Repeated apnea may cause cerebral hypovolemia, which will induce hypoxemia or hypercapnia and seriously endanger patients' life. According to TCM theory, stroke patients have disorder in qi and blood and weakness of muscles in some body parts. Along with pulmonary respiratory dysfunction, their throat are prone to get blocked, which ultimately induces apnea. It is believed in TCM that benefiting the tongue as well as unblocking the throat is the main principle for the treatment of stroke patients with SAS [14].

In this study, after treatment, the sleep latency, sleep duration, sleep efficiency as well as SaO_{2min} increased, the longest apnea time was shortened and AHI decreased in both groups. The overall effective rate after treatment in the observation group was higher than that in the control group, suggesting that for stroke patients with SAS, western medicine treatment combined with acupuncture can reduce AHI more significantly, thus improving the sleep quality of patients and the overall treatment effect. The differences between the observation group and the control group were statistically significant. Silva et al. studied the effect of western medicine treatment alone and the combined treatment of western medicine and TCM on the sleep quality of patients with SAS respectively, and the results showed that the combined treatment is more effective in the improvement of patients' sleep quality [15]. The study of Shergis et al. pointed out that acupuncture treatment helps to shorten the sleep latency, increase the sleep duration, and improve the sleep efficiency of patients with sleep disorders [16]. This is because acupuncture at Lianquan point is effective in dredging the Ren meridian, and acupuncture at this point can activate meridians, benefit the tongue and unblock the throat, improve pharyngeal muscle tone, promote airway opening, and facilitate the recovery of tongue muscle function, thus achieving positive effects in the treatment of SAS apnea [17, 18].

NSE is mainly in neuroendocrine cells and neurons in the brain. When brain tissues or neurons are damaged, the damaged neurons will secrete large amounts of NSE which enters the blood circulation through the damaged blood-brain barrier [19]. It is known that S100β level is quite low in serum and cerebrospinal fluid of patients with non-neurological diseases. When brain tissues are injured, central nervous glial cells and other types of glial cells secrete a large amount of S100β proteins and enter the blood vessels through the damaged blood-

Table 4. Comparison of clinical efficacy between the two groups before and after treatment (n, %)

Groups	Cured	Markedly effective	Effective	Ineffective	Overall effective rate
Observation group (n=44)	20 (45.45)	15 (34.09)	6 (13.64)	3 (6.82)	41 (93.18)
Control group (n=44)	14 (31.82)	12 (27.27)	8 (18.18)	10 (22.73)	34 (77.27)
Z/χ^2	5.447				4.423
P	0.142				0.035

Table 5. Comparison of serum levels of NSE and S100β between the two groups before and after treatment ($\bar{x}$ ± sd)

Groups	NSE (ng/mL)	S100β protein (μg/L)
Observation group (n=44)		
Before treatment	2.87±0.94	144.49±10.04
After treatment	1.22±0.60$^{*,\#}$	97.80±10.47$^{*,\#}$
Control group (n=44)		
Before treatment	2.79±0.86	143.87±12.30
After treatment	1.84±0.78*	113.33±10.99*

Note: Compared with that before treatment, *P<0.05; compared with the control group after treatment, $^{\#}$P<0.05. NSE: neuron-specific enolase; S100β protein: S100 calcium binding protein β.

Table 6. Comparison of MoCA scores between the two groups before and after treatment ($\bar{x}$ ± sd, score)

Groups	MoCA scores
Observation group (n=44)	
Before treatment	22.93±3.33
After treatment	26.67±2.90$^{*,\#}$
Congtrol group (n=44)	
Before treatement	22.50±3.75
After treatment	24.85±3.02*

Note: Compared with that before treatment, *P<0.05; compared with the control group after treatment, $^{\#}$P<0.05. MoCA: Montreal Cognitive Assessment.

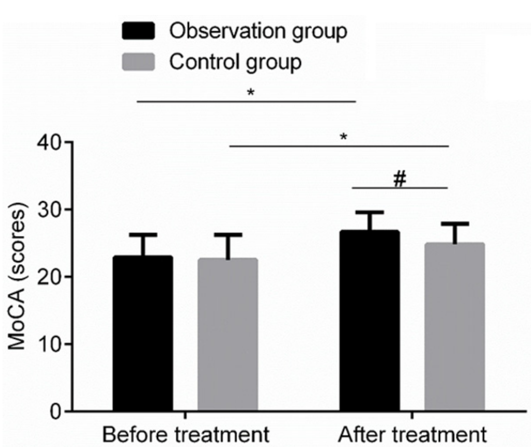

Figure 1. Comparison of MoCA scores between the two groups before and after treatment. Compared with that before treatment, *P<0.05; compared with the control group after treatment, $^{\#}$P<0.05. MoCA: Montreal Cognitive Assessment.

brain barrier, resulting in abnormally increased serum levels [20]. Therefore, it can be concluded that cerebrospinal fluid or serum levels of NSE and S100β are positively correlated with the impairment degree of central nervous system function [21]. In this study, the serum NSE and S100β protein levels in both groups after treatment were lower than those before treatment, and their levels in the observation group were lower than those in the control group, suggesting that western medicine treatment combined with acupuncture can more significantly enhance the neurological function of stroke patients with SAS. It is consistent with the study results reported by Chavez et al., which demonstrated that acupuncture treatment was more effective than western medicine treatment on the improvement of neurological function of stroke patients [22]. It is speculated that because Lianquan belongs to Ren meridians, and Ren meridians regulate many yin meridians. When Lianquan is punctured, it can stimulate nerves as well as maintain muscle excitability and tranquilize the mind, thus improving the patient's neurological function. But the specific effect of acupuncture at Lianquan point in regulating neurological function is still not fully elucidated and it needs to be confirmed by more studies.

In addition, this study is single-centered with a limited sample size, and the specific mechanism of acupuncture at Lianquan point in improving neurological function and cognitive function in stroke patients remains to be explored, which requires further studies.

In summary, western medicine treatment combined with acupuncture can significantly relieve the clinical symptoms of stroke patients with SAS, and improve their sleep quality, neurological function and cognitive function, which is worthy of clinical application and promotion.

Disclosure of conflict of interest

None.

Address correspondence to: Junfeng Xu, Department of Acupuncture, First Teaching Hospital of Tianjin University of Traditional Chinese Medicine, National Clinical Research Center for Chinese Medicine Acupuncture and Moxibustion, No. 314 Anshan West Road, Nankai District, Tianjin 300193, China. Tel: +86-022-27432633; Fax: +86-022-27432633; E-mail: xujunfengz1yd@163.com

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