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Original Article

Secondary prevention for improvements in limb hemiplegia after stroke

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Abstract: Objective: To explore the efficacy of secondary prevention on improvements in limb hemiplegia in stroke patients, and to lay a scientific foundation for clinical diagnosis and management. Methods: A total of 96 patients initially-diagnosed as having upper-limb hemiparesis after stroke, who were admitted to our hospital from October 2012 to July 2015, were randomly divided into the treated group (n=48) and the control group (n=48). The treated group received early medical treatment as secondary prevention, with adjunctive rehabilitation therapy, to control blood pressure, glucose and lipids, and anti-platelet aggregation whereas the control group received physical rehabilitation training alone. The motility of the wrist joints and the hand on the hemiplegic side, and the activities of daily living (ADL) of the patients were assessed using the Barthel Index (BI), functional comprehensive assessment (FCA), and simplified fugl-Meyer assessment scale (U-FMA) within 24 hours before treatment and 3 months after treatment, respectively. After the first three months of treatment was completed, the patients in the control group began to receive secondary prevention for the following three months, followed by assessments on the motility of their limbs on the hemiplegic side. Finally, the efficacy of the intervention therapies was compared between the groups. Results: Compared with those in the control group, the motility of the wrist joints and hands, and activities of daily living (ADL) were improved significantly in the patients in the treated group (n=48) ($P<0.05$). Significant improvements were also observed in the patients in the control group after they received the additional secondary prevention in the latter three months ($P<0.05$). Conclusion: The medical treatment as early secondary prevention can significantly improve the recovery of the motility in the affected limbs of the patients with stroke.

Keywords: Stroke, limb hemiplegia, secondary prevention

Introduction

In recent years, the cerebrovascular diseases have become one of the most devastating causes of death in China. Epidemiological studies have showed that there are 1.5-2 million new stroke patients in China every year and 58-142 deaths per 100,000 person-years. About 80% stroke patients may develop disabling sequelae in various degrees [1]. Stroke has exerted a great threat to patients' health and lives, and hemiplegia after stroke may severely affect their activities of daily life (ADL), making them suffer a lot and increasing burdens to both their families and society. Therefore, it is extremely crucial to carry out the early secondary prevention for better limb motor function in hemiplegia.

Secondary prevention for stroke refers to intervention therapies for preventing the risks of recurrent stroke in stroke patients by controlling risk factors in individuals with cerebrovascular diseases. It can significantly reduce the risks for stroke recurrence and improve clinical outcomes. That is to say, the patients are assigned to appropriate antihypertensive drugs, antiplatelet agents, and lipid-regulating drugs and to strictly follow the principle of "double effectiveness" (i.e., effective dose and drugs) [4] (As for further details, please refer to *The Practice Guidelines for Diagnosis and Treatment of Acute Ischemic Stroke in China*) [2]. Over the years, most of the studies on secondary prevention for stroke in China and other countries are involved in the ways to reduce the risks for recurrent stroke as well as the application of rehabilitation therapies in limb hemiplegia after stroke. However, studies on improvements in paralysis and specific mechanisms are not available after standard secondary prevention for patients with post-stroke limb hemiplegia. As a result, the present study was to explore the significance of early secondary pre-

Table 1. General information of the treated group and the control group

Clinical characteristics	Treated group (n=48)	Control group (n=48)	*P* value
Gender			
Male	28	26	0.07
Female	20	22	0.06
Age	55.7±17.5	57.4±14.8	0.81
Hypertension	21	14	0.11
HPL	25	20	0.09
Diabetes	16	18	0.26

vention for improvement in post-stroke limb hemiplegia.

Subjects and methods

Subjects

The subjects enrolled in this trial were 96 patients admitted to our hospital from October, 2012 to July, 2015, with an initial diagnosis of post-stroke upper-limb hemiparesis. Patients were eligible if they had stroke as demonstrated by cranial computed tomography (CT) or Magnetic Resonance Imaging (MRI) and in accordance with the diagnostic criteria approved at *The Fourth National Conference on Cerebrovascular Disease* [3], unilateral upper-limb hemiplegia in various degrees, the first onset of stroke but without other complicating diseases and voluntarily participated in the study. Patients were excluded if they had reversible cerebral ischemia were excluded or other disorders that may affect limb movement, sensation or cognition, such asmyeleterosis, myopathies, arthropathy, diabetic peripheral neuropathy (DPN). The subjects were randomly divided into the treatment group (n=48) and the control group (n=48). The general data showed no significant difference between the two groups (P>0.05), so they were comparable (**Table 1**). During the treatment, the same symptomatic regimen was assigned to all the patients in the two groups. This trial was approved by the ethics committee on clinical research and all patients signed written informed consents.

Methods

All the patients in the two groups underwent routine neurological medical therapy, namely, they received medicine that contributes to the functional rehabilitation of brain tissues and nutrition to nerve cells (e.g. brain protein hydrolyzate, mecobalamin and oxiracetam) upon admission. When the patients were in stable condition, those in the treated group were assigned to oral atorvastatin (20 mg) and clopidogrel (75 mg) daily, concomitant with physical rehabilitation training. The above treatment lasted for 3 months. By contrast, the control group was given physical rehabilitation training alone, including anticonvulsant posture, sensory stimulation by means of limb ultrasonic massage, active or passive joint stretching or pinching, balance training for sitting and erect positions, standing, weight-bearing loading and gait training, and hand function training, as well as specific hand functional exercise like beading, screwing, finger-finger exercise and grasping. The whole process lasted for 3 months. At 3 months after therapy, the abilities of daily living (including eating, dressing, grooming, bathing, defecation, moving and walking) as well as activity range and motor functions of the muscles in the upper limbs and joints were compared between the two groups. After the first three months of treatment, a three-month secondary prevention was added to the patients in the control group, folllowed by a second comparison between the two groups in the above assessments at different time points.

Assessment indexes

With the use of the Barthel Index (BI), functional comprehensive assessment (FCA), and simplified fugl-Meyer assessment scale (U-FMA), the motility of the wrist and hand on the hemilegic side as well as the ADL were assessed among all the patients within 24 hours before treatment and at 3 months after treatment, respectively, with lower scores indicating worse capacity for self-independence of the elderly patients.

Statistical analysis

The data were analyzed using SPSS software, version13.0, and statistical charts were generated with the use of Graph PAD Prism 5. All the measurement data were expressed as Mean ± SEM. The between-group differences were compared using the t test, and the data was detected with the use of the homogeneity of variance test. The comparison across groups was performed using univariate analysis of vari-

Table 2. Comparison of the pre- and post-treatment functional scores between the two groups ($\overline{X}\pm S$)

Group	Cases	Time	U-FMA	BI	FCA
Treated group	48	24 h pre-treatment	32.6±5.81	27.43±17.21	69.12±10.52
		3 m post-treatment	60.77±9.20$^{*,\#}$	54.23±19.37$^{*,\#}$	93.21±8.86$^{*,\#}$
		6 m post-treatment	61.65±9.45	56.34±19.89	96.54±9.35
Control group	48	24 h pre-treatment	33.70±6.35	28.67±15.29	66.21±6.45
		3 m post-treatment	42.26±8.77$^{\#}$	35.51±16.77$^{\#}$	88.82±5.27$^{\#}$
		3 m post-secondary prevention	58.38±8.63$^{\#}$	50.78±12.96$^{\#}$	91.03±7.76$^{\#}$

Note: post-treatment comparison with the control group, *P<0.05; pre- and post-treatment comparison within the same group, $^{\#}$P<0.05.

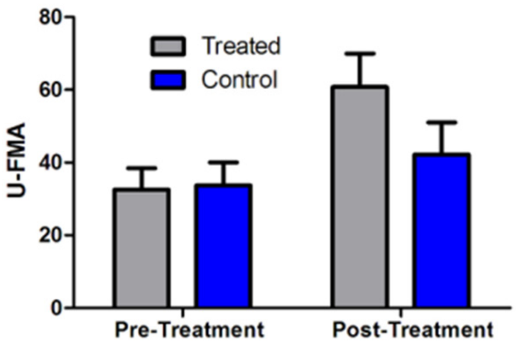

Figure 1. Comparison of the pre- and post-secondary prevention U-FMA scores between the two groups (score, $\overline{X}\pm s$). Significant differences at various time points were found within the same group (*P<0.05), and significant differences at the same time points were also found between the two groups (**P<0.05).

ance whereas the comparison between groups was performed using the SNK test. The data at different time points before and after the intervention were compared using the repeatedly measured and designed two-way ANOVA (time as intragroup factors, and treatment as intergroup factors) among the patients in the two groups. The significance level α equals to 0.05, and P<0.05 was considered statistically significant difference.

Results

The general data including age, gender, hypertension, hyperlipidemia and other basic disease data were not significantly different among the patients in the two groups (P>0.05). After three months of effective early secondary prevention, the stroke patients' scores for MBI, FCA, U-FMA were improved in some degree, and the improvements in hand functions were significantly greater in the treatment group than in the control group (P<0.05, **Table 2**).

U-FMA scores

There were no significant differences in U-FMA scores between the two groups before treatment (P>0.05), but both groups improved in the U-FMA scores at 3 months after treatment (P<0.05), with more significant improvements in the treatment group (P<0.01). After the first three months, secondary prevention was added to the patients in the control group for the second three months. After that, the U-FMA scores were significantly higher than those before the secondary prevention (P<0.05), but at six months after treatment they were insignificantly higher in the control group than in the treated group (**Figure 1**).

BI indexes

There were no significant differences in BI scores between the two groups before treatment (P>0.05), but both groups improved in the BI indexes scores at 3 months after treatment (P<0.05), with more significant improvements in the treatment group (P<0.01). The BI indexes scores were significantly higher in the control group after the second secondary prevention was added (P<0.05), but at six months after treatment they were insignificantly higher in the control group than in the treated group (**Figure 2**).

FCA scores

No significant differences were found in FCA scores before treatment between the two groups (P>0.05). At 3 months after treatment, the FCA scores of both groups were higher (P<0.05), and the treatment group improved more significantly than the control group (P< 0.01). The FCA index score was significantly higher in the control group after the second

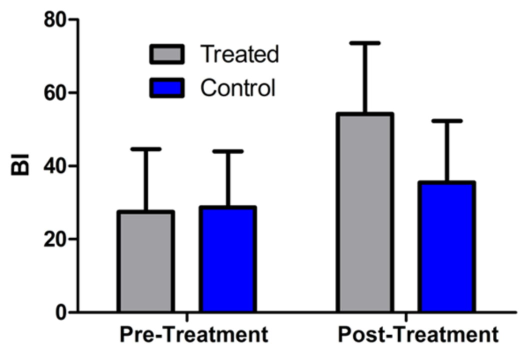

Figure 2. Comparison of the pre- and post-secondary prevention BI scores between the two groups (score, $\overline{X}\pm s$). Significant differences at various time points were found within the same group (*P<0.05), and significant differences at the same time points were also found between the two groups (**P<0.05).

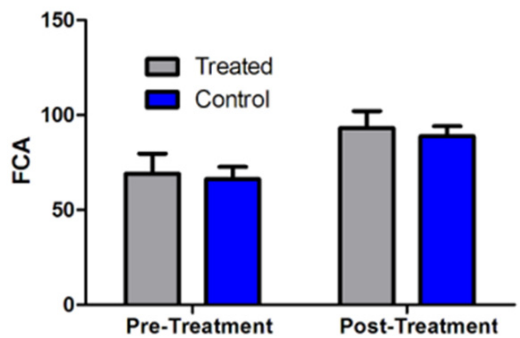

Figure 3. Comparison of the pre- and post-secondary prevention FCA scores between the two groups ($\overline{X}\pm S$). Significant differences at various time points were found within the same group (*P<0.05), and significant differences at the same time points were also found between the two groups (**P<0.05).

three-month secondary prevention was added (P<0.05), but at six months after treatment it was insignificantly higher in the control group than in the treated group (P<0.05, **Figure 3**).

Discussion

The findings of the present study showed various degrees of improvements in the motility of the wrist joints and hand on the hemiplegic side, as well as in ADL of the patients. The differences in Barther indexes and FMA scores were statistically significant between the two groups (P<0.05). Related studies suggest that early secondary prevention improves post-stroke limb hemiplegia and prevent from the recurrence of stroke in the patients [5]. In addition, the scores for the motility of the patients in the control group were significantly higher after three-month additional secondary prevention, but insignificantly lower than those of the patients in the treated group after the first three-month secondary prevention. The findings of the present study forcefully confirmed that the early secondary prevention plays a crucial role in the prognosis of limb hemiplegia after acute stroke.

Lower extremity and hand functional impairments in various degrees may occur in most stroke patients with limb hemiplegia in the process of functional rehabilitation [6]. The functional rehabilitation in hemiplegic patients begins several days upon onset of cerebrovascular diseases, and the fastest rehabilitation can be seen in the first three months. The rehabilitation slows down after the first 3 months due to secondary disorders like disuse syndrome and misuse syndrome, with the better rehabilitation in the lower limbs than in the upper ones [7, 8]. The upper limbs are responsible for flexible, coordinated and skill-based activities, so their functions are difficult to be compensated in case of hemiplegia, especially the functions of the hands, recover slowly, and may even lead to some sequelae [9, 10]. The results of our study indicated that compared with the control group, the stroke patients with post-stroke limb hemiplegia in the treated group improved significantly in limb functions after three-month consecutive medical treatment (including administration of anti-platelet aggregation and lipid-lowering drugs) and intense training for rehabilitation; and the difference was statistically significant. It is suggested that patients with post-stroke limb hemiplegia undergo early secondary prevention therapy with concomitant trainings for rehabilitation can be more likely to recover the functions of their paralyzed limbs and prevent the risk for recurrent stroke.

Braun et al. [13] found that the mechanisms for secondary prevention to improve the conditions of stroke patients with limb hemiplegia may be the reasons that the regulation of blood lipids, blood glucose and blood pressure reduces the risk for vascular injuries, promotes the repair and recanalization of injured blood vessels, and prevent from re-occlusion of the injured blood vessels, leading to reductions in the recurrence of stroke.

After the attack of primary stroke, the patients may have nine times higher risks for recurrent stroke than the general population and their prognosis of recurrent stoke is worse. About 70% to 80% of such events often contribute to severe disability or death. In the past thirty years, the United States has witnessed remarkable achievements in the primary prevention for stroke (control of risk factors and prevention of stroke events), so its incidence is decreasing year by year [11, 12]. The secondary prevention for stroke is to prevent the recurrence of stroke in patients by means of various relevant preventative measures. According to epidemiological data, a patient, after the first attack of cerebral thrombosis, may develop cerebral embolism in case of the recurrence of cerebral thrombosis; about 38% of cerebral embolism may develop into other disorders like thrombosis; and more than half of lacunar infarcts in patients may develop into cerebral thrombosis when it recurs [14, 15]. Currently, the medical measures as secondary prevention for cerebrovascular diseases are to further recognize or control the patients' cerebrovascular attacks or the potential risk factors, with the aim to prevent any death, disability or recurrence in the patients with cerebrovascular diseases [16, 17].

The main strategies of secondary prevention for stroke include 1) controlling the risk factors (hypertension, diabetes, hyperlipidemia (HPL), hyperviscosity, smoking and unhealthy life styles); 2) anti-platelet medicine (mostly aspirin, aspirin plus ginko biloba extrat/dipyridamole and clopidogrel), which is the first-line treatment for most ischemic strokes; 3) anticoagulation, used only for cardiogenic stroke (warfarin); 4) statin therapy for lipid-lowering and plaque stability; 5) surgical/endovascular treatment, among which, carotid artery stenting technique has not been verified in most cases [18-20]. In addition, it is also crucial to make regular neurological examinations, necessary auxiliary examinations and laboratory tests and to improve stroke patients' compliance of secondary prevention.

However, the patients enrolled in our trial were inpatients. As a result, some patients might be excluded from the trial because they were not hospitalized. Some valid information was lost, which gave rise to a bias of selection. In addition, the patients varied in previous physical conditions, medication, and family environments, which may affect the results of the trial. All these factors result in the errors in the trial results, therefore measures should be taken to further improve the trial methods.

In summary, this trial confirms the early secondary prevention can improve limb hemiplegia after stroke, and delay its aggravation. Thus, it is worthy of extensive clinical application, but in real life, due to the patients' poor compliance, and weak preventive consciousness, more efforts should be made to control the risk factors by carrying out secondary prevention for stroke. Medical staff should enhance the education of patients and their families and take regular follow-ups. In this way, that they can acquire more relevant knowledge, with which, they can reduce the chances of recurrent stroke, leading to more effective secondary prevention.

Disclosure of conflict of interest

None.

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