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Effects of electroacupuncture on the arterial stiffness in stroke patients

IWAMOTO Eisuke[1)], MURASE Kentaro[2)], TANINOKUCHI Machiko[1)], MOTOISHI Nozomi[1)]

1) Division of rehabilitation medicine, Okatsu Hospital

2) Kagoshima college of acupuncture and moxibustion

Abstract

[Objective] It seems that in Japan's aging society, investigating the position of acupuncture and moxibustion for the treatment of arteriosclerotic diseases is important. In this report we evaluated the effects of electroacupuncture (EA) on stroke patients by measuring changes in pulse wave velocity (PWV), brachial-ankle PWV (baPWV), ankle brachial pressure index (ABI), blood pressure (BP) and heart rate (HR).

[Method] The subjects were 210 initial stroke patients. Stroke patients were randomly allocated to three groups, those only taking drug therapy (drug group), those taking drug therapy combined with rehabilitation (rehab group), and those taking drug therapy and rehabilitation combined with EA (EA group). 81 cerebral thrombosis patients (drug group n = 25, rehab group n = 28, EA group n = 28), 68 cerebral embolus patients (drug group n = 24, rehab group n = 20, EA group n = 24) and 61 cerebral hemorrhage patients (drug group n = 20, rehab group n = 21, EA group n = 20) were examined. For the evaluation method blood pressure pulse wave measuring equipment was used to measure PWV, baPWV, ABI, BP, and HR after two months, four months, and six months from the onset of treatment.

[Results] After two months and four months there was no significant difference in blood vessel elasticity of the three cerebral thrombosis groups. Whereas after six months, compared to the drug group, the baPWV in cerebral thrombosis patients significantly decreased for the rehab group ($P < 0.05$) and EA group ($P < 0.01$). There were no significant differences in ABI, BP, or HR. Cerebral hemorrhage and cerebral embolism patients showed no significant difference in baPWV, ABI, BP, and HR.

[Conclusion] We examined the effects of adding EA to the treatment of patients who suffered cerebral thrombosis, cerebral embolism, or cerebral hemorrhage. These results show that adding EA to drug treatment and rehabilitation significantly improves blood vessel elasticity and suggests that using EA would reduce the risk of cerebral thrombosis and its reoccurrence.

Key words: *electroacupuncture, pulse wave velocity (PWV), brachial-ankle PWV (baPWV), ankle brachial pressure index, stroke*

I. Introduction

In Japan, stroke is the third leading cause of death and at the top of the list of diseases with which patients are highly likely to become bedridden. In addition, the recurrence rate for stroke is high. Approximately 10% of stroke cases have a recurrent stroke within one year, and approximately 50% of them have one within ten years[1)]. Stroke is classified as an arteriosclerosis disease, and pulse wave velocity (PWV), an index for arteriosclerosis, has been widely used for the prediction of the onset of stroke, because PWV is measured in an easy and non-invasive way[2)]. Exploring how acupuncture can be helpful in treating cases of arteriosclerosis may greatly contribute to preventing stroke onset or reducing the risk of stroke recurrence. There have been some reports on the effects of acupuncture treatment on the sequelae of stroke; however, it was not included as a recommended treatment in the 2009 Japanese Guidelines for the Management of Stroke[3)].

We examined the effects of electroacupuncuture (EA)

Corresponding author: Iwamoto Eisuke, Division of Rehabilitation Medicine, 3-95 Masagohonmachi, Kagoshima-shi, Kagoshima 890-0067, Japan

E-mail address: rmggb534@yahoo.co.jp

in combination with drug therapies and rehabilitation on the arterial stiffness in cases of cerebral thrombosis, cerebral embolism or cerebral hemorrhage in the subacute and convalescent phases.

II. Subjects

The subjects were initially 243 cases of incipient stroke, consisting of 98 cases of cerebral thrombosis, 77 cases of cerebral embolism, and 68 cases of cerebral hemorrhage other than subarachnoid hemorrhage.The criteria for inclusion as a subject were: (1) the patient's or his or her family's consent to participate in the present study, (2) being affected by incipient stroke, (3) being in the sub-acute phase, approximately two months from the onset, (4) being in Brunnstrom stage IV or higher, and (5) being available to trace and observe the progress for six months from the onset.

Criteria for excluding subjects included: failing to satisfy all the criteria for inclusion, discovery of severe complications (e.g., visceral diseases such as renal diseases) that were not associated with the stroke, or determined to be unsuitable for the study by a doctor.

We divided the subjects randomly into a drug therapy group (drug group), in which the patients were treated only by drug therapies allocated to them by the envelope method according to their disease type; a rehabilitation group (rehab group) in which drug therapies were combined with rehabilitation and an EA group (EA group) in which drug therapies were combined with EA treatment. During the course of the study, some cases were dropped, for example, because of systemic deterioration, and the number of subjects was finally reduced to 81 cases of cerebral thrombosis consisting of 25 cases in the drug group, 28 cases in the rehab group, and 28 cases in the EA group; 68 cases of cerebral embolism consisting of 24 cases in the drug group, 20 cases in the rehab group, and 24 cases in the EA group; and 61 cases of cerebral hemorrhage other than subarachnoid hemorrhage consisting of 20 cases in the drug group, 21 cases in the rehab group, and 20 cases in the EA group. (Fig. 1) The present study was conducted with the approval of the Ethics Committee of Okatsu Hospital.

III. Methodology

1. Measuring equipment and measurement methods

For the measurements, the PWV/ABI measuring equipment (Model BP-203 RPE from Nippon Colin) was used. Not after exercise or physical activity but after approximately 10 minutes of resting in bed in a supine position, each subject was monitored with a heartbeat sensor, ECG clips, and cuffs on the right and left brachia and ankles for sensing blood pressure and pulse waves. The elasticity of the blood vessels in terms of brachial-ankle PWV (baPWV), the degree of constriction in terms of ankle brachial pressure index (ABI), the systolic blood pressure (SBP), the diastolic blood pressure (DBP), and the heat rate (HR) were simultaneously measured. More specifically, the heart beat waveforms, and the pulse waveforms at the upper and lower limbs, were measured for 30 seconds, and the mean values of the waveforms were automatically calculated and recorded as measurement values. The baPWV value for a single pulse was obtained by determining the length between the aortic valve orifice and the brachia (Lb) and the length between the aortic valve orifice and the ankle (La) by estimating the height, and dividing the value

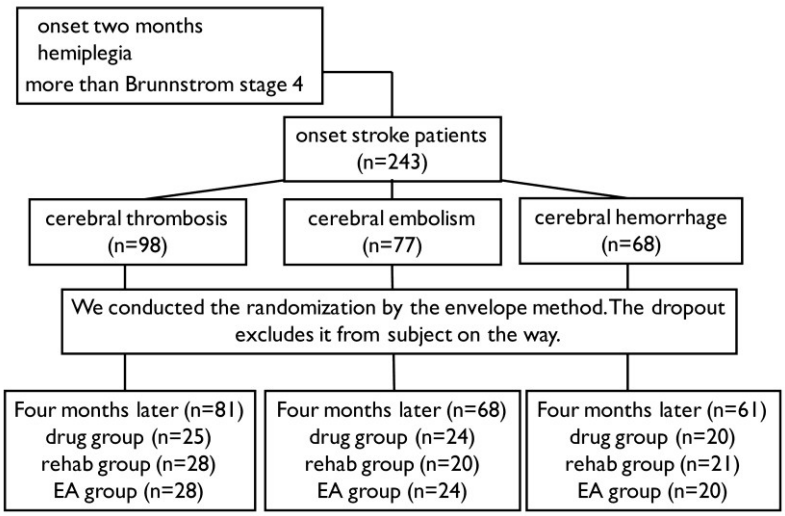

Fig.1 Subjects The drug group gave only pharmacotherapy. The rehab group combined rehabilitation with pharmacotherapy. The EA group combined EA with pharmacotherapy and rehabilitation.

obtained from the equation "La - Lb" by the latency difference in the rise of the pulse wave between the brachial and the ankle. Thus, the equation for this calculation was baPWV (cm/sec) = La — Lb/⊿t, and the mean of the baPWV values for the heart beats (at least three beats) measured for 30 seconds was obtained. ABI was recorded as the blood pressure at the ankle or at the brachial, whichever was higher. A blood vessel may have a hardened arterial wall, a stenosis or an occlusion because of the person's age or lifestyle. The decline of elasticity of arterial walls due to hardening can be assessed in terms of baPWV, and the constriction of blood vessels in terms of ABI. The subjects were examined by means of the measuring equipment mentioned above at two months, four months, and six months from the stroke onset. Measurements were conducted between 16:00 and 17:00, at least 24 hours after rehabilitation therapy or the EA treatment had been administered. Drugs for the drug therapy were administered at different times according to each case, and measurements were conducted two hours after drug administration.

2. Drug therapy and rehabilitation

The subjects in the present study were in the convalescent phase with moderate to mild systemic disorders or motor impairment. The goals for treatment were mainly to prevent stroke recurrence and complications such as pneumonia, and to combat motor impairment. The subjects were given instructions and guidance on lifestyle. Anti-thrombotic agents, hypoglycemic agents, hypotensive agents, hypolipidaemic agents, and/or anti-inflammatory analgesic agents were administered as appropriate. For the convalescent rehabilitation, a team approach was taken by the rehabilitation-related staff. The basic rehabilitation program involved training to improve the voluntary movement of paralyzed limbs, training to improve the articular range of motion, walking training, balance training, muscle strengthening exercises, etc., with the aim to improve these functions for daily life and reduce brain dysfunction.

3. EA treatment

For the EA treatment, acupuncture points LI 10 – LI 4 of the hand, and acupuncture points ST 36 – SP 6 of the foot, on the paralyzed half of the body were stimulated with No. 20 stainless needles 48 millimeters long from Unico inserted approximately 5-10 mm deep. The electrification device used in the present study was an Ohm Pulser LFP-4000A from Zeniryo, and the electrical stimulation was of bipolar pulse waves at 2 Hz and was given for 15 minutes. The strength of the stimulation was such that it could not give pain but recognized as a stimulation (non-twitch stimulation). This treatment was administered five days every week.

The stimulation points were selected on the basis of a prior study that reported that acupuncture stimulation at each of the acupuncture points LI 10 of the hand and the acupuncture point ST 36 of the foot had improved the elasticity of blood vessels in healthy adults[4]. In the present study, EA treatment rather than acupuncture treatment was administered on the basis of a prior study that showed that EA had increased the blood flow in the brains of patients with cerebral vascular disorders[5] and another prior study that showed that EA stimulation to rats with cerebral infarction had significantly reduced the infarct areas[6]. The strength of electrical stimulation was based on a report of cases in which sensory stimulation at strengths less than the motor threshold had improved the hemiplegia and the elasticity of blood vessels[7].

4. Statistical analysis

For the statistical analysis, the temporal variations in each assessment item were processed and the results for the three groups were compared with one another by Stat View Ver. 5.0 (SAS Institute Inc.). With regard to the temporal variations according tosex, age and mean values, the results data were tested by one-way analysis of

Table.1 Subjects background in cerebral thrombosis, cerebral embolism, and cerebral hemorrhage.

	cerebral thrombosis (n=81)			cerebral embolism (n=68)			cerebral hemorrhage (n=61)		
	drug group	rehab group	EA group	drug group	rehab group	EA group	drug group	rehab group	EA group
subject	25	28	28	24	20	24	20	21	20
man/woman	13/12	12/16	18/10	10/14	9/11	11/13	12/8	10/11	11/9
age (year)	75.5	75.9	76.1	80.9	76.9	80.4	79.9	75.2	76.4
height (cm)	157.1	156.2	155.4	157.6	155.5	155.9	150.4	155.2	157.7
weight (kg)	50.9	52.2	54.3	56.0	58.2	57.3	56.2	61.9	57.3
BMI (kg/m²)	22.2	21.1	23.4	22.9	24.3	22.4	24.4	25.7	23.4
hypertension (case)	9	8	7	13	10	9	15	11	13
dyslipidemia (case)	6	3	8	12	16	13	10	8	8
diabetes (case)	2	5	3	12	11	11	8	9	6
use drug (case)									
antithrombotic	20	17	17	13	15	19	6	7	9
antihypertensive	11	9	8	14	11	12	8	6	5
hypoglycemic agent	2	4	6	10	17	12	15	12	12
lipid descent	9	8	12	12	12	11	6	5	9
other medicine	17	12	15	19	18	19	19	15	18

variance and then by Dunnet's multiple comparison test. The significance level was set at 5%. The numerical values were all shown in the form of mean ± standard deviation.

IV. Results

1. Attributes of subjects

There were no significant differences in the subjects' attributes including age, sex, body type, underlying disease, and administered drugs among the drug group, rehab group, and EA group (Table 1).

2. Temporal variations, and comparison of the groups in terms of baPWV

(1) Comparison according to disease type

1) Cerebral thrombosis

The baPWV for cerebral thrombosis for the drug group was 2352.0 ± 1014.1 cm/sec after two months, 2211.6 ± 912.7 cm/sec after four months, and 2289.0 ± 886.9 cm/sec after six months, and thus, there were no significant differences over time. The baPWV for cerebral thrombosis for the rehab group changed from 2281.8 ± 821.2 cm/sec after two months, to 2270.5 ± 791.7 cm/sec after four months, and to 2008.9 ± 546.0 cm/sec after six months, and thus, the results after six months were significantly lower than those after two months ($P < 0.05$). The baPWV for cerebral thrombosis for the EA group changed from 2334.4 ± 974.9 cm/sec after two months to 2144.0 ± 1032.8 cm/sec after four months and to 1778.8 ± 508.1 cm/sec after six months, and thus, the results after six months were significantly lower than those after two months ($P < 0.01$).

The comparison in terms of baPWV for cerebral thrombosis for the three groups showed that there were no significant differences between the result after two months and those after four months for each of the groups, while there were significant differences between the results after two months and those after six months for the rehab group ($P < 0.05$) and the EA group ($P < 0.01$). In addition, the results after six months for the EA group were significantly lower than those after six months for the rehab group ($P < 0.05$). (Fig. 2)

2) Cerebral embolism

The baPWV for cerebral embolism for the drug group was 2179.7 ± 697.8 cm/sec after two months, 2247.1 ± 864.7 cm/sec after four months, and 2019.5 ± 692.9 cm/sec after six months, and thus, there were no significant differences over time. The baPWV for cerebral embolism for the rehab group was 2303.8 ± 719.6 cm/sec after two months, 2119.8 ± 507.3 cm/sec after four months, and 2194.5 ± 793.9 cm/sec after six months, and thus, there were no significant differences over time. The baPWV for cerebral embolism for the EA group was 2201.4 ± 904.9 cm/sec after two months, 2168.8 ± 727.2 cm/sec after four months, and 1930.1 ± 818.5 cm/sec after six months, and thus, there were no significant differences over time.

The comparison in terms of baPWV for cerebral embolism for the three groups showed that there were no significant differences among the results after two

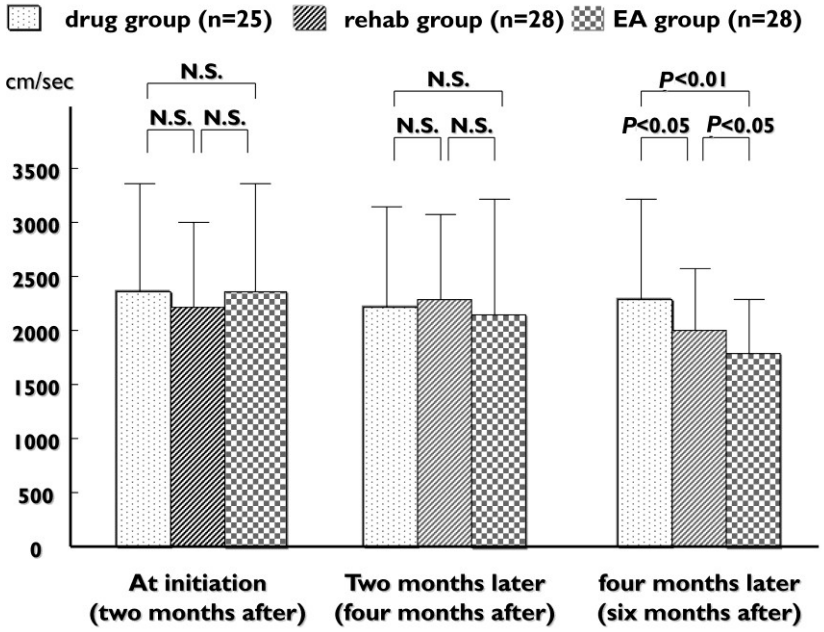

Fig.2 3 comparisons between groups of baPWV in subjects with cerebral thrombosis.
There were no significant differences at time and four months time for two months. We sometimes recognized significant low

months, after four months, and after six months for each of the groups. (Fig. 3)

3) Cerebral hemorrhage

The baPWV for cerebral hemorrhage for the drug group was 2239.6 ± 755.5 cm/sec after two months, 1925.8 ± 643.2 cm/sec after four months, and 2205.3 ± 561.1 cm/sec after six months and thus, there were no significant differences over time. The baPWV for cerebral hemorrhage for the rehab group was 2050.2 ± 660.3 cm/sec after two months, 2032.3 ± 757.1 cm/sec after four months, and 2314.1 ± 894.7 cm/sec after six months, and thus, there were no significant differences over time. The baPWV for cerebral hemorrhage for the EA group was 2059.7 ± 741.9 cm/sec after two months, 2011.6 ± 772.9 cm/sec after four months, and 2350.0 ± 703.5 cm/sec after six months, and thus, there were no significant differences over time.

The comparison in terms of baPWV for cerebral hemorrhage for the three groups showed that there were no significant differences between the result after two months, after four months, or after six months for each of the groups. (Fig. 4)

(2) The mean values of baPWV according to sex and age

The normal values of baPWV are 1641 ± 289 cm/sec for males in their 60's, 1577 ± 273 cm/sec for females in their 60's, 1832 ± 328 cm/sec for males in their 70's, and 1742 ± 298 cm/sec for females in their 70's. The normal ABI is in a range of 0.9 < ABI < 1.3.

1) Difference by sex

For differences by sex in baPWV for cerebral thrombosis for the drug group, there were no significant differences between male subjects (n = 13) and female subjects (n = 12) over time. For differences by sex in baPWV for cerebral thrombosis for the rehab group, there were no significant differences between male subjects (n = 12) and female subjects (n = 16) over time.

For differences by sex in baPWV for cerebral thrombosis for the EA group, the results for males subjects (n = 18) were 2375.2 ± 735.3 cm/sec after two months, 2096.6 ± 740.3 cm/sec after four months, and 180.6.6 ± 531.4 cm/sec after six months, and thus, the results after six months were significantly lower than those after two months (P< 0.05). The results for female subjects (n = 10) were 2254.8 ± 538.6 cm/sec after two months, 2136.5 ± 519.8 cm/sec after four months, and 1718.8 ± 375.5 cm/sec after six months, and thus, there was a decreasing trend, but no significant difference over time. The comparison in terms of baPWV between male subjects and female subjects showed that there was no significant difference after two months, after four months, or after six months.

There were no significant differences by sex in terms of baPWV for cerebral thrombosis and cerebral hemor-

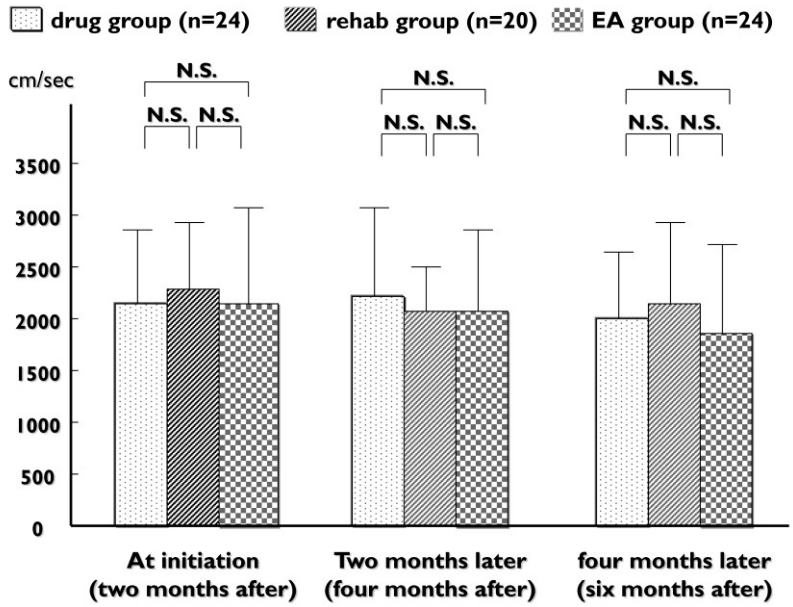

Fig.3 3 comparison between groups of baPWV in subjects with cerebral embolism.
In both periods, there were no significant differences in three groups. Displayed with mean ± S.D.

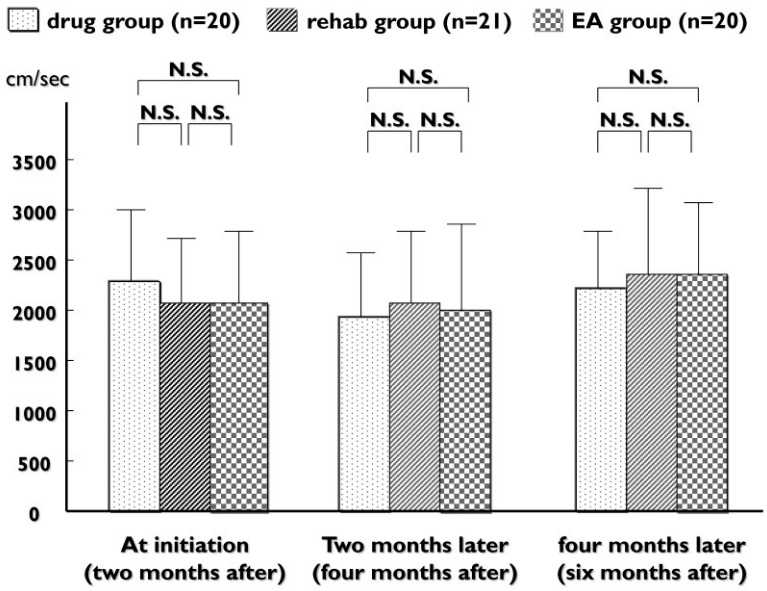

Fig.4 3 comparisons between groups of baPWV in subjects with cerebral hemorrhage.
In both periods, there were no significant differences in three groups. Displayed with mean ± S.D.

rhage for the drug group, rehab group, or EA group.

2) Differences by age

The variations in baPWV after two months, four months, and six months were analyzed according to age. The subjects included only a few patients in their 90's, and therefore, those of age 80 or more were put into one group.

The results for cerebral thrombosis for the drug group showed no significant differences in terms of baPWV for patients in their 60's (n = 5), those in their 70's (n = 10), or those in their 80's or older (n = 10).

The results for cerebral thrombosis for the rehab group showed that there were no significant differences after two months, after four months, or after six months for patients in their 50's (n = 4), those in their 60's (n = 8), and in their 80's or older (n = 3). On the other hand, the results for patients in their 70's (n = 13) were 2384.0 ± 928.2 cm/sec after two months, 2162.4 ± 736.2 cm/sec after four months, and 1792.6 ± 301.1 cm/sec after six months, and thus, the results after six months were significantly lower than those after two months ($P < 0.05$).

The results for patients in their 60's (n = 6) and those in their 70's (n = 9) for the EA group showed no significant differences over time. The results for those in their 80's or older (n = 13) were 2521.4 ± 776.0 cm/sec after two months, 2167.8 ± 755.1 cm/sec after four months, and 1673.9 ± 453.1 cm/sec after six months, and thus, the results after six months were significantly lower than those after two months ($P < 0.05$).

The results for cerebral thrombosis and cerebral hemorrhage showed no significant differences according to age.

3) Analysis with respect to mean values two months after stroke onset

The results for cerebral embolism for the drug group were analyzed according to sub-groups divided by their mean values. For the rehab group, for which the mean was 2281.8 cm/sec after two months, the results for the sub-group consisting of patients with less than the mean value were 1775.9 ± 377.8 cm/sec after two months, 1648.9 ± 309.0 cm/sec after four months, and 1914.5 ± 506.5 cm/sec after six months, and thus, there were no significant differences over time. On the other hand, the results for the sub-group consisting of patients with the mean value or more were 3032.8 ± 685.9 cm/sec after two months, 2914.7 ± 666.3 cm/sec after four months, and 2096.7 ± 584.9 cm/sec after six months, and thus, the results after six months were significantly lower than those after two months ($P < 0.05$). For the EA group, for which the mean was 2322.0 cm/sec after two months, the results for the sub-group consisting of patients with less than the mean value were 2930.6 ± 512.2 cm/sec after two months, 2276.8 ± 734.9 cm/sec after four months, and 1808.7 ± 471.7 cm/sec after six months, and thus, the results after four months and after six months were both significantly lower than those after two months ($P < 0.05$ after four months and $P < 0.01$ after six months). The results for the sub-group consisting of those with less than the mean were 1883.4 ± 315.3 cm/sec after two months, 1986.4 ± 590.9cm/sec after

four months, and 1750.3 ± 493.7 cm/sec after six months, and thus, there were no significant differences over time.

The results for cerebral thrombosis and cerebral hemorrhage showed no significant differences according to the sub-groups.

(3) Comparison among the three groups in terms of ABI, SBP, DBP, and HR

None of the results for ABI, SBP, DBP and HR for cerebral thrombosis, cerebral embolism, or cerebral hemorrhage showed significant differences after two months, four months, or six months among the three groups (Tables 2, 3, and 4).

V. Discussion

1. Subjects' cases

We selected patients two months after the onset of

Table.2 3 comparisons between groups of ABI, SBP, DBP and HR in subjects with cerebral thrombosis. In both periods, there were no significant differences in three groups. Displayed with mean ± S.D.

		At initiation (two months after)	Two months later (four months after)	four months later (six months after)
ABI	drug group	1.1±0.1	1.1±0.1	1.1±0.1
	rehab group	1.1±0.1	1.1±0.1	1.1±0.1
	EA group	1.1±0.2	1.1±0.1	1.1±0.2
SBP (mmHg)	drug group	129.4±20.1	132.0±26.6	137.1±18.1
	rehab group	134.8±25.6	138.6±27.1	134.5±28.7
	EA group	134.2±20.4	124.4±15.5	129.0±27.9
DBP (mmHg)	drug group	78.6±15.7	74.9±13.7	78.6±9.9
	rehab group	77.8±14.7	80.4±14.2	79.4±15.4
	EA group	75.3±12.6	71.8±12.8	73.9±15.8
HR (bpm)	drug group	75.5±12.3	76.4±13.3	74.2±18.2
	rehab group	75.4±17.9	74.7±13.4	74.2±12.4
	EA group	75.9±18.3	77.1±17.9	76.3±13.8

Table.3 3 comparisons between groups of ABI, SBP, DBP and HR in subjects with cerebral embolism. In both periods, there were no significant differences in three groups. Displayed with mean ± S.D.

		At initiation (two months after)	Two months later (four months after)	four months later (six months after)
ABI	drug group	1.0±0.2	1.1±0.2	1.1±0.1
	rehab group	1.1±0.1	1.1±0.1	1.1±0.1
	EA group	1.0±0.2	1.1±0.1	1.1±0.1
SBP (mmHg)	drug group	134.8±31.4	118.5±23.4	117.3±19.1
	rehab group	135.2±29.3	126.8±17.5	135.6±27.5
	EA group	134.2±17.7	133.0±24.9	129.7±24.9
DBP (mmHg)	drug group	74.3±15.4	72.3±10.6	72.3±10.6
	rehab group	79.5±16.7	69.6±12.4	69.6±12.4
	EA group	78.4±15.6	75.9±11.9	75.9±11.9
HR (bpm)	drug group	77.1±10.9	70.3±13.7	70.3±13.7
	rehab group	73.9±19.2	72.6±13.3	72.6±13.3
	EA group	74.0±14.6	72.2±12.6	72.2±12.6

Table.4 3 comparisons between groups of ABI, SBP, DBP and HR in subjects with cerebral hemorrhage. In both periods, there were no significant differences in three groups. Displayed with mean ± S.D.

		At initiation (two months after)	Two months later (four months after)	four months later (six months after)
ABI	drug group	1.1±0.2	1.0±0.2	1.1±0.1
	rehab group	1.1±0.1	1.0±0.1	1.1±0.1
	EA group	1.1±0.1	1.1±0.1	1.1±0.1
SBP (mmHg)	drug group	121.8±22.6	129.9±21.7	130.0±27.4
	rehab group	131.1±21.2	137.3±13.1	135.9±25.6
	EA group	123.5±22.7	129.7±22.3	133.5±18.7
DBP (mmHg)	drug group	70.6±12.3	72.8±10.9	79.5±15.9
	rehab group	72.7±13.2	77.3±15.1	76.7±14.6
	EA group	71.3±12.3	77.0±12.5	75.7±13.3
HR (bpm)	drug group	76.5±17.3	72.1±11.9	79.6±20.8
	rehab group	75.2±15.7	76.4±12.2	74.7±13.6
	EA group	78.6±17.1	71.4±12.6	80.2±21.2

their strokesas subjects of this study, because general care is particularly important for some time after stroke onset, there are various factors that might affect the measurement of PWV, and the condition of stroke patients generally becomes stable after two month. We did not initially consider including Brunnstrom stage as a criterion for excluding subjects, but the Ethics Committee of Ohkatsu Hospital approved our study plan on the condition that the subjects would be restricted by Brunnstrom stage. So we set Brunnstrom stage IV or higher as a criterion for inclusion. In addition, we limited the period of observation for this study to six months following stroke onset, because (1) at present, rehabilitation or recovery from stroke is extremely difficult after six months (180 days) from onset, and (2) such rehabilitation is most effective within six months from onset.

2. Arteriosclerosis and PWV

Blood vessels are hardened by aging or lifestyle. Hardened blood vessels may eventually cause stroke or arteriosclerotic diseases such as cardiac infarction and arteriosclerosis obliterans. For the assessment of arteriosclerosis, ultrasonic echo and flow-mediated dilation have been used so far, and PWV has also been considered useful for examining arteriosclerotic diseases. Arteriosclerosis includes atherosclerosis, in which cholesterol is deposited on arterial walls, and macrophages that devour the deposits pile up to form a plaque, and Monckeberg arteriosclerosis, in which the arterial walls themselves gradually degenerate and harden. For assessment of arteriosclerosis in terms of PWV, ABI is an indirect index for such plaque and baPWV is an index for the hardening of smooth vascular muscles. In the present study, ABI was in its normal range, and baPWV was far beyond its normal range two months after the stroke onset. This suggests that the latter must have been the main cause of the arteriosclerotic lesions. The degrees of hardening of blood vessels in the subjects were estimated to be moderate to severe. Nakano, et al., reported on groups of healthy aged people, patients with subarachnoid hemorrhage, patients with hypertensive cerebral hemorrhage, and patients with cerebral infarction who were compared with one another in terms of baPWV. The baPWV values for the hypertensive cerebral hemorrhage group and the cerebral infarction group were significantly higher and suggested that baPWV might be a predictive index for possible stroke onset. In the present study, the subjects were patients with cerebral thrombosis, those with cerebral embolism, and those with cerebral hemorrhage, in reference to the report by Nakano, et al.

3. Reasonswhy EA was effective only on cerebral thrombosis

The results of PWV assessment on the patients with cerebral thrombosis, those with cerebral embolism, and those with cerebral hemorrhage under EA treatment showed that baPWV was significantly lowered only for those with cerebral thrombosis. In light of the baPWV and ABI values two months after stroke onset, the different mechanisms for formation of pathological conditions, of thrombus, and of different disease types were indicated by the above results, although the elasticity of the blood vessels was low for each of the disease types.

Blood flow factors (i.e., blood stagnation and shear stress), components of blood vessel walls (i.e., endothelium of the walls and the smooth muscles of the vessels), and blood components (i.e., fibrins, platelets, and white blood cells) are important factors in the formation of pathological conditions and of thrombus in cases of stroke. Such important factors affect each pathological condition, influence one another, and have different weights according to such conditions.

Cerebral hemorrhage may occur when the blood vessels are exposed for long periods to a hypertensive condition, and there have been impact loads on the perforated arteries. Blood flow factors (i.e., shear stress due to hypertension) are mostly associated with such hemorrhage, followed by the components of the blood vessel wall, and then by blood composition. Cerebral embolism often occurs when blood stagnant in the left atrium of heart forms thrombi (fibrin thrombus) and such thrombi flows into cerebral blood vessels. Thus, the blood flow factor (i.e., blood stagnation) and blood components (mainly fibrins) are most important. Cerebral thrombosis often occurs when endothelial injuries or degeneration of vascular media due to dyslipidemia, hypertension, or diabetes mellitus results in thrombi (platelet thrombi). Thus, the components of the blood vessel wall and other blood components (mainly platelets) are mostly associated with cerebral thrombosis.

In the present study, although we did not examine blood flow factors or blood components associated with the disease types, we concluded that EA was effective only on cerebral thrombosis, which is mostly associated with the components of the blood vessel walls.

4. Relationships between baPWV, drug therapy, and rehabilitation

The present study showed that the drug group did not make any significant improvement for any of the disease types. With regard to the relationship between therapeutic drugs and PWV, Takami, et al., reported that administering various hypotensive agents to aged hypertensive patients lowered baPWV, though to various degrees[10]. In the present study, the blood pressures of the subjects were within a normal blood pressure range two month after the stroke onset, and thus, the lowered blood pressures affected baPWV values. The blood pressures of the subjects did not change after two months, after four months, or after six months. These stable results must have been produced by blood pressure control. Apart from the foregoing, drugs may affect blood glucose and lipids in the subjects; however, no appropriate reports on such matters were found. These should be, therefore, studied in the future.

With regard to the relationship between exercise therapy and PWV, it was reported that baPWV in patients with cerebral infarction is correlated with the amount of muscles and bones. However, with regard to the type of exercise, short-duration, low-intensity exercises lowered baPWV, but concentric resistance training increased it.[11), 12)] Thus, what type of exercise is most effective for the recovery from stroke has not been demonstrated. In the present study, therefore, rehabilitation was determined and performed by each therapist in accordance with the Japanese Guidelines for the Management of Stroke. Consequently, the results for cerebral embolism and cerebral hemorrhage did not show significant differences over time, but those for cerebral thrombosis showed significant improvement in the elasticity of blood vessel walls six months after stroke onset. This seems to be because the above-mentioned formation of pathological conditions affected the results. For cerebral hemorrhage, the blood pressures of the patients were lowered by drug therapy, but no change was seen in the elasticity of the blood vessels of the patients, because years of hypotension produced a heavy load on the blood vessel walls, which in turn diminished the relaxation response[13)]. For cerebral embolism, no change was seen in the elasticity of the blood vessels of the patients because the components of the blood vessel walls are much less involved in such embolism than in cerebral thrombosis[9)]. This suggests that the type of rehabilitation does not make a difference in the in the recovery from cases of stroke, but the various pathological conditions create different influences over the elasticity of blood vessels in the patients under rehabilitation.

We have searched for reports that indicate the effects of drug therapy combined with exercise therapy, but we could not find any. Such effectsshould be studied in the future.

5. Relationship between baPWV and EA treatment

The results of the present study showed that EA treatment in combination with other therapies reduced baPWV the most. A prior study reported that baPWV was correlated to the vascular resistance index[14)]. This suggests that an improvement in the elasticity of blood vessels reduces vascular resistance, which in turn increases blood flow.

The mechanism of improvement of the elasticity of blood vessels by EA treatment in combination with other therapies may be associated with changes in functional or in organic conditions. Changes in functional conditions can be caused by the suppression of activities of sympathetic vasoconstrictor fibers[15)], vasodilation substances[16), 17)], or angiogenetic effects[18)]. Kurono, et al., reported that EA stimulation did not affect blood pressure or heart beat rates, but it did reduce muscle sympathetic nerve activities[15)], and Sato, et al., reported that vascular dilation in rats under the anesthesia that occurred after EA simulation did not depend on the systemic blood pressure, but was mediated by a calcitonin gene-related peptide (CGRP)[16)]. It was, therefore, suggested that those activities or peptides might produce such dilation. In the present study, measurements were conducted approximately 24 hours after the EA treatment was administered, but the rehab and EA groups did not show any significant changes until six months after onset. This suggests that long-term repetitive stimulation, as well as neural regulation and humoral regulation, might affect the results. Vascular endothelial growth factor (VEGF), which has an angiogenetic effect, might be involved. Nagasaka, et al., reported that VEGF was produced in ischemic rats as a result of five days of electrical stimulations at a strength less than the motor threshold[18)]. However, the present study differed from the study by Nagasaka, et al., in the period of stimulation and the level of ischemia. The involvement of VEGF is, therefore, a matter to be studied in the future.

For organic changes, the insulin-like growth factor-1 (IGF-1) might be involved. It was reported that CGRP released by stimulation to capsaicin-sensitive C-fibers acted on systemic parenchymal cells to accelerate the production of IGF-1[19)]. IGF-1 acts on the cardiovascular system to prevent arteriosclerosis. There have been no reports that acupuncture stimulation is associated with the production of IGF-1; however, in light of the fact that acupuncture stimulates capsaicin-sensitive C-fibers[20)] and the fact that CGRP is released systemically as a result[17)], it cannot be denied that such stimulation is associated with the production of IGF-1.

EA treatment in combination with therapeutic drugs and rehabilitation seems to be useful for the prevention or improvement of arteriosclerosis, and the prevention of stroke onset or recurrence. How acupuncture treatment can be used will be explored by considering it from various angles.

VI. Conclusion

We examined the effects of EA treatment in combination with therapeutic drugs and rehabilitation on patients with cerebral thrombosis, cerebral embolism or cerebral hemorrhage. The results showed that EA treatment combined with drug treatment or rehabilitation improved the elasticity of blood vessels in patients with thrombosis. This suggests that EA treatment combined with drug therapy and rehabilitation is useful for the prevention and recurrence of cerebral thrombosis.

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