Clinical Report 1 (Japan)

Peripheral Arterial Disease (PAD) and Acupuncture and Moxibustion

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Introduction

Japan is moving toward an aging society unprecedently faster than any other country in the world. The disease structure that used to mainly consist of acute disorders has changed, and chronic lifetsyle-related diseases and geriatric diseases occupy a large share of the structure. Typical is arteriosclerosis among them.

If arteriosclerosis occurs in the cerebral blood vessels, it results in cerebrovascular disease such as cerebral infarction. If it occurs in the blood vessels of the heart, ischemic heart disease such as a heart attack or myocardinal infarction is caused, whereas peripheral arterial disease (hereafter PAD) is caused by arteriosclerosis occurring in the arteries of four limbs.

PAD is a disease that has narrowings or blockage of arteries of four limbs due to progression of limbs arteriosclerosis, resulting in circulatory impairment in the blood perfusion area. It is anticipated that PAD will increase significantly with the growth of aging population. And dietary problems from westernized lifestyles, lack of physical activity or a sedentary lifestyle, and increased stresses are also contributing factors to develop PAD.

Main symptoms of PAD are cold sensation and intermittent claudication and advanced cases lead to ulcers and gangrene, both of which are symptoms caused by circulatory obstruction in the lower limb arteries.

Treatment of PAD differs depending on its severity. For PAD of Stages I and II of Fontaine Classification[1],nonsurgical procedures are mainly used[2]. However, if they do not have effects, a surgery procedure may be used.

Meanwhile, acupuncture treatment is recognized as being effective for improving disturbances of peripheral circulation. And a few reports on effects of acupuncture treatment on sensitivity to cold or cold sensation[3] and **Raynaud's phenomenon** symptoms[4-6] have been released. Cases of PAD that showed improvements in symptoms[7-9] have also been reported, although limited in number. From these, there may be possibilities of acupuncture treatment as a conservative procedure.

We have administered acupuncture treatment to patients with PAD to verify clinical effects and the range of indications and also eclucidate a part of these mechanisms. With the results being analyzed, we will introducea a summary and the cases as below:

1. Clinical effects of acupuncture treatment on PAD

1) Subjects

Subjects were 21 patients (male 17, female 4, average age 72.1±7.3) having subjective ischemic symptoms in the lower legs (lower thighs) with the diagnosis of PAD confirmed through angiography (or MR angiography). In the Fontaine Classification showing the levels of ischemia in the lower legs, PAD was categorized as Stage I (cold sensation and numbness) in 1 patient , as Stage II (intermittent claudication) in 17 ptients, as Stage III (rest pain) in 2 patients, and as Stage IV (ulcers and gangrene/necrosis) in 1 patient.

2) Methods

Measurement items were lower leg skin temperature (by thermography), heart rate, blood pressure, plasma CGRP level, the ratio of the blood pressure in the lower limbs to the blood pressure in upper limbs (arms); Ankle Brachial Pressure Index (hereafter ABPI), intermittent claudication distance, pain, and cold sensation (based on pain scores). In the treatment of two

patients (one with Stage I and the other with Stage IV), ordinary acupuncture needling (leaving needles in place and sparrow pecking technique) was performed, whilst low frequency current was applied to insertion needles for the crural muscles of the lower limbs presenting ischemic symptoms.

The assessments of ABPI, intermittent claudication distance, pain and cold sensation were carried out before the beginning of the treatment and after 16 times of the treatment (hereafter assessment time). The treatment period was 1 to 3 months.

3) Results

The skin temperatures of the affected leg regions were measured and a comparison was made with those of before-treatment against those read during the period from 15 minutes from the beginning of the treatment to 15 minutes from the end of the treatment, showing significant increases. In terms of Fontaine Classification, the patients with Stage I and the patients with Stage II manifested more distinguished increases than those of Stage III and Stage IV. The heart rates and blood pressures measured simultaneously did not show significant changes from the beginning to the end of the treatment. Plasma CGRP levels showed significant increases after 15 minutes from the end of the treatment compared to before the treatment.

ABPIs in all patients remained same. At the time of the assessment, intermittent claudication distance showed a significant extension compared to before the treatment.

Both pain and cold sensation showed significant decreases at the time of the assessment compared to the VAS values assessed prior to the treatment. In view of Fontaine Classificaton, the patients with Stage I and patients with II had marked decreases, whereas those with Stages III and those with IV had small decreases.

Through the entire treatment period, any adverse event causing disadvantages to the patients was not observed.

A case of PAD will be introduced as follows.

2. Case of PAD (Fontaine Classification Stage II)

Relatively many patients who want acupuncture and moxibustion treatment visit our hospital with the complaints such as cold lower legs, pain, and pain when walking. Since these symptoms may have developed due to spinal canal stenosis or PAD, knowing their clinical conditions accurately is necessary and important when acupuncture and moxibustion treatment is performed.

The following patient, who had been a patient of the hospital I had previously worked for, was referred to our hospital by her previous orthopedist due to“crural muscle pain in the lower legs.” According to the patient, “the legs became painful after dancing (social). Probably dancing shoes did not fit.” The patient was a 68-year old woman. After the interview, arteries of lower limbs were palpated, but below-knee popliteal artery on one side could not be felt. Then, a queston was made to her whether or not she had pain while walking and stopped walking to get rest, and became able to walk after rest. She said “yes.” Then another question was asked: “how far she could walk before she had to stop.” She said “about 80 meters.” From the conversation, PAD was assumed and treatment was started. At the same time, I made a hospital referral for her.

1) Case

[Case] Female of 75 years old

[Chief complaint] Pain in the right lower limb (dull pain with a feeling of heaviness in the calf muscles)

[History of present illness] The patient began to take up dance lessons five months ago. Around the time, the symptom of her chief complaint appeared. She thought it was caused by the heels she seldom wore and had shiatsu and massages. Since there were no changes in the condition, she visited the Orthopedics and had X-ray photography with the diagnosis of lumber spine osteoarthritis and osteoporosis. The pain in the left lower limb was diagnosed as muscle pain and the patient was referred to us for acupuncture and moxibustion treatment.
[Past medical history] No special mention
[Family history] Younger sister (cardiac disease, died at the ge of 50), younger brother (brain hemorrhage, died at the age of 53)
[Complication] High blood pressure (from the age of 68 to the present): receiving treatment (with drugs) by an internal medicine specialist of a nearby hospital. Ischemic heart disease (from the age of 70 to the present): receiving treatment (with drugs) by an internal medicine specialist of a nearby hospital.

[History of life] Smoking (-), drinking a little alcohol.
[Conditions at the initial visit] Height 152cm, weight 43kg, blood pressure120/60mmHg, pulse 70/min (regular)

The range of lumber motion was sufficient. Pain accompanied by motions (-), FFD 0 cm, SLR-either right or left 90 degrees (-), kemp signs (-), lower limb muscular power - normal, lower limb muscle atrophy (-), Babinski reflex (-), PTR(+)/(+), ATR(±)/(±), tactile sense and pain sense-normal. Limb skin temperatures - lowerd on the left, and calf pain (+) left>right.

Pulse: Femoral arteries-right and left palpable, popliteal arteries-right palpable, left decreased and weak.

Posteria tibial arteries; right - palpable, left - difficult to palpate, dorsalis pedis arteries – palpable on the right and decreased and weak on the left.

Lower limb pain appeared in the calf muscles when the patient walked up to the distance of 80 meters at a slower pace. Constricting pain on the left was marked, so she had to stop when she walked 120 meters. Cold sensation: left legs (+), feeling of numbness in the left sole (±), rest pain and ulcers (-).

Straight leg raising test: Left (±), right (-). Straight leg lowering test: Left (±), right (-), edema (-), cyanosis (-), ABPI; Right 0.71, left 0.53

2) Acupuncture treatment and the purpose

Since the patient had pain behind the lower thighs, the acupuncture treatment was administered by applying low frequency current to the regions of triceps surae muscles of the calf with the aim of relieving ischemic pain. The needling points were heyang (the motion point of the triceps surae muscles) and chengshan (paninful region of calf muscles) (Fig. 1) with the needling depth of 20 to 30 mm. Stainless needles 50mm long with a diameter of 0.22 mm were used. Stimulation conditions were 1 Hz, pulse width 0.25 ms, stimulating intensity 1 mA, at which the patient did not feel unpleasant and is high enough to cause contractons of triceps surae muscles. The time to apply current was 20 minutes. The low frequency acupuncture equipment Ohm Pulser 4000A (for all medical cares) was used.

Drugs used previously were maintained during the treatment periodd with same dosages.

3) Assesssment of treatment effects

Skin temperatures and heart rates, and the ratio of the blood pressures in the upper limbs to the blood pressure in the lower limbs; Ankle Brachial Pressure Index (ABPI), intermittent claudication distance, pain and coldness were reviewed and studied. Concerning ABPIs, the intermittent claudication distance, pain, and

coldness were assessed before the beginning of treatment and after three months.

(1) Lower limbs skin temperature and heart rate/blood pressure

Skin temperatures caused by acupuncture were measured in a constant temperature room maintained at 26.5±0.5 Celsius with humidity 55±5 % using a thermography machine (Thermoviewer JTG-5370 manufactured by Nippon Denshi (JEOL Ltd.). Before measurements, it was ensured that skin temperatures became in a stable equilibrium state after the patient had been at rest in the recumbent position for more than 15 minutes. Tempertures were taken 10 times in total with the frequency of every 5 minutes: before the acupuncture treatment, during 20 minutes of the treatment and till 20 minutes from the end of the treatment. For analyzing variations in lower limb skin temperatures, the nail bed of the second toe finger on the affected side was determined as a fixed point and temperatures were read from the thermographic images. At the same time, blood pressures and heart rates were also measured (with Omron Automatic Blood Pressure Monitor).

(2) Ankle Brachial Pressure Index (hereafter ABPI) (Ratio of the blood pressures in the leg joints to the blood pressure in the upper arms)

Systolic blood pressures in the upper arms and leg joints at rest were measured using an ultrasonic Dopper bloodflow meter (ES-1000SPⅡ, ARS Inc.): specifically blood pressures in the right and left brachial arteries, and posterior tibial artery on the affectd side and dorsal pedis arteries. The highest values were used, based on which ABPIs were derived using the following equation.

$$\text{ABPI} = \frac{\text{Leg joint blood pressure (mmHg)}}{\text{Upper arm blood pressure (mmHg)}}$$

(3) Intermittent cludication distance

To determine intermittent claudication distance, the distance that the patient was able to walk on the flat (hospital level corridor) before she had to stop due to pain was measured.

(4) Pain and cold sensation

Changes in subjective symptoms of pain and cold sensation were self-recorded by the patient on the Visual Analogue Scale (hereafter VAS). In regard to pain, the left end of the straight line 100 mm in length was made as “absolutely no pain.” In regard to cold sensation, it was made as “absolutely no cold sensation.” The right end in terms of pain was for “most cruel pain the patient had ever experienced” whle in terms of cold sensation, it was for “most unbearably cold than ever.” For the intensity of the symptom the patient felt, the patient wrote the mark「＼」on the line. Intensities were assessed by the length (distance) of the line from the left end.

4) Results

(1) Lower limb skin temperature and heart rate/blood pressure

The leg skin temperature on the affected side was 30.3 Celsius before the treatment. It rose to 31.4 Celsius when 5 minutes elapsed from the beginning of the treatment and reached a peak temperature of 31.4 when 5 minutes elapsed from the end of the treatment. Then, it lowered slightly 20 minutes from the treatment being finished to 31.0, which was higher than that of pre-treatment. Heart rate, systolic blood pressure, and diastolic blood did not change practically from the beginning of the treatment and to 20 minutes after the end of the treatment.

(2) The ratio of the blood pressure in the upper limbs and the blood pressure in the lower limbs; Ankle Brachial Pressure Index (ABPI)

The ABPI of pre-treatment was right 0.71and

left 0.53, showing no changes from the values of right 0.71and left 0.53 gained at the time of assessment.

(3) Intermittent claudiction distance

Whereas the caludication distance of pre-treatment was 120 meters, it extended to 200 meters when the assessment was made. The patient became able to walk twice faster than she could before treatment.

Further, the recovery time from becoming unable to walk to resuming walking was shortened.

(4) Pain and cold sensation

Whereas the VAS of pain before the treatment was 85.0 mm, it became 70.9 mm at the time of assessment.

(5) Adverse event

Through the entire treatment period, any adverse event causing disadvantages to the patient was not observed.

Moreover, as the patient was suspected of having PAD as soon as the treatment began, an examination request was made to the Department of Angiology. As a result, anteriography indicated common femoral artery occulsons on both sides with the diagnosis of PAD. In the patient, there were risk factors of her being elderly (76) and a complication of cardiac disease and hypertension. The patient had also intermittent claudication. Symptoms were prominent on one side. Lower limb arteries could not be palpated. On the basis of these, PAD was presumed.

5) Discussion

(1) Mechanism of acupuncture treatment (from a case series of 21 cases)

In order to elucidate part of the mechanism producing acupuncture treatment effect in the patient, skin temperatures and plasma CGRP levels were measured. The results showed that the skin temperature of the leg being treated significantly increased during the time from 15 minutes from the beginning of the treatment to 15 minutes from the end of the treatment. Plasma CGRP levels also significantly increased after the end of the treatment. However, almost no changes took place in blood pressures. These results suggest the possibilities that the rise in the skin temperature after the treatment was not caused by a blood-pressure-dependent passive increase of the blood flow but rather it was related to the peripheral circulation that was improved in association with vasodilation caused by the secretion of CGRP, a vasodilatory substance.

In regard to effects of low frequency electroacupuncture on the peripheral circulation, there is a study by Sakai, et al.[10] who performed low frequency electroacupunture on triceps surae muscles in a similar manner as we did for the patient. With healthy adults as study subjects, they have verified in the study that after applying low-frequency electroacupuncture stimulation to triceps surae muscles, the lower thigh deep temperature of the muscles rose and muscle blood flow volume and skin blood flow as well as the pain threshold also increased.

Similarly, Tokutake, Yoshikawa, et al.[11,12] have also reported that stimulating the lower thigh by low frequency electroacupuncture caused an increase in the deep temperature of the targeted muscles. They pointed out that its mechanism might have involved the muscle pumping function performed by muscle contractions. In the case of the low frequency electroacupuncure we conducted, a similar mechanism might have worked, in addition to the action of the vasodilatory substance like CGRP.

For the treatment of PAD, bypass surgery or percutaneous angioplasty is carried out. And there is a document reporting that these procedures significantly increase lower limb skin temperature

and that a strong correlationship exists between an increase after surgery in ABPI, which is an index of perfusion pressure in the peripheral site of the lower leg, and an increase in skin temperature of the lower thigh peripheral site[13]. These improvements are attributable to the surgery resolving the stenotic lesion, resulting in a marked increase in the blood flow volume in the major artery of the lower limb and the skin blood flow volume. This means that in tissues of such as a PAD affected leg that have extremely reduced supplies of blood, an increase of blood flow in the major artery diretly induces skin blood flow and the ABPI to increase. However, there were effects on pain and cold sensation from 1-3 month treatment but no changes occurred in the ABPI. This indicates that improvements in organic lesions such as constriction or obstruction of a blood vessel cannot be expected from acupuncture treatment for a short period of 1-3 months.

However, the result showing that the intermittent cludication distance, pain, and cold sensation significantly improved prompted us to think of the possibility that collateral blood circulation paths gradually developed. Recently, Oda, et al.[14] conducted an experiment with rats and histologically verified the findings of VEGF production by applying low-frequency electroacupuncture stimulation using an ischemic muscle model of rats' anterior tibial muscles. From the findings, it may be possible that the electroacupuncture for PAD induced the production of VEGF and the development of collaterial blood routes. We want to leave this matter as one of the agenda to be investigated in the future.

(2) Acupuncture indication range for PAD

For chronic artery obstructions such as PAD, Fontaine Classification for lower limb ischemic symptoms [1] is widely used to classify disease stages. Non-surgical procedures for PAD are used for the patients with Stage I and the patients with Stage II according to the Fontaine Classificationc [2]. Since acupuncture treatment is one of non-surgical methods, acupuncture was administered mainly to the patients with Stage I and the patients with Stage II. Furthermore, in order to find out and study indications and the limit of acupuncture treatment for PAD, acpunture treatment was also provided to as few as three patients with Stage III and Stage IV respectively.

In terms of effects on clinical symptoms, both pain and cold sensation of pre-treatment significantly improved from post-treatment. From the viewpoint of the Fontaine Classification, the intensites of these symptoms markedly decreased in Stage I and Stage II while their improvements in Stage III and Stage IV were slight.

The intermittent claudication distance after acupuncture treatment improved significantly compared to that before the treatment with an extension of the distance. On the other hand, almost no changes were shown in ABPIs in all lpatients.

In regard to the method of PAD treatment, severe cases of chief complaints such as ulcer, necrosis, and rest pain are considered positive candidates for surgery such as revascularization surgery. In the case of the patient with Stage IV (necrosis developed on the toe) in this report, the skin temperature increased after the acupuncture treatment but cold sensation and pain did not change and subsequent treatment did not yield effects, leading to a toe amputation. In the two patients with Stage III of Fontaine Classification, cold sensation and pain were relieved slightly, not to the extent that they could be assessed as clinical effects. Changes in ABPIs were also not observed. As shown above, serious cases were only three patients, but acupuncture has a limit to its effects if the severity of ischemia from artery obstruction is high, which exceeds the indication range of acupuncture.

From the results above, we consider that the treatment with acupuncture for clinical symptoms of PAD with Fontaine Stage I and Stage II is effective and Stage I and Stage II symptoms are within the indication range of acupuncture treatment.

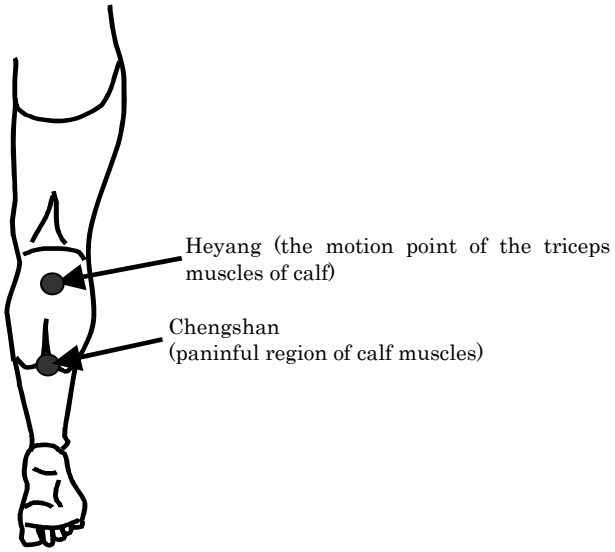

Figure 1　Acupuncture points to insert needles

Fig. 1 shows acupuncture points to insert acupuncture needles in the low frequeny electroacupuncture stimulation method. The insertion depth was 20-30 mm. Stainless steel needles 50 mm long with a diameter of 0.20 mm were used. Stimultion conditions were 1 Hz, pulse width 0.25 ms, and pulse strength 1 mA, the intensity that did not make patient feel unpleasant but strong enough to cause contractions of triceps surae muscles.

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Introduction of Tokyo Ariake University of Medical and Health Sciences (TAU)

About TAU

Tokyo Ariake University of Medical and Health Sciences (TAU) opened in 2009 in Ariake of Tokyo the capital of Japan is a four-year university. Ariake is a waterfront area included in the new Tokyo Waterfront Subcenter of the urban project developed by the metropolitan government. Ariake is one of the most promising areas in Tokyo with good access to urban central areas as there are two public transportation systems (Rinkai Line and Yurikamome Line) and the networks of Tokyo Metropolitan expressways.

Hanada Gakuen, the mother organization of TAU was founded in 1956 by Hanada Tsutou who made great contributions to improving the status of Japanese traditional medicine and developing the traditional medicine after the war. The school is a traditional college that has so far produced over 15,000 acupuncture/ moxibustion practitioners and Judo therapists.

TAU is organized with the Faculty of Healthcare to which the Department of Acupuncture and Moxibustion and the Department of Judo Therapy belong, and the Faculty of Nursing. Education is provided by 43 full-time teachers and a team of vastly-experienced part-time instructors. TAU aims to contribute to the society by training well-balanced specialists that have a wealth of knowledge and solid techniques as well as an investigative point of view and can give consideration to the position of patients and their needs.

Department of Acupuncture and Moxibustion

In the Department of Acupuncture and Moxibustion of TAU, education is given by full-time teachers (1 doctor, 1 doctor of traditional Chinese medicine, 3 researchers of basic researches, 13 practitioners of acupuncture and moxibustion, and 1 athletic trainer (AT) who is a certified practitioner of acupuncture and moxibustion) and other 90 part-time specialists. The education aims to nurture practical human resources so that it is not only designed for students to gain a wide range of medical knowledge relating to acupuncture and moxibustion but also field-oriented, focusing on on-the-job trainings about the optimal implementation method of acupuncture and moxibustion under the modern medical care system and evidence-based indications and contraindications of acupuncture and moxibustion treatment. The education has also an important purpose of contributing to the development of acupuncture and moxibustion medicine through basic clinical research and studies.

Adjunct facilities of TAU

A center for acupuncture and moxibustion with 17 beds will open as adjunct facilities of TAU in September 2009. In the center, practitioners of acupuncture and moxibustion of the Department of Acupuncture and Moxibustion will perform clinical activities on a rotating system to help maintain and improve health of the community residents. And at the same time, students of the Department of Acupuncture and Moxibustion will have on-the-job trainings. Furthermore, a clinic of modern medicine (internal medicine and orthopedics) and a Judo-therapy center are planned to open two years later. Through their cooperation, these centers will assume a role of becoming an implementation example of integrated medicine in Japan.

(Tomoaki Kimura, Department of Acupuncture and Moxibustion)

Tokyo Ariake University of Medical and Health Sciences (TAU)