Effects of Acupuncture on Lower Limb Ischemia

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Objective: To investigate the efficacy of acupuncture treatment for lower limb ischemia.

Design: We quantitatively measured the effects of electro-pulsed acupuncture on cutaneous blood flow and oxygenation, by determining skin perfusion pressure (SPP) and transcutaneous oxygen tension (TcPO2), respectively. The Zusanli and Sanyinjiao acupoints on the right leg were stimulated with electro-pulsed acupuncture at 1 Hz for 10 minutes, then SPP levels at 4 measurement points before and after, and TcPO2 levels at those points before, during, and after treatment were measured. The control group (20 healthy volunteers, average 33.8 years old) received treatment once, while the patient group (9 patients with peripheral arterial disease [PAD], average 65.1 years old) received once-a-week acupuncture treatments and accompanying measurements for 4 weeks, and were also administered a set of questionnaire (VAS in pains and general conditions, KDQOL™, and the Medical Outcomes Study Short Form-36 Health Survey [SF-36]) on the first and final acupuncture treatment days.

Results: Blood flow and oxygenation were increased in peripheral areas in the control group. In the PAD patients, blood flow was significantly increased in the dorsum of the foot and ankle after the first and at all 4 points after the final treatment, whereas cutaneous oxygenation was not significantly increased. In addition, the patient group reported improvements in answers to the Physical Function of SF-36.

Conclusion: Our results indicate that acupuncture is effective as therapy for lower limb ischemia.

Keywords: acupuncture, blood flow, blood oxygenation, diabetes, diabetes mellitus, electro-pulsed acupuncture, lower limb ischemia, peripheral arterial disease (PAD), skin perfusion pressure (SPP), transcutaneous oxygen tension (TcPO2), Short Form-36 (SF-36)

INTRODUCTION

Improvement of limb circulation is a challenging problem when treating patients with peripheral arterial disease (PAD) and/or diabetic foot. Various approaches to increasing lower limb blood flow have been reported, including oral, local, and systemic prostaglandin¹⁵, angioplasty, and bone marrow mononuclear cell transplantation²¹, peripheral blood mononuclear cell transplantation³¹, and peripheral blood stem cell transplantation⁴¹. Unfortunately, even with combinations of those treatments, many patients with lower limb ischemia remain unable to avoid amputation.

Acupuncture has been shown to be effective in increasing blood flow, as documented by several different studies⁵⁻⁹. The goal of the present study was to provide objective and quantitative data to support the use of electro-pulsed acupuncture for increasing cutaneous blood flow and oxygenation, as a potential treatment for lower limb ischemia. We applied
electro-pulsed acupuncture to the Zusanli (ST36) and Sanyinjiao (SP6) acupoints, both of which are commonly used by acupuncture practitioners because of their effects to increase cutaneous blood flow in the lower limbs. Next, we measured the effects of the treatments on skin perfusion pressure (SPP) and transcutaneous oxygen tension (TcPO2) in both healthy volunteers and PAD patients. To evaluate the qualitative aspects of the treatment in the patient group, a series of questionnaires was given.

MATERIALS AND METHODS

Ethical approval

The study was reviewed and approved by the Saitama Medical University Institutional Review Board.

Participants

The trial was conducted at Saitama Medical University from August 2006 to June 2007 for the control group and April to October 2007 for the patient group. We enlisted 20 healthy adults (10 males, 10 females; average age 33.8 years old) as the control group and 9 PAD patients (7 males, 2 females; average age 65.1 years old), each of whom were receiving hemodialysis therapy, as the patient group. We selected patients from those receiving hemodialysis, since PAD is more prevalent among them. Table 1 shows the characteristics of the patient group.

Interventions

Using a 40 mm, No. 18 acupuncture needle (Seirin Corporation, Japan), the Zusanli (Leg Three Li; ST 36) and Sanyinjiao (Three Yin Crossing; SP 6) acupoints of the right leg were stimulated with electro-pulsed acupuncture for 10 minutes at 1 Hz. The Zusanli acupoint is located outside of the lower leg, a few inches below the kneecap on the tibialis anterior muscle, while the Sanyinjiao acupoint is 3 cun (the distance between the second and third knuckles) above the prominence of the medial malleolus, in a depression close to the medial crest of the tibia (Figure 1). A pulse generator (Suzuki Medical, Japan, Model PG-306) was used to provide the electric pulses. The control group received one acupuncture treatment, whereas the patient group received once-a-week treatments for 4 weeks (i.e. 5 times, 1 treatment at the beginning of the trial, and then 1 treatment every 7 days for the next 4 weeks). All acupuncture treatments were performed by one of the co-authors, Dr. Omata, a professional practitioner of acupuncture for 23 years.

Quantitative hemodynamic measurements

To avoid psychological effects, we chose two different quantitative hemodynamic measurements considered to be unaffected by emotion or will. SPP and TcPO2 were measured at 4 points before and after electro-pulsed acupuncture treatment, as follows: (a) the distal-dorsal point of the metatarsus of the first toe (first toe); (b) the proximal-dorsal point of the metatarsus of the first toe (dorsum of foot); (c) a point 5 cm proximal of the medial malleolus (ankle); and (d) a point 5 cm distal of the distal end of the knee cap on the medial face of the tibia (below knee) (Figure 1). The treatment room was kept at an average temperature of 24.7 ± 1.7°C, with an average humidity of 57.6 ± 11.4%.

Table 1. Characteristics of the PAD patient group

<table>
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<tr>
<th>Patient</th>
<th>Gender</th>
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<th>Fontaine Stage</th>
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<th>Hemodialysis</th>
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<td>69</td>
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<td>(+)</td>
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<td>M</td>
<td>63</td>
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<tr>
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<td>F</td>
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<td>III</td>
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</tbody>
</table>

*Age is shown in years. M = male, F = female, (+) = present, (−) = not present.

Fig. 1. Schematic view of the 2 acupoints of Zusanli (ST36) and Sanyinjiao (SP6) and 4 measurement points.
TcPO2 was determined using Clark-type oxygen-sensing electrodes (TCM400, Radiometer Medical, Denmark), which were attached to the skin, and a controlled heating element around the electrode was warmed to 44°C. Measurements were performed at all 4 measurement points at the same time with the participant resting in a supine position.

Qualitative measurements

The patient group received once-a-week acupuncture electro-therapy (AET) for a total of 5 times over 4 weeks. On the first and final days, each were administered 3 different questionnaires before receiving acupuncture, which were composed of questions scored with a visual analogue scale (VAS) (0-100 mm), a Kidney Disease Quality Of Life (KDQOL™) study, and a Medical Outcomes Study Short Form-36 (SF-36) Health Survey. 11, 12)

(1) Questions scored by VAS

The following 2 questions were asked to the patients: “How much pain do you have today?” and “How much physical difficulty are you having today?”, which were scored using a VAS.

(2) Kidney Disease Quality of Life (KDQOL™) Study

Using the KDQOL™, we asked the patients to give an assessment of how they were feeling based on 11 different categories: Symptoms/Problems; Effects of Kidney Disease; Burden of Kidney Disease; Work Status; Cognitive Function; Quality of Social Interaction; Sexual Function; Sleep; Social Support; Dialysis Staff Encouragement; and Patient Satisfaction. For the KDQOL™, higher scores in each category indicated that the patient was feeling better.

(3) Medical Outcomes Study Short Form 36 (SF-36) health survey

The SF-36 asks patients to describe how they are feeling based on 8 different categories: Physical Functioning; Role Limitations due to Physical Problems; Bodily Pain; General Health Perceptions; Vitality; Social Functioning; Role Limitations due to Emotional Problems; and General Mental Health. For each category, the higher the score, the better the patient is feeling.

Statistical analysis

Statistical testing of the SPP data was based on the differences in SPP before and after acupuncture treatments for the control and patient groups, with the data analyzed using a Wilcoxon signed-rank test. We compared between before and after treatment in the control group. In the patient group, we compared between before and after the first treatment, before and after the final treatment, and before the first and before the final treatment.

Statistical testing of the TcPO2 data was based on the differences in TcPO2 before, immediately after,

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**Fig. 2.** Timeline of SPP and TcPO2 measurements before, during, and after acupuncture treatments. Note that SPP was measured before and after treatment, whereas TcPO2 was measured before, during and immediately after the 10-minute treatment period.
5 minutes after, and 10 minutes after beginning the 10-minute acupuncture treatment in the control group, and was analyzed using Fisher’s least-significant-difference and multiple comparisons tests. The same protocol was used for the patient group for the first and final treatments. In addition, difference in TcPO2 before the first and before the final treatment in the patient group was analyzed using a Wilcoxon signed-rank test.

A Wilcoxon signed-rank test was also used to compare the VAS, SF-36, and KDQOL\textsuperscript{TM} scores obtained on the first acupuncture treatment day with those obtained on the final day. All statistical analyses were conducted using Microsoft Stat Excel 2006 for Windows\textsuperscript{®} (Microsoft Corporation, Seattle, WA). We defined statistical significance at a confidence level of 95%.

RESULTS

Quantitative measurements – SPP and TcPO2

Control group – SPP

Following the acupuncture treatment, SPP values in the control group were significantly increased in the first toe and ankle (Figure 3). Further, the increase in SPP value in the dorsum of the foot was just outside the 95% confidence level, whereas the change below the knee was not significant.

Control group – TcPO2

The TcPO2 values changed significantly in the first toe at 10 minutes after the start of the acupuncture therapy, as well as in the dorsum of the foot at both 5 and 10 minutes after the start in the control group (Figure 4).

Patient group – SPP

The effects of the initial acupuncture treatment in the patient group were somewhat different from those in the control group. Following the first treatment, the SPP values were significantly different for the dorsum of the foot and ankle in the patient group (Figure 5).

Thereafter, the patient group then received once-a-week treatments for 4 weeks (total of 5 treatments). The effects of the final acupuncture treatment were evaluated by comparing the SPP values before and after the final treatment. Those values were significantly increased at all 4 measurement points (Figure 6).

Patient group – TcPO2

After the first acupuncture treatment, the TcPO2 values showed no significant changes at any of the 4 measurement points. Those values on the final treatment day were also compared among before, just after insertion of the needles, 5 minutes after insertion, and 10 minutes after insertion. However, the TcPO2 values did not change significantly at any of the measuring points on the final day.

Qualitative measurements – VAS, KDQOL\textsuperscript{TM}, and SF-36

Wilcoxon signed-ranks test

\( n = 20 \text{ mean} \pm \text{S.D.} \)

*\( p < 0.05 \)

Fig. 3. Control group. Changes in SPP before and after acupuncture treatment.
Although the average of both sets of VAS scores was decreased, neither showed statistical significance. The average score for physical difficulty decreased from 50.67 to 43.89 (p-value, 0.4008), while that for pain decreased from 48.78 to 40.11 (p-value, 0.3270). Among the 8 conditions addressed in the SF-36, only the physical functioning condition showed a significant increase after the fourth treatment, as the average score increased from 33.33 to 45.00 (p-value, 0.0284) (Figure 7). For the patient group, none of the 11 areas of the Kidney Disease Quality of Life (KDQOL™) study showed a statistically significant change after the fourth treatment.

**DISCUSSION**

Acupuncture treatment has been reported to improve lower limb circulation, and a previous study of patients with collagen disease showed that the therapy raised cutaneous temperature and increased cutaneous blood flow, as shown by laser Doppler flowmetry results. In addition, acupuncture treatment for healthy adults was found to increase the blood flow in the chorioretinal

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**Fig. 4.** Control group. Changes in TcPO2 before and after acupuncture treatment.

**Fig. 5.** Patient group. Changes in SPP before and after first acupuncture treatment.
area\textsuperscript{6}, while that in rats resulted in increases in permeability of the vascular wall and production of local free-radicals, as observed microscopically\textsuperscript{7}. Thus, effects of acupuncture on blood flow have been observed, with relative increases determined in a qualitative manner.

Other studies have taken a more clinical approach to the effects of acupuncture and acupressure on lower limb blood flow. Yasuno et al. revealed that PAD patients at Fontaine stage I and II experienced an easing of pain and numbness after acupuncture treatments\textsuperscript{8}. Also, Li et al. performed acupressure treatment for Fontaine stage II PAD patients and observed increases in TcPO\textsubscript{2} levels in the lower limbs\textsuperscript{9}. However, neither study directly measured the effects of acupuncture/acupressure on cutaneous blood flow. In addition, other studies have suggested the microbiological effects of acupressure and acupuncture, though little has been proven\textsuperscript{13-16}.

The mechanism of the effects of acupuncture has been reported in a number of studies, as noted by Li et al\textsuperscript{9}. Acupuncture stimulation has been shown to be effective in regulating the autonomic nervous system\textsuperscript{17-19}. In addition, based on observations of the patients

\begin{figure}[h]
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\includegraphics[width=\textwidth]{fig6.png}
\caption{Patient group. Changes in SPP before and after fifth (final) acupuncture treatment.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig7.png}
\caption{Patient group. Changes in SF-36 scores after 4 weeks of acupuncture treatments.}
\end{figure}
undergoing sympathectomy treatments, vasoactive neuropeptides, such as calcitonin gene-related peptide (CGRP) and substance P (SP), are considered to take part in increased blood flow caused by acupuncture\(^{20,21}\). Acupuncture may also relax the sphincter, allowing microvessels to drain tissue fluid, resulting in an increase in interstitial fluid and expansion of blood capillaries\(^{17}\). Based on these previous reports, Figure 8 shows a proposed schematic view of acupuncture related mechanisms lead to blood vessel dilation.

The results of the present study indicate that acupuncture stimulation to the Zusanli (Leg Three Li, ST36) and Sanyinjiao (Three Yin Crossing, SP6) acupoints in healthy adults increases SPP at more distal points of the legs. In the case of our PAD patients as well, the first acupuncture treatment increased SPP in the distal areas (the dorsum of foot and ankle). Four weeks later, after the patients had received four treatments, the effects of the fifth acupuncture treatment were greater than those of the first, as SPP was increased significantly at all 4 points of the lower leg and foot after the final treatment. This indicates that the efficacy of the acupuncture therapy was lower at first, whereas it increased with repeated treatments (Figure 9). These results showing increased SPP by acupuncture support previous studies in which acupuncture was shown to increase blood flow in the skin and chorioretinal area\(^{5,6}\).

In contrast, there was no significant sustained increase in SPP after 4 weeks of acupuncture electro-therapy as compared with the initial SPP measurements, thus 4 weeks of once-weekly acupuncture treatments was not enough to maintain SPP at significantly high levels throughout the treatment interval period (1 week). One week after the fourth treatment (i.e. just before the final treatment), SPP was not increased significantly as compared with before the first treatment.

Increased cutaneous blood flow, which is determined by measuring increased SPP, provides more oxygen to cutaneous tissues, which is determined by measuring increased TcPO2. The effects of acupuncture on TcPO2 in healthy adults were shown to be greater at the distal measurement points (first toe and dorsum of foot). On the other hand, TcPO2 values for the patient group did not increase significantly throughout the observation period (Figure 10). Deeper tissues, including muscle and bone, are more likely to be susceptible to hypoxia than superficial tissue, namely skin. Patients with PAD chronically suffer from hypoxia, while oxygen provided by increased cutaneous blood flow may be consumed not only by the skin, but also by such deeper tissues. Thus, it is possible that the...
increased blood flow seen in the patient group may have first provided oxygen to deeper tissues, while cutaneous tissue may not have received oxygen immediately by the increased blood flow. The control group consisted of healthy adults and deeper tissues of the lower limbs in those likely received sufficient oxygen prior to the acupuncture treatment. In such a condition, increased oxygen provided by increased cutaneous blood flow is not consumed by tissue with hypoxia and is measured as increased TcPO2. This discrepancy in sensitivity between healthy adults and patients has been shown in previous studies. For example, Omata et al. observed the secretion of sweat in the palm areas as an indicator of peripheral sympathetic nerve system, and found that patients with collagen diseases secreted sweat for a longer period than healthy adults following acupuncture therapy.

Other factors of the blood flow of deeper tissue to influence cutaneous blood flow include the mechanical design of the SPP measurement apparatus and accompanying effects of the acupuncture therapy. Since SPP measurement requires the process of avascularization, the measurement value may reflect not only the cutaneous blood flow but also the blood flow in the deeper tissue. During the acupuncture treatment, muscles at the site of acupuncture point contract and this may also contribute the cutaneous blood flow to be influenced by the blood flow in the deeper tissue. We also evaluated qualitative changes in the patients as a result of the acupuncture therapy. Although the VAS scores and KDQOL study results did not show significant differences, the Physical Functioning category of the SF-36 had a significant improvement after 4 weeks of treatments. A high score in Physical Functioning indicates that the patient is able to perform all types of physical activities including the most vigorous without limitations due to health. Those who can perform the activities in this category are capable of doing most of the daily activities without someone’s support. Questions asked in this category include those related to bathing, dressing, lifting and carrying groceries, climbing stairs, bending, kneeling, and walking moderate distances. Each of these activities requires muscle movements and the muscles of the lower limbs plays a key role, especially in individuals suffering from lower limb ischemia. Acupuncture treatment increases blood flow to the lower limbs, which fuels such muscle movements. Thus, a quantitative improvement can be realized by patients in their daily activities, as reflected by qualitative results. This correspondence of quantitative to qualitative data is also seen in the study of Myers et al., in which absolute claudication time for PAD patients was correlated with physical functioning shown in the SF-36. PAD patients desire improvements in such fundamental activities in everyday life and acupuncture therapy is one potential solution.

CONCLUSIONS

Acupuncture treatment applied to the Zusanli and Sanyinjiao acupoints resulted in increased blood flow in the lower limbs in both healthy adults and PAD patients, which in turn improved the activities of daily life for those patients. Our findings suggest that the acupuncture is effective as therapy for lower limb ischemia.

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AUTHOR DISCLOSURE STATEMENT

No competing financial interests exist.

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下肢血流障害に対する鍼治療の効果
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目的：下肢血流障害に対する鍼治療の効果を検証する。
デザイン：通電鍼刺激の皮膚血流および酸素化への効果を定量的に検証するため、皮膚還流圧（SPP）および経皮酸素分圧（TcPO2）を測定した。右下肢の足三里穴および三陰交穴を1Hzの通電鍼刺激によって10分間刺激し、右下肢の4計測点（右第一中足骨遠位・足背・足関節・膝下）についてSPPおよびTcPO2の変化を測定した。このうちSPPについては通電鍼刺激前後の測定を行い、TcPO2については刺激前、刺激中、および刺激後の測定を行った。コントロール群（20人の健常者で平均年齢33.8歳）については通電鍼刺激および測定を1回のみ行った。患者群（9人の末梢動脈疾患患者[PAD]で平均年齢65.1歳）は週1回の鍼治療を4週間、計5回受け、初回および5回目についてSPPおよびTcPO2の測定を行った。患者群についてはさらに、初回および5回目の鍼治療開始前に一連のアンケート調査（疼痛および全般についてVAS score、KDQOL™、及びMedical Outcomes Study Short Form-36 Health Survey [SF-36]）を行った。
結果：鍼刺激により、コントロール群では皮膚血流および酸素化が末梢領域で上昇を認めた。PAD患者群では初回鍼治療によって足背および足関節部での皮膚血流が上昇し、5回目の鍼刺激によって4計測点すべての血流が上昇したが、患者群での酸素化の上昇は認めなかった。患者群では更に、SF-36の身体機能について有為な改善を認めた。
結論：下肢血流障害に対する治療法として、鍼治療が有効であることが示された。

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