

Treatment of primary Raynaud's syndrome with traditional Chinese acupuncture

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Abstract. Appiah R, Hiller S, Caspary L, Alexander K, Creutzig A (Medizinische Hochschule Hannover, Department of Angiology, Hannover, Germany). Treatment of primary Raynaud's syndrome with traditional Chinese acupuncture. *J Intern Med* 1997; **241**: 119–24.

Objective. Evaluation of the effects of a standardized acupuncture treatment in primary Raynaud's syndrome.

Design. A controlled randomized prospective study.

Setting. A winter period of 23 weeks, angiological clinic of Hannover Medical School.

Subjects. Thirty-three patients with primary Raynaud's syndrome (16 control, 17 treatment).

Interventions. The patients of the treatment group were given seven acupuncture treatments during the weeks 10 and 11 of the observation period.

Main outcome measures. All patients kept a diary throughout the entire observation period noting daily frequency, duration and severity of their

vasospastic attacks. A local cooling test combined with nailfold capillaroscopy was performed for all patients at baseline (week 1) and in weeks 12 and 23, recording flowstop reactions of the nailfold capillaries.

Results. The treated patients showed a significant decrease in the frequency of attacks from 1.4 day⁻¹ to 0.6 day⁻¹, $P < 0.01$ (control 1.6 to 1.2, $P = 0.08$). The overall reduction of attacks was 63% (control 27%, $P = 0.03$). The mean duration of the capillary flowstop reaction decreased from 71 to 24 s (week 1 vs. week 12, $P = 0.001$) and 38 s (week 1 vs. week 23, $P = 0.02$) respectively. In the control group the changes were not significant.

Conclusions. These findings suggest that traditional Chinese acupuncture is a reasonable alternative in treating patients with primary Raynaud's syndrome.

Keywords: acupuncture therapy, capillaroscopy, laser-Doppler flowmetry, peripheral vascular disease, Raynaud's syndrome.

Introduction

Primary Raynaud's syndrome is defined as idiopathic intermittent vasospastic attacks of the acra—mainly of the hands—triggered by cold or emotions. Its prevalence varies from country to country and is estimated at 5–10% in the German population [1]. Occurring mainly in people between the ages of 20 and 30 years, it affects twice as many women as men. Symptoms may range from mild painless pallor of one single digit to painful ischaemia of all fingers and toes. Ulcerations though, are not seen in primary Raynaud's syndrome.

In contrast to secondary Raynaud's syndrome, where the attacks are due to an underlying disease, there are no organic changes to be found causing primary Raynaud's syndrome. From primary

Raynaud's syndrome there seems to be no threat to the health of the patients. Yet many patients feel their social life being compromised by this disease.

Patients with primary Raynaud's syndrome are advised to avoid cold exposure. Only if this does not lead to satisfactory control of the symptoms, further treatment is required. Many approaches, ranging from autosuggestive and relaxation therapies to sympathectomy, have been evaluated.

Today one of the therapeutic options for severe primary Raynaud's syndrome is the prescription of the calcium-channel antagonist nifedipine. This drug decreases the severity of attacks by about 70–90% in roughly 70% of the patients [2–7]. A similar effectiveness has only been shown in uncontrolled studies evaluating autosuggestive strategies and relaxation therapies [8–10]. Yet quite a few patients abandon

therapy with nifedipine because of undesirable side-effects. This is understandable as primary Raynaud's syndrome is often associated with low blood pressure.

In recent years acupuncture has become more and more popular for treating functional diseases. At the same time the number of patients asking for treatments other than drug administration has increased. Concerning primary Raynaud's syndrome and acupuncture several case-reports have been published [11–13], but no controlled studies have been performed yet.

In a controlled randomized prospective study we wanted to evaluate the effect of traditional Chinese acupuncture on patients with primary Raynaud's syndrome as an alternative to standard treatment.

Patients and methods

From the patients of the angiological clinic of the Medical School Hannover we found 33 subjects meeting the following criteria: age between 18 and 60 years, primary Raynaud's syndrome according to the criteria of Allen & Brown [14] (intermittent vasospastic attacks triggered by cold or emotions, duration of the disease at least 2 years, symmetrical symptoms, no trophic lesions, no organic manifestations), normal blood count, no antientomere

or antinuclear antibodies, no cryoglobulines, no rheumatoid factor, no clotting disorders, no anti-coagulative therapy, normal morphology of nailfold capillaries, no use of vasoactive drugs during the study and 6 weeks before, no history of myocardial infarction or angina pectoris, no pregnancy, informed written consent.

The upper limit of age was set at 60 years. This is much higher than the usually observed onset of primary Raynaud's syndrome which is around 20 years. Most patients who finally seek professional help in our angiological clinic have a long history of vasospastic attacks, resulting in a higher mean age. Pregnant women were excluded from the study, as there is not enough data on the effect of pregnancy on primary Raynaud's syndrome. Patients with history of myocardial infarction or angina pectoris were rejected because of a hypothetical possibility of acupuncture worsening these conditions. Table 1 shows relevant clinical data of the participating patients. There were no significant differences between the two groups.

The study was designed according to the declaration of Helsinki (Hong Kong revision 1989) and approved by the Council for Ethics of the Medical School Hannover.

The patients were randomly assigned to one of the two groups 'control' or 'treatment', resulting in 17 patients in the treatment group and 16 patients as controls. All patients were asked to keep a diary noting daily frequency, duration and severity of their vasospastic attacks during a 23-week period, lasting from November 1993 to April 1994. The severity of the attacks was judged by the patients on a 10-point visual scale. The recorded data was calculated for 2 periods with the weeks 1–9 as 'period 1' and the weeks 12–23 as 'period 2'. The data of the 2 weeks in which the patients of the treatment group were acupuncture did not contribute to the evaluation.

The patients of the treatment group were treated with acupuncture during the weeks 10 and 11 every second day—making a total of seven treatments for each patient. Acupuncture-points were chosen according to the Shanghai School [15]. The control group received no treatment. Corresponding to the international nomenclature [15] the following points were used: Lu9, St36, St40, Sp1, SI3, UB15, Liv3, Ren12, Ren14. The points Ren12, SI3 and Sp1 were treated with moxibustion only, whereas all other points were acupuncture with sterile single-use

Table 1 Clinical data of participating patients

	control (n = 16)	treatment (n = 17)
Men/women	5/11	5/12
age (years, mean \pm SD)	41.5 \pm 10.7	45.5 \pm 11.5
Duration of disease (years, mean \pm SD)	11.4 \pm 11.1	16.1 \pm 14.6
Nicotine consumption	3	2
Attacks		
Frequency per day (mean \pm SD) ^a	1.6 \pm 1.3	1.4 \pm 1.1
Duration per attack (min, mean \pm SD) ^a	36.5 \pm 21.1	23.6 \pm 17.4
Severity per attack (mean \pm SD) ^{a,b}	4.8 \pm 2.1	4.0 \pm 1.8
Localisation		
fingers	16	17
toes	5	8
Triggered by		
cold	16	17
emotions	5	3
Previous therapies		
vasoactive drugs	7	6
sympathectomy	2	1

^aFrequency, duration and severity of attacks were calculated for 'period 1' i.e. before the acupuncture therapy.

^bThe severity of attacks was recorded by means of a 10-point visual scale.

needles (Seirin, Germany). Moxibustion is a kind of heat therapy where a burning cigar of *artemisia vulgaris* is held over the acupuncture point so that the patient records an agreeable heat sensation. As some of the acupunctured points are associated with similar effects, we treated St40 alternating with St36 and SI3 alternating with Ren12.

In weeks 1, 12 and 24 a local cooling test, adopted from Mahler *et al.* [16], combined with nailfold capillaroscopy was performed for all patients and capillary flow-stop reactions were recorded. This technique has been used to study the disturbances of skin microvascular reactivity in different types of Raynaud's syndrome. Both sensitivity and specificity have been found to be 0.95 [17, 18].

For this investigation a capillary-microscope (Zeiss, Germany) with attached video-camera (Panasonic, Japan), video-recorder (Sony, Japan) and video-timer (For.A, Japan) was used. We selected a finger with an even nailfold to achieve a good picture quality of the observed capillaries. To ensure standardized conditions for each investigation the patients were allowed to acclimatize for at least 20 min to the 23°C warm examination room. In addition, the patients immersed both latex-gloved hands for 3 min into a waterbath at 40°C. Furthermore the same finger was examined in each of the three investigations. With the patients sitting upright and the hand at heart level the selected finger was placed under the microscope and capillary blood flow was recorded for 5 min.

Quickly decompressing carbon dioxide was then directed through a plastic tube and an attached aluminium pipe onto the observed nailfold for 90 s. The distance between the mouth of the pipe and the nailfold was 5 cm, the angle between finger and pipe 45°. A digital thermometer in the air-stream allowed the regulation of the carbon dioxide flow and achieved a constant cooling temperature of $-15 \pm 2^\circ\text{C}$. Following the cooling, the capillary blood flow was recorded for further 13.5 min, resulting in a total observation time of 20 min.

The evaluated parameters were the number of capillaries with a flowstop reaction for more than 5 s in relation to the total seen capillaries and the average duration of flowstop reactions in all observed capillaries.

As a control for these investigations, 10 healthy subjects of similar age (four men, six women, 39.1 ± 11.5 years) and with no history of vascular

disease were examined twice within 2 weeks according to the above described procedure.

Since a normal distribution (Kolmogorov–Smirnov test for normal distribution with $P > 0.1$) could not be assumed for all parameters of the study we only used the non-parametrical Wilcoxon test for statistical evaluation. All tests were performed with SPSS for windows, version 6.0.1. The level for significance was set to $P < 0.05$.

Results

Eleven out of the 17 treated patients reported a subjective improvement of their Raynaud's syndrome. This was confirmed by the evaluation of the diaries. In the group of treated patients the frequency of attacks was significantly reduced from 1.4 day^{-1} to 0.6 day^{-1} ($P < 0.001$). The control group showed a non-significant reduction in frequency from 1.6 day^{-1} to 1.2 day^{-1} ($P = 0.08$). Figure 1 shows the mean frequency of attacks per group and per patient for both periods.

The parameters duration and severity of attacks showed no significant changes either in the treatment group or in the control patients. The improvement concerning the frequency of attacks lasted throughout the entire second part of the observation period of 3 months. We questioned the treated patients 7 months later, after the beginning of the following

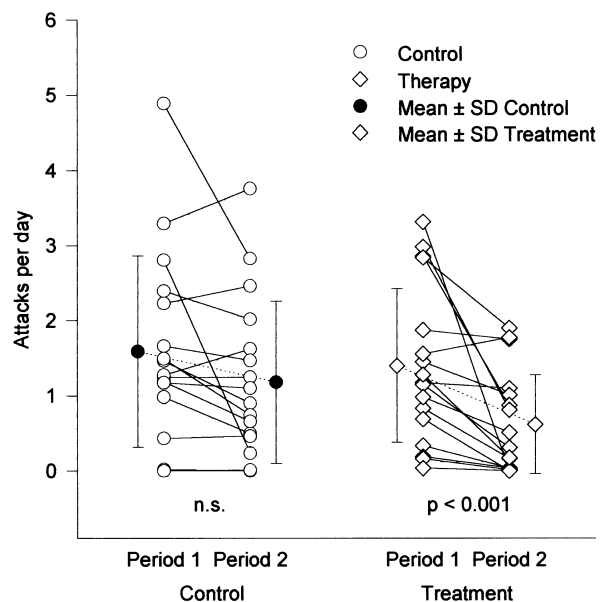


Fig. 1 Frequency of attacks during period 1 and period 2 per patient and per group.

Table 2 Mean number of capillaries with a flowstop reaction in relation to total seen capillaries and mean duration of flowstop reaction for each examination. Also given are [minimum - maximum, median].

	Capillaries with a flowstop reaction in relation to total seen capillaries (%)		Mean duration of flowstop reaction (s)	
	Control (n = 16)	Treatment (n = 17)	Control (n = 16)	Treatment (n = 17)
Examination 1 (week 1)	73.6 [20-100, 87.5]	79.7 [0-100, 100.0]	62.7 [5-130, 58.0]	70.9 [0-167, 57.0]
Examination 2 (week 12)	45.6 [0-100, 33.3] (NS)	24.8 [0-100, 0.0] (<i>P</i> = 0.0014)	36.5 [0-164, 17.2] (NS)	28.4 [0-189, 0.0] (<i>P</i> = 0.0097)
Examination 3 (week 23)	56.0 [0-100, 60] (NS)	38.3 [0-100, 16.7] (<i>P</i> = 0.017)	41.2 [0-160, 33.3] (NS)	29.4 [0-119, 12.4] (<i>P</i> = 0.0217)

The stated significance values are calculated against the values of the first examinations. NS, not significant.

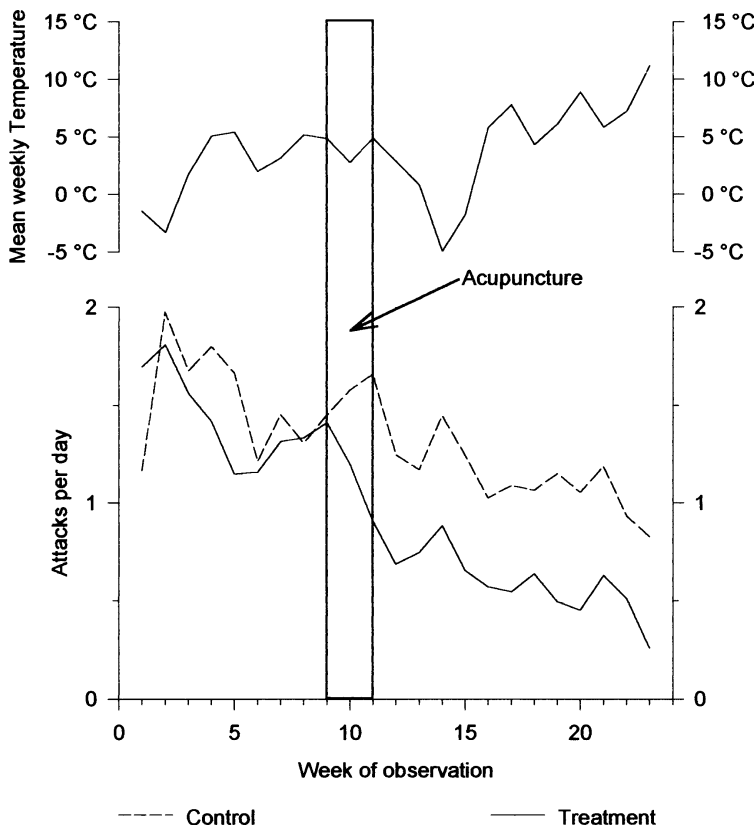


Fig. 2 Frequency of attacks per group and mean weekly temperature.

cold period (November 1994). Still 10 out of the 17 patients reported a lasting improvement.

Regarding the capillaroscopic parameters of the treatment group we found a significant reduction in the percentage of capillaries with a flowstop reaction as well as a reduction in the duration of the blood stasis. Changes of these parameters in the control

group were not significant (Table 2). Within the healthy subjects, the percentage of capillaries with a flowstop reaction increased insignificantly from 13.9% to 21% (range 0-100% and median = 0 in both examinations). The mean duration of the flowstop reaction remained unchanged (17.9 s. vs. 17.4 s, range 0-100% and median = 0 each time).

Discussion

In this study we found a significant reduction of the frequency of attacks in the patients treated with traditional Chinese acupuncture. This effect lasted throughout the entire observation period after the treatment. According to the questionnaires the patients completed in the following cold period, it seems that the duration of beneficial effects goes beyond 10 months. The untreated control group showed a slight decrease of attacks as well, which was not significant and should be due to the warmer weather in the second part of the observation period (Fig. 2). Also contributing to the decrease of attacks in the control group is the fact that two of the patients spent longer holidays in warmer countries, where they had no attacks. This did not occur in the treatment group.

It might be suggested that the reduction of attacks in the treated group is due to a placebo effect. To evaluate this, it was not possible to treat the control group with placebo-acupuncture, as patients who have already had experience with acupuncture are able to tell the difference between real and placebo acupuncture [19]. Another thought might have been to treat the control group with nifedipine. This would have reduced the number of participating patients, because many of our patients had already been treated with vasoactive drugs and aborted the treatment because of side-effects.

Treating patients with Raynaud's syndrome, Coffman *et al.* found a placebo effect causing an 18% reduction of symptoms [20]. With 63% in our study, the reduction of attacks in the treated patients is so great that we presume that the vast proportion of this result is caused by the acupuncture treatment. Even if there should be a greater placebo effect, we share the opinion of Götzsche, that a therapy showing a large effect, compared with no treatment, is a useful intervention, no matter what its nature is [21].

Comparing this result with those of studies using vasoactive drugs [2–7, 20, 22–28] we find acupuncture to be similarly effective. It should be mentioned that none of the treated patients reported any side-effects except the disappearance of a long-lasting tinnitus and the improvement of a chronic sinusitis.

Despite much investigation the pathophysiology of primary Raynaud's syndrome still is poorly understood. Several neural and biochemical mechanisms

regulating the cutaneous vascular tone have been identified, with recent research focusing on the interactions of the endothelium with calcitonin gene-related peptide (CGRP), nitric oxide and endothelin-1 [29,30]. Regarding acupuncture effects on primary Raynaud's syndrome two mechanisms could be postulated: a reduction of the sympathetic tone and the release of vasoactive mediators, especially CGRP.

It has been shown that an increased sympathetic tone plays an important role in eliciting attacks in primary Raynaud's syndrome [31, 32]. Concerning the effects of acupuncture it could be presumed that a reduction of the sympathetic tone is achieved. This mechanism has been confirmed in experimental studies with spontaneous hypertensive rats [33].

Furthermore it has been shown that acupuncture releases substance P and CGRP from peripheral terminals of primary sensory neurons [34], the latter being one of the most potent vasodilators [35]. As a deficiency of CGRP has been found in patients with primary Raynaud's syndrome [36] and Kjartansson *et al.* describe the effect of acupuncture on ischaemia to be more similar to CGRP than to a reduction of the sympathetic tone [37], this might be a more adequate explanation of the effects found in this study. Still there are no studies that could confirm this effect to be a causative factor for the observed long-term effects.

A question still remaining is why the mean duration and the mean severity of attacks showed no significant changes. It is possible that with acupuncture therapy only the threshold for eliciting an attack has been elevated. If an attack is provoked, it seems to have the same duration and severity as usual. Coffman *et al.* have made similar findings treating patients with vasoactive drugs [20].

The results drawn from the diaries are confirmed by the data obtained through the nailfold capillaroscopy: significant reductions in the number of capillaries with flowstop reactions and in the mean duration of the blood stasis could be shown for the treated patients.

In conclusion, traditional Chinese acupuncture seems to induce a long-lasting reduction of attacks in primary Raynaud's syndrome. It appears that the effectiveness of a standardized acupuncture therapy is comparable to that described for nifedipine but without showing any side-effects.

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Received 9 April 1996, accepted 16 September 1996.

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