Research Article

Determination of vascular responses to manual PC6 acupuncture in subjects healthy and diabetics by the second derivative of the finger photoplethysmogram waveform

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Abstract

Background: Diabetes is known to be associated with increased arterial stiffness. Indices obtained from the second derivative of photoplethysmogram (SDPTG) have been proposed to characterize vascular aging and arterial rigidity. Pericardium 6 (PC6) is an acupoint that has been shown to improve cardiovascular functioning. **Objective**: To assess if manual acupuncture in PC6 modifies the SDPTG indices in type 2 diabetic subjects compared to healthy subjects. **Materials and methods**: AGI, b/a, and d/a indices based on the wave components of SDPTG of healthy subjects (n=15, 44.6 years old) versus type 2 diabetic subjects (n=15, 48.3 years old) were compared. The photoplethysmogram (PTG) was obtained by measuring infrared light transmission through the finger. Of each subject, a PTG registration 30 min long was obtained. PC6 right was stimulated by manual needling for 5 min (1-6 min). SDPTG indices were compared in each subject in the pre- versus post-acupuncture periods (1 versus 30 min, respectively). **Results**: At baseline, we found a significantly higher value of AGI in diabetic subjects (p= 0.002). Comparing pre- versus post-acupuncture periods, AGI improved significantly in diabetics subjects; and b/a and d/a did not modify significantly. **Conclusion**: This study provides evidence that manual acupuncture in PC6 can modify the SDPTG index related to arterial stiffness in subjects with type 2 diabetes. Clinical trials are needed to assess this acupuncture treatment for improving the arterial stiffness in diabetic subjects.

Keywords: acupuncture; type 2 diabetes; arterial stiffness; Pericardium 6

Introduction

Arterial stiffness is a major contributor to high cardiovascular morbimortality and independent marker of cardiovascular disease in type 2 diabetic subjects (Mansour et al., 2013); type 2 diabetes is associated with a greater age-related stiffening of the aorta, regardless the level of hypertension (De Angelis et al., 2004).

Type 2 diabetes mellitus is a significant risk factor in the development and progression of arterial stiffness (Elias et al., 2018); and a is a key determinant of left ventricular remodeling, arterial stiffness, adverse pulsatile hemodynamics, and ventricular-arterial interactions in subjects with heart failure (Chirinos et al., 2019). Moreover, in subjects with impaired fasting glucose arterial stiffness was higher than in subjects with normal fasting glucose (Paik et al., 2012).

Epidemiologic studies strongly support the assertion that among patients with established DM, arterial stiffness is closely related to the progression of complications of DM, including nephropathy, retinopathy, and neuropathy (Prenner and Chirinos, 2015).

The detailed analysis of the second derivative of the finger photoplethysmogram (SDPTG) waveform permits the assessment of peripheral circulation and changes elicited by vasoactive agents (Takazawa et al., 1998). The SDPTG allows

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more accurate recognition of the circulation phases, and it is easier to interpret than the DVP waveform analysis. Population studies have shown that SDPTG waveform reflects both the elasticity of the aorta and peripheral arteries and that it is associated closely with age and other risk factors for atherosclerotic vascular disease (Takazawa et al., 1998; Bortolotto et al., 2000; Miyai et al., 2001). Hashimoto et al. reported that SDPTG might be worthwhile for detecting vascular aging accelerated by hypertension (Hashimoto et al., 2005).

Previous preliminary studies have suggested that the stimulation of acupoints or nerve underlying acupoints can elicit different effects on arterial blood pressure (Longhurst and Tjen-A-Looi, 2017). Besides, PC6 acupoint is one of the primary acupoints used clinically in traditional Chinese medicine to treat cardiovascular diseases (Tam and Yiu, 1975; Richter et al., 1991; Chen, 1994).

Among many acupoints, we were interested in the PC6 (Neiguan) acupoint because it has been considered to affect the cardiovascular system, and to reduce systolic blood pressure in subjects with hypertension (Li et al., 2015). A previous study showed that electroacupuncture at PC6 acupoints improved hemodynamics and increased cardiac contractility in anesthetized open-chest dogs under normotensive conditions (Syuu et al., 2001). We examined the acute effects of manual needling PC6 on SDPTG indices in healthy subjects and type 2 diabetic subjects.

Materials and Methods

This study is designed as an experimental non-randomized, single-center trial to check if manual acupuncture in right PC6 modifies the SDPTG indices in type 2 diabetic subjects compared to healthy subjects.

Subjects

Healthy subjects were recruited from the community around our institution by advertisement. The study reference group comprised 15 (4 female) healthy subjects with a mean (± SD) age of 44.6 ± 7.2 years. At the time of the study, all subjects were normotensive (office blood pressure <140/90 mm Hg and none had total serum cholesterol values >200 mg/dl. None had cardiac or renal diseases or were taking any medications. Study diabetic group comprised 15 (9 female) with type 2 diabetics with a mean (± SD) age of 48.3 ± 7.9 years, with type 2 diabetes diagnosed between a period of 5 – 9 years and on continuous medical management with oral hypoglycemic agents. A fasting blood glucose of <200 mg/dl was required as an inclusion criterion. The exclusion criteria were the presence of cardiovascular or renal diseases.

All subjects were studied fasting, having abstained from caffeine, alcohol, or smoking in the previous 12 h. The trial was approved by the Ethics Committee of Health and Biological Sciences Division, Metropolitan Autonomous University at Iztapalapa (2007.6.01.03). Written informed consent was obtained from all participants.

Second Derivative of PTG (SDPTG)

The second derivative of the PTG wave contour was obtained using the Origin, Scientific Graphing, and Analysis Software, v. 7.5 (Microcal Software, Inc., Northampton, MA) to specify inflection points (Figure 1). Typically, the d2PTG/dt2 waveform comprises five distinct waves: *a* to *f*. The height of each wave was measured from the baseline, the values above the baseline being positive and those under it negative, as previously described (Hashimoto et al., 1998).

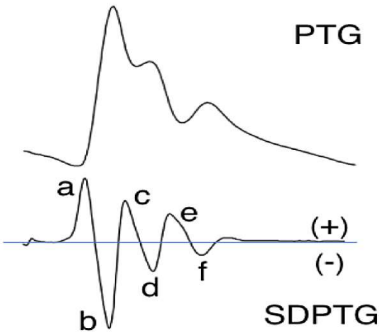

Figure 1. Typical traces of the finger photoplethysmogram (PTG, top) and its second derivative (d2PTG/dt2, bottom). The SDPTG consists of the *a, b, c, d*, and *e* waves. The b/a ratio was calculated as the ratio of the absolute value for the height of the *b* wave to that of *a* wave, and the d/a ratio was calculated as the ratio of the absolute value for the height of the *d* wave to the *a* wave. The AGI was defined as (*b-c-d-e*)/*a*.

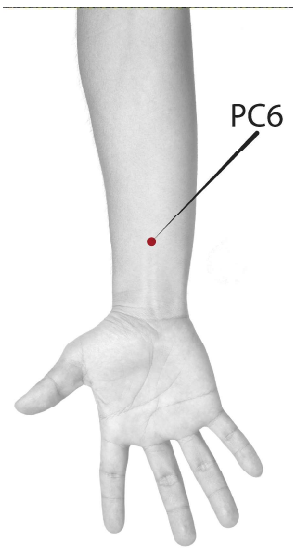

Figure 2. Pericardium 6 (PC6) acupoint.

Acupuncture

Acupuncture treatment was given by a physician trained in both orthodox Western medicine and traditional Chinese medicine. We used 5-cm-long, 0.22-mm-wide disposable stainless steel needles (SHARP, Suzhou, Beijing, China) with no additional electrical or laser stimulation. In healthy subjects and type 2 diabetics subjects, the diagnostic workup included the recording of medical history and symptoms. Acupuncture needle was inserted unilaterally into PC6 (Figure 2) at 1.5 cm deep in the right arm and was manually stimulated until acupuncture characteristic sensation (*DeQi)* was obtained. The needle was maintained in place for 5 min (1-6 min) and removed thereafter. Healthy subjects and diabetic subjects were assessed in the same way, were given the same amount of attention, and received the same acupuncture treatment, which was left for the same length of time, as their pairs. The trial was blinded for clinical investigator calculating SDPTG indices, who were not aware of the healthy or diabetic character of the subjects.

Assessment method

The measurements were performed with each subject in the supine position. All recordings were made at the morning in a laboratory with a temperature 24±1 ºC. All subjects rest for at least 30 min before recordings commenced. A photoplethysmograph TSD200 (BIOPAC Systems, Inc., Goleta, CA, United States) transmitting infrared light at 860 nm±90 nm placed on the index finger of the right hand was used to obtain the PTG (Figure 1). The frequency response of the photoplethysmograph was flat to 10 Hz. The digital output from the photoplethysmograph was recorded through a 12-bit analog-to-digital converter with a sampling frequency of 200 points per second BIOPAC Systems, MP150 (BIOPAC Systems, Inc., Goleta, CA, United States) using AcqKnowledge v. 4.1 software (BIOPAC Systems, Inc., Goleta, CA, United States). Of each subject, a PTG continuous registration 30 min long was obtained. After a 1 min basal record, PC6 was stimulated in the right arm manually until obtaining the DeQi reaction, contralateral to the PTG registry side. PC6 right was stimulated by manual needling for 5 min (1-6 min). Continuous and high-quality 20–40 SDPTG indices were extracted from beat to beat PTG and calculated for every subject in the basal (pre-acupuncture) and post-acupuncture periods (minutes 1 and 30, respectively). The SDPTG indices for each group were averaged and then tested for statistically significant differences between the two groups.

Data analysis

Based on absolute values for the height of waves *a*, *b*, c, and *d* of the raw PTG we comprehensively calculated and analyzed the following variables: b/a, (i.e., the ratio of the height of the b wave to that of the b); and analogously, d/a; (b-c-d-e)/a (the so-called Aging Index or AGI) (Takazawa et al., 1998). Representative traces of the photoplethysmogram and its second derivative are shown in figure 1.

Statistical analysis

Data were expressed as mean ± SD. The Student *t*-test was used for comparison of normally distributed continuous variables. The P value of $p<0.05$ was considered significant. All statistical analyses were performed with SPSS software version 11.0 (SPSS Inc., Chicago, IL).

Results

Characteristics of the healthy subjects and diabetic subjects are shown in table 1. Demographic and physiological data were not significantly different between the two subject groups.

The SDPTG indices in healthy subjects before and its changes after acupuncture are shown in table 2. Comparing pre- vs. post-acupuncture periods, any of the SDPTG indices did not show significant differences among healthy subjects.

The SDPTG indices in type 2 diabetics subjects before and its changes after acupuncture are shown in table 3. Manual acupuncture stimulation in PC6 significantly improved de SDPTG aging index ($p=0.013$) when comparing the pre- to post-acupuncture values. Otherwise, there was no significant difference in b/a and d/a indices.

Table 1. Demographic and clinical data for study groups

Demographic and clinical parameter	Healthy subjects	Diabetics subjects
No. (female)	11 (4)	6 (9)
Age (yr)	44.6 ± 7.2	48.3 ± 7.9
Brachial systolic BP (mm Hg)	123 ± 12.2	128 ± 14.1
Brachial diastolic BP (mm Hg)	74.1 ± 9.2	76.3 ± 10.5
Heart rate (bmp)	74.5 ± 8.2	75.4 ± 9.4

Data are mean ± SD.

Table 2. Comparison of SDPTG indices in healthy subjects in the pre- versus post- acupuncture periods

SDPTG index	Pre-acupuncture	Post-acupuncture	p
AGI	-0.60 ± 0.23	-0.41 ± 0.20	0.088
b/a	-0.97 ± 0.33	-0.99 ± 0.24	0.792
d/a	-0.10 ± 0.14	-0.14 ± 0.09	0.403

*P < 0.05; AGI= Aging index defined as (*b-c-d-e*)/*a*; b/a= Calculated as the ratio of the absolute value for the height of the *b* wave to that of the *a* wave. d/a= Calculated as the ratio of the absolute value for the height of the *d* wave to *a* wave.

Table 3. Comparison of SDPTG indices in type 2 diabetic subjects in the pre- versus post- acupuncture periods.

SDPTG index	Pre-acupuncture	Post-acupuncture	p
AGI	-0.12 ± 0.04	-0.52 ± 0.24	0.013
b/a	-0.94 ± 0.47	-1.03 ± 0.19	0.545
d/a	-0.16 ± 0.14	-0.12 ± 0.11	0.500

*P < 0.05; AGI= Aging index defined as (*b-c-d-e*)/*a*. b/a= Calculated as the ratio of the absolute value for the height of the *b* wave to that of the *a* wave. d/a= Calculated as the ratio of the absolute value for the height of the *d* wave to *a* wave.

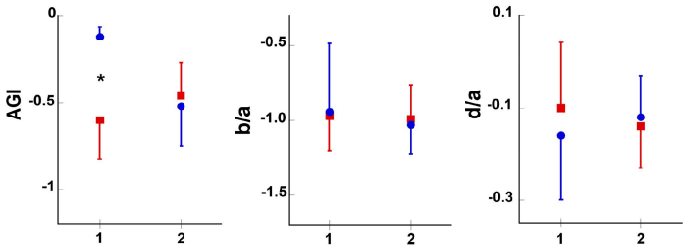

Figure 3. Comparison of indices of SDPTG between healthy subjects —■— and type 2 diabetics —●— in the pre- (1) and post-acupuncture (2) periods. AGI= Ageing index; b/a= b/a index d/a= d/a index; *p < 0.01.

The comparison of SDPTG indices before and its changes after acupuncture between healthy subjects and the type 2 diabetic subjects are shown in figure 3. At baseline, there was no difference in b/a and d/a indices between healthy subjects and type 2 diabetic subjects. However, we found that AGI was significantly higher in diabetic subjects (p=0.0016).

Discussion

The salient finding of this study was in type 2 diabetic subjects, AGI-SDPTG index was improved with manual acupuncture in PC6 when comparing before to after acupuncture values. We also found that the baseline AGI of SDPTG was significantly different between healthy subjects and diabetic subjects; however, there was no significant difference between the groups in the AGI-SDPTG after acupuncture.

Takazawa et al. (1998) showed that the second derivative of the PTG might be used to infer changes in the systemic circulation related to the effects of ageing or drugs; and have reported that the ageing index was higher in subjects with any history of diabetes mellitus, hypertension, hypercholesterolemia, and ischemic heart disease than in age-matched subjects with such a history.

Nonetheless, factors affecting AGI-SDPTG could be modified by miscellaneous pathophysiological factors, including changes in heart and vascular physiology. The effects of needling PC6 on AGI-SDPTG in both healthy and hypertensive subjects could be related to a decrease in arterial vascular tone. The AGI-SDPTG has been proposed specifically as a marker and for evaluation of vascular aging (Bortolotto et al., 2000).

PC6 is one of the primary acupoints used experimental and clinically to treat hypertension, cardiovascular ailments, and other autonomic nervous conditions (Chen, 1994; Syuu et al., 2001; Tam and Yiu, 1975). Stimulation of the median nerve produces a sympathoinhibitory effect, and this inhibition involves some nucleus of the hypothalamus with projection to the rostral ventrolateral medulla (Li, 1991). Acupuncture in healthy persons is associated with changed activity in the sympathetic and parasympathetic nervous system related to the site and kind of stimulation (Haker et al., 2000). PC6 seems to possess a specific capacity to modifies arterial stiffness (Rivas-Vilchis et al., 2007), which could support its cardioprotective effects observed in clinical studies.

In our findings, AGI-SDPTG was higher in diabetics subjects than in a matched population. This finding agreed with previous reports of diabetes as a risk factor for vascular aging, and an accelerated arterial stiffness occurs in those with diabetes (Goh and Cooper, 2008). Moreover, some data suggest that arterial stiffness can predict the onset of diabetes (Prenner and Chirinos, 2015). Otherwise, arterial stiffness may be a result of or a cause of diabetic vascular complications such as diabetic nephropathy and retinopathy (Stehouwer et al., 2008). Several biomechanical changes in the arteries occur as a result of diabetes that could stiffen arteries (Vlassara, 1997)

Limitations of the study. There were differences in the baseline characteristics of the diabetic and nondiabetic groups. This is not a significant drawback in the current study because the aim was not to compare absolute parameters between groups but to compare the effects of manual acupuncture in PC6.

Conclusion

This study provides evidence that manual acupuncture in PC6 can acutely modify the SDPTG aging index related to arterial stiffness in subjects with type 2 diabetes. Further prospective trials and intervention studies are needed to assess if this acupuncture treatment could improve the arterial stiffness in diabetic populations.

Conflict of interest

The authors declare no conflicts of interest.

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