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Effect of Acupuncture on Heart Rate Variability in Primary Dysmenorrheic Women

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Running title: [Acupuncture and HRV in dysmenorrheic women](#)

Abstract: Primary dysmenorrhea is a common gynecological complaint among young women which is related to an autonomic nervous system (ANS) disturbance. Acupuncture is one of several therapeutic approaches for primary dysmenorrhea since it can modulate ANS function. The heart rate variability (HRV) parameters such as high frequency (HF), low frequency (LF) and LF/HF ratio are generally accepted tools to assess ANS activity. The purpose of this study was to investigate the effects of acupuncture applied at Hegu (LI4) and Sanyinjiao (SP6) points on HRV of women with primary dysmenorrhea during the late luteal phase. The experimental design was a crossover and patient-blinded procedure. All subjects participated in Sham (SA) and Real Acupuncture (RA) procedure, separated by one month, in a crossover sequence. The participants included 38 women (mean age 22.3 years; weight 53.8 kg; height 162.6 cm). HRV measurement was for 15 min before and after an acupuncture procedure. The RA procedure was performed at two bilateral acupoints, but needles were inserted subcutaneously to the acupuncture points for the SA procedure. The RA induced a significant decrease in LF/HF ratio and a significant increase in the HF power, while SA treatment caused a significant increase only in the HF power. Manual acupuncture at bilateral acupoints of LI4 and SP6 may play a role in dysmenorrhea treatment with autonomic nervous system involvement.

Keywords: Acupuncture; Dysmenorrhea; Heart rate variability; High frequency; Low frequency.

Introduction

Primary dysmenorrhea is a common problem in women of reproductive age (French, 2005); the prevalence rate is 18 to 81% depending on methods of measurement (Latte *et al.*, 2006). It affects the working population and can cause economic losses in productivity from absenteeism (Burton *et al.*, 2003). Symptoms of primary dysmenorrhea include abdominal cramps, headache, backache, spasmodic pains, vomiting, fatigue and other somatic discomforts (Chen and Chen, 2010). The initial choice for treatment of primary dysmenorrhea is usually nonsteroidal anti-inflammatory agents to reduce myometrial activity, however this treatment is controversial due to a number of side effects (French, 2005). In other studies, pain due to dysmenorrhea has been managed with acupuncture (Proctor *et al.*, 2002; White, 2003; Yang *et al.*, 2008).

Acupuncture is one of the most popular forms of complementary medicine for various medical fields. In gynecology, it has been reported to have adjunctive therapeutic effects on menstrual disorders such as dysmenorrhea (Cho and Hwang, 2010) by modulating the autonomic nervous system (ANS, Lee *et al.*, 2010). The relative homeostasis of the human internal environment depends largely on the orchestrations of the sympathetic nervous system (SNS) and the parasympathetic nervous system (PNS). Therefore, a slight disharmony of these two systems could induce a range of symptomatology (Matsumoto *et al.*, 2006). When we consider that SNS activity is significantly increased and PNS activity is apparently decreased in the late luteal phase in subjects with menstrual disorder (Matsumoto *et al.*, 2006; Matsumoto *et al.*, 2007; Baker *et al.*, 2008), we suggest that a decrease of SNS activity and an increase of PNS activity with acupuncture intervention could be helpful to treat menstrual disorders.

A comprehensive exploration of ANS function is now possible via power spectral analysis of heart rate variability (HRV) which is derived from electrocardiogram (ECG) monitoring. Reliability of HRV as a noninvasive index of ANS activity is well documented (Park and Watanuki, 2005). The high frequencies (HF) of HRV are major contributor to reflecting PNS activity, while the low frequencies (LF) of HRV are dually mediated by both PNS and SNS activities (Matsumoto *et al.*, 2006). Further, LF/HF ratio of HRV is considered to mirror sympatho-vagal balance (Montano *et al.*, 1994). In human studies, women with severe primary dysmenorrhea with regular menstrual cycles displayed a higher HF value than non-dysmenorrheic women (Park and Watanuki, 2005). However, the SNS activity significantly increased and the PNS activity apparently decreased in subjects with bearable premenstrual symptomatology (Matsumoto *et al.*, 2006). Li and colleagues (2005) found that healthy subjects treated with acupuncture

exhibited a significant increase in HF power, and a decrease in LF power and LF/HF ratio as compared to the individuals in the sham control group after all participants had fatigue induced with a 3 hour driving simulation.

Accordingly the present study evaluates the relevance of acupuncture treatment to ANS of dysmenorrheic women in the late luteal phase by means of HRV power spectral analysis.

Materials and Methods

Participants

The dysmenorrheic participants consisted of 18 women in group A and 20 women in group B. To be eligible to take part in this study, participants were required to be female between the ages of 18 to 30 years, with a regular menstrual cycle varying from 28 to 30 days in length during the past 3 months, with a visual analog scale (VAS) of menstrual pain ≥ 6 and taking pain killers for ≥ 3 months. We excluded patients who had neurological or psychiatric disorders (eg, schizophrenia, epilepsy, alcoholism, drug addiction, anorexia nervosa, bulimia nervosa), a medication history (eg, anti-depressants, barbiturate, psychoactive medication), pregnancy intention and those patients who had no adequate contraceptive method. The subjects had a mean age of 22.3 years (range 18-30), a mean weight of 53.8 kg (range 40-76), a mean height of 162.6 cm (range 150-174), a mean menarche of 13.1 years (range 10-16) and a VAS of 8.3 (range 7-10). Informed consent was obtained from all participants after a full explanation of the study. The institutional review board of Kyung Hee Oriental Medical Center approved this study in October 2008 (KOMCIRB 2008-10).

Study Design

This study was a crossover and patient-blinded design. All participants visited 2 ± 1 days before the next expected menstrual bleeding. In the 1st session, group A was treated with real acupuncture (RA) treatment and group B with sham acupuncture (SA). After one month of wash-out period, group A was treated with SA treatment and group B with RA treatment in the 2nd session. All treatments were performed by the same acupuncture practitioner with more than 3 years of experience.

Measurements

Subjects were instructed not to eat, drink alcohol and smoke 2 hours prior to treatment. In a supine position, the patient was connected to an ECG measuring system of FM-150 (Hukuda Denshi, Japan) during the study. They had 15 min rest and the acupuncture procedure lasted another 15 min. Following the removal of needles, subjects rested for 15 min in a supine posture. ECG was recorded throughout the 45 min session. Power spectral analysis of the RR-interval variability was performed by a 512 point Fast Fourier Transformation. Frequency-domain analysis of HRV was performed to obtain HF power (0.141-0.391 Hz) and LF power (0.031-0.141 Hz) components.

Acupuncture Procedure

The manual acupuncture procedure required fine needle insertion at two bilateral acupoints of LI4 (Large Intestine 4, Hegu, located on the dorsum of the hand approximately at the midpoint of the second metacarpal bone in the belly of the first interosseus dorsalis muscle) and SP6 (Spleen 6, Sanyinjiao, located on the medial leg, 3 cun superior to the medial malleolus, on the posterior border of the tibia). Disposable stainless steel needles (0.25 mm × 40 mm, Dongbang, Korea) were used. For the sham procedure, the superficial needle insertion technique with Park sham devices (Dongbang, Korea) was used. A Park sham device consists of a ring-base unit and an oversized tube (Park tube, Dongbang, Korea). The standard guide tube that is included with the real acupuncture needle product, slides into place inside the Park tube. Precut guide tubes were made and fitted into the Park tube for predetermining the penetration depth of the real needles. This achieved the penetration depth of approximately 15-20 mm for the real needles. The same length of guide tubes was also used for the sham needles. A practitioner attached the Park sham devices on four of selected acupuncture points. No manipulation was performed. The acupuncture needle remained inserted in each acupoint for 15 min during the acupuncture and sham procedure.

Pain Visual Analogue Scale (VAS)

VAS of menstrual pain was reported by telephone-interview after 5 days of menstrual bleeding.

Statistical Analysis

All analyses were conducted according to the protocol used. The data are presented as the mean ± standard error. Comparison of HRV components between the pre-stimulation period and the post-stimulation period were tested by Wilcoxon signed rank test. All p values are two-tailed, and significance was set at $p < 0.05$. All statistical analyses were performed using the SPSS ver.12.0 for windows.

Results

Table 1 shows the mean values of LF power, HF power and LF/HF ratio. A significant increase ($p < 0.001$) was observed in the HF power and a significant decrease ($p = 0.001$) in LF/HF ratio was exhibited following the stimulation of Hegu points and Sanyinjiao points. At the same time, the SA procedure caused a significant increase in the HF power ($p = 0.004$) during the post stimulation period. [Both RA and SA caused a significant decrease in menstrual pain VAS after treatment \(data not shown\).](#)

Table 1. Mean \pm Standard Error Values of Heart Rate Variability Components of Low Frequency (LF) Power, High Frequency (HF) Power and LF/HF Ratio during the Pre-stimulation and Post-stimulation Period from either Real Acupuncture (RA) Procedure or Sham Acupuncture (SA) Procedure

		Pre-stimulation	Post-stimulation	P value
RA (n = 38)	LF (msec ²)	554.59 \pm 61.31	694.07 \pm 111.32	.171
	HF (msec ²)	562.83 \pm 96.33	806.73 \pm 119.12	<.001
	LF/HF ratio	1.60 \pm 0.21	1.05 \pm 0.12	.001
SA (n = 38)	LF (msec ²)	562.18 \pm 69.15	609.41 \pm 60.99	.204
	HF (msec ²)	729.06 \pm 141.09	806.00 \pm 150.26	.004
	LF/HF ratio	1.33 \pm 0.18	1.12 \pm 0.11	.117

Discussion

A disturbance of ANS has been postulated as a pathogenetic factor in menstrual disorders which could involve suppressed vagal and/or enhanced sympathetic functions (Li *et al.*, 2005). It was suggested that perceived stress was associated with painful menses (Wang *et al.*, 2004). Dysfunction of ANS is a potential mechanism that connects psychosocial stress to dysmenorrhea. It has been shown that ANS is influenced by intense acute, repetitive and chronic psychosocial stress (Sloan *et al.*, 1994; Dishman *et al.*, 2000; Schommer *et al.*, 2003). When the load of stressors in an individual is too large, when ANS is chronically addressed, or when the capacity of ANS to adjust is diminished, ANS dysfunction may develop (Chrousos and Gold, 1992). Park and Watanuki (2005) found that dysmenorrheic women show different ANS responses when compared to healthy women. The SNS activity significantly increased and the PNS activity apparently decreased in women with premenstrual syndrome compared to healthy women (Matsumoto *et al.*, 2006; Matsumoto *et al.*, 2007; Baker *et al.*, 2008). Yildirim *et al.* (2006) reported that women with polycystic ovary syndrome had significantly higher LF power and LF/HF ratio, and significantly lower HF power compared to controls. Since deregulation of ANS is a major aspect in the pathophysiology of primary dysmenorrhea, acupuncture intervention can be one treatment approach. As acupuncture has been shown to induce distinct autonomic effects (Andersson and Lundberg, 1995), the clinical effects in dysmenorrhea might be mediated by a modulation of ANS.

In the present study, we have shown that the real acupuncture intervention caused a significant increase in the HF power and a significant decrease in the LF/HF ratio. These findings might be explained by the role of LI4 which is known to decrease the sympathetic activities and increase the parasympathetic activities following the acupuncture (Li *et al.*, 2005). A greatly increased activity in the parasympathetic system during the post-stimulation period might be suppressing the jointly increased sympathetic tone, thus resulting in an ultimate increase parasympathetic activity. This possibly explains the relaxation, calmness and reduced feelings of distress commonly experienced by the patients. We suppose these findings could be helpful for dysmenorrheic women, considering that there was positive correlation between severity of dysmenorrhea and the LF power and the LF/HF ratio, while there was negative correlation between severity of dysmenorrhea and the HF power (Lee *et al.*, 2007). A significant increase in the HF power with no modification in sympatho-vagal balance in our study concurs with observations from another study (Haker *et al.*, 2000). Furthermore, both RA and SA caused

a significant decrease in menstrual pain VAS after intervention. We suppose, in the sham acupuncture as the superficial needle insertion technique, nociceptive signals originating from pricking stimulation might have played a role. Even a non-painful mechanical stimulation might excite nociceptive primary afferents (Kolzenburg and Handwerker, 1994).

Using a placebo-needle, which does not penetrate the skin, some practitioners found no difference in the clinical response compared with real acupuncture. Acupuncture is a complex intervention which is characterized by a close interaction between patient and therapist. Paterson and Dieppe (2005) recently argued that psychologic factors which are categorized as 'unspecific' (placebo) in the context of drug trials might be considered as characteristic and thus "specific" within acupuncture therapy. These factors, equally present in SA and RA, have certainly also contributed to the observed effects in the current study and future studies should be undertaken to further investigate the role of unspecific sensory stimulation and patient-therapist interactions in acupuncture therapy. Although the relationship between acupuncture and ANS response is still ambiguous, we suggested that this acupuncture maneuver is noteworthy for dysmenorrheal treatment with ANS involvement.

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