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BLOOD PRESSURE VARIATIONS DURING DIFFERENT PHASES OF MENSTRUAL CYCLE

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ABSTRACT
Blood pressure (BP) is not constant throughout the day, on different days in a month and on different times of a cyclical event like menstrual cycle. Variation in BP during different phases of menstrual cycle can also be attributed to the effect of female sex hormones on cardiovascular function. To evaluate the variation in BP during different phases of menstrual cycle and whether these changes can warrant an increase or decrease in the dose of antihypertensive drugs in hypertensive women of reproductive age group. This study was conducted on a healthy female subject with regular menstrual cycle of 28 days duration using ambulatory BP monitor (TM-2430, A&D Co., Japan). 24-hour BP was recorded on alternate days for a period of 2 consecutive menstrual cycles. BP data was divided into four groups: menstrual phase (days 2 and 4), proliferative phase (days 6, 8, 10 and 12), ovulatory phase (day 14) and secretory phase (days 16, 18, 20, 22, 24, 26 and 28). Though the differences were noted between different phases of menstrual cycle, they were not statistically significant. Cardiovascular homeostatic mechanisms are strong enough to correct the subtle BP changes brought about by the action of ovarian hormones on the cardiovascular system.

KEY WORDS: Menstrual cycle, BP, ambulatory BP monitoring.

INTRODUCTION

Cardiovascular system (CVS) functions in an oscillatory manner to adjust with the variations in the external and internal environment throughout the day, so also the blood pressure (BP) which shows diurnal variation. Variation in BP during different phases of menstrual cycle can also be attributed to the effect of ovarian hormones on cardiovascular function. Since the hormonal changes follow a non-linear trend throughout the menstrual cycle, it may have unpredicted effect on BP regulation. If the BP changes are cyclical, it can warrant an increase or decrease in the dose of antihypertensive medication in hypertensive women of reproductive age group. The incidence of coronary artery disease (CAD) and hypertension (HTN) is relatively low among women in reproductive age, with a sharp rise after menopause (Farhat *et al.*, 1996). Estrogen has beneficial effect on CVS by decreasing LDL cholesterol and increasing HDL cholesterol (Malinow *et al.*, 1963); and direct action on blood vessels causing vasodilatation through an endothelial nitric oxide synthase (eNOS) dependant genomic mechanism (Miller and Duckles, 2008) and through calcium-dependant NOS (Collins *et al.*, 1996). Estrogen produces slow genomic effect by acting via ERα and ERβ whereas it produces fast non-genomic effect by action through membrane receptor: G-protein coupled estrogen receptor (GPER) (Miller and Duckles, 2008). Estrogen is also known to reduce the development of HTN in pre-menopausal women through peripheral actions such as up-regulation of endothelium-derived vasodilator factors with simultaneous down-regulation of vasoconstrictor factors. Estrogen might protect against elevated arterial pressure by inhibiting sympathetic nervous activity (Kotchen and Kotchen, 2003). Progesterone lowers BP and blunts the response to angiotensin II either independently or in conjunction with estrogen by decreasing calcium L-currents and hence delays vascular smooth muscle (VSM) contraction. Progesterone receptors have also been localized in the myocardium and thus may have effect on cardiac contractility (Barbagallo *et al.*, 2001). It may also cause cyclo-oxygenase (COX) activation leading to increased vascular prostacyclin production. It inhibits angiotensin II induced endothelin-1 production in endothelial cells whereas it up-regulates AT-1 receptor (Khalil, 2005). These direct vascular actions explain the lower BP and increased renin-angiotensin system (RAS) activity during the secretory phase (Barbagallo *et al.*, 2001). However, the action of progesterone on vascular parameters in an estrogen-deprived environment is less clear. It has been shown that progesterone given without estrogen does not adversely affect vascular function in post-menopausal women (Honisett *et al.*, 2003). Progesterone inhibits aldosterone binding to the mineralocorticoid receptor and has natriuretic properties. Therefore, progesterone-induced natriuresis leads to compensatory activation of the renin-angiotensin-aldosterone system (RAAS) thus increasing aldosterone production during the secretory phase (Szmuilowicz *et al*., 2006).

Therefore, we hypothesized that the variation in BP during different phases of menstrual cycle may follow the cyclical hormonal changes and the purpose of this study was to document these variations and to elucidate the mechanisms by which ovarian hormones interact in bringing about cardiovascular changes during menstrual cycle.

MATERIALS AND METHODS

The study was conducted on a healthy nulliparous female volunteer, 28 years, BMI=14.6, with regular menstrual cycles of 28 days duration and 5 days menstrual flow, after taking written informed consent and approval by institutional ethics committee. 24-hour BP was recorded using ambulatory BP monitor (TM-2430, A&D Co., Japan). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were recorded every 15 min from 07:00 AM to 10:00 PM and every 30 min from 10:00 PM to 07:00 AM on alternate days for 2 consecutive menstrual cycles. 79 data points were recorded on each day. Pulse pressure (PP) and mean arterial blood pressure (MABP) were calculated. BP data was divided into four groups: menstrual phase (days 2 and 4), proliferative phase (days 6, 8, 10 and 12), ovulatory phase (day 14) and secretory phase (days 16, 18, 20, 22, 24, 26 and 28).

Statistical analysis

Statistical analysis was performed using PASW 18.0 (SPSS Inc., Chicago, USA) and Origin 8.0 Pro. One-way analysis of variance (ANOVA) or Welch/Brown-Forsythe test was done depending on the significance of Levene's test of homogeneity of variances. Tukey's HSD (Equal variances assumed) and Tamhane's (Equal variances not assumed) Post-Hoc tests were performed for statistical significance. Statistical significance was set at $p < 0.05$.

TABLE 1. Blood pressures (in mm Hg) during different phases of menstrual cycle.

	Phases	N	1st Cycle (Mean ± SD)	2nd Cycle (Mean ± SD)
Systolic BP	Menstrual phase	158	96.48 ± 13.18	96.22 ± 12.97
	Proliferative phase	316	98.15 ± 17.47	98.64 ± 18.25
	Ovulatory phase	79	96.64 ± 15.09	96.64 ± 15.09
	Secretory phase	553	95.81 ± 14.74	95.86 ± 16.08
Diastolic BP	Menstrual phase	158	64.18 ± 12.96	64.07 ± 11.69
	Proliferative phase	316	64.10 ± 13.22	64.03 ± 15.00
	Ovulatory phase	79	60.95 ± 12.93	60.95 ± 12.93
	Secretory phase	553	61.63 ± 11.45	62.69 ± 13.65
Pulse Pressure	Menstrual phase	158	32.30 ± 7.15	32.15 ± 9.23
	Proliferative phase	316	34.05 ± 12.52	34.62 ± 12.00
	Ovulatory phase	79	35.69 ± 13.55	35.69 ± 13.55
	Secretory phase	553	34.23 ± 12.70	33.63 ± 12.03
Mean Arterial BP	Menstrual phase	158	74.95 ± 12.59	74.79 ± 11.32
	Proliferative phase	316	75.45 ± 13.54	75.57 ± 15.13
	Ovulatory phase	79	72.84 ± 12.11	72.84 ± 12.11
	Secretory phase	553	73.03 ± 11.10	73.75 ± 13.09

RESULTS

Table 1 shows various BP parameters. SBP and DBP recordings were near lower limit of normalcy, which may be attributed to lower BMI in this subject. Even though the differences were observed, there were no statistically significant variations in mean SBP (1st month, p=0.19; 2nd month, p=0.15), DBP (2nd month, p=0.20), PP (1st month, p=0.15; 2nd month, p = 0.08) and MABP (2nd month, p=0.18) during different phases of menstrual cycle. Only significant variations observed (Fig. 1) were during 1st month between proliferative and secretory phase in DBP (p=0.023) and MABP (p=0.024).

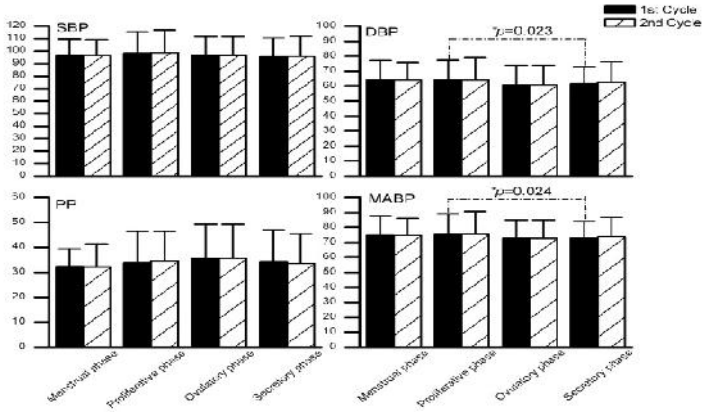

FIGURE 1. Blood pressures (in mm Hg) during different phases of menstrual cycle.

DISCUSSION

Blood pressure changes during normal menstrual cycle are not well documented and previous studies have shown conflicting results. Dunne *et al.* (1991) showed that both SBP and DBP were higher in the menstrual phase than during other phases of menstrual cycle, also DBP was

lower during days 17-26 than during the remainder of the cycle. Resting SBP was significantly higher in the ovulatory phase than in other phases, but resting DBP did not differ significantly between phases (Moran *et al.*, 2000). SBP was lower during the follicular phase while DBP and HR were lower during the menstrual and follicular phases (Tsai *et al.*, 2003). Resting DBP was lower during luteal phase and higher during follicular phase whereas SBP remained uniform across the menstrual cycle (McFetridge and Sherwood, 2000). Differences in the BP parameters during different phases in our study were statistically not significant. Nevertheless, in both the months, SBP was higher during proliferative phase than other phases, which is in disagreement with above studies and DBP was higher during menstrual phase than other phases, which is in confirmation with Dunne *et al.* (1991); and McFetridge and Sherwood (2000). In our study, SBP was lowest in secretory phase and DBP was lowest in ovulatory phase. Scarce literature is available on changes in PP and MABP. This study revealed that PP was highest during ovulatory phase and lowest during menstrual phase while MABP was highest during proliferative phase and lowest during ovulatory phase in both cycles.

Changes in hemodynamic function during the secretory phase, relative to the proliferative phase, should reflect the influence of estrogen. Lower DBP during secretory phase and higher DBP during proliferative phase suggest that estrogen may mediate vasodilatation and reduce vascular tone; these findings were consistent with those of McFetridge and Sherwood (2000). Ovarian hormone variations along the menstrual cycle are associated with significant changes in multiple neurohormonal homeostatic mechanisms regulating the CVS. The increase in plasma renin activity, aldosterone, plasma nor-epinephrine and plasma volume in the high hormonal environment during the luteal phase is counter-balanced by a decrease in β_1 adrenoreceptor sensitivity and an increase in cardiovagal baroreflex activity. These opposite influences of the gonadal hormones result in BP, HR and orthostatic stress responses to remain unchanged throughout the menstrual cycle (Hirshoren *et al.*, 2002). Our study also did not show significant change in the above. Brosnihan *et al.* (1997) demonstrated that estrogen may shift the vasoconstrictor-vasodilator balance of the RAAS. The vascular effects of estrogen are antagonized by increase in the RAAS hormones during the luteal phase of the cycle (Ounis-Skali *et al.*, 2006). Circulating RAAS components peak when the plasma estrogen levels are highest, i.e., during the secretory phase of the cycle. Despite an increase in these circulating components, the system is blunted rather than activated at the tissue level either by a direct effect on receptors or through the counter-regulatory impact of NO (Chidambaram *et al.*, 2002). Also autonomic mediated baroreflex control seems to be greater in the mid-luteal phase than in other phases of menstrual cycle (Kotchen and Kotchen, 2003).

CONCLUSIONS

Cardiovascular changes are brought about by the action of ovarian hormones on heart and blood vessels but these subtle changes are corrected by multiple neurohumoral homeostatic mechanisms. However, to substantiate our findings further investigation is required with more subjects.

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