Impact of Menstrual Cycle on Cardiac Autonomic Function Assessed by Heart Rate Variability and Heart Rate Recovery

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Abstract

Objective: The purpose of the present study was to investigate autonomic tone during the follicular and luteal phases of the menstrual cycle using heart rate variability (HRV) and heart rate recovery (HRR) in healthy women. *Subjects and Methods:* Thirty women aged 22–37 years with regular menstrual cycles were included in the study. The HRV and HRR were measured at the follicular and luteal phases. The HRV was obtained using the time domain method with 24-hour long-term recordings. For time domain analysis, the following were obtained: standard deviation of all normal sinus R-R intervals during 24 h (SDNN), mean of the standard deviation of all normal sinus R-R intervals for all 5-min segments (SDNN index), standard deviation of average normal sinus R-R intervals for all 5-min segments (SDANN), root mean square of the successive normal sinus R-R interval difference (rMSSD), and percentage of successive normal sinus R-R intervals longer than 50 ms (pNN50). The HRR was calculated at the first, second, and third minute of recovery after the cessation of peak exercise using a treadmill test. The paired sample t test was used for the comparison of both phases of the menstrual cycle. *Results:* The SDNN (136 ± 39 vs. 154 ± 32 ms; p = 0.015) and SDANN (122 ± 36 vs. 142 ± 36 ms; p = 0.004) were significantly lower during the luteal phase than during the follicular phase. The HRR, rMSSD, and pNN50 were not different between the 2 phases. *Conclusion:* Parasympathetic tone markers of HRV and HRR were unaffected by the menstrual phase. Lower SDNN and SDANN during the luteal phase than during the follicular phase could have resulted from enhanced sympathetic activity during the luteal phase.

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Introduction

Endogenous sex hormone levels continuously change during the menstrual cycle. While estrogen starts to increase halfway through the follicular phase to reach a peak just before ovulation, both estrogen and progesterone are elevated during the midluteal phase. Different hormonal environments during the follicular and luteal phases may have implications for cardiac autonomic function.

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In the investigation of the effect of the menstrual cycle on heart rate variability (HRV) at various times during the cycle, higher sympathetic activity in the luteal phase than in the follicular phase have been reported [1–5]. However, others have reported higher parasympathetic activity in the luteal phase [6, 7], although Leicht et al. [8] did not find any phase differences in HRV. Therefore, there is no consensus at present regarding the interaction between the menstrual cycle and HRV.

Heart rate (HR) gradually decreases to its resting values in the period of recovery after exercise [9]. The rapid decline in HR during the first 2–3 min following exercise cessation [heart rate recovery (HRR)] primarily results from parasympathetic reactivation at the sinus node [10]. However, it appears that the influence of the menstrual cycle on the HRR has not been reported. Therefore, the aim of this study was to investigate autonomic tone changes of the HRV and HRR in the follicular and luteal phases of the menstrual cycle in premenopausal women, which could provide supplementary information about the impact of parasympathetic activity on HR.

Subjects and Methods

Subjects

Thirty nonobese healthy female volunteers aged 22–37 years were included in the study. The length of the menstrual cycle was determined by counting the number of days from the first day of a bleeding episode up to and including the day before the start of the next bleeding episode. For at least 12 months prior to the study, their menstrual cycles were regular and ranged from 25 to 30 days in length. The menstrual cycle was considered normal when menstruation regularly occurred between 25- and 31-day intervals [11]. All subjects were sedentary and nonsmokers. They underwent detailed physiological and clinical examination. Each participant completed a health history questionnaire and none of them had any chronic disease that could influence cardiovascular autonomic modulation. None of the participants was pregnant and/or lactating. They did not take any medications including estrogen/progesterone contraceptives, hormone replacement therapy, or other drugs.

The study was approved by the Ethics Committee of Konya Education and Research Hospital. All subjects gave written informed consent prior to participation.

Protocol

The volunteers were investigated at each of the following phases of the menstrual cycle: the late follicular phase (9–13 days after the first day of bleeding) and the midluteal phase (19–23 days after the first day of bleeding).

The HRV measurements were obtained using 24-hour Holter ECG monitoring (DMS 300 Holter Recorder). Holter recordings longer than 20 h were included in the analysis. Errors in the software's automated detection of R-waves were corrected by visual

Table 1. Time domain HRV parameters in the follicular and luteal phases

	Follicular phase	Luteal phase	p
SDNN, ms	154±32	136±39	0.015
SDNN index	61±11	63±21	n.s.
SDANN, ms	142±36	122±36	0.004
rMSSD, ms	38±12	41±27	n.s.
pNN50, %	14±9	14±14	n.s.

Results are presented as means ± SD.

Table 2. HRR indexes in the follicular and luteal phases

	Follicular phase	Luteal phase	p
Basal HR, bpm	98±18	94±13	n.s.
Peak HR, bpm	175±10	174±12	n.s.
HRR[1], bpm	32±10	33±8	n.s.
HRR[2], bpm	50±10	51±8	n.s.
HRR[3], bpm	56±12	56±14	n.s.

Results are presented as means ± SD. [1] 1st minute of the recovery phase. [2] 2nd minute of the recovery phase. [3] 3rd minute of the recovery phase.

inspection. The recordings were edited for abnormal beats and artifacts. The HRV was analyzed in the time domain; the following 5 standard parameters were calculated in the time domain: (1) standard deviation of all normal sinus R-R intervals during 24 h (SDNN), (2) mean of the standard deviation of all normal sinus R-R intervals for all 5-min segments (SDNN index), (3) standard deviation of average normal sinus R-R intervals for all 5-min segments (SDANN), (4) root mean square of the successive normal sinus R-R interval difference (rMSSD), and (5) percentage of successive normal sinus R-R intervals longer than 50 ms (pNN50). The SDNN and SDANN are related measures. While the SDNN (a measurement of overall HRV) reflects the balance between the sympathetic and parasympathetic activities on the sinus node, the pNN50 and rMSSD predominantly reflect the influence of parasympathetic tone on the sinus node. A reduction of the SDNN is considered to reflect an alteration of the physiological balance between sympathetic and parasympathetic activities, consisting of a decreased parasympathetic and an increased sympathetic modulation of the sinus node.

All subjects underwent a symptom-limited treadmill exercise test using the standard Bruce protocol. Subjects were encouraged to exercise until they experienced maximal exhaustion because achieving the target HR alone was not enough to terminate the testing exercise. Following peak exercise, all subjects spent at least 1 min in a cool-down period at a speed of 2.4 km/h and a grade of 0% during the treadmill testing. The HR and rhythm were recorded during the standing pre-exercise period, 60 s before the end of

each stage, during peak exercise, and after the cessation of peak exercise. The HRR was calculated as the difference between the maximal HR achieved during exercise testing and HR at the first, second, and third minute of recovery after the cessation of peak exercise.

Statistical Analysis

All statistical analyses were performed using SPSS version 15.0 for Windows (SPSS Inc., Ill., USA). The values are presented as means ± SD. The paired sample t test was used for the comparison of both phases of the menstrual cycle. The relationship between the HRV and HRR parameters was evaluated using Pearson correlation analysis. A p value of <0.05 was considered statistically significant.

Results

The HRV and HRR measurements during the late follicular and midluteal phases of the menstrual cycle are given in tables 1 and 2. The SDNN (136 ± 39 vs. 154 ± 32 ms; p = 0.015) and SDANN (122 ± 36 vs. 142 ± 36 ms; p = 0.004) were lower during the midluteal phase than during the late follicular phase (p < 0.05); however, there were no observed differences in the other HRV parameters and HRR indexes between the cycle phases.

Discussion

In the present study, the parasympathetic tone parameters of HRV (rMSSD and pNN50) and HRR were not affected by the menstrual phases; however, SDNN and SDANN significantly decreased, indicating that sympathetic tone was greater, during the luteal phase.

The SDNN and SDANN are related parameters; the SDNN behaves much like the SDANN. The SDNN linearly decreases as a function of increased HR as has been reported [12–15]. Rosano et al. [16] suggested a greater incidence of arrhythmias in the luteal phase than in the follicular phase in women with regular menses and paroxysmal supraventricular tachycardia. Myerburg et al. [17] reported that menstrual cycle-dependent paroxysmal supraventricular tachycardia was induced during the luteal phase but not during the follicular phase. Because sympathetic stimulation has an arrhythmic effect, these data support increased sympathetic activity in the luteal phase.

Our findings are similar to previous studies in which sympathetic activity increased more by HRV in the luteal phase when compared to other phases [1–5]. Contrary to our findings, Princi et al. [6] and Chung and Yang [7]

found a greater increase in parasympathetic activity in the luteal phase. Inconsistent findings regarding the interaction between the menstrual cycle and HRV may be due to the differences in the sample size, age, and physical condition of subjects; ECG recording time; method used to evaluate HRV; phase studied (menstruation, follicular phase, ovulation, luteal phase), and methods used to identify normal menstrual function and to verify the menstrual phase.

The major limitation of this study was that serum endogenous sex hormone levels were not measured during the cycle phases. Thus, our findings could not be attributed to specific hormones.

Conclusion

In this study, the parasympathetic activity assessed in terms of HRV and HRR was unaffected by the menstrual phase. The lower SDNN and SDANN during the midluteal phase in comparison to the late follicular phase could have resulted from enhanced sympathetic activity during the luteal phase. These findings suggest that the different hormonal status in the follicular and luteal phases could contribute to the autonomic modulation of the heart. Our study could be supported by large randomized controlled trials investigating the combined influence of age, BMI, endogenous sex hormone levels, and menstrual cycle on the HRV and HRR.

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