Research Article

Heart rate variability among reproductive and postmenopausal women

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Abstract

Background: Heart rate variability (HRV) has been proposed as the most sensitive indicator of autonomic function especially for the assessment of sympathovagal balance. It has also been proposed that there is sympathetic hyperactivity in postmenopausal women and parasympathetic dominance in women of reproductive age group due to the effect of estrogen.

Objectives: The aim of the study was to compare the basal cardiovascular parameters and HRV between premenopausal and postmenopausal women.

Materials and Methods: This was a cross-sectional observational study carried out in Sri Venkateshwaraa Medical College Hospital and Research Centre, Puducherry. After 15 min of rest, ECG was recorded among 38 premenopausal and 37 postmenopausal women in the supine position for 5 min using PHYSIOPAC-PP_4 (Medicaid Systems Chandigarh). The frequency domain parameters of HRV were analyzed using a Kubios analyzer. The data were presented as mean(SD). Student's unpaired *t*-test was used to find the statistical difference between the two groups. *p*-Value < 0.05 was considered statistically significant.

Results: Systolic blood pressure ($p = 0.022$), pulse pressure ($p = 0.033$), and rate pressure product ($p = 0.003$) values were significantly higher in postmenopausal women compared to premenopausal women. Total power ($p = 0.003$), an index of parasympathetic activity, was significantly higher among premenopausal women. LF (nu), HF (nu), and LF/HF ratio were similar among both the groups.

Conclusion: Though LF (nu), HF(nu), and LF/HF ratio between the two groups remain unchanged, the total power shows increased parasympathetic activity in premenopausal women. This effect could be attributed to the effect of estrogen, which is higher among premenopausal women compared to postmenopausal women.

KEY WORDS: Autonomic functions, HRV, menopause

Introduction

Heart rate variability (HRV) is the beat-to-beat variation (variation in cardiac cycle length) of the heart, a phenomenon that occurs mainly due to variation in cardiac activity during the respiratory cycle (respiratory sinus arrhythmia) at rest. HRV is dependent on the rate of discharge of the sino-atrial (SA) node, which is influenced by autonomic nervous system. Parasympathetic nervous system mainly controls SA nodal discharge and respiratory sinus arrhythmia is due to variation in vagal tone during inspiration and expiration. Thus, HRV is largely influenced by parasympathetic activity though sympathetic activity also influences it. HRV is very useful in the assessment of sympathovagal balance.

The power spectrum of HRV has two components**.** They are high frequency (HF) component and low frequency (LH) components. HF component is indicative of parasympathetic activity and LF component is indicative of sympathetic activity. LF/HF ratio reflects sympathovagal balance. There is

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also another parameter called total power, which is indicative of parasympathetic activity. Increased HF, reduced LF, and LF/HF ratio indicate parasympathetic predominance whereas reduced HF, increased LF, and LF/HF ratio indicate sympathetic predominance. Predominant parasympathetic activity favors good cardiovascular health. Predominant sympathetic activity is an important cardiovascular risk factor.

Menopause is cessation of women's reproductive ability due to cessation of ovarian function. Menopause is characterized by various physiological changes that occur in the reproductive organs and other systems of the body. One change that occurs in the cardiovascular system is modulation of autonomic activity.

Postmenopausal women had lower total power, lower HF in absolute power, higher relative power of LF, and higher LF/HF ratio.[1] Menopause causes an imbalance of the autonomic nervous control of the cardiovascular system that shifts toward sympathetic hyperactivity.[2] Vagal and sympathetic activities in the postmenopausal group were lower and higher respectively than those of the premenopausal group. In addition, postmenopausal women with conjugated estrogen replacement therapy had significantly increased vagal and reduced sympathetic modulations of the heart rate.[3] Postmenopausal women had alteration in their autonomic status with higher sympathetic and lower vagal tone compared to premenopausal women.[4] Postmenopausal women not taking hormone replacement therapy (HRT) had increased sympathetic tone.[5]

Epidemiological studies have indicated that women have a lower incidence of cardiovascular disease compared to their male counterparts but this difference decreases after menopause.

Although many Western studies have shown that there is sympathetic hyperactivity in postmenopausal women compared to pre menopausal women, very few studies have been conducted in Indian population. Hence the aim of the present study was to compare HRV between premenopausal (reproductive) and postmenopausal women among Indian population. The aim of the study was also to compare the basal cardiovascular parameters and HRV between premenopausal and postmenopausal women.

Materials and Methods

This study was a cross-sectional study carried out at Sri Venkateshwaraa Medical College Hospital and Research Centre after obtaining approval from the institutional ethics committee. The study population was divided into two groups. One group included 38 premenopausal women aged 20–38 years and the other group included 37 postmenopausal women aged 40–60 years who had attained menopause naturally at least 2 years ago. Written informed consent was obtained from the subjects.

Women with diabetes, hypertension, or cardiovascular disease were excluded. Others such as smokers, alcoholics, on oral contraceptive pills, hormonal replacement therapy, or drugs that alter the cardiovascular functions, with menorrhagia, metrorrhagia, dysfunctional uterine bleeding, or abnormal menstrual cycles were also excluded.

The experimental procedures were performed during the follicular phase in reproductive age group. The subjects were asked to refrain from coffee or tea for 2 h before the procedure.

The height and weight of all subjects were measured. After 15 min of rest, heart rate, blood pressure, and ECG were recorded. ECG recording was performed in supine position in our physiology research laboratory, in the morning time (room temperature was maintained at 20–25 °C) using the instrument PHYSIOPAC-PP4 (Medicaid System, Chandigarh). The data analysis was then carried out using a Kubios HRV Analyzer. The spectral analysis of HRV assessed included frequency domain measures-total power, normalized low-frequency power (LFnu), normalized high-frequency power (HFnu), and ratio of low-frequency power to high-frequency power (LF/HF ratio). Total power and HFnu are measures of parasympathetic activity and LFnu and LF/HF ratio are measures of the sympathetic activity.

Statistical analysis

The data are presented as mean(SD). Analysis was conducted by using GraphPad Prism, version 6. Student's unpaired *t*-test was used to find the statistical difference between the two groups. *p*-Value < 0.05 was considered statistically significant.

Results

Table 1 shows body mass index (BMI) and basal cardiac parameters of the two groups. It was observed that the BMI was comparable between the two groups. It was seen that the systolic blood pressure ($p = 0.022$), pulse pressure ($p = 0.033$), rate pressure product ($p = 0.003$) were significantly higher in postmenopausal women compared to premenopausal women though the parameters were within normal limits in both the groups. The diastolic blood pressure, mean arterial pressure, and heart rate were similar among both the groups.

Table 2 shows the frequency domain measures of HRV of the two groups. In HRV, only total power ($p = 0.003$), an index of parasympathetic activity, was significantly higher among premenopausal women. LF and LF/HF ratio, which are indicative of sympathetic activity, were similar among both the groups.

Discussion

In a study by Rosano et al.[6], it was found that predominant sympathetic activity in postmenopausal women decreased after estrogen replacement therapy for 4 months. Ribeiro et al.[7] showed a decrease in HRV in postmenopausal

Table 1: BMI and basal cardiovascular parameters of premenopausal women and postmenopausal women, expressed as mean(SD)

Parameters	Premenopausal age group	Postmenopausal age group	*p*-Value
BMI (kg/m^2)	21.72 (3.06)	22.14 (4.03)	0.617
Systolic BP (mm Hg)	108.42 (10.27)	115.41 (15.20)	0.022*
Diastolic BP (mm Hg)	73.42 (7.45)	75.95 (10.13)	0.222
Pulse pressure (mm Hg)	35.00 (7.62)	39.46 (9.98)	0.033*
MAP (mm Hg)	85.09 (7.70)	89.09 (11.10)	0.072
Heart rate (beats/min)	50.12 (7.32)	52.74 (7.98)	0.142
RPP	54.13 (8.17)	60.43 (9.64)	0.003*

BMI - Body Mass Index, MAP - Mean Arterial Pressure, RPP - Rate Pressure Product
Statistical analysis was done by Student's unpaired *t*-test. *p*-Value < 0.05 was considered statistically significant.

Table 2: Frequency domain indices of HRV in premenopausal and postmenopausal women, expressed as mean(SD)

Parameters	Premenopausal age group	Postmenopausal age group	*p*-Value
Total power (ms^2)	2963.13 (461.9)	1368.43 (203.8)	0.003*
LF(nu)	84.35 (3.10)	84.57 (2.13)	0.722
HF(nu)	15.65 (3.10)	15.43 (2.13)	0.722
LF/HF ratio	5.60 (1.15)	5.61 (1.02)	0.966

LF(n.u.), Low-frequency expressed in normalized units; HF(n.u.), High-frequency expressed in normalized units
Statistical analysis was done by Student's unpaired *t*-test. *p*-Value < 0.05 was considered statistically significant.

women (decrease in parasympathetic activity) compared to young women on analysis of time domain measures of HRV. Mercuro et al.[8] studied HRV in women before and after oophorectomy and found that surgical menopause led to an increase in sympathetic activity and decrease in parasympathetic activity. This study also showed that estrogen replacement therapy for 3 months reverted autonomic activity back to baseline.

Stampfer et al.[9] concluded that postmenopausal women on estrogen replacement therapy had a lower risk of cardiovascular disease compared to postmenopausal women devoid of estrogen therapy. Ottenson and Sorensen[10] also showed that estrogen offered cardiovascular protection in postmenopausal women. Saeki et al.[11] showed that parasympathetic activity was predominant during the follicular phase of menstrual cycle during which estrogen level was elevated. Yang et al.[12] concluded that sympathetic activity, as indicated by LF/HF ratio, was lower among postmenopausal women treated with estrogen only compared to postmenopausal women treated with combination of estrogen and progesterone. Tanu et al.[13] compared HRV between premenopausal and postmenopausal women and demonstrated increased parasympathetic activity as indicated by high total power and high HF in premenopausal women. They also showed increased sympathetic activity as indicated by high LF and high LF/HF ratio in postmenopausal women. Brockbank et al.[14] compared heart rate and its variability between premenopausal and postmenopausal women and found that the variability of heart rate decreases significantly after menopause.

Thus, various studies have shown that parasympathetic activity is predominant among premenopausal women, and sympathetic activity is predominant among postmenopausal women through analysis of HRV. These effects have been attributed to the presence or absence of estrogen.

Our study has shown that parasympathetic activity is predominant among premenopausal women though we failed to demonstrate sympathetic hyperactivity in postmenopausal women. It is hypothesized that endogenous estrogen contributes to parasympathetic predominance in premenopausal women. Estrogen increases cholinergic activity at central and peripheral levels, which suppresses sympathetic tone and elevates parasympathetic tone.[15] It has been found that there are estrogen receptors in hypothalamic neurons, and it is well known that hypothalamus is the center for autonomic nervous system. Thus, estrogen modulates autonomic activity by acting through these neurons. In addition, the presence of estrogen receptors in the heart, vascular smooth muscle, and autonomic brainstem centers (e.g., nucleus tractus solitarius, ventrolateral medulla) suggests the involvement in regulation of cardiovascular system.[3]

Thus, estrogen might be responsible for elevated parasympathetic activity in premenopausal women in our study. But we are not able to prove the effect of absence of estrogen in postmenopausal women. The limitation of our study is the lower sample size.

Conclusion

Estrogen might be associated with increased parasympathetic activity in premenopausal women. This might be responsible for the cardioprotective role of estrogen in premenopausal women. HRV can be used as a screening tool

to detect autonomic dysfunction in postmenopausal women and thus it can be used to select postmenopausal women who require HRT.

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