Cardiovascular Autonomic Functional Modulation in Polycystic Ovarian Syndrome – A Cross Sectional Study

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Abstract

Context: Cardiac autonomic dysfunction may develop in patients with polycystic ovary syndrome (PCOS). **Purpose**: evaluation of cardiovascular autonomic functional modulation by using HRV in females with PCOS.

Methodology: Thirty patients with PCOS and 30 healthy female volunteers who were matched for age and body mass index (BMI) were enrolled in the study. Frequency domain power spectral analysis of heart rate variability (HRV) did using non-parametric method of Fast Fourier Transform, using Kubios HRV analysis software.

Results: compared to controls females with PCOS demonstrated a significant reduction in Total power of HRV & High frequency (HF) during rest compared to controls (p=0.016) (p=0.00) & significant increase in Low frequency (LF) (p=0.0134) and LF/HF ratio. (p=0.000).

Conclusion: we conclude that females with PCOS have altered cardiac autonomic modulation during rest in terms of decreased parasympathetic tone and increased sympathetic tone.

Key words: Stress, Parasympathetic tone, Hyperandrogenism, Heart rate variability, Polycystic ovarian syndrome.

Access this article online	
Quick Response Code:	**Website:** www.innovativepublication.com
	DOI: 10.5958/2394-2126.2016.00008.6

Introduction

Polycystic ovary syndrome (PCOS) is a common endocrine disorder of women in their reproductive years, with a prevalence of up to 10%.[1] In addition to the typical association of hyper androgenism and ovulatory dysfunction, an increase in cardiovascular risk factors has also been identified in several studies in patients with PCOS when compared with healthy women of the same age, including obesity, lipid abnormalities[2,3], insulin resistance (IR)[4], hypertension[5] and elevations in C-reactive protein.[6] That, in turn, has led to concern about the effect of PCOS on long-term health, particularly with regard to diabetes, hypertension and coronary heart disease.

It has been recognized that there is a significant relationship between the autonomic nervous system and cardiovascular mortality.[7] Metabolic and cardiovascular disorders are related to autonomic dysfunction, in which there is a compromise of blood pressure and heart rate and reduced HRV.[8]

It has long been known that earliest indicator of cardiovascular autonomic imbalance is reduced heart rate variability (HRV). Frequency domain measurements got by power spectral analysis (PSA) of HRV can quantify both sympathetic and parasympathetic components of ANS and recognize sympatho- vagal imbalance. The analysis of variations in heart rate (heart rate variability) has also been used to determine the balance between sympathetic and vagal nerve activities in the heart.[9]

Various studies have shown sympathovagal imbalance in PCOS.[10,11] But there is limited data to prove the sympathovagal imbalance is due to underlying obesity or due to insulin resistance or occur independently.

So aim of our study is to evaluate cardiovascular autonomic functional modulation in patients with polycystic ovarian syndrome .We hypothesizes that there is decreased HRV in PCOS.

Methodology

The proposed study was conducted in the department of physiology and gynecology, after obtaining approval from the Institutional Ethical Committee and consent from the PCOS females and the controls for participation in the study.

Cases and controls

30 newly diagnosed PCOS patients (n=30) in the age group of 15-35 years who are attending to OBG Department considering the exclusion criterion were taken as cases. PCOS was diagnosed according to the Rotterdam criteria: clinical hyperandrogenism and oligo/amenorrheic cycles; <9 cycles/year; with PCO appearance at ultrasound. Hirsutism was defined as a modified Ferriman Gallwey score > 8.[12] Age matched females with normal, regular menstrual cycles (cycle

duration of 28-35 days) were considered as controls. (n=30).

PCOS females who are already on the treatment were excluded from the study. Subjects or controls were not taken Drugs known to interfere with hormonal levels (such as OC pills, antiandrogens, metformin, fibrates, statins) for at least 3 months before the study. Women diagnosed with other hyperandrogenic disorders (nonclassic congenital adrenal hyperplasia, Cushing syndrome, androgen-secreting neoplasms), thyroid disorders, or hyperprolactinemia were excluded.

Study design: The study conducted during the follicular phase for controls and in amennorhic phase for PCOS. Participants were instructed to abstain from caffeine, other products containing stimulants, alcoholic beverages, and heavy exercise for 24 hours before the test. Subjects rested quietly in the supine position, in a silent and semidark room for 20 minutes At the end of 5 min of rest in supine position, resting heart rate (HR) recorded. Systolic blood pressure (SBP), diastolic blood pressure (DBP) recorded using mercury sphygmomanometer.

HRV analysis was done using ECG recorded at rest in supine position for 5 min. ECG recorded using disposable Ag/AgCl electrodes. ECG data in standard lead II configuration acquired using portable ECG data acquisition equipment (Niviqure Meditech Systems, Bangalore, India). Frequency domain analysis was done using non- parametric method of Fast Fourier Transform, using Kubios HRV analysis software. In the frequency domain following values were recorded; (1) very low frequency (VLF) power, defined as the power ≤0.04 Hz, (2) low frequency power, the power between the 0.04 to 0.15 Hz, (3) high frequency power, the power between the 0.15 and 0.40 Hz and (4) total spectral power, the power between the 0.0 and 0.40 Hz were measured. Measurement LF and HF power components were presented in absolute values of power (ms2) and (nu).

Statistical analysis

Statistical Analysis has done using IBM SPSS 20 software. Comparison of the HRV during rest between PCOS and Controls were done by unpaired Student's t test. With the confidence interval of 95%, p value < 0.05 considered as significant and p value < 0.001 as highly significant.

Results

This is a cross-sectional study done on 30 PCOS (n=30) and 30 healthy controls (n=30). The mean age group of PCOS and controls were 27.13±4.53 and 25.87±6.54 years respectively. BMI of PCOS and controls were 23.22±2.78 and 22.67±34 respectively.

Table 1 shows the comparison of study parameters during rest in controls and PCOS. There is a significant reduction in Total power of HRV in PCOS during rest compared to controls (p=0.016). there is significant reduction in LF (ms^2) and HF (nu). There is significant increase in LF (nu) (p= 0.0134) and LF/HF ratio (p=0.000).

Discussion

Our study evaluated HRV in PCOS female during rest and compared with controls. Our study evaluated HRV during rest in PCOS & it show impaired autonomic modulation even during rest, predominantly in vagal HRV indices, as evidenced by reduction in HF (nu) with significant increase in LF (nu) and LF/HF ratio compared with controls. A few previous studies have evaluated HRV in PCOS; show impaired cardiac autonomic modulation at rest [10, 11] and during 24 hours [13] in women with PCOS in comparison with controls.

Androgens could be responsible for blunted autonomic responses seen in PCOS. Even though this is the limitation of the study that we have not measured the total androgen levels, studies shows negative correlation between androgen levels and frequency domain of HRV in PCOS women.[14] Even the insulin resistance (IR) found in PCOS could also be responsible for the blunted response to stress in PCOS. Again this is the limitations of the study that parameters to assess insulin resistance have not measured, studies show evidence of an association between IR and cardiovascular risk reflected by changes in HRV in hyperinsulinemic and diabetic patients [15], regardless of age.

Augmentation of the sympathetic innervations may play a role in the polycystic ovaries. Rats with estrogen-induced polycystic ovaries have been shown to have high uptake and levels of norepinephrine and a high degree of transmitter release after electrical stimulation of the ovary.[16] Moreover, there is data suggesting altered peripheral noradrenalin deamination and/or uptake in adolescent patients with PCOS. Insulin resistance, observed both in obese and lean subjects with PCOS, and sympathetic activity are linked in a positive-feedback fashion that leads to their reciprocal reinforcement. Small sample size is the main limitation of this study that limits the generalization of our findings. With use of instrument that measures sympathetic activity accurately like MSNA should be used to assess the exact increase in sympathetic activity.

Table 1: Comparison of Frequency domain HRV parameters during rest in controls and PCOS. (n=30 each)

Parameter	Rest (controls)	Rest (PCOS)	T value	P value
Total power (ms2)	2983.03±320.14	1786.60±338.33	2.499	0.016 *
Lf(ms2)	992.43±150.97	536.86±87.32	2.363	0.022 *
Lf(nu)	44.32±2.97	52.24±4.23	-3.575	0.0134 *
Hf(ms2)	1335.05±316.02	740.73±118.88	1.516	0.136
Hf(nu)	53.46±2.50	31.40±1.42	6.921	0.000 **
Lf/hf	0.9452±0.12	1.988±0.16	-5.043	0.000 **

Values expressed as mean±SEM. Lf- low frequency, Hf- High Frequency
$p < 0.05$ considered as significant *, $p < 0.01$ considered highly significant **

Conclusion

From this study we conclude that females with PCOS have altered cardiac autonomic modulation during rest in terms of decreased parasympathetic and increased sympathetic tone. They also show failure to cope up to mental stresses as shown by insufficient sympathetic response to stress. We also conclude that frequency domain analysis of HRV during induced acute mental stress is a powerful non-invasive tool for early diagnosis of cardiovascular autonomic neuropathy in asymptomatic PCOS patients. More studies with large sample size are needed to support our findings.

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