Original Article

Effect of Progressive Muscle Relaxation on the Adverse Cardiovascular Profile in Women with Polycystic Ovarian Syndrome

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ABSTRACT

Background: The altered stress reactivity in polycystic ovarian syndrome (PCOS) may constitute a link between depression, overweight, and cardiovascular risk factors. **Aims:** To study the effects of progressive muscle relaxation (PMR) on the stress levels of PCOS patients and their influence on the cardiovascular risk factors. **Subjects and Methods:** This prospective pilot project was conducted on 100 PCOS patients in a tertiary care hospital of West Bengal, after receiving approval from the Institutional Ethical Committee and informed consent of the subjects. The stress levels were assessed and conventional autonomic function tests and the lipid profi les were analyzed. The subjects were divided into two groups using an online randomizer. One group received medication, while the other group received medication and practiced progressive muscle relaxation (PMR) for three months. All parameters were re-evaluated at the end of three months. **Results:** The perceived stress scale was significantly less in subjects practicing relaxation exercises, as compared to subjects only on medication. The waist/hip ratio, pulse rate, and systolic blood pressure were significantly lower, while there was no difference in the body mass index (BMI) and diastolic blood pressure. Results of the autonomic function tests showed a significant parasympathetic tilt in subjects practicing PMR. In patients with PCOS, who were on PMR, cholesterol, triglycerides, and low-density cholesterol (LDL) were significantly lower and high-density cholesterol HDL was significantly higher. **Conclusions:** PCOS patients are a high-risk group for developing the metabolic syndrome and relaxation therapies may be recommended as an adjuvant therapy, to tilt the autonomic balance to parasympathetic dominance, to improve the cardiovascular profile.

KEY WORDS: Autonomic functions, cardiovascular system, polycystic ovarian syndrome, stress

INTRODUCTION

The polycystic ovary syndrome (PCOS) is one of the most common endocrinopathies affecting 6.5-8% of the women.[1,2] The syndrome is characterized by oligomenorrhea and hyperandrogenism and the presence of associated risk factors for cardiovascular disease, including obesity, glucose intolerance, and dyslipidemia. PCOS may be associated with mood and eating disorders.[2-5] Women with PCOS are a specific group, who have several aspects of the metabolic syndrome (MBS). Concomitantly, MBS may be a part of the metabolic abnormalities present in PCOS. Stress has been linked to aggravate the metabolic abnormalities present in MBS. The PCOS patients show an enhanced hypothalamic-pituitary-adrenal (HPA)-axis and heart rate reactivity as well as a reduced upregulation of IL-6 in response to stress. The altered stress reactivity in PCOS patients may constitute a link between depression, overweight, and cardiovascular risks.[1-7]

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Progressive muscle relaxation (PMR) developed by Edmund Jacobson,[8] is a technique for reducing stress and anxiety. Muscle tension accompanies anxiety; one can reduce anxiety by learning how to relax the muscular tension. Relaxation can be attempted in order to create a pleasant mental state, reduce anticipatory anxiety, reduce anxiety as a response to stress, increase parasympathetic activities, increase knowledge concerning muscle tension, and autonomous stimuli. The autonomic nervous system plays a central role in governing the response to stress and how the body recovers following a stressor. Functional magnetic resonance imaging (MRI) has been used in studies to examine the hypothesized heart–brain connection and has found concurrent associations between vagal influenced

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heart rate variability and changes in blood flow through areas of the brain known to be involved in emotional responses, attention, and working memory.[7]

The present study was conducted to study the effects of PMR on the stress levels of PCOS patients and its influence on the cardiovascular risk factors, by assessing the autonomic functions and lipid profile.

SUBJECTS AND METHODS

This prospective pilot project was conducted in a tertiary care hospital of West Bengal in a time span of two years, after receiving approval from the Institutional Ethical Committee. Informed consent was taken from the subjects.

Inclusion criteria

Patients in the age group of 20-30 years (24.65 ± 2.81), with newly diagnosed polycystic ovarian disease, visiting Gynecology outdoor of the hospital, were included in the study. PCOS was diagnosed according to the Rotterdam criteria, that is, oligomenorrhea/amenorrhea, clinical or biochemical signs of hyperandrogenism, and polycystic ovaries on ultrasound.

Exclusion criteria

Subjects suffering from chronic debilitating diseases such as cardiac arrhythmias, hypertension, diabetes, ischemic heart disease, retinopathy, nephropathy, respiratory diseases or smokers, were excluded. Subjects on treatment for psychiatry problems, pregnant women, puerperal mothers, sportswomen, yogis, and subjects on a regular meditation and exercise regime were excluded. Hypothyroids, subjects having adrenal disorders, and androgenic/anabolic drug users were not included. Subjects who had come with a history of infertility were excluded as the treatment modality differed in these subjects.

Methods

Sampling was done using multistage cluster sampling. One hundred and twenty eight newly diagnosed PCOS patients attended the outdoor in this time interval. Six patients were not in the age group of our study and two had come for treatment of infertility. On the first appointment, histories of the subjects were carefully recorded. Twelve patients did not fit into the study as per the inclusion and exclusion criteria (two subjects were already under psychiatric treatment, four were hypothyroid, two were diabetic, four were practicing other exercise regime). Thus, the sample size came down to 108.

Measures of stress

The stress-related behavioral parameters studied were the presumptive life event stress scale (PSLES)[9] and perceived stress (PSS-14).[10] a general health questionnaire (GHQ-12)[11] was administered to assess the psychological morbidity.

Subjects were asked to tally a list of 43 life events based on a relative score. Accordingly, they were categorized into no stress, less/moderate stress, and severe stress. A stress score up to 40: No stress; 41-200: Less/moderate stress; More than 200: Severe stress. Finally, 106 females with scores above 200 were chosen for the study, as they had a higher risk of developing illness. Six patients refused to participate in the study. Finally 100 patients were administered questionnaires.

The General Health Questionnaire (GHQ-12) developed by Goldberg and Williams was administered to measure the evidence of stress/psychological distress in the individual during the past week. The GHQ scores on a Likert scale were as follows; 'better than usual' =0, same as usual = 1, less than usual = 2, much less than usual = 3. The possible range of scores was 0-36. A total score of 15 or more was considered as a 'GHQ case' and attributed with a higher risk of psychological morbidity. GHQ has been validated in the Indian population. All the patients had a score >15 (19.2 ± 2.3).

Perceived stress

Perceived stress is an outcome variable measuring the experienced level of stress as a function of objective stressful events, coping processes, and personality factors. Perceived stress among the patients is assessed using the the perceived stress scale (PSS-14) developed by Cohen *et al*. It is a 14-item scale that measures the degree to which situations in one's life have been appraised as stressful during the past month. A higher degree and longer duration of self-perceived stress, is indicated by a higher score, which is considered a risk factor for a clinical psychiatric disorder.

After clinical examinations were conducted and pre-test instructions were given to avoid consumption of any drugs that may alter the autonomic function, 48 hours prior to the test, the subjects were advised to have a good restful sleep. The subjects were advised to have light dinner within 8 p.m. and go to bed early, and avoid stressful situations during the day before the tests were conducted.

Fasting blood samples were drawn to exclude diabetes. Baseline anthropometric measurements, echocardiography (EKG), Fasting sugar, and lipid profile analysis were analyzed. Body Mass Index (BMI), Waist/Hip ratio, pulse, and blood pressure were recorded.

Subjects had a light breakfast at least three hours prior to testing and at least 24 hours of abstinence from alcohol, tobacco, tea, and coffee. The conventional autonomic function tests[12] were performed at laboratory room temperature, controlled at 22-24°C in the morning, between 11 a.m. and 1 p.m. It was ensured that they had not undergone any strenuous work or exercises three hours prior to the tests.

The subjects were made to rest for 15 minutes in a supine position. The resting time given to the subjects in between the two tests was five to ten minutes. All the tests were done in post the menstrual phase, five to ten days of menstrual cycle, to exclude the stress effects of premenstrual period and effects of hormonal variation on the autonomic functions, during the different phases of menstrual cycle.

Heart rate response to postural change (30:15 ratio)

The subject was instructed to stand erect from the supine position as quickly as possible (within three seconds) with continuous EKG recording for at least 30 seconds.The ratio of the longest R-R interval around the thirtieth beat after standing to the shortest R-R interval around the fifteenth beat after standing were calculated for a result of the 30:15 ratio.

Heart rate variation during deep breathing

The patient was instructed to take deep inspiration over five seconds, followed by expiration over the next five seconds, completing six respiratory cycles in one minute. The mean of the minimum R-R intervals in the six inspiratory cycles was calculated and the heart rate determined. Also the mean of the maximum R-R interval in the six expiratory cycles of the same tracing were calculated for the heart rate during expiration. The difference of the heart rate between the maximum in the inspiratory cycle and the minimum in the expiratory cycles were calculated and were used as the result of the test and an Expiration: Inspiration ratio of the R-R interval was also calculated.

Heart rate response to the Valsalva maneuver

The subject was instructed to exhale forcefully through the mouth piece of a modified mercurial sphygmomanometer and to maintain pressure in the manometer up to 40 mmHg for 15 seconds. An EKG recording was taken during the Valsalva maneuver (VM) and continued for about 30 seconds after the performance. The ratio of the longest R-R interval after blowing to the shortest R-R interval during blowing was calculated.

Orthostatic tolerance test

The basal blood pressure was recorded. Then the patient was asked to stand up and the blood pressure was recorded immediately. The difference between the systolic blood pressures of the one recorded in the supine position and the one taken in the erect posture was calculated. The fall in systolic pressure was taken as the result of orthostatic tolerance test (OTT).

Blood pressure response to sustained isometric handgrip

The basal blood pressure was measured. Then the subject was told to perform the maximum grip of the handgrip dynamometer in the sitting position with the dominant hand, and the maximum capacity was noted. After five minutes, the subject was asked to hold the grip with 30% of the maximum capacity for five minutes and the blood pressure was recorded just after release of the grip. The rise in diastolic blood pressure was calculated and taken as the result of the isometric handgrip (IHG) test.

Cold pressor test

The subject was asked to immerse the hand in cold water maintained at 4-6°C

The Blood Pressure from the other arm was recorded at 30 second intervals for a period of two minutes. After two minutes the subject was allowed to remove the hand. The maximum increase in systolic and diastolic blood pressures was recorded.

The patients were subsequently allocated into two groups using an online randomizer Group A (n = 50) and Group B (n = 50). Both groups were age- and BMI-matched, and had similar stress levels. There was no significant difference in pulse, blood pressure, autonomic function test results, hormonal status or treatment modalities at the beginning of study between the two groups [Table 1].

Table 1: Shows the different parameters of subjects before practicing PMR and receiving medication

Parameter	No=50 mean (SD)		*P* value
	Group B (control)	Group A (study)	
PSS	29.94 (2.61)	29.42 (3.09)	0.33
Waist/Hip ratio	0.98 (0.07)	0.99 (0.08)	0.29
BMI (kg/m²)	26.4 (2.9)	27.1 (2.2)	0.19
Pulse rate (beats/min)	80.2 (2.6)	80 (2.6)	0.7
Systolic BP (mm of Hg)	128.5 (2.9)	129.4 (2.97)	0.139
Diastolic BP (mm of Hg)	84.2 (4.6)	83.2 (2.09)	0.185
Valsalva ratio	1.4 (0.02)	1.365 ± 0.019	0.0569
Deep breath test (I-E)	23.7 (0.9)	23.5 (1.04)	0.3
Deep breath test (E : I)	1.3 (0.01)	1.32 (0.01)	0.259
30:15 R-R ratio	1.3 (0.06)	1.3 (0.07)	0.526
IHG (mm of Hg)	20.8 (2.8)	19.4 (4.1)	0.054
OTT (mm of Hg)	10.8 (3.3)	10.4 (1.8)	0.432
CPT (SBP)	23.2 (1.9)	22.7 (1.9)	0.16
CPT (DBP)	18.2 (1.9)	18 (1.6)	0.73
Cholesterol (mg/dl)	170 (10.2)	172.7 (6.4)	0.107
Triglyceride (mg/dl)	131.4 (7.1)	132.1 (4.9)	0.57
HDL (mg/dl)	49.2 (5.1)	48.4 (4)	0.399
LDL (mg/dl)	113.6 (5)	114 (3.8)	0.62

PMR – Progressive muscle relaxation, SD – Standard deviation, IHG – Isometric handgrip, BP – Blood pressure, OTT – Orthostatic tolerance test, BMI – Body mass index, PSS – Perceived stress, HDL – high density lipoprotein, LDL – Low density lipoprotein, DBP – Diastolic blood pressure, SBP – Systolic blood pressure, CPT – Cold pressor test

All subjects of group A (study group) were given a training of PMR. Training involved tensing the specific muscle groups for 7-10 seconds, followed by releasing them (relaxing) for 15-20 seconds, as per Jacobson's protocol.[8] They were asked to practice this technique at home for 20 minutes every day, for three months, and come for follow-up. The subjects were followed up at regular intervals during this period. Group B (control group) received treatment only from gynecologists, with no stress management program used to reduce their stress. Subjects in both groups continued to take medications as advised by gynecologists. All patients received the same treatment protocol, that is, Metformin and low-dose oral contraceptives, and the medications were standardized for BMI.

After three months, the lipid profile, vital parameters, and stress levels were rechecked, and the subjects of both groups were asked to repeat the tests.

The computer software "Statistical Package for the Social Sciences (SPSS) version 16 (SPSS Inc. Released 2007. SPSS for Windows, Version 16.0. Chicago, SPSS Inc.) was used to analyze the data. The difference between the groups was considered significant and highly significant if the analyzed probability values (*P* value) were $P < 0.05^{*}$ and $P < 0.01^{**}$, respectively.

Intragroup comparisons were not done as the subjects were all on medications that could alter autonomic functions and lipid metabolism. Changes in response after medications occurred due to altered autonomic activity resulting from modulation of the neurotransmitter on account of hormonal fluctuation.[13]

RESULTS

The most common mode of presentation of PCOS patients was menstrual irregularities and they all belonged to an urban population. All patients had a good education-minimum up to graduation level-and they all came from upper middle class families. Sixty eight percent of the patients were married. Treatment by a gynecologist consisted of birth control pills and Metformin.

The perceived stress scale was significantly less in subjects practicing relaxation exercises (21.8 (1.59) vs. 29.3 (4.5)), as compared to the group that was only on medication. Waist/hip ratio (0. 88 (0.02) vs. 0.91 (0.02)) and pulse rate were significantly lower, while there was no significant difference in BMI (25.06 (1.5) vs. 25.06 (1.5), *P* value: 0.55) and diastolic blood pressure (81.52 (3.03) vs. 82.4 (1.6)), *P* value: 0.063. Among the autonomic function tests, results of the eep breath difference test (29.6 (4) vs. 25.3 (4.5) and 1.45 (0.1) vs. 1.34 (0.1)), 30: 15 R-R ratio (1.1 (0.008) vs. 1.1 (0.01)), isometric hand grip test, and cold pressor test results showed a significant parasympathetic tilt in subjects practicing PMR. Cholesterol (139.1 (11.8) vs. 157.5 (13.4)), triglycerides (106.3 (6.8) vs. 123.03 (3.6)), and LDL cholesterol (98.9 (12.2) vs. 108.8 (14.1)) were significantly lower and HDL (53.7 (4.24) vs. 50.9 (3.98)) was significantly higher in patients of PCOS, who were on PMR [Table 2]. No difference in insulin levels was seen due to PMR.

DISCUSSION

Stress either physical or mental leads to cardiovascular morbidity. Psychological stress is a risk factor for hypertension and coronary artery disease. The purpose of the present study has been to assess the impact of stress on cardiac autonomic regulation in patients with PCOS, as they have an increased risk of developing cardiovascular diseases.[4-7] The significant better results of the autonomic functions and lipid profile following relaxation exercises in our study group may be due to the positive effect of mental relaxation on autonomic function and lipid metabolism. A study by Goyal *et al*., in 2010,[14] exposed the study group to noise levels (stressor) of more than 80 dB (A) for more than eight hours a day for a period of six months. Various autonomic function tests were carried out in both the groups. The significant greater worsening of autonomic functions in the study group was attributed to increased sympathetic activity. Thus, the stressor was shown to significantly alter autonomic functions.

Physical adaptation occurs due to stress, principally to promote an adaptive redirection of energy. Thus, oxygen and

Table 2: Shows different parameters of subjects practicing PMR and subjects only on medication

Parameter	No=50 mean (SD)		*P* value
	Group B (control)	Group A (study)	
PSS	29.3 (4.5)	21.8 (1.56)	<0.001**
Waist/Hip ratio	0.9 (0.01)	0. 88 (0.02)	<0.001*
BMI (kg/m²)	25.7 (1.8)	25.06 (1.53)	0.55
Pulse rate (beats/min)	77.9 (3.9)	75.2 (3.3)	0.001**
Systolic BP (mm of Hg)	126.5 (2.6)	122.1 (1.9)	<0.001**
Diastolic BP (mm of Hg)	82.4 (1.6)	81.5 (3)	0.06
Valsalva ratio	1.4 (0.1)	1.414 (0.01)	0.69
Deep breath test (I-E)	25.3 (4.5)	29.6 (4)	<0.001*
Deep breath test (E : I)	1.3 (0.1)	1.5 (0.1)	<0.001**
30:15 R-R ratio	1.1 (0.01)	1.1 (0.008)	0.0196*
IHG (mm of Hg)	20 (2.7)	17.5 (2.4)	<0.001**
OTT (mm of Hg)	8.95 (2.2)	7.99 (1.4)	0.06
CPT (SBP)	23.3 (2.1)	21.9 (2.4)	0.032*
CPT (DBP)	18.1 (1.9)	14.6 (3.1)	<0.001**
Cholesterol (mg/dl)	157.5 (13.4)	139.1 (11.8)	<0.001*
Triglyceride (mg/dl)	123.03 (3.6)	106.3 (6.8)	0.03*
HDL (mg/dl)	50.9 (4)	53.7 (4.2)	0.005**
LDL (mg/dl)	108.8 (14.1)	98.9 (12.2)	0.003*

PMR – Progressive muscle relaxation, SD – Standard deviation, IHG: Isometric handgrip, BP – Blood pressure, OTT – Orthostatic tolerance test, BMI– Body mass index, PSS – Perceived stress, HDL – high density lipoprotein, LDL – Low density lipoprotein, DBP – Diastolic blood pressure, SBP – Systolic blood pressure, CPT – Cold pressor test, * – $P < 0.05$ Significant, ** – $P < 0.01$ highly significant nutrients are shunted to the central nervous system (CNS) and the stressed body site(s), where they are needed the most. Increases in cardiovascular tone, respiratory rate, and intermediate metabolism (gluconeogenesis, lipolysis) all work in concert to promote availability of vital substrates, while energy consuming functions, such as, digestion, reproduction, growth, and immunity are temporarily suspended. Restraining forces are also activated during stress, in order to prevent a potential excessive response of the components of the stress system.[15-17] The ability of the individual to develop the restraining forces that prevent such an over-response accurately and in time is equally essential for a successful general adaptive response. If the counteracting forces of the body fail to control the elements of the stress response in a precise manner, the prolongation of the initial adaptive responses may turn maladaptive and contribute to the development of disease. Relaxation exercises may help in improvement of these adaptive responses.[8]

Stress in a known factor responsible for the development of dyslipidemia, and dyslipidemia is known to alter autonomic functions by decreasing heart rate variability and baroreceptor sensitivity.[15,18-20] This effect of stress is also evident in the present study. Stress also alters distribution of body fats[15,18-20] and this is the cause of a significant decrease in the waist/hip ratio in the study group, as compared to the control, however, there is no significant decrease in the BMI.

A study in 2013, explored whether viewing pictures of nature prior to a stressor altered the autonomic function during recovery from the stressor. Natural scenes are known to produce relaxation effects on the mind.[16] Parasympathetic activity was significantly higher during recovery following the stressor when viewing scenes of nature compared to viewing scenes depicting built environments. Thus, viewing nature scenes prior to a stressor alters the autonomic activity in the recovery period. Our study also demonstrates an improvement in autonomic functions following mental relaxation.

Study of the autonomic function basal heart rate, basal blood pressure, and systolic and diastolic response to cold stimulus was carried out by Rode *et al*. on females, in 2010,[17] during the premenstrual and postmenstrual phase. Increased sympathetic activity was observed during the premenstrual phase and this was positively correlated with the stress levels. To avoid stress effects of the premenstrual phase, we examined our subjects during the postmenstrual phase.

Changes in the autonomic function may be responsible for some of the symptoms produced through endorphins that have been held responsible for behavioral changes.[15-17] We also noticed significantly less PSS in our study group as compared to the control and significant improvement in the autonomic functions following relaxation exercises.

Bhimani *et al*. in 2011[21] studied the effect of Pranayama on stress and cardiovascular autonomic function. The stress level was reduced after two months of practicing pranayama and there was significant reduction in the sympathetic drive to the heart and increase in parasympathetic output. Two months of practice of pranayama resulted in a better sympathovagal balance, with the resting balance tilting toward better parasympathetic control. Our study also demonstrated similar results with PMR training.

The stress levels in healthy students were assessed in 2006.[12] Cardiac autonomic regulation was tested using both conventional tests and spectral analysis of heart rate variability. Nine subjects who obtained scores on the stress scale in the upper quartile were classified as the 'stress' group and the rest constituted the 'no-stress' group ($n = 27$). There were no significant differences between the two groups on any of the conventional tests of autonomic nervous activity. However, in our study we found significant differences in the conventional autonomic function tests. Our study and control groups were PCOS patients, not normal healthy subjects, and the study group was practicing PMR for three months, which may be the cause of variance. The low frequency power in normalized units and low frequency high frequency ratio of heart rate variability in the supine posture, was significantly higher in the 'stress' group compared to the 'no stress' group, in the above study. The low frequency power in normalized units was significantly and positively correlated with the total stress score. The changes were suggestive of a tilt in the resting cardiac autonomic balance toward increased sympathetic activity. A similar influence of stress was seen in studies by Kulshreshtha *et al*., in 2013.[22] Our study also indicates a similar tilt of cardiac autonomic balance, with increased levels of stress.

Progressive muscle relaxation helps in the modulation of heart rate, blood pressure, and lipid profile in healthy individuals. Significant decreases in resting HR and SBP and DBP of subjects were observed after PMR training by Khanna *et al*.[23] in 2007. This decrease may be a result of a complex interplay of physiological and psychological mechanisms, to reduce the anxiety in subjects practicing PMR,[8,24] as PMR training is known to increase parasympathetic activity, reduce muscle tension; improve concentration, and lead to a sense of well-being.[8] Our study also demonstrates similar results in PCOS patients.

Limitations

Heart rate variability (HRV) analysis would have been a better choice to measure the autonomic functions, but it was not available in our laboratory.The study groups were not randomized for insulin levels, which adds limitations to the present study.

CONCLUSIONS

The cardiovascular risk factors were significantly decreased in PCOS patients following relaxation therapy. These patients were a high-risk group for developing metabolic syndrome, and relaxation therapies could be recommended as an adjuvant therapy to tilt the autonomic balance to parasympathetic dominance, to improve the cardiovascular profile.

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