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RESEARCH ARTICLE

Comparative analysis of sympathetic nervous system activity in pre-menopausal and post-menopausal women

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ABSTRACT

Background: Post-menopausal women suffer from various complications like autonomic dysfunction which predisposes them to cardiovascular morbidity. Decline in estrogen levels after menopause is associated with increased cardiovascular risks. Timely evaluation of such derangements and active intervention can play an important role in the prevention of cardiovascular morbidity. **Aims and Objective:** The aim is to compare the sympathetic autonomic nervous system activity in pre-menopausal and age-matched post-menopausal women. **Materials and Methods:** This study was conducted on two groups of 40 women each. Group I included pre-menopausal women and Group II included post-menopausal women. Sympathetic nervous system assessment was done using cold pressor test (CPT), handgrip test (HGT), and blood pressure (BP) response to standing. Statistical analysis was performed using Student's *t*-test. **Results:** Evaluation of sympathetic functions between the two groups showed that the mean rise in systolic BP (SBP) in response to CPT was lower in Group I than in Group II ($P < 0.01$). Mean rise in the diastolic BP (DBP) in response to HGT was also lower in Group I as compared to Group II ($P < 0.01$). Fall in SBP on standing in Group I was more than in Group II ($P < 0.01$). **Conclusion:** Sympathetic nervous system evaluation showed sympathetic hyperactivity in the post-menopausal group as compared to the pre-menopausal group.

KEY WORDS: Menopause; Sympathetic; Cardiovascular; Estrogen

INTRODUCTION

Menopause is defined as the stage of aging process which marks the transition from the reproductive phase of life to the post-reproductive phase. Menopause generally begins around the age of 40 years and varies considerably from one woman to another.[1] Technically, it is the last menstrual period which is termed as menopause, but the process begins months or years before the actual event.[2] The ovaries begin with a finite number of follicles and these atrophies at a steady rate throughout the reproductive years. Menopause in humans is characterized by reduced circulating estradiol level which is due to falling numbers of functional follicles as the age advances.[3] Menopause predisposes women to many diseases and changes their quality of life.[4] Menopausal symptoms that impair the quality of life of menopausal women include hot flushes, night sweats, sleep disorders, sexual dysfunction, and alterations in mood.[5] Alteration in autonomic nervous system (ANS) functions primarily due to changes in estrogen level is responsible for symptoms associated with menopause.[5]

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Pre-menopausal women have a lower risk of coronary heart disease as compared to men of same age. In post-menopausal age group, the incidence of coronary heart disease becomes equal in both sexes.[6] Data from the Framingham study shows a two-fold age-adjusted increase in risk for coronary heart disease in post-menopausal compared with pre-menopausal women.[7] Young women with bilateral oophorectomy have an increased risk of coronary heart disease if they are not treated with estrogens.[8] These observations, along with the favorable effect of hormonal replacement therapy on cardiovascular morbidity and mortality in post-menopausal women, have led to the assumption that ovarian hormones, especially estrogens, protect women from coronary heart disease.[9]

Autonomic modifications of cardiovascular control have also been observed with aging. In women, both aging and post-menopausal hormonal changes contribute to modifications of the autonomic control of the cardiovascular system. Menopause causes an imbalance of the autonomic nervous control of the cardiovascular system with a shift toward sympathetic hyperactivity. This shifts explains, in part, the increased incidence of cardiovascular diseases observed in post-menopausal women.[10] Cardiovascular function is under constant control by the sympathetic and parasympathetic nervous systems and any change in autonomic activity enhances the risk of cardiovascular disease and this aspect of cardiovascular function is also modulated by estrogen.[11] It has been observed that replacement estrogen therapy can reduce the post-menopausal morbidity and mortality of cardiovascular disease by about 50%.[11] Various animal and human studies have evaluated the effect of the hormonal changes on ANS function in various phases of menstruation and among the pre-menopausal and post-menopausal females.[12]

Animal studies have demonstrated that estrogen reduces the pressor responses to restraint (stress) in the ovariectomized rats.[13]

Some human studies have shown that pressor responses to mental stress were enhanced in the post-menopausal women as compared to the pre-menopausal women. There is an exaggerated cardiovascular and neuroendocrine response to behavioral stressors in post-menopausal women.[14,15] Menopause is often associated with an increased incidence of palpitations and with worsening of pre-existing arrhythmias.[16]

Menopausal changes in ANS may be responsible for the increased cardiovascular morbidity in women. Evaluation of such changes in post-menopausal females can lead to the formulation of preventive strategies for cardiovascular morbidity and mortality in such patients. Hence, we set out to look for the changes that occur in sympathetic activity of ANS following menopause.

MATERIALS AND METHODS

The present study was conducted in the Department of Physiology, Government Medical College, Amritsar, Punjab, India. Prior approval from the Institute Ethics Committee was taken. This study was conducted on two groups of 40 women each.

- Group I: Included 40 pre-menopausal women of age group 40-45 years.
- Group II: Included 40 post-menopausal women of age group 45-50 years, who had their last menstrual cycle 1 year back or more.

Participants were taken from the general population of city of Amritsar. Before initiation of this study, written informed consent was obtained from the participant after full explanation of elements contained in the research protocol. While selecting the participants, women with a history of cardiac disease, diabetes mellitus, or who were on hormone replacement therapy which is likely to influence the interpretation of sympathetic nervous activity were excluded from this study. Electrocardiogram (ECG) for sympathetic function testing was done with cardiart-108T/MK-VI ECG machine of BPL make, using standard limb lead II. Blood pressure (BP) was recorded using sphygmomanometer. Before sympathetic nervous system evaluation, pulse rate, systolic BP (SBP), and diastolic BP (DBP) were compared between two groups.

Sympathetic nervous system assessment was done using following tests.[17]

1. Cold pressor test (CPT)
2. Handgrip test (HGT)
3. BP response to standing.

CPT

In this test resting, BP was recorded with the participant sitting comfortably. Participant was asked to immerse her hand in cold water maintained at 4°C. BP measurements were made from the other arm at 30 s interval for 2 min. After 2 min, the participant was allowed to remove her hand. Maximum increase in the SBP before and after the test was determined and results recorded.

HGT

In this test, the participants were instructed to grasp a dynamometer and sustain fixed, isometric contraction for 3 min. BP was measured before and at 1 min interval during handgrip. The results were expressed as the difference between the DBP during handgrip and reading before handgrip began.

BP Response to Standing and Lying

The test was performed by measuring the participant's BP with a sphygmomanometer while she was lying down quietly

and 1 min after she was made to stand up. The postural fall in BP was taken as the difference between the SBP while lying and SBP on standing. Statistical analysis was performed using unpaired *t*-test using Microsoft Excel. The $P < 0.05$ was taken as statistically significant.

RESULTS

The present study was conducted with the objective to compare the sympathetic nervous system activity between pre-menopausal (Group I) and post-menopausal (Group II) women. The various ANS tests were performed to evaluate the integrity of sympathetic divisions of the ANS. The results were expressed as a mean ± standard deviation.

The average age in the pre-menopausal group and post-menopausal group was comparable (Table 1).

The pre-test values for mean pulse rate, mean SBP, and mean DBP were lower in pre-menopausal women as compared to post-menopausal group ($P < 0.05$) (Table 2).

Evaluation of sympathetic functions between the two groups showed that the mean rise in SBP in response to CPT was lower in Group I than in Group II ($P < 0.01$). Mean rise in the DBP in response to HGT was also lower in Group I as compared to Group II ($P < 0.01$). Fall in SBP on standing in Group I was more than in Group II ($P < 0.01$) (Table 3).

Table 1: Comparison of age (mean±SD) in pre-menopausal and post-menopausal groups

Groups	Number (*n*)	Age (mean±SD)
Pre-menopausal (Group I)	*n*=40	43.57±1.34
Post-menopausal (Group II)	*n*=40	46.55±1.45

SD: Standard deviation

Table 2: Comparison of pre-test values of pulse rate, SBP, and DBP (mean±SD) in pre-menopausal (Group I) and post-menopausal (Group II) groups

Parameters	Pre-menopausal (Group I)	Post-menopausal (Group II)
Pulse rate (beats/min)	82.4±8.51	91.9±7.27*
SBP (mmHg)	125.15±4.57	134.5±4.16*
DBP (mmHg)	82.85±5.31	89.2±4.52*

*$P<0.05$ versus corresponding values in Group I. SBP: Systolic blood pressure, DBP: Diastolic blood pressure

Table 3: Comparison of sympathetic functions in pre-menopausal (Group I) and post-menopausal (Group II) groups

Parameters	Pre-menopausal (Group I)	Post-menopausal (Group II)
CPT (rise in SBP) (mmHg)	15.6±1.58	18.85±4.27**
HGT (rise in DBP) (mmHg)	13.6±2.18	18.1±3.56**
SBP fall on standing (mmHg)	9.95±2.73	7.65±2.35**

**$P<0.01$ versus corresponding values in Group I. CPT: Cold pressor test, SBP: Systolic blood pressure, HGT: Handgrip test, DBP: Diastolic blood pressure

DISCUSSION

The average age of the women in the pre-menopausal (Group I) was comparable to the post-menopausal (Group II). The average age of onset of menopause is between 40 and 50 years.[18] The average age of women in Group II is comparable to the population mean. The pre-menopausal group was selected from among the females in the age group of 40-45 years to prevent variation in sympathetic nervous system function tests due to age factor.

The statistical analysis showed that the mean values of pulse rate were higher in the post-menopausal group as compared to pre-menopausal group ($P < 0.05$). This finding is in agreement with an earlier study wherein autonomic functions of 24 post-menopausal women were evaluated.[3] Various other studies also support our findings of tachycardia in post-menopausal women.[19]

Mean pre-test SBP recordings in the post-menopausal group were higher as compared to the pre-menopausal group. Similarly, mean pre-test DBP recordings in the post-menopausal group were more as compared to the pre-menopausal group. Our finding matches with the study conducted on 38 pre-menopausal and 28 post-menopausal women which showed that basal SBP and DBP were significantly higher in post-menopausal women as compared to pre-menopausal women.[20]

Mean SBP rise in response to CPT is significantly higher in post-menopausal group. These results match with the results of a study conducted on 24 post-menopausal women for ANS assessment.[3] Another population-based study done on 9864 men and women aged 18-70 years and followed for 18 years also showed that pressor response to cold was higher in menopausal as compared to fertile women.[21]

HGT which measures BP response to sustained isometric exercise showed an increase of DBP in post-menopausal group as compared to the pre-menopausal group. The results are supported by a study showing reversal of augmented sympathetic vasoconstriction in exercising forearms of post-menopausal women on estrogen therapy.[22] Similar results were obtained in another study assessing ANS functions in 24 post-menopausal women.[3]

BP response to standing showed a lesser fall in SBP in post-menopausal women as compared to pre-menopausal women. Our results are in accordance with the various studies carried

out to evaluate autonomic function in post-menopausal females.[3]

Evaluation of the sympathetic activity of ANS revealed that there is an increase in sympathetic activity in the post-menopausal women as compared to pre-menopausal women as indicated by all the tests performed to assess sympathetic activity, namely, resting heart rate, BP, CPT, HGT, and BP response to standing.

Increased sympathetic activity in post-menopausal women as compared to pre-menopausal women can be attributed to changes in catecholamines and 5-hydroxytryptamine levels in both hypothalamus and extrahypothalamic areas in the brain.[23] This is due to decrease in levels of circulating estrogens and change in number of estrogenic receptors in the brain after menopause.[4] Various vasomotor symptoms such as hot flushes, sweating are mediated by increased sympathetic activity.

Limitations

The catecholamine and estrogen levels were not evaluated in the present study. Their evaluation could have substantiated findings of the study.

CONCLUSION

Sympathetic dominance was observed in post-menopausal women as compared to pre-menopausal women of similar age group. The various signs and symptoms of menopause can be attributed to sympathetic overactivity being influenced by hormonal imbalance after menopause.

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