National Journal of Physiology, Pharmacy and Pharmacology

RESEARCH ARTICLE

Parasympathetic nervous system changes after the menopause: A comparative study

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Received: February 06, 2019; **Accepted:** March 04, 2019

ABSTRACT

Background: Autonomic nervous system control is a major determinant in various cardiovascular diseases. Onset of menopause in women results in increased risk of cardiovascular mortality. Early assessment of the changes in autonomic activity after menopause can help reduce the prevalence of cardiovascular mortality in women. **Aims and Objectives:** The aim of the study is to compare the parasympathetic autonomic nervous system activity in age-matched pre- and post-menopausal women. **Materials and Methods:** The study was conducted in the physiology department of Government Medical College, Amritsar. Two groups of 40 women each were enrolled in the study. We enrolled pre-menopausal women in Group I and post-menopausal women in Group II. Parasympathetic nervous system assessment was done using 30:15 ratio, standing: lying ratio (S: L ratio), Valsalva ratio, and deep breathing test (DBT). Statistical analysis of the collected data was done using student *t*-test. **Results:** Parasympathetic functions tests did not reveal any significant change in the mean 30:15 ratio, S: L ratio, Valsalva ratio, and the mean value for DBT ($P > 0.05$). **Conclusion:** No significant variation in parasympathetic activity between the pre-menopausal and post-menopausal groups was observed.

KEY WORDS: Parasympathetic; Menopause; Cardiovascular

INTRODUCTION

The autonomic nervous system plays an essential role in the natural course of cardiovascular diseases and serves as a potential target for the treatment of pathophysiological conditions such as myocardial ischemia, arrhythmias, increased blood pressure, and peripheral vascular diseases.[1] Various studies evaluating autonomic nervous system changes show sympathetic overactivity after menopause.[2,3] However, studies of parasympathetic nervous system changes after menopause are few and inconclusive.

Access this article online	
Website: www.njppp.com	Quick Response code
DOI: 10.5455/njppp.2019.9.0203904032019	

Sympathetic and parasympathetic branches of the autonomic nervous system control the cardiovascular system. Any alteration in its activity increases the risk, which results in cardiovascular morbidity and mortality.[4] The pre-menopausal women suffer from cardiovascular diseases less often than men but once menopause sets in, this difference in incidence becomes less apparent.[5,6] Studies suggest that estrogen which is the primary female hormone modulates this aspect of the cardiovascular functions.[4] This risk is reduced to 50% in the post-menopausal females who are prescribed estrogen replacement therapy.[4] The gender-specific differences may be due to dissimilarity in the hormones. Variation in the hormone levels is responsible for autonomic system variations seen in pre- and post-menopausal women and also in different phases of menstrual cycle.[1] A study has revealed that reduced estrogen levels in post-menopausal females lead to impairment of parasympathetic division of the autonomic nerve function.[7] Various studies comparing women of

different age groups show that parasympathetic tone of the cardiovascular system is reduced in women of elderly age group.[8] Atrial baroreflex stimulation as a result of change in posture is mediated by both parasympathetic and sympathetic nervous systems. Parasympathetic nervous system control of the baroreflex is deranged in post-menopausal women and men of the same age, signifying that menopause has no effect on the parasympathetic activity while the same is not true for the sympathetic nervous system control. Changes in female hormones are partly responsible for this difference.[8] Similarly, an another study has concluded that parasympathetic modulation of the variability of heart rate at rest decreases in post-menopausal females when compared to younger females.[9]

Symptoms of menopause, namely, hot flushes, weight gain, sweating, hypertension, etc., are due to neuroendocrine changes which result from fall in female hormonal synthesis by the ovaries.[10,11]

Changes in autonomic nervous system (ANS) after the onset of menopause have been observed to be responsible for increased cardiovascular morbidity in women. Assessment of these changes in post-menopausal females can help in laying down preventive methods (lifestyle modifications, yoga, meditation, etc.) for cardiovascular diseases. The earlier studies included women with wider gap in age in pre-menopausal and post-menopausal groups. Since age is an important factor while assessing autonomic changes, we, in this study enrolled women in both groups of similar age to look for any deviation in parasympathetic activity due to the onset of menopause without the age influencing the results.

MATERIALS AND METHODS

We did this study in the Department of Physiology of Government Medical College at Amritsar after obtaining approval from the Institute Ethics Committee.

Two groups comprising of 40 women each were formed.

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

We selected the participants randomly from the city of Amritsar and obtained written informed consent after full explanation of elements contained in the research protocol. Women with a history of cardiac ailments, diabetes, and those taking hormone replacement therapy (which is likely to influence the interpretation of parasympathetic nervous activity) were excluded from the study. Electrocardiography (ECG) for parasympathetic function testing was done with cardiart-108T/MK-VI ECG machine of BPL make, using limb lead-II. Sphygmomanometer was used to record blood pressure. Pre-test recordings of pulse and BP were taken.

Parasympathetic nervous system evaluation was done using following tests.

- 30:15 ratio[12]
- S: L ratio (Standing: lying ratio)[13]
- Valsalva ratio[12]
- Deep breathing test (DBT).[12]

30:15 Ratio

In this test, the heart rate of the participants was monitored on the E.C.G machine for 3 min continuously, in lying down position. The participants were then made to stand without any support, and this point was marked on electrocardiograph. The ratio of longest to shortest interval between two consecutive R-waves recorded near 30th beat and the shortest near 15th beat after standing was measured.

The S/L (Standing to Lying) Ratio

Participants were made to stand first and then asked to lie down unsupported. We simultaneously recorded E.C.G from 20 beats and 60 beats after lying down. The ratio of the maximum interval between two consecutive R-waves during the 5 beat interval before lying, and minimum interval after lying was taken as S/L ratio.

Valsalva Ratio

In this test, the participants were asked to blow in a mercury manometer through mouthpiece against closed glottis. They were told to hold it at a pressure of 40 mmHg for the duration of 15 s. E.C.G was recorded while the participants were blowing against closed glottis. After 45 s, ECG was recorded again, and Valsalva ratio was calculated. It is the ratio of longest R-R interval (after blowing) to the shortest R-R interval (during blowing).

Heart Rate (R-R interval) Variation during Deep Breathing

In this test, the participants were made to breathe deeply for 1 min at the rate of six breaths per minute with equal inhalation and exhalation time duration. ECG was recorded continuously during deep breathing. Onset of each inspiration and expiration was marked on the ECG with a marker pen. Ruler was used to measure the longest and the shortest R-R intervals in each of the breathing cycles, and these values were changed to beats per minute. The average difference between maximum and the minimum heart rates in beats per minute for each of the six deep breathing cycles was calculated.

Data obtained from the study were analyzed using the Unpaired *t*-test. $P < 0.05$ was taken as statistically significant.

RESULTS

This study was done with the aim to compare the parasympathetic nervous system activity between pre-menopausal and post-menopausal women. The various autonomic tests were conducted to assess the integrity of parasympathetic divisions of ANS. The results were expressed as mean ± standard deviation.

The average age in the Group-I and in Group-II was comparable [Table 1].

The pre-test values for mean pulse, mean systolic, and diastolic blood pressure were lower in pre-menopausal women in comparison to post-menopausal women ($P < 0.05$) [Table 2].

Intergroup comparison of parasympathetic functions showed that the mean 30:15 ratio, S: L ratio, Valsalva ratio, and DBT were not statistically significant ($P > 0.05$) [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

P<0.05 versus corresponding values in Group-I. SD: Standard deviation

Table 2: Comparison of pre-test values of pulse rate, systolic blood pressure, and diastolic blood pressure (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*
Systolic blood pressure (mm Hg)	125.15±4.57	134.5±4.16*
Diastolic blood pressure (mm Hg)	82.85±5.31	89.2±4.52*

**P*<0.05 versus corresponding values in Group-I. SD: Standard deviation

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

Parameters	Pre-menopausal (Group-I)	Post-menopausal (Group-II)
30:15 ratio	1.07±0.05	1.06±0.06**
S/L ratio	1.19±0.04	1.17±0.05**
Valsalva ratio	1.21±0.07	1.21±0.06**
DBT	13.25±1.99	12.47±1.76**

***P*>0.05 versus corresponding values in Group-I. S/L ratio: Standing: lying ratio, DBT: Deep breathing test

DISCUSSION

Various tests, namely, 30:15 ratios, S: L ratio, Valsalva ratio, and DBT that were performed to evaluate changes in the parasympathetic nervous system due to the onset of menopause did not show significant variation.

In the present study, the average age in the two groups is comparable. Moreover, the average age of post-menopausal group is comparable to the population mean which is 40–50 years.[14] A study determining the factors which affect the age of menopause onset concluded that the average age in women of Indian origin is 46.2 years which matches our study.[15] The mean pre-test readings of pulse, systolic, and diastolic blood pressures in post-menopausal women were higher in comparison to pre-menopausal group ($P < 0.05$). Our finding matches with various other studies showing increased heart rate in post-menopausal women.[16-18] The increase in these values of systolic and diastolic blood pressure in post-menopausal woman is supported by a similar study, which showed that basal systolic and diastolic blood pressure were significantly higher after menopause. These findings could result from the increased sympathetic tone.[19] The variation in mean 30:15 ratio in the two groups was statistically not significant. Our results do not match with previous study conducted on small group of women.[7] Disagreement of results could be due to age group of pre-menopausal women chosen in that study, which was much lower (mean age 24.30 ± 3.88 years) as compared to our study (mean age 43.57 ± 1.34 years). S/L ratio for the cardiac parasympathetic activity showed that there was no significant difference. It may result partly from the fact that difference in average age of pre-menopausal and post-menopausal women included in our study was minimal. Valsalva ratio which is another tool used to assess parasympathetic activity did not achieve statistical significance ($P > 0.05$). These findings are in accordance with a study which compared parasympathetic function in post-menopausal to pre-menopausal women and showed similar values of Valsalva ratio.[20] DBT which is a measure of changes in heart rate resulting from deep breathing showed statistically insignificant difference in both the groups.

Assessment of parasympathetic functions tests did not reveal significant variation after the onset of menopause. Minimal difference in the average age of the two groups may have been the reason for these results. Moreover, age-related effects are more pronounced in parasympathetic cardiovascular functions and have a little effect on sympathetic cardiovascular function.[21] In our study, we have compared parasympathetic activity in age-matched groups, and so, it may be the reason for insignificant results. Thus, due consideration to age of the participant should be given while evaluating the tests of autonomic nervous function tests.

Strength and Limitations

In our study, the average age of women in pre- and post-menopausal groups was similar, thus avoiding any variations that may reflect in the tests due to difference in age alone. In our study, we have not measured the levels of estrogens which could have helped us understand and interpret the results with more clarity.

CONCLUSION

No significant alteration in parasympathetic nervous system activity was observed after the onset of menopause in age-matched women.

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How to cite this article: Dureja S, Bachhel R, Gupta M, Bhandari V. Parasympathetic nervous system changes after the menopause: A comparative study. Natl J Physiol Pharm Pharmacol 2019;9(5):383-386.

Source of Support: Nil, **Conflict of Interest:** None declared.