

Autonomic reactivity in premenopausal, perimenopausal and postmenopausal Women

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Abstract

The autonomic nervous system controls most of the visceral functions of the body through the sympathetic and the parasympathetic nerve fibers. In postmenopausal women, the risk of cardiovascular diseases gradually increases and alterations in autonomic nerve functions commonly affect cardiac vagal control. In women, the withdrawal of the hormones in the perimenopausal and the menopausal period is gradual. The present study was aimed to assess the autonomic functions in premenopausal, perimenopausal and postmenopausal women. This study was conducted on 210 women volunteers, who were divided into three groups of 70 each, namely Group I (premenopausal), Group II (perimenopausal) and Group III (postmenopausal). The sympathetic function tests performed were blood pressure, blood pressure response to standing (orthostasis) and the isometric handgrip strength test (IHST). The parasympathetic tests conducted were standing to lying (S/L) ratio, 30:15 ratio, valsalva ratio and tachycardia ratio. All parameters were reported as mean and standard deviation. The study concluded that there is predominant sympathetic activity in postmenopausal women in comparison to premenopausal women. Parasympathetic activity altered slightly but not significantly in postmenopausal women.

Keywords: Autonomic nervous system, Postmenopausal, Sympathetic, Parasympathetic, Nerve fibers, Cardiac vagal control

Introduction

Menopause is a normal aging phenomenon in women.⁽¹⁾ The risk of cardiovascular diseases gradually increases in postmenopausal women, which may be due to lower level of estrogen.⁽²⁾ Alteration in autonomic nerve functions may occur in menopausal women and it commonly affects cardiac vagal control and usually is associated with sympathetic hyperactivity.⁽³⁾ Changes in neuroendocrine system due to the loss of ovarian function at menopause have an important bearing in the control of reproductive and non-reproductive functions.

The high incidence of ischemic heart disease after menopause suggests a close association between ovarian hormone levels and the cardiovascular system.⁽⁴⁾

A woman in her reproductive period, gradually transcends into perimenopause and later after a couple of years, into menopause. Perimenopause is a hormonally distinct time in midlife. It is a transitional stage which is prior to menopause and in this stage the menstrual cycles are irregular, with a 30 per cent reduction in estrogen and a decrease in progesterone and ovulation becomes inconsistent.⁽⁵⁾

Common clinical characteristics of transition are a change in the women's usually regular menstrual periods and the beginning of the vasomotor symptoms like hot flushes and night sweats. These menopausal vasomotor symptoms suggest an alteration of either cardiovascular reflexes or the local control of blood flow to skin, *i.e.* an alteration of autonomic haemodynamic control.

The present study was done to evaluate the autonomic functions in premenopausal, perimenopausal

and postmenopausal women, so as to assess any significant deviation from normal in sympathetic as well as in parasympathetic reactivity.

Material and Methods

This study was carried out in the Postgraduate Department of Physiology, Government Medical College, Jammu for a one year period from November 2012 to October 2013 after approval from the Institutional Ethical Committee. Care was taken to exclude subjects with illnesses known to affect autonomic reactivity. The study was conducted on 210 subjects, who were divided into three groups – Group I of premenopausal women, Group II of perimenopausal women and Group III of postmenopausal women—with 70 women in each group. The nature of the study was explained to all the subjects and a written informed consent was obtained from them. A detailed history and general physical examination was done. Physical parameters were recorded as per standards recommended by W.H.O. Age of the subjects in years was recorded as per their statement. The various autonomic function tests which were performed were sympathetic and parasympathetic function tests.

For assessing sympathetic activity, the parameters recorded were:

1. Blood pressure, recorded by auscultatory method—using a sphygmomanometer.
2. Orthostasis (blood pressure response to standing): Recorded as change in systolic and diastolic blood pressures in response to change in position from supine to standing position.⁽⁶⁾

3. Handgrip test (blood pressure response to static exercise): The response was considered as the difference between maximum blood pressure obtained after exercise and resting blood pressure.⁽⁷⁾

For assessing parasympathetic activity, parameters evaluated were:

1. Standing to lying down (S/L) ratio: It was calculated as longest respiratory rate (R-R) interval during 5 beats before lying down to the shortest R-R interval during 10 beats after lying down.⁽⁸⁾

2. 30:15 ratio: It was calculated as ratio of R-R interval at beat 30 to R-R interval at beat 15 in the ECG recorded after subject stands up from supine position.⁽⁹⁾

3. Valsalva ratio: It was calculated as ratio between maximal R-R interval after release of strain and maximum R-R interval during the strain.⁽¹⁰⁾

4. Tachycardia ratio: It was calculated as the ratio of shortest R-R interval during the valsalva maneuver divided by the longest R-R interval before this maneuver.⁽¹¹⁾

Statistical analysis was carried out by unpaired student 't' test, where the mean values of all parameters tested in all the subjects were compared with established normal values. The p value less 0.05 was considered as significant.⁽¹²⁾

Results

The present study showed a significant increase in sympathetic activity in perimenopausal and postmenopausal women, with no change in parasympathetic activity.

The results of tests carried out for recording sympathetic activity are shown in Table 1.

Table 1: Comparison of mean values of sympathetic parameters among subjects of three groups

Sympathetic parameters		Group I Mean \pm SD (Range)	Group II Mean \pm SD (Range)	Group III Mean \pm SD (Range)	p-value
Blood pressure (mm Hg)	SBP	114.91 \pm 7.34 (90-130)	120.28 \pm 8.88 (90-130)	128.14 \pm 9.48 (90-160)	0.000***
	DBP	74.74 \pm 6.53 (60-100)	77.60 \pm 6.59 (60-90)	82.80 \pm 6.92 (60-92)	0.000***
Orthostasis test (mean changes in mm Hg)	SBP	2.14 \pm 1.37 (0-10)	2.31 \pm 1.05 (0-6)	1.48 \pm 1.51 (0-6)	0.000***
	DBP	0.71 \pm 1.18 (0-4)	1.31 \pm 1.44 (0-6)	1.11 \pm 1.11 (0-4)	0.03**
Handgrip test (mean changes in mm Hg)	SBP	2.4 \pm 3.54 (0-20)	1.74 \pm 2.25 (0-10)	0.82 \pm 1.57 (0-6)	0.002***
	DBP	7.34 \pm 2.67 (2-12)	8.05 \pm 2.25 (2-12)	6.05 \pm 2.88 (0-10)	0.001***

Significant; *Highly significant

Both mean systolic blood pressure and mean diastolic blood pressure showed statistically significant differences between Group-I and Group-II and between Group-II and Group-III.

With orthostasis the change in mean systolic blood pressure was not statistically significant between Group-I and Group-II, but the difference between Group-I and Group-III as well as between Group-II and Group-III was statistically highly significant. In case of change in mean diastolic blood pressure with orthostasis, significant difference was observed only between Group-II and Group-III.

With the Handgrip-dynamometer test the mean systolic blood pressure showed non-significant difference between Group-I and Group-II and between Group-II and Group-III, but showed a statistically highly significant difference between Group-I and Group-III. And for mean diastolic blood pressure there is non-significant difference between Group-I and Group-II and highly significant difference between Group-I and Group-III and between Group-II and Group-III.

The tests carried out for determining parasympathetic reactivity showed a slight decrease in S/L ratio and tachycardia ratio, though not statistically significant, whereas the values of 30:15 ratio and tachycardia ratio are almost similar in all the three groups of women (Table 2).

Table 2: Comparison of mean values of parasympathetic parameters among subjects of three groups

Parasympathetic parameters	Group I Mean \pm SD (Range)	Group II Mean \pm SD (Range)	Group III Mean \pm SD (Range)	p-value
S/L ratio	1.02 \pm 0.11 (0.74-1.31)	0.98 \pm 0.11 (0.64-1.26)	0.98 \pm 0.10 (0.77-1.31)	.059*
30-15 ratio	1.01 \pm 0.10 (0.73-1.33)	1.01 \pm 0.06 (0.86-1.26)	1.02 \pm 0.07 (0.89-1.133)	.728*
Valsalva ratio	1.27 \pm 0.24 (0.9-2.08)	1.26 \pm 0.20 (0.56-1.83)	1.26 \pm 0.19 (0.73-1.83)	.989*
Tachycardia ratio	0.88 \pm 0.23 (0.6-2.26)	0.88 \pm 0.13 (0.4-1.47)	0.85 \pm 0.10 (0.52-1.06)	.428*

* Not significant

All the parameters recorded for assessing parasympathetic activity i.e. S: L ratio, 30:15 ratio, valsalva ratio and tachycardia ratio showed no significant difference between Group-I and Group-II, between Group-II and Group-III or between Group-I and Group-III.

Discussion

Assessment of cardiovascular autonomic reflexes is a critical element in evaluation of autonomic function in humans. Cardiovascular autonomic reflexes are essential for the maintenance of arterial blood pressure during the orthostatic stress (adopting a standing posture) and or preventing wide fluctuations of arterial blood pressure in response to stress, exercise and other adaptive responses.⁽¹³⁾

Perimenopause is a critical period in life during which striking endocrinological, somatic and psychological alteration occurs in the transition to menopause. The perimenopausal period encompasses the changes from the ovulating cycle to the anovulating cycle up to the cessation of menses and is marked by an irregularity of menstrual bleeding. In perimenopausal women, the serum estradiol levels do not decline until less than a year before menopause. The circulating estradiol levels are higher in men as compared to postmenopausal women.⁽¹⁴⁾

Menopause is the permanent cessation of menses as a result of the irreversible loss of a number of ovarian functions including ovulation and estrogen production. It has long been suggested that estrogen protects against atherosclerosis because the incidence of the cardiovascular disease is lower in women than men in the reproductive age group. In menopausal women, the risk of cardiovascular disease gradually increases due to the lack of estrogenic protective effect. The effect of the sympathetic stimuli on the uterus is highly variable depending on the estrogen and progesterone secretions.⁽¹⁵⁾

The sympathetic function tests conducted were blood pressure, blood pressure response to standing (orthostasis) and isometric handgrip strength test. The findings of the present study are that both baseline systolic and diastolic blood pressure altered

significantly in all the three groups, with postmenopausal having higher systolic and diastolic blood pressures as compared to those of pre or perimenopausal women. Our findings are consistent with the findings of Reckelhoff, who reported that the blood pressure is higher in men than in age matched premenopausal women. However, after menopause, blood pressure increases in women to levels even higher than that of men.⁽¹⁶⁾ The present study is also similar to the study of Higashi *et al.* who showed that both menopause and hypertension are associated with endothelial dysfunction and are risk factors for coronary heart disease.⁽¹⁷⁾

There is predominant sympathetic activity in postmenopausal women in comparison to the premenopausal women. The increase in the sympathetic activity in the menopausal women in the present study was consistent with those in the previous studies which were conducted by Rosano *et al.*⁽¹⁸⁾ and Farag *et al.*⁽¹⁹⁾

Perimenopausal women also showed an increase in the sympathetic activity and this was consistent with the findings of Kumar *et al.* with an increase in the total body norepinephrine spillover. There was a decrease in the norepinephrine-induced vasoconstriction after the estrogen supplementation.⁽²⁰⁾

Mercuro *et al.* also showed that surgical menopause induces a decline in cardiac vagal modulation with a shift towards sympathetic hyperactivity.⁽³⁾ Du *et al.* have also shown that cardiovascular protection by estrogen is partly mediated through modulation of autonomic nervous system.⁽²¹⁾

The parasympathetic tests done were standing to lying ratio, 30:15 ratio, valsalva ratio and tachycardia ratio. There was decrease in S/L ratio, valsalva ratio and tachycardia ratio in postmenopausal women in comparison to premenopausal women, although the difference was not statistically significant. The 30:15 ratio was almost equal in all the three groups.

The cause of decrease in the parasympathetic activity was a reduction in the cardiac parasympathetic tone in the older women as compared to that in the younger women. The arterial baroreflex control of the parasympathetic nerve activity was impaired in

postmenopausal women, which was consistent with the study of Saeki et al.⁽²²⁾

Bhat et al. in their study found significant alterations in sympathetic as well as on parasympathetic activity in postmenopausal period when compared with normal established range of response to various term of autonomic reactivity. The parameters reflecting predominantly sympathetic activity showed significant variations in postmenopausal women. The parasympathetic activity, *i.e.* Valsalva ratio, heart rate response, 30:15 ratio also showed significant variation in postmenopausal women.⁽²³⁾ All these findings are inconsistent with our study but the result of insignificant variation in S/L ratio is similar in both the studies.

Conclusion

As a female passes through different stages of her reproductive life- from premenopausal, through perimenopausal, to postmenopausal phases- altered autonomic reactivity may be present due to the effect of prevailing levels of sex hormones as the female transits through these phases. And cardiovascular autonomic reflexes are believed to be important for normal cardiac health in our day to day life.

The results of our study showed significant increase in sympathetic reactivity in perimenopausal and postmenopausal women- presumably as the sex hormone levels fall with onset of perimenopause. However, parasympathetic functions showed statistically insignificant change.

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