Original Article

Physiology

Evaluation of the Autonomic Functions in Perimenopausal and Menopausal Women

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ABSTRACT

Background and Objectives: The autonomic nervous system controls most of the visceral functions of the body through the sympathetic and the parasympathetic nerve fibers. In women, the withdrawal of the hormones in the perimenopausal and the menopausal period is gradual. This study was aimed to assess the physiological changes in the autonomic function tests in them.

Material and Methods: 60 normal women volunteers, perimenopausal and postmenopausal, were divided into 2 groups of 30 each, Group I (perimenopausal) and Group II (postmenopausal). The parasympathetic function tests included the standing to lying ratio (S/L ratio), the 30:15 ratio and the valsalva ratio. The sympathetic function tests like the blood pressure response to the isometric handgrip (IHG) and the blood pressure response to standing (BPS) were also done. The above 5 tests were recorded in the groups I and II subjects.

Results: By the independent sample 't' test, we found the mean difference of the S/L ratio, the 30:15 ratio, the valsalva ratio, the IHG test and BPS between the perimenopausal and the menopausal women, with a 'p' value >0.5.

Conclusion: The comparison of the autonomic functions in the perimenopausal and menopausal women showed no significant changes. The parasympathetic activity was reduced because the values which were obtained in the parasympathetic function tests were reduced to below the normal values. The sympathetic activity was increased in both the groups, indicating an increased risk of cardiovascular disease in women even before menopause.

Key Words: Autonomic functions, Menopausal women, Perimenopausal women

KEY MESSAGE

- This study highlights the importance of risk factor screening for cardiovascular diseases, even prior to menopause in women, in order to prevent it.

INTRODUCTION

The autonomic nervous system controls most of the visceral functions of the body through the sympathetic and the parasympathetic nerve fibers. The peripheral nerves mediate the autonomic control of the heart rate and the blood pressure and their influence on the uterus depends on the oestrogen and progesterone secretions [1]. The autonomic functions are altered, which is due to the gradual withdrawal of the hormones and a decline in the physical function due to aging [2].

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 [which can range from 2 to 10 years, the average being 6 years] 30-50 years. It is only in this stage that the menstrual periods are irregular, with a 30% reduction in oestrogen and a decrease in progesterone and when the normal ovulation becomes inconsistent [3].

Menopause is the total cessation of menstruation and this occurs between the age group of 45 and 60. Menopause is defined as the absence of menstrual periods for 12 consecutive months and thereafter [4].

Earlier study reports document the autonomic changes in the reproductive period with respect to the menstrual cycle [5,6,7] and pregnancy [8], but there is no proper documentation regarding the autonomic function tests in perimenopausal and menopausal women. This study was done to demonstrate the physiological changes in the autonomic function tests in perimenopausal and menopausal women.

MATERIALS AND METHODS

This study was conducted in the Department of Physiology, PSG Institute of Medical Sciences and Research (PSGIMS and R), Coimbatore. Prior to the commencement of the study, the permission of the Institute Research Council and the Institute Ethics Committee were obtained.

This study was carried out on 60 normal human women volunteers who were aged from 40 to 60 years. Subjects having diabetes, hypertension and other cardiac problems and those who did not have the natural course of menopause (i.e,) in whom hysterectomy was done, were excluded from the study. The subjects were randomly divided into two groups.

Group I consisted of 30 perimenopausal women who had menstrual periods once in 2 months or 3 months. Group II consisted of 30

menopausal women who had complete cessation of menstruation for a period of one year and more.

The nature of the study was explained to all the subjects and a written informed consent was obtained from all of them. The various autonomic function tests which were performed were the standing to lying ratio (S/L ratio), the 30:15 ratio, the valsalva ratio, the blood pressure response to a sustained isometric hand grip and the blood pressure response to standing. The first three tests detected the parasympathetic function and the next two detected the sympathetic function The following parameters were recorded by using BIOPAC systems, Inc, MANB5L3S, student version. The methodology which was adopted for the autonomic assessment was as under:

1. The Standing to Lying Ratio (S/L Ratio): Each subject was asked to stand quietly and to then lie down without any support, while a continuous ECG was recorded from 20 beats before to 60 beats after lying down. The point at which the subject started to lie down was marked. The S/L ratio was calculated as follows S/L Ratio = (longest R-R interval during 5 beats before lying down)/(shortest R-R interval during 10 beats after lying down). The maximum ratio of three trials was taken. An S/L ratio of >1.01 was taken as normal [9].
2. The 30:15 ratio: Each subject lay quietly for 3 minutes, then stood up and remained motionless. A continuous ECG was recorded and a point was marked to identify the point of standing. The 30:15 ratio was calculated by taking the ratio of the R-R interval at beat 30 and at beat 15 after standing [9]. Values which were >1.04 were taken as normal.
3. The Valsalva ratio: Each subject performed the valsalva maneouver for 15 seconds by blowing against a closed glottis through a mouthpiece which was attached to an aneroid Manometer and maintained a pressure of 40 mm Hg for 15 sec. Three trials were performed at intervals of 5 minutes. A continuous ECG was recorded 1 min before the maneouver (resting period), during the maneouver (strain period, 15 sec.) and 60 seconds subsequent to the strain period. The Valsalva ratio was calculated as the ratio of the maximum R-R interval after the strain to that of the shortest R-R interval during the strain, with values >1.21 being taken as normal [9].
4. The Blood Pressure Response to a Sustained Isometric Hand Grip Test, (IHGS): The subject was asked to apply pressure on a hand grip dynamometer for 1 minute at 30% of the maximal voluntary contraction and simultaneously, the blood pressure changes were observed. The difference between the diastolic blood pressure (DBP) just before the release of the contraction and that before the handgrip began was taken as a measure of the response. A rise in DBP to >10 mm Hg was considered as normal [9].
5. The Blood Pressure Response to Standing: In this test, the subject's blood pressure was measured with a sphygmomanometer while lying supine and immediately after standing up. The recording was done three times and the mean was calculated. The postural fall in the blood pressure was taken as a difference between the systolic pressure in the lying and the systolic pressure in the standing posture. The normal systolic fall would be upto less than 20 mmHg [10].

The data which were collected from the 60 subjects were subjected to statistical analysis by using the independent sample 't'- test.'P' values of less than 0.05 were considered as significant [11].

RESULTS

The comparison of the autonomic function tests in perimenopausal and menopausal women showed no significant changes with p values which were > 0.05, or as shown in [Table/Fig-1].The values which were obtained in the parasympathetic function tests were reduced to below the normal values, thus denoting a reduction in the parasympathetic activity. The values which were obtained in the sympathetic function tests were increased to above the normal values, thus denoting an increase in the sympathetic activity.

	S/L ratio	30:15 ratio	Valsalva ratio	IHGS Test (mm/Hg)	BPS (mm/Hg)
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
GROUP I [PM]	0.801±.06	0.804±.05	0.728±.08	13.20±5.7	13.00±6.9
GROUP II(M)	0.776±.07	0.825±.05	0.686±.09	13.30±5.5	15.20±7.3
'p'value	0.16*	0.12*	0.07*	0.94*	0.23*

[Table/Fig-1]: Comparison of Autonomic Functions in Perimenopausal subjects (n=30) and Menopausal women subjects (n=30)

PM-perimenopause: M-menopause,*P>0.05; S/L ratio-standing to lying ratio; IHGS-Isometric HandGrip Strength test; BPS – Blood pressure response to standing

DISCUSSION

Perimenopause is a critical period in life during which striking endocrinological, somatic and psychological alterations occur in the transition to menopause. The perimenopausal period encompasses the change from the ovulatory cycle to the anovulatory cycle upto the cessation of menses and is marked by an irregularity of menstrual bleeding. In perimenopausal women, the serum oestradiol levels do not decline until less than a year before menopause. The circulating oestradiol levels in the perimenopausal age group are higher as compared to those in the menopausal age group.

Menopause is the permanent cessation of menses as a result of the irreversible loss of a number of ovarian functions including ovulation and oestrogen production. The ovarian functions gradually become diminished and so, the oestrogen production from the granulosa cells of the ovary also reduces, but the follicle stimulating hormone levels are very highly raised. It has long been suggested that oestrogen protects against atherosclerosis, because the incidence of cardiovascular disease is lower in women than in men in the reproductive age group. In menopausal women, the risk of cardiovascular diseases gradually increases due to the lack of the oestrogenic protective effects and the incidence of cardiovascular disease is equal to that in men.It is not so in perimenopausal women because of the highly circulating oestradiol levels. The effect of the sympathetic stimulation on the uterus is highly variable, depending on the oestrogen and progesterone secretions [1].

The sympathetic function tests were the isometric hand grip strength test and the blood pressure response to standing. In our study, the blood pressure response to standing was below the normal mean values of 20mm of Hg systolic pressure, thus indicating an increase in the sympathetic activity, though it was not statistically significant. The increase in the sympathetic activity in the menopausal women was consistent with those in the previous studies which were done by Rosana et al [12] and Noha H Farag et al [13]. Perimenopausal women also showed an increase in the sympathetic activity and this was consistent with the findings of Sudhir K. et al [14] , with an increase in the total body norepinephrine spill over. There was a decrease in the norepinephrine induced vasoconstriction after the oestrogen supplementation.

In the isometric hand grip strength test, the blood pressure increase was due to an increase in the sympathetic activity and oestradiol does not have any effect on the muscle strength or the mobility.

The mechanisms by which oestrogen affects the cathecholeamine levels are also uncertain. The bulk of the circulating epinephrine appears to originate from the adrenal medulla and that of the norepinephrine from the sympathetic neuron, although under the condition of stress, the adrenal secretion of norepinephrine increases predominantly under neuronal control [15]. There is evidence that oestrogen modulates cathecholamine synthesis in the neural tissue [16] and that it also increases the urinary cathecholamine clearance in post-menopausal women.

The parasympathetic function tests like the standing to lying ratio, the 30:15 ratio and the valsalva ratio showed a decrease in the values which were statistically insignificant, thus indicating that the parasympathetic functions were diminished in both perimenopausal and menopausal women. The cause for the 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 earlier study reports of Saeki Y et al [17]. Our findings revealed that the sympathetic dominance and the decreased level of oestrogen in postmenopausal women produced the unfavourable alterations in the cardiac function.

CONCLUSION

From the present study, we conclude that the comparison of the autonomic functions in perimenopausal and menopausal women showed no significant changes .The parasympathetic activity was reduced because the values which were obtained in the parasympathetic function tests were reduced to below the normal values. The sympathetic activity was increased in both the groups, thus indicating an increased risk of cardiovascular disease in both the perimenopausal and menopausal women. This study highlights the importance of risk factor screening for cardiovascular diseases, even prior to menopause, in order to prevent it.

Limitations: This was a short duration study with a small sample size since it was a ICMR project.

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