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Role of estrogen on autonomic functions of postmenopausal women

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Abstract

Introduction and Objectives: Menopause is part of the aging process which is characterized by the natural cessation of menstruation. During this time the reduction in estrogen can cause symptoms and disorders that can interfere with their quality of life. Women are also more susceptible to cardiovascular diseases during this period that these ovarian hormones would be associated with a protective effect on the cardiovascular system. Postmenopausal women are at risk of developing cardiovascular complication associated with alterations in autonomic nerve functions. Thus, this study was aimed to test the role of estrogen in postmenopausal women that alters the autonomic functions.

Materials and Method: Healthy premenopausal and postmenopausal women with the age group of 40-55yrs were selected for the study. Parameters like Pulse rate, Blood pressure, Cold pressor test, Orthostasis for sympathetic functions and Heart rate response-difference, Standing/lying ratio, 30:15 ratio for parasympathetic functions are recorded. Serum estrogen was done for both the groups.

Results: There was a significant increase in the sympathetic activity and reduced parasympathetic activity in postmenopausal women. Sr.estrogen levels were reduced in postmenopausal women. Parameter 30:15 ratio, showed positive correlation with and Orthostasis showed negative correlation with Serum estrogen level in postmenopausal women.

Statistical Analysis: By student 't' test and Pearson Coefficient of Correlation.

Conclusion: There was a significant increase in the sympathetic activity and reduced parasympathetic activity in postmenopausal women due to decreased level of estrogen.

Keywords: Estrogen, Autonomic functions, Post-menopausal women

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Introduction

The average lifespan of a women in India is 65 years while in developed countries it is 80 years, so women of our country deserve special attention.(1) The World Health Organization defines menopause (mensis= month; pausis= pause) as the permanent cessation of menstruation due to the loss of ovarian follicular activity. A large number of postmenopausal women in our country are at risk of developing postmenopausal complication including cardiovascular disease associated with autonomic nerve dysfunctions.(2) Alterations in autonomic nerve functions may occur in menopausal women and it commonly affects cardiac vagal control and usually associated with sympathetic over activity.(3)

Autonomic control of heart plays an important role in the cardiac mortality. The ovarian hormones seem to play an important role in the autonomic control of heart rate and blood pressure. A reduction in ovarian hormones causes an autonomic imbalance and increases the risk of cardiovascular diseases. Thus, this study was aimed to test the role of estrogen in postmenopausal women that alters the autonomic functions.

Materials and Method

This study was undertaken to test the Autonomic functions in the premenopausal and postmenopausal women. Case-control type of study was done. The subjects were selected from Thanjavur Medical College Hospital and Raja Mirasudar Hospital, Thanjavur. This study was performed on healthy women of age 40-55 yrs. of premenopausal and postmenopausal women. The ethical committee clearance was obtained and an informed consent was taken after explaining the procedure to the subjects.

Exclusion Criteria: Subjects with Diabetics, Hypertension, Cardiovascular disorders, Renal disorder, Liver disorder, smoking, Alcohol, Oral Pills, Hormone Replacement therapy were excluded. A detailed history was obtained. Clinical examination was done. ECG was recorded by a simple compact Electrocardiograph (Eden) to assess the autonomic functions.

To assess sympathetic function Pulse rate, Blood pressure, Cold pressor test, Orthostasis are recorded and Heart rate response-difference, Standing/lying ratio, 30:15 ratio for parasympathetic functions were recorded. Oestrogen levels were determined in all the subjects by the method of electro-chemiluminescence immunoassay.

Statistical Analysis: Statistical analysis was done by using statistical package for social sciences (SPSS) XVIII version. The results were analysed by the student 't' test. Data's were expressed as mean with standard deviation.

Results

The results were analysed by the student 't' test. The statistical significance was considered $P < 0.05$.

Table 1: Tests for sympathetic function

Parameters		Study Mean±SD	Control Mean±SD	't' value	'p' value
PR		87.4±7.063	81.4±7.456	3.664	0.0005 <0.05 Significant
BP	SBP	120.65±7.25	114.9±9.71	-3.000	0.04 <0.05 Significant
	DBP	77.10 ± 5.728	74.75± 5.98	-1.794	0.07 >0.05 Not Significant
Orthostasis	SBP	103.07±7.960	106.35±10.68	-3.567	0.02 <0.05 Significant
	DBP	61.98±4.356	71.75±5.006	1.716	0.09>0.05 Not Significant
	Variation	17.30±8.259	8.55±10.749	-3.852	0.01<0.05 Significant
CPT	SBP	121.55±8.283	119.75±7.334	T=-1.029	0.307>0.05 Not Significant
	DBP	79.75±4.797	78±6.485	T=-1.372	0.174>0.05 Not Significant

Table 1 shows higher values of mean for three sympathetic function tests in study groups (postmenopausal women) than controls (premenopausal women) that reflects increased sympathetic activity.

Table 2: Tests for parasympathetic function

Sl. No	Sample	Mean	S.D	Statistical inference
1	**30:15 Ra**			T=4.936 .001<0.05 Significant
	Control (n=40)	1.0660	.07635	
	Study (n=40)	0.9675	.10051	
2	**S:L Ra**			T=1.062 .292>0.05 Not Significant
	Control (n=40)	3.7232	16.91081	
	Study (n=40)	0.8837	.11401	
3	**HRR-diff**			T=2.651 0.010<0.05 Significant
	Control (n=40)	12.9000	5.4716	
	Study (n=40)	10.6500	7.08031	

Table 2 shows parasympathetic function that reveals lower values of mean in study groups when compared to control groups. It suggests that decreased parasympathetic activity in postmenopausal women which is statistically significant.

Table 3: Serum Estrogen levels in the study and the control groups

Sl. No	Estrogen Pg/dl	Mean	S.D	Statistical Inference
1	Control (n=40)	90.3375	45.1545	T=4.639 .001<0.05 Significant
	Study (n=40)	45.0586	46.103	

This table shows decreased estrogen level in postmenopasal women**.**

Table 4: Correlation of Serum. Estrogen levels with 30:15 ratio in the study groups

Estrogen	Correlation value 'r'	'p' value
30:15 Ratio	0.3136	0.004

This table shows the positive correlation between the sr. estrogen levels of the study groups and the 30:15 ratio, which was found to be statistically significant.(p=0.004<0.05)

Table 5: Correlation of Sr. Estrogen levels with 30:15 ratio in the control group

Estrogen	Correlation value 'r'	'p' value
30:15 Ratio	-0.2584	0.107

30:15 ratio showed negative correlation with Sr.estrogen levels in the control groups. It was found to be statistically insignificant.(p=0.107<0.05)

Table 6: Correlation of Sr.Estrogen levels with Fall in the SBP of study groups

Estrogen-study	Correlation value 'r'	'p' value
Fall in SBP	-0.1170	0.472

Fall in SBP showed negative correlation with Sr.estrogen levels in the study groups. It was found to be statistically insignificant.($p=0.472<0.05$).

Discussion

The postmenopausal women often suffer from various menopausal complications including autonomic nerve dysfunction. The present study shows significant alteration in the autonomic function tests, that includes increased sympathetic and decreased parasympathetic activity respectively. In this study, Sr. estrogen levels of postmenopausal women showed significantly reduced values, when compared to the premenopausal women.

Anjali Nadir Bhat et al., have studied the autonomic functions in healthy postmenopausal women. Their results showed high significant variation in the pulse rate. The present study congruent with this literature cited. Similar findings were observed in the previous studies.[4,5,6,7] The supine SBP were found to be significantly elevated in the postmenopausal women that reflects the increased sympathetic activity.

Naher LAD[8] et al., performed sympathetic function tests in postmenopausal women and their results showed increased resting SBP and DBP, which again reflects the increased sympathetic activity. The present study is also congruent those found by Neves et al, Anjali Nadir Bhat et al, Shaher Lavi et al., This study also coincides with the previous study done by Ronald E. De Meersman[9] et al., who showed decreased systolic and diastolic blood pressure after estrogen replacement therapy. The present study showed significant fall in systolic BP after standing from lying position, which indicates sympathetic hyperactivity in postmenopausal women. The study also showed negative correlation of fall in SBP with Sr.estrogen in postmenopausal women, which was not statistically significant. Latifa Afrin Dill Naher et al., observed significant fall in systolic BP after standing from lying position and was found to be negatively correlated with the estrogen levels in postmenopausal women. In the present study, Cold pressor test (SBP, DBP) showed increased mean values, thus indicating an increase in the sympathetic activity, though it was not statistically significant. L. Mouret[10] et al., showed CPT triggers an increase in blood pressure in the healthy subjects, that may be due to increased cardiac output and increase in muscle sympathetic nerve activity. Similar findings were observed in the previous studies by Victor RG[11] et al. In this present study, 30:15 ratio in the postmenopausal women showed significantly reduced value and also showed significant positive correlation with Sr.estrogen level in postmenopausal women. Naher et al observed significant variation in postmenopausal and also showed positive correlation with Sr.estrogen level in postmenopausal women, reflecting reduced parasympathetic activity. The Standing / Lying ratio were found to be reduced, though it was not statistically significant. Anjali Nadir Bhat et al also observed the variation in S/L ratio, which was statistically insignificant. G.V. Lathadevi[12] et al showed reduced values of S/L ratio that was not statistically significant. The present study is in accordance with the literature cited.

The present study tested the hypothesis that estrogen exerts regulatory influence on ANS in postmenopausal women. Estrogen has a sympatho-inhibitory effect. Estrogens increases density as well as the function of presynaptic α2 adrenoreceptors, thereby resulting in significant decrease of nor-epinephrine induced responses. So, estrogen deficiency in postmenopausal women may lead to increased basal level of Nor-epinephrine and its vasoconstrictor responses.[13,14,15] Estrogen also acts peripherally to increase vasodilation by increasing the production of Nitric oxide and prostacycline or by decreasing the release of endothelin from endothelium.[16] It has direct effect on vascular smooth muscle to cause muscle dilatation.[17] Estrogen have effects on central Baroreflex mechanism. It facilitates the glutaminergic transmission in the nucleus tractus solitarious. It also increases the Baroreflex sensitivity as well as vagal tone. So, estrogen deficiency in postmenopausal women leads to decreased baroreflex activity, HRV, lowered parasympathetic activity.[18] The decreased level of estrogen shifts the autonomic balance toward the sympathetic dominance in the postmenopausal women.

Conclusion

The study concludes that there was a significant alteration in the Autonomic functions of postmenopausal women with the premenopausal women. The results obtained in the present study showed decreased parasympathetic activity and increased sympathetic activity in postmenopausal women. Estrogen levels were reduced in the postmenopausal women, when compared to the premenopausal women, which exerts the regulatory influence on Autonomic functions**.** Thus detecting autonomic dysfunction earlier in postmenopausal women we can improve the quality of life by proper medication and lifestyle modification**.**

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