The relationships of parasympathetic nerve function parameters with endogenous estrogen level in postmenopausal women


Abstract

Background: The risk of cardiovascular diseases gradually increases in postmenopausal women may be due to decreased level of estrogen in this period of life. This study was carried out to observe relationships of estrogen with parasympathetic nerve function parameters, which may help in early detection of parasympathetic nerve dysfunction in this group of women. Methods: This cross sectional study was carried out in the Department of Physiology, BSMMU, Dhaka from January 2007 to December 2007. For this study 60 subjects were selected among them 30 were postmenopausal women aged 45 to 60 years (study group) and 30 were premenopausal women aged 20 to 30 years (control group). Premenopausal women were studied during the follicular phase of menstrual cycle. Serum estrogen level was measured in each subject by MEIA (microparticle enzyme immunosorbent assay) method and parasympathetic nerve functions were evaluated by three non invasive cardiovascular reflex tests. Results: Estrogen level was significantly (p<0.001) lower in postmenopausal women than that of premenopausal women during follicular phase of menstrual cycle. Parasympathetic nerve function parameters such as heart rate response to deep breathing and heart rate response to standing were significantly (p<0.001 and p<0.01 respectively) lower in postmenopausal women than premenopausal women. Again, valsala ratio (r=0.531, p=0.003**), heart rate response to deep breathing (r=0.450, p=0.013*) and heart rate response to standing showed (r=0.419, p=0.021*) significant positive correlation with serum estrogen level in postmenopausal women. Conclusion: Therefore, parasympathetic nerve functions are related with serum estrogen level and reduced level of this hormone in postmenopausal women may lead to decrease in parasympathetic nerve function.

Key words
Postmenopausal women, parasympathetic nerve function, estrogen.

Introduction

Women, during their childbearing age have reduced risk of cardiovascular diseases than man. However, this risk gradually increases in postmenopausal women, which may be due to decreased level of estrogen in this period of life1. Moreover, alterations in autonomic nerve function have been observed in postmenopausal women that commonly affect cardiac vagal control2. Alteration in autonomic nerve function may lead to hypertension, cardiac arrythmia or sudden cardiac death3,4.

Cardiovascular autonomic balances are related to baroreceptor sensitivity and heart rate variability (HRV)4. It has been observed that in women, ovariectomy suppresses baroreflex sensitivity and HRV5. Estrogen supplementation increases baroreflex sensitivity and HRV as well as
parasympathetic control of the heart in postmenopausal women. Therefore, cardiovascular autonomic dysfunctions may be improved following hormone replacement therapy (HRT). However, some other group of investigators have demonstrated no improvement in cardiac autonomic dysfunctions following estrogen administration.

In several countries the relationships of decreased level of estrogen with autonomic nerve dysfunction has been observed. However, no published available data were reported in our country. In the present study, the relationships of parasympathetic nerve dysfunction with estrogen levels have been observed in healthy Bangladeshi postmenopausal women. So, this study may contribute to identify the parasympathetic nerve dysfunction in postmenopausal women population, which may also help the physicians to take appropriate measure for the improvement of health status.

Methods
The present cross sectional study was carried out in the Department of Physiology, BSMMU, Dhaka from January 2007 to December 2007. In this study a total number of 60 apparently healthy subjects were selected, of whom 30 postmenopausal women with age ranged from 45 to 60 years were included in the study group (group B) and 30 premenopausal women with age ranged from 20 to 30 years were selected as control group (group A2). Control group was studied during follicular phase (9th to 14th day) of menstrual cycle. The duration of natural and surgical menopause was at least one year and they were not on any form of HRT.

Objectives of the study were explained to each of the subject in details and then written informed consent was taken. Parasympathetic nerve functions of each of the subject were evaluated by cardiovascular autonomic nerve function test like heart rate response to valsalva maneuver, heart rate response to standing and heart rate response to deep breathing. Serum estrogen level of each subject was measured by MEIA method.

All the parametric variables were expressed as mean±SD (Standard Deviation). Comparison between the groups were done by unpaired students 't' test. 'r' value was obtained by Pearson's correlation coefficient. The statistical analysis was done by SPSS program version-11.5. "p" value <0.05 was considered as statistically significant.

Results
The mean (±SD) age and Body Mass Index (BMI) of the subjects are shown in Table 1. The mean value of estrogen was significantly (p<0.001) lower in group B (postmenopausal women) than that of group A2 (premenopausal women during follicular phase) (Figure 1).

Table 1: Age and BMI in different groups (n=60)

<table>
<thead>
<tr>
<th>Variables</th>
<th>A2 (n=30)</th>
<th>B (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>24.30±3.88 (20-30)</td>
<td>50.53±3.02 (47-60)</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>20.80±1.40 (18.4-22.94)</td>
<td>22.18±3.08 (18.42-28.20)</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD. Figures in parentheses indicate ranges

A2= Premenopause during follicular phase (control)
B = Postmenopause (study), n = Total number of subjects

Parasympathetic nerve function status had been observed in both the groups and comparisons were made among them (Table 2). The mean value of valsalva ratio was higher in group B than that of group A2, however the differences were not statistically significant. Significantly lower value of heart rate response to deep breathing (p<0.001) and
heart rate response to standing (p<0.01) were observed in group B than that of group A2.

Table 2: Parasympathetic nerve function parameters in different groups (n=60)

<table>
<thead>
<tr>
<th>Parasympathetic nerve function parameters</th>
<th>Group A2 (n=30)</th>
<th>Group AB (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate response to valsalvamaneuver (valsalva ratio)</td>
<td>1.41±0.18 (1.11-1.89)</td>
<td>1.44±0.32 (1.11-2.63)</td>
</tr>
<tr>
<td>Heart rate response to deep breathing (beats/min)</td>
<td>26.79±7.09 (11.83-39.57)</td>
<td>12.62±3.83*** (5.72-21.82)</td>
</tr>
<tr>
<td>Heart rate response to standing (30th: 15th)</td>
<td>1.20±0.26 (1.04-2.50)</td>
<td>1.07±0.08** (0.93-1.30)</td>
</tr>
</tbody>
</table>

Data are shown as mean ± SD. Figures in parentheses indicate ranges
A2 = Premenopausal during follicular phase (control)
B = Postmenopause (study)
*** = significant at the p<0.001, ** = significant at the p<0.01
n = Number of subjects

Valsalva ratio was positively correlated with serum estrogen level both in group B and in group A2 but the relationship was statically significant (p<0.01) only in group B (Figure 2).

Heart rate response to deep breathing showed significant (p<0.05) positive correlation with serum estrogen level in both group B and in group A2 (Figure 3).

Again, heart rate response to standing also showed significant (p<0.05) positive correlation with serum estrogen level in group B. In group A2 this relationship was negative and non significant (Figure 4).

Discussion
In this study serum estrogen level was significantly (p<0.001) lower in postmenopausal women compared to the follicular phase of the premenopausal women. Fadel et al. (2004) also observed similar findings in postmenopausal women in comparison to follicular phase of premenopausal women13.
Again, serum estrogen showed significant positive correlation with valsalva ratio, heart rate response to deep breathing and heart rate response to standing in postmenopausal women. Some group of investigators of different countries had also observed the relationship of the autonomic nerve function with estrogen level in postmenopausal women. However, they have used other non invasive parameters like time domain and frequency domain indexes of HRV. Neves et al. (2007) observed significant positive correlation of estrogen with HFnu (high frequency normalized unit) in postmenopausal women, which represent parasympathetic nerve function.

In premenopausal women heart rate response to deep breathing showed significant positive correlation with estrogen level during follicular phase. However, relation with valsalva ratio and heart rate response to standing were non significant. Anthony, David and Graham (2003) reported significant positive correlation of estrogen with all the absolute measures of HRV (heart rate variability) like LF, HF and TP (low frequency, high frequency and total power respectively) during follicular phase of premenopausal women. However, Matsumoto et al. (2006) observed non significant relationships of parasympathetic nerve functions with estrogen level during follicular phase.

In this study significant positive correlation of estrogen with parasympathetic nerve function parameters indicates that reduced parasympathetic nerve functions are associated with decreased level of estrogen in postmenopausal women and this also suggestive of decreased baroreflex activity and vagal tone. However, the role of estrogen on the modulation of the autonomic nerve function has not yet been established. Several investigators have demonstrated that estrogen has regulatory influences on parasympathetic nerve function.

It has been suggested that estrogen acts on central neural pathway of baroreceptor reflex arc and facilitates the baroreflex sensitivity as well as the activity. The exact central mechanisms involved in the baroreflex enhancement by estrogen have yet to be established. However, some investigators suggested that estrogen has facilitatory roles on glutamatergic neurotransmission in nucleus tractus solitarius (NTS) and thereby modulate the central baroreflexes and vagal tone. Therefore, decrease in baroreflex sensitivity and HRV may be the consequences of estrogen deficiency in postmenopausal women.

Conclusion
Postmenopausal women may suffer from alteration of parasympathetic nerve function due to lack of estrogen hormone and estrogen has positive relationships with parasympathetic nerve function. However, exact mechanisms involved for this impairment of autonomic nerve function in postmenopausal women cannot be elucidated from this type of study. Supplementation with estrogen hormones in this group of women can give a more conclusive finding.

References
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