Status of estradiol in premenopausal women with essential hypertension in Karkuk City: A cross-sectional study

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Abstract

High Blood Pressure (BP) results from a complex interaction of genetic, environmental and demographic factors. The level of endogenous estrogens may be a critical risk factor in hypertensive diseases. Estrogens exert an effect on the endothelium and smooth muscle cells in the vascular wall, where they inhibit cell proliferation and induce vasodilatation. The aim of this study is to assess the status of estradiol in women with HyperTension (HTN). The present study is a cross-sectional study that was carried out between 2011 to 2012 at Karkuk Teaching Hospital/Karkuk governorate/Iraq.

Parameters measured include serum estradiol and calculating Body Mass Index BMI) in premenopausal women with HTN. The results of this study shows a total of 100 Premenopausal women with HT were involved in this study G1: (n=100). A matching group of hundred apparently healthy women who were included as controls (n=100), Serum estradiol was significantly reduced in Premenopausal women with HT G1 when compared with controls (p < 0.05); a significant negative correlation was found between estradiol and Body Mass Index (n=100; r = 0.8; P< 0.05). In conclusion, women with HT were having low level of serum estradiol compared with controls; this estradiol was negatively correlated with body mass index. The above results suggest importance of hormone therapy in maintenance of vascular tone.

Keywords: Estradiol, hypertension, premenopose

INTRODUCTION

Blood Pressure (BP) in human population is distributed normally, and the cut-off point for high BP is arbitrary. In most cases, high BP results from a complex interaction of genetic, environmental and demographic factors. The recent search for genes that contributed to the development of essential hypertension (HTN) has found the disorder is polygonic in origin (Oparil, 1992).

Within the last decade, a decrease in mortality has been observed due to diseases developing on the background of atherosclerosis; however, despite this tendency, these diseases are still the main cause of death in many countries (Islami et al., 2011). Hence, it is necessary to apply prophylaxis, including, among other that the main risk factors of atherosclerosis are obesity and lipid disorders (Matyjaszczyk et al., 2011). Based on the results of studies, it was confirmed that the intensification of atherosclerotic changes is positively correlated with obesity and the levels of Low Density Lipoprotein (LDL) and Very Low Density Lipoprotein (VLDL) cholesterol, and negatively correlated with the level of HDL cholesterol, irrespective of race, age, and gender (Berenson, 1998).

Population studies show that among young women, morbidity due to ischemic heart disease is approximately 6 times lower compared to males in analogous age things, the control of risk factors. Many studies confirm groups (Gerhard and Ganz, 1995). Nevertheless, this gender-related difference decreases after menopause,
when the frequency of occurrence of atherosclerosis and arterial hypertension in females drastically increases (Hu et al., 1999; Mendelsohn and Karas, 1999). These observations suggest that the reduction in the level of endogenous estrogens after menopause may be a critical risk factor in these diseases. Studies of the genetic risk factors of cardiovascular diseases, including atherosclerosis, are still being continued. Although many candidate genes of cardiovascular diseases have been found, the role of genes participating in the impact of sex hormones still remains unclear. Estrogens exert an effect on the endothelium and smooth muscle cells in the vascular wall, where they inhibit cell proliferation and induce vasodilatation (Mendelsohn and Karas, 1999). Estrogens also affect the hepatic cells, resulting in decreased LDL cholesterol fraction (Lundeen et al., 1997; Mendelsohn and Karas, 1994) and increase in HDL cholesterol fraction in blood (Mendelsohn and Karas, 1999; Lundeen et al., 1997).

The physiological process of estrogen works by binding to estrogen receptors (Mendelsohn and Karas, 1999).

In this study, we aimed to describe Estradiol status and the correlation between BMI and estradiol in hypertensive pre-ovulatory women.

MATERIAL AND METHODS

This was a cross-sectional study conducted at the Teaching Hospital of Karkuk Medical College/Karkuk governorate/Iraq between September 2011 to September 2012. The protocol for the study was approved by the Ethical committee of Karkuk Medical College, and informed signed consent was given by each subject. A total of 100 essential hypertensive premenopausal female patients aged between 20-45 years, were enrolled in this study.

Exclusion criteria were that any Patients with previous history of cardiac, renal, hepatic, thyroid disease or hormonal disturbances were excluded. Other exclusion criteria included; pregnancy and breast feeding, acute infections and blood diseases.

The participants were asked to fast for 12 hours prior to blood sampling. The body weight and height were measured for all patients included. Body Mass Index was calculated by dividing the body weight over the square of the height (Kg/m$^2$).

Various blood samples were taken; the sera were separated by centrifugation at (3000 rpm) for 15 minutes. And the serum was stored frozen at -20°C until assay.

The blood samples were taken one day before ovulation, which was calculated by the “mean” of three consecutive menstrual cycles, with subtraction of 14 days to determine the date of ovulation.

Then each serum sample was analysed for estradiol. All assays were obtained by running duplicates for the test and standard. Estradiol was estimated using miniVIDAS Estradiol Kit (Biomerieux, France).

Patients with hormonal disturbance, renal disease, thyroid disease, or using antidepressant drugs or contraceptive pills were excluded from the study.

It should be mentioned that all study patients were diagnosed with essential hypertension. The data of the research were saved in Microsoft Excel Spread sheet and analyzed on the computer using Microsoft Excel program (2010) and SPSS (v.17).
RESULTS

A total of 100 women with essential hypertension included in hypertensive (HT) group, these were compared with 100 apparently healthy subjects who were included in the control-group the clinical criteria for both groups was shown in Table 1.

Serum Estradiol was significantly reduced (P < 0.05) in HT group when compared with the control group (P < 0.05) As in Table 2. Also a significant (n=100; r = 0.8; P< 0.05) negative correlation was found between Estradiol and body mass index in HT women as in Figure 1; however, this correlation was lost in healthy women.

DISCUSSION

HyperTensioN (HTN) is considered a major health problem that emerges from the wide occurrence of its cardiovascular complications (Rupal et al., 2014).

To our knowledge, this is the first study to show a reduced plasma estradiol levels in HT premenopausal women apart from other studies that show the same results but either in postmenopausal as in Schuit et al study (Schuit et al., 2004) or diabetic women as in Zinah and Al-Zaidi study (Zinah and Mahmood, 2011). This might indicate that lack of estrogens play a vital role in vascular arteriosclerosis.

Many studies show that the frequency of occurrence of cardiovascular diseases increases after menopause. It is considered that a decrease in endogenous estrogens is responsible for this unfavorable effect (Ferrero et al., 2003; Nordström et al., 2003). A few studies suggest that there is no reliable evidence for a rapid increase in morbidity due to Cardio Vascular Diseases (CVD) at postmenopausal age; however, a constant, proportional increase in the occurrence of these diseases is observed with age, caused by the co-existence of risk factors such as obesity, hypertension, lipid disorders, and glucose intolerance (Tworoger et al., 2006). Thus, the question of whether estrogens exert a direct effect on the development of cardiovascular diseases or whether this effect is related to their impact on lipidogram, arterial hypertension, and body weight, remains to be answered.

Clinical studies indicate that estrogens greatly affect the amount of fatty tissue. A decrease in their level is related to an increase in the amount of fatty tissue in women (Tworoger et al., 2006). It is noteworthy that estrogens may increase the level of HDL-cholesterol, which explains the lower frequency of occurrence of cardiovascular diseases in pre-menopausal women. This observation has not been confirmed based on the presented material.

Attempts were undertaken to take advantage of the beneficial effect of estrogens on the cardiovascular system in women by applying hormone replacement therapy (HRT).

In addition, the present data revealed an inverse correlation between serum estradiol level and Body Mass Index (BMI). Tworoger et al. (2006) suggested two hypotheses to prove the inverse correlation between BMI and estradiol level. First, a high BMI may be associated with ovulatory insufficiency beyond its known role in increasing ovulatory cycles. The hypothesis is also supported by epidemiological data suggesting that a BMI as low as 24 kg/m² is associated with an increased risk of ovulatory infertility (Tworoger et al., 2006). A second hypothesis may be through an indirect regulation by sex hormone binding globulin (SHBG). As SHBG declines, free estradiol should increase. Therefore, in response to...
decreased SHBG, follicle-stimulating hormone levels may
decrease to lower total estradiol production by the
ovaries, thus keeping free estradiol relatively constant.
Additionally, the molecular clearance rate of estradiol is
positively associated with weight, also potentially
reducing total estradiol levels (Nordström et al., 2003;
Tworoger et al., 2006).

There are only a small number of studies on the
differences in endogenous hormone levels between
racial/ethnic groups in the United States. Also, most of
the studies were in women during their ovulatory time
and not pre-ovulatory period and the women were not
diabetic (Nordström et al., 2003; Tworoger et al., 2006).

Even so, Stefania et al. (2005) studied the differences
in serum sex hormones levels in Caucasian and African-
American premenopausal women and concluded that
race is an important determinant of plasma sex hormone
levels, even after adjustment for differences in body size.
A significant association between endogenous estradiol
and HDL-C levels exists in premenopausal women,
independent of their race (Lamon-Fava et al., 2005).

In 2007, Ausmanas et al. (2007) studied estradiol,
FSH and LH profiles in nine ethnic groups of
postmenopausal Asian women and concluded that the
levels of FSH, LH and particularly of Estradiol differed
substantially among ethnic groups of postmenopausal
Asian women, but the clinical significance (if any) of
these differences remains to be investigated.

The main limitation of our study is the small number of
incident cases, which may yield a lack of statistical
power.

Conflict of Interest

The authors declare that they have no conflict of interest.

CONCLUSION

From this study, it can be concluded that Iraqi
hypertensive premenopausal women at their pre
ovulatory period exhibit a proatherogenic risk profile
because of their abnormal BMI, lower estradiol levels.

REFERENCES

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