

Assessment of Endometrial Thickness in Postmenopausal Women with and without Hypertension

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ABSTRACT :

BACKGROUND:

Hypertension in postmenopausal women is a risk factor for endometrial hyperplasia.

OBJECTIVE:

To examine whether the endometrium of hypertensive postmenopausal women is thicker than that of non hypertensive postmenopausal women, to determine whether this thickening is directly related to the antihypertensive drugs and whether is associated with abnormal pathology.

METHODS:

A Case control study of Forty five hypertensive asymptomatic postmenopausal women was conducted in Al Yarmouk Teaching Hospital, (22) were treated with B- blockers combination medication and (23) were treated with other medications. They were compared with each and with (25) non hypertensive women. All women were interviewed; blood tests were performed and endometrial thickness in antero-posterior diameter was measured by vaginal ultrasonography. Endometrial sampling had been taken for those with increased endometrial thickness more than 5mm.

RESULTS:

24.44% of hypertensive women and 4.00% of non hypertensive women had an endometrial thickness more than 5mm. There was no statistically significant difference between those who treated with medication including B- blocker and those who were treated with other medication. The histological findings were mainly of endometrial hyperplasia for those with thickened endometrium.

CONCLUSION:

Hypertension may have a role in endometrial thickness. We were unable to substantiate an association between the type of treatment administered and the increase in endometrial thickness. Those with increased endometrial thickness more than 5mm, the histological findings were mainly of endometrial hyperplasia.

KEYWORDS: hypertension, menopausal women, endometrial hyperplasia.

INTRODUCTION:

Endometrial cancer is the fourth most common cancer ranking behind breast, lung and bowel cancer and it's the eighth leading cause of death from malignancy in women. Over all about 2-3% of women develop cancer during their life time, (1,2)

Studies reported a four folds increase in

women. (3). A possible mechanism that might be responsible for endometrial thickness in patient incidence of hypertension in postmenopausal with hypertension, as well as in those with obesity and glucose intolerance is that of hyperinsulinemia, insulin resistance and hence to insulin like growth factor I, which has been related to cell growth and neoplastic progression (4,5). Long term treatment with conventional B-blockers either non-selective e.g. propranolol, or B1-selective, significantly decreased insulin sensitivity in hypertensive women. They alter the insulin secretion from pancreatic B-cells which plays an important role in controlling post load glycemia, so that more insulin is needed. B-Blockers also attenuate insulin in insulin resistant patients leading to

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>10% higher steady state plasma insulin level; the resulting hyperinsulinemia could down regulate the insulin receptors and consequently lower insulin sensitivity.^(4,6,7)

Transvaginal ultrasound is accurate in delineating endometrial thickness. No endometrial thickness threshold completely excludes the possibility of an early endometrial carcinoma, which can be present in women who have no PMB, but have been scanned for other reasons and found to have a thickened endometrium as an incidental finding.^(8, 9,10) Endometrial Aspiration has the advantage that it can be done as an outpatient procedure. Many physicians generally perform the endometrial biopsy without anesthesia, and most patients are able to tolerate this well. However, the use of a paracervical block, as well as non steroidal anti-inflammatory drugs, greatly improves the patient tolerance and compliance.⁽¹¹⁾

PATIENTS AND METHODS:

A case control study was conducted in Al-Yarmouk Teaching Hospital in the time period between March 2008 and June 2009.

Eighty asymptomatic women (no history of postmenopausal bleeding) who were at least one year after menopause were considered for enrollment in this study and divided in to the following three groups:

1. Women without hypertension.
2. Women with essential hypertension treated with a combination of medication including B-blockers.
3. Women with essential hypertension treated with other medication that did not include B-blockers. The non hypertensive control women were those who came for a routine gynecologic examination or who complained of gynecological symptoms other than vaginal bleeding, like vaginal discharge of genital infection, symptoms of urinary tract infection or symptoms of pelvic organ prolapsed. Women with essential hypertension treated with medication for at least one year duration were enrolled from the medical clinic. Specially designed questionnaire was used. Women were interviewed for a history of infertility, hormonal disturbance, smoking, and medical diseases. Blood pressure, weight and height were measured then BMI was calculated. Blood tests for fasting blood sugar and FSH level were performed. Vaginal ultrasonography with a 7.5 MHz probe was then performed for measuring the endometrial thickness in anterior-posterior diameter and to exclude an ovarian

pathology. For the purpose of this study an endometrial thickness more than 5 mm was considered thick. Endometrial sample was taken from a woman with a thickened endometrium and sent for histopathology. The sample was taken by sharman curette as an outpatient endometrial biopsy and if the patient refused or the procedure failed to obtain a biopsy because of cervical stenosis then dilatation and curettage was done under general anesthesia.

Other instruments (out patient endometrial aspiration) by using pipelle or vabra aspirators were not available during the period of study.

Exclusion criteria:

Diabetic women or women with an abnormal fasting blood sugar level.

Obese women (BMI >30).

Women who had been taken hormonal medications or hormonal replacement therapy during the last year.

Women with a history of hormonal disturbance, infertility or polycystic ovarian syndrome.

Women with any malignant disease or ovarian tumor, whether benign or malignant.

Smokers or who had smoked during the past year.

Finally seventy women were included in the study, (10) women were excluded because : (5) of them proved to have diabetes, three refused examination by TVUS and the last two discovered to have ovarian mass by ultrasound.

Statistical analysis:

The significance of differences of different percentage (data) was tested using person Chi-squared test (χ^2 - test).

The significance of differences for two independent means was tested using t- test.

Statistical analysis was considered significant when the P-value was less than 0.05.

RESULTS:

A total of eighty women were considered for enrollment in this study, ten of them were excluded for the reasons detailed in the method section. The age of the participants is ranged between 50 and 68 years.

Forty five women with hypertension enrolled in the study: 22 were treated with a combination of medication including B-blockers and 23 were treated with other medications. The two groups were compared with a group of 25 non hypertensive women.

As shown in Table -1- both hypertensive groups were similar to the control group in all aspects.

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Table 1: Characteristics of patient's medical history.

	Non-hypertensive group N=25	Hypertensive group N=45		
		With B-blocker combination medication	With other combination medication	Total
Age (years) \pm SD	61.60 \pm 4.97 (55.0-68.0)	62.68 \pm 5.22 (53.0-67.0)	62.87 \pm 5.36 (50.0-67.0)	62.78 \pm 5.23 (50.0-67.0)
Age at menopause (years) \pm SD	51.96 \pm 1.40 (48.0-54.0)	51.50 \pm 1.37 (49.0-54.0)	51.57 \pm 1.31 (48.0-54.0)	51.53 \pm 1.32 (48.0-54.0)
Age at menarche (years) \pm SD	12.80 \pm 0.76 (12.0-14.0)	12.91 \pm 0.97 (11.0-14.0)	12.57 \pm 0.95 (11.0-14.0)	12.73 \pm 0.96 (11.0-14.0)
Parity (number) \pm SD	8.68 \pm 1.68 (4.0-12.0)	8.09 \pm 1.54 (4.0-12.0)	8.22 \pm 1.68 (4.0-12.0)	8.16 \pm 1.59 (4.0-12.0)

Data presented as mean \pm SD (Range).

*Significant difference from non hypertensive using t-test for two independent means at 0.05 level of significance.

#Significant difference from hypertensive with B-blocker combination medication using t-test for two independent means at 0.05 level of significance.

Each of the three groups was compared with one another by using student-t-test.

Table 2 shows that although a diastolic blood pressure was similar among all women as a result of treatment for hypertension, the systolic blood

pressure was higher among the hypertensive group.

There was no significant difference in BMI between the hypertensive group and non hypertensive group.

Table 2: Patient's physical characteristic.

	Non-hypertensive group N=25	Hypertensive group N=45		
		With B-blocker combination medication	With other combination medication	Total
BMI(kg/m2) \pm SD	27.33 \pm 0.34 (26.6-28.1)	27.51 \pm 0.83 (25.8-29.1)	27.04 \pm 1.18 (25.4-29.0)	27.45 \pm 1.05 (25.4-29.1)
Body mass index				
Weight (kg) \pm SD	69.28 \pm 1.37 (68.0-72.0)	69.59 \pm 1.44 (66.0-71.0)	69.87 \pm 1.82 (65.0-75.0)	69.73 \pm 1.63 (65.0-75.0)
Height (cm) \pm SD	159.20 \pm 1.00 (158.0-160.0)	159.09 \pm 2.41 (155.0-166.0)	157.91 \pm 2.86 (153.0-166.0)	158.49 \pm 2.69 (153.0-166.0)
SBP (mmHg) \pm SD	129.80 \pm 3.38 (120.0-135.0)	149.55 \pm 7.85* (140.0-160.0)	150.43 \pm 8.25* (140.0-160.0)	150.00 \pm 7.98* (140.0-160.0)
Systolic blood pressure				
DBP(mmHg) \pm SD	79.80 \pm 2.27 (70.0-85.0)	80.45 \pm 6.35 (70.0-90.0)	81.83 \pm 5.80 (70.0-90.0)	81.67 \pm 6.12 (70.0-90.0)
Diastolic blood pressure				

Data presented as mean \pm SD (Range).

*Significant difference from non hypertensive using t-test for two independent means at 0.05 level of significance.

As shown Table 3 there was significant difference in FBS level between each group of hypertensive women and that of non hypertensive group. It was higher in the hypertensive group, but there was no significant difference in FBS level between each group of hypertensive women. FSH level was similar among the three groups.

Table 3 also shows that there was significant difference in endometrial thickness between each group of hypertensive women and that of the non hypertensive group, but there was no significant difference in endometrial thickness between women treated with B-blockers medication and those who treated with other medication.

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Table 3: Laboratory and ultrasonographic findings.

	Non-hypertensive group N=25	Hypertensive group N=45		
		With B-blocker combination medication	With other combination medication	Total
FBS level (mg/dl) \pm SD Fasting blood sugar	90.80 \pm 3.44 (80.0-100.0)	100.45 \pm 5.10* (90.0-110.0)	99.35 \pm 5.07* (90.0-110.0)	99.89 \pm 5.06* (90.0-110.0)
FSH level (mIU/ml) \pm SD Follicular stimulating hormone	61.04 \pm 11.36 (40.0-70.0)	59.68 \pm 10.96 (40.0-70.0)	60.78 \pm 9.14 (40.0-70.0)	60.24 \pm 9.97 (40.0-70.0)
Endometrial thickness (mm) \pm SD	2.32 \pm 0.85 (2.0-6.0)	6.55 \pm 5.52* (3.0-22.0)	6.39 \pm 6.46* (2.0-25.0)	6.47 \pm 5.95* (2.0-25.0)

Data presented as mean \pm SD(Range).

*Significant difference from non hypertensive using t-test for two independent means at 0.05 level of significance.

#Significant difference from hypertensive with B-blocker combination medication using t-test for two independent means at 0.05 level of significance.

As shown in Figure 1, the percentage of women with endometrial thickness (>5mm) in hypertensive group was 24.44%, while that of non hypertensive group was 4.00% which means

that there was a significant difference between the two groups by using Pearson Chi- squared test.

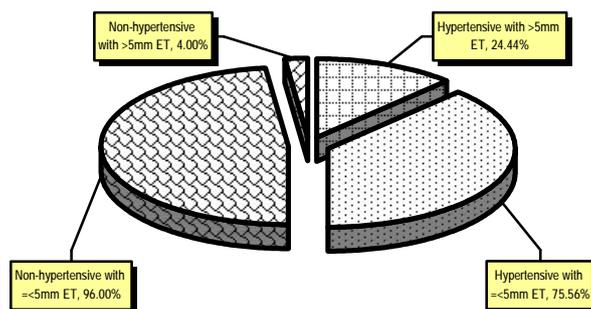


Figure 1: The percentage of endometrial thickness in the two groups (using Pearson chi- squared test, P = 0.030).

The histological findings of endometrial biopsies:

In hypertensive group, the total number was 45 patients, eleven of them had endometrial thickness more than 5mm and the histological findings were:

Five samples (simple endometrial hyperplasia)
Two samples (complex endometrial hyperplasia)
One sample (atypical endometrial hyperplasia)
Two samples (non-secretory endometrium), and the last one (proliferative endometrium).

In non hypertensive women (total number 25) only one patient had endometrial thickness >5mm and the histological finding was non secretory endometrium.

DISCUSSION:

The screening for endometrial cancer or its precursors may be justified for certain high risk women such as those receiving postmenopausal estrogen therapies without progestin. The apparent association between hypertension and endometrial cancer had been repeatedly arisen over the years. Transvaginal ultrasound is a non invasive method that yield detailed image of the uterus.⁽¹²⁾The main finding in this study was that 24.44% of the asymptomatic post- menopausal women, who were hypertensive, had increased endometrial thickness whereas only 4.00% of non hypertensive women had increased endometrial thickness which was significant. The cutoff point of endometrial thickness in this

study was 5mm. This was in agreement with a study done by Jacob Bornstein who concluded that 20% of hypertensive postmenopausal women were found to have increased endometrial thickness, forty five hypertensive women were enrolled in the study and other risk factors for endometrial cancer had been excluded.⁽⁵⁾ Our study was unable to verify a significant association between the type of treatment administered whether B-blockers were included or not and the increase in endometrial thickness which was in agreement with a study done by Jacob Bornstein.⁽⁵⁾ A possible mechanism that may be responsible for endometrial thickness in hypertensive women is that of hyperinsulinemia and insulin resistance⁽⁴⁾. The treatment with conventional B-blockers had detrimental effect on insulin sensitivity; this can be seen from several studies⁽⁴⁾. In large prospective atherosclerosis risk in communities cohort study after adjustment for all potentially important confounders showed that those treated with B-blockers had 28% higher risk of type 2 diabetes, compared to those taking no medication whereas users of thiazide diuretics, angiotensin converting enzyme inhibitors or calcium channel blockers were not at significantly higher or lower risk for subsequent type 2 diabetes than untreated hypertensive.⁽¹³⁾

Originally it was intended to enroll an additional group of untreated hypertensive women to distinguish between the role of hypertension itself and that of medication. Unfortunately it becomes clear that in most cases the treatment was initiated on discovery of hypertension and that's the reason we couldn't enroll a sufficient number of untreated hypertensive women.

In this study the endometrium of a woman with more than 5mm thickness was sampled to find whether it was associated with significant endometrial abnormality. Endometrial hyperplasia are generally considered premalignant disorders of the uterus which are clinically important because they may cause abnormal bleeding and precede or occur simultaneously with endometrial cancer, so they need long term follow up by TVUS⁽¹⁴⁾.

Clinically significant hyperplasia usually evolves within a background of proliferative endometrium as a result of protracted estrogen stimulation in the absence of progestin influence^(1,14).

Our study showed that there was significant difference in FBS level between hypertensive

and non-hypertensive groups which was higher in the former group, this may be explained by the concept of metabolic syndrome which suggests that a decrease in insulin sensitivity would not result in elevation of blood glucose level as long as pancreatic B-cells would secrete the necessary amount of insulin, however after a certain period of time B-cells would no longer be able to compensate for the increase in insulin resistance and type 2 diabetes would appear. The decrease in insulin sensitivity may be caused by the anti hypertensive drugs or the hypertension itself. (4)

Conclusion & Recommendation

CONCLUSION:

1. Hypertensive postmenopausal women were found to have increased endometrial thickness, which is assessed by TVUS when other risk factors (Diabetes, Obesity, Hormonal effect) have been excluded.
2. We were unable to substantiate an association between the type of the treatment whether B-blockers included or not and the increase in the endometrial thickness.

Recommendation

1. On the basis of the findings of this study; we suggest a study performing TVUS on discovery of hypertension in postmenopausal women before the antihypertensive treatment is begun to elucidate whether the hypertension itself or the treatment is responsible for the increase in endometrial thickness.
2. It's better to advice asymptomatic postmenopausal women who are hypertensive to be examined by periodic TVUS to measure the endometrial thickness.
3. It may be warranted to obtain endometrial biopsy specimens from hypertensive asymptomatic postmenopausal women with a thickened endometrium (>5mm) to know whether these women have an increased incidence of endometrial carcinoma or hyperplasia.

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