

DOOPLER ULTRASONOGRAPHY IN EVALUATING THE ENDOMETRIUM OF POSTMENOPAUSAL WOMEN RECEIVING HRT

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ABSTRACT

Objective: In this study we investigated the value of Doppler ultrasonography (DUSG) in evaluating the endometrium of postmenopausal women receiving hormone replacement therapy (HRT).

Material and Method: Sixty-five postmenopausal women constituted the material of our study. Pelvic DUSG was used to evaluate endometrial thickness and resistance index (RI) values before and after one year of hormone replacement therapy HRT. Forty-two patients completed the study and statistical analysis was performed using paired t-test and variables using multiple regression analysis.

Results: Endometrial thickness was measured as 3.5(1.5 mm after one year of therapy. The increase in thickness was statistically significant ($p<0.05$). Although there was a slight decrease in RI values, this finding was not considered to be statistically significant ($p>0.05$).

Conclusion: In this study we concluded that uterine artery RI does not change significantly after HRT; this conclusion contradicts other studies in the literature. This difference may be due to the short duration of menopause in our study group.

Key Words: Doppler ultrasonography, Menopause, HRT

INTRODUCTION

Menopause is a milestone affecting women's health both physically and psychologically. Cultural and social attitudes and beliefs are important in the way a woman accepts this era (1).

The necessity of regular evaluation of the endometrium and breast in postmenopausal women using hormone replacement therapy (HRT) is universally acknowledged. Methods and intervals of evaluation are still controversial.

Doppler ultrasonography (DUSG) is an acceptable method in detecting gynaecological malignancies (2). Low vascular impedance due to angiogenesis in the tumor and high diastolic blood flow is typical for malignancies. However, diastolic blood flow is lowered and almost absent because of the atrophic endometrium and increased vascular impedance is present in the uterine artery in postmenopausal women (3,4).

In this study we aimed to investigate the effects of HRT on the endometrium and uterine artery perfusion.

MATERIAL AND METHODS

Sixty-five healthy postmenopausal women with an age range 29-67 presenting to the Haydarpaşa Numune Hospital Outpatient Menopause Clinic constituted the material of our study. None had received HRT before and at least one year had passed after the onset of menopause. Criteria for inclusion in the study group were: 1. FSH > 40 IU/L, 2. A minimum of one year's amenorrhea, 3. E2 < 50 pg/ml.

Blood lipids, fasting glucose, liver and kidney function tests and hemogram were performed and mammography, bone mineral density, pelvic Doppler USG and pap-smears were evaluated in all women before starting HRT.

All women received oral estradiol valerat for 21 days with cyproterone acetate for the last 10 days in a cyclic-sequential regimen. 1g of oral calcium was added. Routine follow-ups were scheduled on the 3rd, 6th and 12th months.

Blood samples were checked on 3rd and 6th months and every parameter including pelvic Doppler USG was reevaluated at the end of the 12th month.

Doppler USG was evaluated using a colour Doppler Toshiba Sonolayer SSA 270-A with a 7.5 mHz transducer both before and after HRT. We assessed the resistance index (RI) in the uterine artery. Endometrial thickness was measured from the thickest part of the longitudinal axis of the uterus. Control Doppler ultrasonographies were performed on the 20-21th days of the cycle.

Statistical analysis was performed using paired t-test and variables using multiple regression analysis.

RESULTS

Forty-two patients completed the study. The average age of the 42 patients was 51 and the average age of menopause was 48. The average duration of menopause was 4.4 years. The patients selected had not received HRT before.

The mean endometrial thickness measured using transvaginal Doppler ultrasonography

before HRT was found to be 3.5 ± 2.1 mm. Endometrial biopsies were performed in 2 patients with endometrial thicknesses > 5 mm. Pathology reports of their samples showed inactive endometrium in both. The average uterine RI values were 0.84 ± 0.009 (Range 0.70-1.00) in this group.

Endometrial thickness after one year of HRT was measured as 5.71 ± 1.5 mm (Range 3.60-11.3 mm) and mean uterine artery RI values were 0.79 ± 0.05 (Range 0.70-0.88).

By using multiple regression analysis to compare uterine artery RI values with endometrium thickness, duration of menopause, and age, we found no correlation ($p > 0.05$). The result was the same for correlation analysis.

The increase in endometrial thickness after HRT was statistically significant ($p < 0.05$). Although RI values dropped after HRT this decrease was not considered to be statistically significant ($p > 0.05$).

Endometrial biopsies were performed in 15 patients with endometrial thickness > 5 mm. After HRT pathology reports of these samples revealed inactive endometrium in 8, proliferative endometrium in 1 and secretory endometrium in 6 patients.

A positive correlation existed between age and duration of menopause whereas duration of menopause and endometrial thickness showed negative correlation.

DISCUSSION

Evaluation of the endometrium using transvaginal ultrasonography before and during use of HRT is a commonly accepted method. Recently Doppler ultrasonography is used to detect endometrial pathologies (1,2,5).

In a study performed by Kurjak et al (6) the average RI of postmenopausal women with duration of menopause between 1 to 5 years not receiving HRT was 0.89, whereas this value was 0.94 for women with duration of menopause > 16 years. The mean RI was 0.85 for women receiving HRT for 1 to 5 years and 0.83 for women receiving HRT for over 6 years. This

study showed that RI decreased as the duration of menopause increased.

Bonilla et al showed that the mean RI fell to $87\% \pm 4\%$ of baseline values during the first month of therapy (7). Their findings suggested that the increase in vascular flow occurred even in women who began HRT long after menopause. Jakap stated that the positive vascular changes and increased peripheral perfusion in women taking HRT detected by Doppler ultrasonography are due to the vasodilator effect of oestrogen leading to cardiovascular and cerebrovascular protection (8). While studies show that sequential combined HRT lowers arterial impedance (9), the same effect is not seen in continuous HRT and RI values are unchanged (10,11). However, Doren et al showed that continuous HRT did lower uterine RI values (12). In a study by Bekavac et al, analysis of uterine arteries flow velocities showed a significant positive correlation between RI and years of menopause with a higher value for patients with longer menopause duration. After six months of HRT, plasma estradiol concentrations inversely correlated with RI of uterine arteries. They concluded that Doppler studies of the uterine arteries could provide specific and precise pathophysiological information to assess blood flow variations in correlation with combined HRT (13). Kurjak et al's study also confirmed these findings and they concluded that uterine artery RI does not change significantly in the first postmenopausal years thus supporting the thesis that the aging process initially affects the uterus less than the ovary. Furthermore, they also noted that proper hormonal stimulation could even delay this aging process (5). In our study we found that mean uterine artery RI was 0.84 before HRT. This decreased to 0.79 after HRT but the difference was not considered to be statistically significant ($p > 0.05$). This may be caused by the short duration of menopause of the patients in our study group.

Varner et al (14) studied 80 postmenopausal women and performed endometrial biopsies in 20 patients with endometrium thickness of more than 4 mm and compared the pathological results with transvaginal sonographic scanning. They found proliferative, secretory or hyperplastic endometrium and in one case low-grade

carcinoma. We performed endometrial biopsies in 15 cases with endometrial thickness > 5 mm and found inactive endometrium in 8, proliferative endometrium in 1 and secretory endometrium in 6 of these patients.

In our study, mean endometrium thickness was 3.5 ± 2.1 mm before and 5.7 ± 1.5 mm after a year of HRT. This increase was statistically significant ($p < 0.05$). There was an inverse correlation between duration of menopause and endometrial thickness. This finding was congenial with the results of other authors (15-17).

Sheth et al (18) investigated if endometrial blood flow analysis could be used to differentiate between benign and malignant causes of endometrial thickening in postmenopausal women. They concluded that low-impedance arterial flow is observed in various diseases of the endometrium, but that there is an overlap between the RI of benign and malignant lesions.

We concluded that although HRT lowers uterine artery RI values slightly, the difference cannot be considered to be statistically significant. Transvaginal USG together with Doppler ultrasonography is useful in the evaluation of women receiving HRT and will reduce the number of invasive procedures performed.

REFERENCES

1. Danska A, Szpurek D, Kedzia H, Spaczynski M. Doppler USG for detection of pathologic changes in uterine body endometrium. *Ginekol-Pol* 1997; 68: 604-609.
2. Bourne T, Campbell S, Steer CV, Royston P. Detection of endometrial cancer by TV USG with color flow imaging and blood flow analysis. A preliminary report. *Gynecol Oncol* 1991; 40:253-225.
3. Rotmensch S, Copel JA, Hobbins JC. Introduction to Doppler Velocimetry in obstetrics. *Obstet Gynecol Clin North-Am* 1991; 18:823-843.
4. Fleischer AC. *Sonography in Obstetrics and Gynecology. Principles and Practice.* New Jersey: Appleton and Lange, 1996:863-864
5. Kurjak A. Endometrial carcinoma in postmenopausal women. Evaluation by TV color Doppler USG. *Am J Obstet Gynecol* 1993; 169:1597-1603.

6. Kurjak A, Kupesic S. Ovarian senescence and its significance on uterine and ovarian perfusion. *Fertil Steril* 1995; 64:532-537.
7. Bonilla MF, Marti MC, Ballester MJ, Raga F. Normal uterine arterial blood flow in postmenopausal women assessed by TV color Doppler sonography: the effect of HRT. *J Ultrasound Med* 1995; 14:497-501.
8. Jakap A Jr. Management of menopause and HRT by ultrasound. *Eur J Obstet Gynecol Reprod Biol* 1997; 71:155-162.
9. Van Baal WM, Kenemans P, Stehouwer CD, Peters-Muller ER, van Vugt JM, van der Mooren MJ. Sequentially combined hormone replacement therapy reduces impedance to flow within the uterine and central retinal arteries in healthy postmenopausal women. *Am J Obstet Gynecol* 1999; 181:1365-1373.
10. Tanawaltanacharoen S, Panyakhamlera K, Chaikittisilpa S, Taechakraichana N, Limpaphayom KK. Uterine blood flow response to hormonal replacement therapy in asymptomatic postmenopausal women: a transvaginal Doppler Study. *J Med Assoc Thai* 2000; 83:368-373.
11. Zalud I, Conway C, Shulman H, Trinca D. Endometrial and myometrial thickness and uterine blood flow in postmenopausal women: the influence of hormonal replacement therapy and age. *J Ultrasound Med* 1993; 12:737-741.
12. Doren M, Suselbeck B, Schneider HP, Holzgreve W. Uterine perfusion and endometrial thickness in postmenopausal women on long-term continuous combined estrogen and progestogen replacement. *Ultrasound Obstet Gynecol* 1997; 9:113-119.
13. Bekavac I, Kupesic S, Mihaljevic D, Kurjak A. Vascular impedance of uterine, inferior vesicle, and ophthalmic arteries in postmenopausal women receiving hormonal replacement therapy: comparative Doppler study. *Croat Med J* 2000; 41:235-239.
14. Varner RE, Sparks JM, Cameron JD, Roberts LL, Soongs J. Transvaginal sonography of the endometrium in postmenopausal women. *Obstetrics Gynecol* 1991; 78:195-199.
15. Jones KP. Estrogens and progestins: What to use and how to use it. *Clinical Obstet Gynecol* 1992; 35:871-883.
16. Sobel NB. Progestins in preventive hormone therapy. Including pharmacology of the new progestins, desogestrel, norgestimate, and gestodene: are there advantages? *Obstet Gynecol Clin North Am* 1994; 21:299-319.
17. Colditz GA, Elgan KM, Stampfer MJ. HRT and risk of breast cancer. Results from epidemiologic studies. *Am J Obstet Gynecol* 1993; 168:1473-1480.
18. Steth S, Hamper UM, McCollum ME, Caskey CI, Rosenshein NB, Kurman RJ. Endometrial blood flow analysis in postmenopausal women: Can it help differentiate benign from malignant causes of endometrial thickening? *Radiology* 1995; 195:661-665.