Uterine Blood Flow Response to Hormonal Replacement Therapy in Asymptomatic Postmenopausal Women : A Transvaginal Doppler Study

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Abstract

To evaluate the effect of continuous hormonal replacement therapy (HRT) on Doppler parameters of uterine blood flow in asymptomatic postmenopausal women. Thirty-eight asymptomatic postmenopausal women were recruited into the study from the outpatient menopause clinic, Department of Obstetrics and Gynaecology, Faculty of Medicine, Chulalongkorn University. The study population was divided into 20 cases without any HRT (group 1) and 18 cases using continuous conjugated equine estrogen 0.625 mg/day combined with medroxyprogesterone acetate 2.5 mg/day (group 2). The duration of HRT was 21.3 $\pm$ 9.5 (13–56) months. A transvaginal colour flow imaging system (ALOKA SSD-2000 MultiView, Tokyo, Japan) was used to assess uterine blood flow. Quantitative data from areas of colour were evaluated by pulsed Doppler spectrum analysis. Resistance indices (RI) were measured as indicators of uterine perfusion. Both groups were statistically similar with respect to age, parity, age at menopause, height and weight. The endometrial thickness in group 1 and 2 were 3.8 $\pm$ 0.8 and 4.1 $\pm$ 0.6 millimetres, respectively. The left uterine artery RIs of group 1 and 2 were 0.86 $\pm$ 0.08 and 0.84 $\pm$ 0.07, respectively ($p = 0.33$) The right uterine artery RIs of group 1 and 2 were 0.87 $\pm$ 0.07 and 0.83 $\pm$ 0.06, respectively ($p = 0.06$). In conclusion, continuous HRT had a non-significant influence on uterine blood flow in the postmenopausal women.

Key word : Uterine Blood Flow, Hormonal Replacement Therapy, Transvaginal Doppler

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The menopausal period is the phase of a woman's life which makes the transition from being reproductive to non-reproductive. In this period, several organs undergo degenerative changes which are caused by estrogen deficiency. Postmenopausal women show significantly higher whole blood viscosity, plasma viscosity and red cell rigidity while there is no significant rise in the hematocrit and plasma fibrinogen. The postmenopausal period, therefore, is associated with significant change in blood rheology(1). It is likely that blood perfusion of the genital organs decreases during this period;

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the impedance to blood flow in the uterine arteries increases after the cessation of menses[2,3].

Hormonal replacement therapy (HRT) is being increasingly used in postmenopausal women. The influence of HRT on the postmenopausal endometrium has been widely studied[4-6]. To date, although a thick endometrium may be a sign of pathological processes, no morphological features that are unique to malignant disease have been identified[7]. Recently, the use of colour flow imaging and blood flow analysis has been reported to help in detection of endometrial carcinoma in women with postmenopausal bleeding[2,8,9]. However, in one study no Doppler variable differentiated better between benign and malignant or between normal and pathologic endometrium than did endometrial thickness as measured by ultrasonography[10].

Although there are increasing data on the value of transvaginal colour flow Doppler in symptomatic postmenopausal women, knowledge of the long-term effects of HRT on uterine perfusion is limited. The first report which showed that HRT reduced arterial impedance and decreased vascular tone in postmenopausal women was published in 1990[11]. As a matter of fact, there are only a few studies dealing with the long-term effects of HRT on uterine circulation[12-15]. We conducted the present study to evaluate the effect of continuous HRT on Doppler parameters of uterine blood flow and endometrial thickness in asymptomatic postmenopausal women.

MATERIAL AND METHOD

Asymptomatic postmenopausal women were included in the study from the outpatient menopause clinic, Department of Obstetrics and Gynaecology, Faculty of Medicine, Chulalongkorn University. After explanation of the nature of the study, the patient voluntarily signed an informed consent statement. The study population was divided into two groups :

Group 1 Postmenopausal women without any HRT.

Group 2 Postmenopausal women using continuous combined HRT (Conjugated equine estrogen 0.625 mg/day combined with Medroxy-progesterone acetate 2.5 mg/day).

High-frequency transvaginal ultrasonographic examinations with 5-MHz transducer were performed on all patients. Only patients who had thin endometrium of < 5 millimetres, which was considered normal and did not necessitate endometrial biopsy for confirmatiom, were included in the study. Patients with abnormal ultrasonographic findings, such as uterine fibroid or ovarian tumour, were excluded from the study. A transvaginal colour flow imaging system (ALOKA SSD-2000 MultiView, Tokyo, Japan) was then used to explore uterine blood flow. We detected the flow velocity waveform of the main branch of the uterine arteries lateral to the supravaginal portion of the cervix, in the longitudinal plane, on both sides of the uterus. Quantitative data from areas of colour were evaluated by pulsed Doppler spectrum analysis. The angle of the transducer was adjusted to obtain a maximum Doppler frequency shift. Resistance indices [(systole – end diastole)/systole] were measured as indicators of uterine perfusion. All examinations were performed by the same investigators (S.T.).

The results of blood flow characteristics in the study and control groups were compared by means of the two-sample *t*-test ; a p-value of < 0.05 was considered significant. Results were presented as mean and standard deviation.

The study was approved by the Ethical Committee of the Faculty of Medicine, Chulalongkorn University.

RESULTS

A total of 38 asymptomatic postmenopausal women were enrolled, 20 cases were in group 1 and 18 in group 2. Table 1 shows the patient characteristics of each group. Both groups were statistically similar with respect to age, parity, age at menopause, height and weight. The duration of HRT in group 2 was 21.3 ± 9.5 (13-56) months.

The measurements of endometrial thickness and RI of both left and right uterine arteries were done in all patients (Fig. 1, 2). In group 1, endometrial thickness was 3.8 ± 0.8 (2.4-5.0) millimetres, compared to 4.1 ± 0.6 (3.0-5.0) millimetres in group 2. The thickness of the endometrium in group 2 seemed to be larger, but these cannot be compared because of the inclusion criteria of < 5 millimetres of endometrial thickness in our study.

The resistance indices of blood flow in both uterine arteries are shown in Table 2. In group 1, the left uterine artery RI was 0.86 ± 0.08 and the right uterine artery RI was 0.87 ± 0.07. In group 2, the left uterine artery RI was 0.84 ± 0.07 and the right uterine artery RI was 0.83 ± 0.06.

Table 1. Patient characteristics.

	Group 1 (N=20) Mean ± SD (Range)	Group 2 (N=18) Mean ± SD (Range)	Significance
Age	53.1 ± 4.6 (45 – 62)	55.2 ± 5.2 (42 – 62)	NS
Parity	2.8 ± 1.7 (0 – 7)	2.5 ± 1.5 (0 – 5)	NS
Age at Menopause	49.4 ± 3.3 (43 – 54)	48.6 ± 3.4 (38 – 53)	NS
Height (cm)	155.1 ± 5.5 (145.8 – 168.0)	153.2 ± 4.0 (145.0 – 160.0)	NS
Weight (Kg)	58.2 ± 9.7 (45.0 – 83.0)	56.7 ± 9.3 (38.0 – 84.0)	NS

NS : No significance

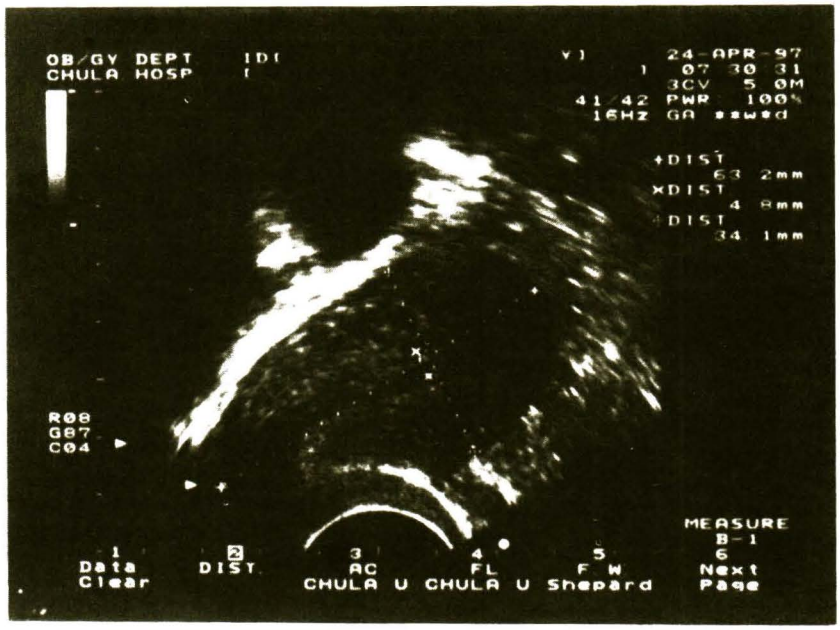

Fig. 1. Transvaginal ultrasound shows endometrial thickness (cursors x) in asymptomatic postmenopausal women, measuring 4.8 mm.

DISCUSSION

Transvaginal ultrasonography makes it possible to show pelvic structures precisely. Additionally, with colour and pulsed Doppler ultrasonography, it is easy to evaluate the quality of blood flow in the uterine or any other pelvic vessels. Thus, Doppler examination adds functional information about morphology obtained with B-mode ultrasonography

The aging process effected the uterine artery blood flow. Several studies showed the effects of HRT on uterine circulation. Bourne et al described the influence of transdermal estrogen and sequential oral norethisterone acetate on uterine artery blood flow after 6 weeks of HRT[11]. Pirhonen et al concluded that the duration of treatment in relation to menopause, discontinuance of HRT, and mode of treatment modified both the normal post-

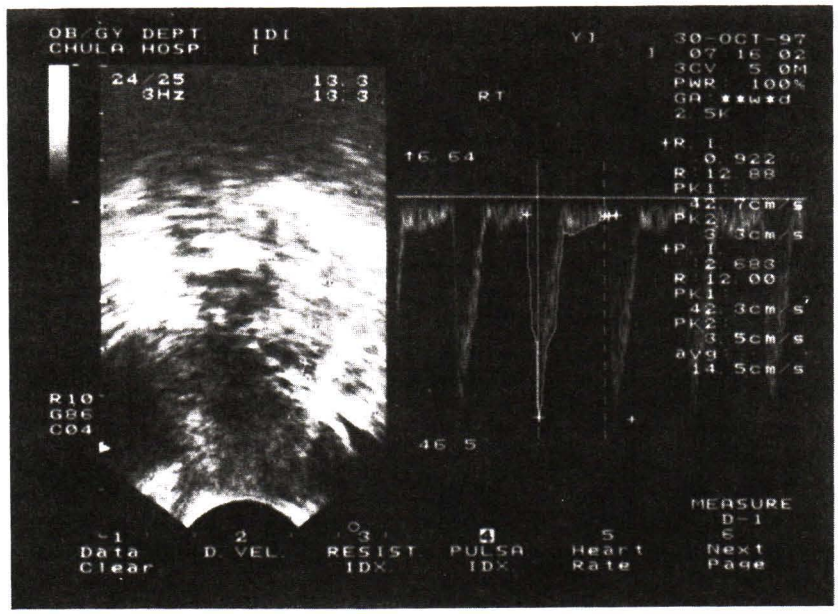

Fig. 2. Uterine artery blood flow velocity waveforms on transvaginal pulsed Doppler ultrasound in asymptomatic postmenopausal women ; RI = 0.922.

Table 2. Resistance index of uterine artery.

	Group 1 (N=20) Mean ± SD (Range)	Group 2 (N=18) Mean ± SD (Range)	Significance (p-value)
Left uterine artery	0.86 ± 0.08 (0.70 – 0.96)	0.84 ± 0.07 (0.72 – 0.93)	NS (0.33)
Right uterine artery	0.87 ± 0.07 (0.73 – 1.00)	0.83 ± 0.06 (0.68 – 0.93)	NS (0.06)

NS : No significance

menopausal endometrial thickness and the uterine vascular resistance[12]. Later, Zalud et al found no statistically significant difference of uterine blood flow between postmenopausal women with and without HRT[13]. Pines et al concluded from their study that the peripheral hemodynamic effects of HRT, such as vasodilatation, are transient, whereas, the central effects (increased inotropism) are long lasting[17]. Our study attempted to establish the influence of continuous HRT on uterine blood flow. We also found the difference of uterine artery RI in each group, but this difference did not reach statistical significance. Except for the reason explained by Pines et al, another possibility may be that the sample size in our study was too small to gain enough statistical power to detect the difference of uterine artery RI between these two groups.

More studies are required to clarify the effects of HRT on peripheral resistance. Attention should also be paid to the therapy protocol such as the beginning, the duration, and the mode of therapy. The normal values of endometrial thickness and uterine artery RI in postmenopausal women, both with and without HRT should be established because these may be useful aids for screening and detection of endometrial carcinoma in this population.

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ผลของการให้ฮอร์โมนทดแทนต่อการไหลเวียนโลหิตของมดลูกในสตรีวัยหมดระดูที่ไม่มีอาการผิดปกติ : การศึกษาคลื่นเสียงด็อพเพลอร์ โดยการตรวจทางช่องคลอด

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ในการประเมินผลของการให้ฮอร์โมนทดแทนที่มีต่อการไหลเวียนโลหิตของมดลูกโดยศึกษาคลื่นเสียง Doppler ได้ทำการคัดเลือกสตรีวัยหมดระดูที่ไม่มีอาการผิดปกติจำนวน 38 รายเข้าร่วมโครงการ โดยแบ่งเป็น 2 กลุ่มได้แก่ กลุ่มที่ 1 เป็นสตรีที่ไม่เคยได้รับฮอร์โมนทดแทน จำนวน 20 ราย และกลุ่มที่ 2 เป็นสตรีที่ได้รับฮอร์โมนทดแทนแบบต่อเนื่องโดยรับประทาน conjugated equine estrogen ขนาด 0.625 มิลลิกรัมต่อวัน ร่วมกับ medroxyprogesterone acetate ขนาด 2.5 มิลลิกรัมต่อวัน จำนวน 18 ราย โดยระยะเวลาที่ได้รับฮอร์โมนทดแทนเฉลี่ยเท่ากับ 21.3±9.5 (13–56) เดือน สตรีทุกรายได้รับการตรวจคลื่นเสียงความถี่สูงด้วยเครื่อง ALOKA SSD–2000 MultiView ของประเทศญี่ปุ่น และใช้ระบบ colour flow imaging เพื่อตรวจดูการไหลเวียนโลหิตภายในเส้นเลือดแดง uterine artery และใช้คลื่นเสียง Doppler วัดค่า Resistance index (RI) เพื่อประเมินการไหลเวียนโลหิตที่มายังมดลูก

พบว่าในสตรีทั้งสองกลุ่มไม่มีความแตกต่างกันในเรื่องอายุ จำนวนบุตร อายุเมื่อหมดระดู ส่วนสูงและน้ำหนัก ความหนาของเยื่อบุโพรงมดลูกในสตรีกลุ่มที่ 1 และ 2 มีค่าเท่ากับ 3.8±0.8 และ 4.1±0.6 มิลลิเมตร ตามลำดับ ส่วนค่า RI ของเส้นเลือดแดง uterine artery ข้างซ้ายในสตรีกลุ่มที่ 1 และ 2 มีค่าเท่ากับ 0.86±0.08 และ 0.84±0.07 ตามลำดับ ($p = 0.33$) และค่า RI ของเส้นเลือดแดง uterine artery ข้างขวาในสตรีกลุ่มที่ 1 และ 2 มีค่าเท่ากับ 0.87±0.07 และ 0.83±0.06 ตามลำดับ ($p = 0.06$) โดยสรุปการให้ฮอร์โมนทดแทนแบบต่อเนื่องมีผลต่อการไหลเวียนโลหิตของมดลูกอย่างไม่มีนัยสำคัญทางสถิติ

คำสำคัญ : การไหลเวียนโลหิตของมดลูก, ฮอร์โมนทดแทน, การศึกษาคลื่นเสียงด็อพเพลอร์

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