Is routine endometrial sampling necessary before hormone replacement therapy?

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Before the initiation of hormone replacement therapy, routine endometrial sampling were performed in 1200 peri-and postmenopausal patients by using Pipelle device. The mean age and duration of menopause of the postmenopausal patients were 50.0±1.0 and 3.8±2.3 years respectively. The mean age of the perimenopausal patients was 48.3±2.8. Transvaginal ultrasonographical examinations were performed and endometrial thickness were measured just before the sampling. Dilatation and curettages were done when there was a discordance between the tissue amount and the endometrial thickness. The histopathological diagnosis were: inactive endometrium in 835 women, proliferative endometrium in 225 women, hyperplasia in 9 women, secretory endometrium in 25 women and insufficient tissue in 106 women. There was no endometrial cancer. The diagnosis of secretory and the hyperplastic endometrium were all belong to the perimenopausal patients. The positive and negative predictive values, sensitivity and specificity of transvaginal ultrasonography in the detection of the endometrial thickness were found as 97.8%, 85.3%, 95.6% and 92.6% respectively. We conclude that the yield for neoplasia is so low that screening endometrial sampling before hormone replacement therapy is not justified in asymptomatic postmenopausal patients. Instead, assessment of the endometrial thickness by transvaginal pelvic ultrasonographical examination can be more convenient. But it is essential in perimenopausal patients even if they are asymptomatic. [Turk J Med Res 1995, 13(3): 97-100]

Key Words: Hormone therapy, Endometrial sampling, Endometrium

Endometrial cancer is the most common gynecologic malignancy and approximately 80% of it occurs in postmenopausal women. Because these patients usually are seen with vaginal bleeding, it has been a dogma in gynecology that the endometrium of the postmenopausal women with this symptom must be sampled (1,2). But the value of the screening the postmenopausal population without symptoms is debatable (3).

Endometrial sampling causes a great deal of anxiety to the postmenopausal patient and moreover almost 70% of the diagnostic curretages result in a diagnosis of a benign condition (4). With the introduction of the transvaginal ultrasonography, the examination of the uterus and the endometrium in postmenopausal women has become very easy and instant (4.5).

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We evaluated the endometrial sampling results taken before the hormone replacement therapy in 1200 asymptomatic and postmenopausal women to determine the incidence of abnormal endometrial histological characteristics and thus to answer the question "Is it worth taking endometrial biopsy before hormone replacement therapy?". Also we compared the histologic diagnosis with the transvaginal ultrasonographically determined endometrial thickness to reveal the effectiveness of this noninvasive method in the detection of the endometrial pathologies.

MATERIALS AND METHODS

The 1200 women included to the study were all volunteers who were interested in hormone replacement therapy for relief of their menopausal complaints. Nine hundred (75%) were postmenopausal and the rest 300 (25%) were perimenopausal patients. Because of the nature of the study all of the patients were required to have an intact uterus and no evidence of a gynecological disease.

Serum estradiol (E2) and follicle stimulating hormone (FSH) were measured in all patients and E2<30

pg/ml, FSH>40 IU/L were accepted as indicators of the postmenopausal period. The postmenopausal patients were amenorrhea for at least one year. The perimenopausal patients were oligomenorrheic and had menopausal symptoms for at least one year.

Each patient underwent a screening endometrial sampling by using Pipelle device. If the specimen was insufficient or the histologic diagnosis did not correlate with the ultrasonographic findings, dilatation and curettages were performed. The endometrial samples were immediately placed in 4% paraformaldehyde in phosphate buffer containing 0.25% acetylpyridinium chloride. All samples were histopathologically evaluated by the same pathologist in Dr.Zekai Tahir Burak Women's Hospital, Department of Pathology. Each biopsy specimen was categorized by using the following criteria:

1. Inactive endometrium: *This broad category includes the patterns of marked atrophy, inactive endometrium of menopausal type. Some epithelial snouts and vacuoles may be present*

2. Proliferative endometrium: *The endometrium shows discernible evidence of stimulation. Small, tubular glands, fine cytoplasmic vacuoles and columnar surface epithelium with ciliation and mitoses in epithelial cells and/or stroma.*

3. Secretory endometrium: *Glands may show subnuclear glycogen vacuoles with more advanced secretory change; glands are tortuous with luminal secretion. Stroma is hypertrophic with periarteriolar cuffing. Mitoses are rare or absent.*

Table 1. Endometrial histology in 1200 menopausal women without symptoms

Histology	n	%
Inactive	835	69.5
Proliferative	225	18.9
Secretory	25	2.0
Hyperplasia	9	0.75
Insufficient tissue	106	8.8
Cancer		

4. *Hyperplastic endometrium: A spectrum of glandular patterns, crowding.*

5. Insufficient ***for*** *definitive diagnosis: These specimens contained fragments of endometrium too less to evaluate, or no discernible tissue at all or contained endocervical tissue.*

Transvaginal ultrasonographic examinations were performed with a Kretz Combison 320-5, 7.5 mHz transvaginal transducer with both sagittal and coronal projections and before endometrial sampling, endometrial thickness of all the patients were measured and registered.

RESULTS

The mean age and duration of menopause in postmenopausal patients were 50.0+1.0 and 3.8+2.3 years respectively. The mean age of the perimenopausal patients was 48.3±2.8.

Nintyfive dilatation and currettage were performed to the patients in whom there was a discordance between the ultrasonographic endometrial thickness and the biopsy specimen taken with Pipelle device.

Results of the 1200 screening biopsies are shown in Table 1. Histopathologic diagnosis of inactive endometrium was noted in 835 patients (69.5%), proliferative endometrium was found in 225 patients (18.8%) while secretory changes were shown in 25 (2%). All of the hyperplastic endometrium specimens were taken from perimenopausal patients and all of them were simple hyperplasia. One hundred six specimens (3.8%) contained insufficient tissue for a diagnosis. There was no endometrial cancer.

Eleven patients with inactive endometrium, 7 patients with proliferative endometrium and 2 patients with secretory endometrium also had cervical polyps. In 4 patients with inactive endometrium there were endometrial polyps.

Results of the measurements of endometrial thickness and comparison with the histopathological diagnosis are shown in Table 2. Thirty four cases out of 835 (4%) with inactive endometrium and 7 cases out of 106 cases (6.1%) with insufficient tissue showed discordance with the ultrasonographic findings. The

Table 2. Results of transvaginal ultrasonography compared with histologic diagnoses

TVU	Histologic diagnosis of specimens										
Endometrial thickness (mm)	Inactive		Proliferative		Secretory		Hyperplastic		Insufficient material		Total
	n	%	n	%	n	%	n	%	n	%	
$5	800	66.6	20	1.6			–	–	100	8.3	920
6-10	34	2.9	205	17	25	2	–	–	6	0.5	271
*11							9	0.7			9
Total	835		225		25		9		106		1200

Table 3. Accuracy of sonography in predicting low estrogen stimulation of the endometrium

TVU Endometrial thickness (mm)	Endometrial histology 1*	2"	Total
*5	900	20	920
>5	41	239	280
Total	941	259	1200

1 -Insufficient tissue, atrophic endometrium
2-Proliferative, secretory, hyperplastic endometrium
Positive predictive value - 900/920x100-97.8%
Negative predictive value - 239/280x100=85.3%
Sensitivity ~ 900/941x100-95.6%
Specificity = 239/259x100-92.6%

positive and negative predictive value, sensitivity and specifity or transvaginal ultrasonographic examination in detection of the endometrial thickness were found as 97.8%, 85.3%, 95.6% and 92.6% respectively (Table 3).

DISCUSSION

Endometrial sampling has been associated with a high degree of sensitivity and specificity for the detection of endometrial cancer in a patient population with symptoms (2,9,10). This gynecologic malignancy manifests early with vaginal bleeding and the expected incidence of the disease is approximately 1 to 2 per 1000 woman years. Screening of high risk women would detect only 50% of cases of endometrial cancer (3,11). But even this low value seems important because it has been appreciated that the postmenopausal hormone replacement therapy has to be initiated to every postmenopausal woman.

Endometrial sampling causes a great deal of anxiety to the postmenopausal patient besides its quite high cost and almost 70% of diagnostic curretage result in a diagnosis of a benign condition (4). The Pipelle device, which does not required suction pump is less expensive, easier to use and associated with less patient discomfort than the other techniques, while obtaining adequate tissue with a 97.5% sensitivity for detecting endometrial neoplasia (6,7,8,12). But yet it is still an invasive procedure and the question "is it worth?" remains to be answered when the result of the studies similar to ours are not alarming.

On the other hand vaginal probe ultrasonographic transducers are of higher accuracy and closer proximity to structures being studied, so it is called "sonomicroscopy" (13). Its positive and negative predictive values, sensitivity and specifity are very high as it is supported in this study (1,8). They can easily be used in peri and postmenopausal patients instead of routine endometrial sampling. With this method we can screen the cases to be biopsied.

As a result we conclude that in asymptomatic postmenopausal patients a careful transvaginal ultrasonographic examination is sufficient and screening endometrial biopsy is not justified. But our results indicate that in perimenopausal patients endometrial biopsy has a value even if they are asymptomatic since all of the hyperplasias were detected in this grup.

Hormon replasman tedavisi öncesi rutin endometrial örnekleme gerekli midir?

7200 peri ve postmenopozal hastaya hormon replasman tedavisine başlamadan önce Pipelle küret ile rutin endometrial örnekleme yapıldı. Postmenopozal hastaların yaş orlamaları 50.0±1.0 ve ortalama menopoz süreleri 3.8±2.3 yıl iken perimenopozal hastaların ortalama yaşları 48.3±2.8 idi. İşlemden hemen önce transvaginal ultrasonogram inceleme ile endometrial kalınlık ölçüldü. Doku miktarı ile ölçülmüş olan endometrial kalınlık arasında uyumsuzluk olan hastalara dilatasyon ve küretaj uygulandı. Histopatolojik tanılar şöyle idi: 835 hastada inaktif endometrium, 225 hastada proliferatif endometrium, 25 hastada sekretuar endometrium, 9 hastada hiperplazi ve 106 hastada yetersiz doku. Endometrial kanser tespit edilmedi. Histopatolojik tanılar ile ultrasonografik olarak tespit edilen endometrial kalınlıklar karşılaştırıldığında transvaginal ultrasonografinin pozitif ve negatif kestirim değerleri, sensitivite ve spesifitesi sırasıyla %97.8, %85.3, %95.6 ve %92.6 olarak bulundu. Sonuçta asemptomatikpostmenopozal hastalarda malignité olasılığı çok düşük olduğundan tedavi öncesi rutin endometrial örneklemenin gerekmediği ama transvaginal pelvik ultrasonografi gibi noninvazif bir işlem ile endometrial kalınlık ölçümünün yapılabileceği kanısına varıldı. Perimenopozal hastalarda ise endometrial patoloji yönünden asemptomatik bile olsalar tedavi öncesi endometrial örnekleme gereklidir.

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