ASSESSMENT OF RELIABILITY OF ENDOMETRIAL BRUSH CYTOLOGY TO DETERMINE THE ETIOLOGY OF ABNORMAL UTERINE BLEEDING AND POSTMENOPAUSAL BLEEDING

Erhan YAVUZ[1], Erdal MALATYALIOGLU[2], Mehmet SAKINCI[3], Ilkser AKPOLAT[4], Migraci TOSUN[2], Fatma Devran BILDIRCIN[2],

[1] Agri Patnos State Hospital, Agrı, Turkey
[2] Department of Gynecology and Obstetrics, Faculty of Medicine, Ondokuz Mayis University, Samsun, Turkey
[3] Department of Gynecology and Obstetrics, Faculty of Medicine, Akdeniz University, Antalya, Turkey
[4] Department of Pathology, Faculty of Medicine, Ondokuz Mayis University, Samsun, Turkey

SUMMARY

Objective: *To demonstrate diagnostic efficacy of endometrial cytologic sampling for detection of endometrial pathologies (endometrial hyperplasias and cancers), by comparing endometrial full curettage and endometrial cytologic smear pathologic results performed in patients with abnormal uterine bleeding.*

Materials and methods: *Totally 109 reproductive and postmenopausal women with abnormal uterine bleeding who applied our clinic between the dates January 2005-June 2010 were included in the study.After measurement of endometrial thickness by transvaginal ultrasound, patients were treated initialy with endometrial cytologic sampling using endometrial brush then endometrial full curettage using sharp curette. Pathology and cytology reports were evaluated retrospectively by reviewing patient's files.*

Results: *The most frequent diagnoses in endometrial cytologic specimens obtained by endometrial brush was nondiagnostic with a rate of 73.7%(n:42) and 53.8%(n:28) in postmenopausal women and reproductive period women, respectively. When all the patients were analysed together, the diagnosis was non-diagnostic in 64.2%(n:70) (38.5% postmenopausal,25.7% premenopausal) of endometrial cytologic samples. Cytologic assessment was resulted as sufficient in only 35.8% (n:39) of the cases. Endometrial full curettage pathologic diagnoses were resulted as insufficient in 56.1%(n:32) of postmenopausal patients and 9.6%(n:5) of reproductive period cases.The second most frequent diagnosis was endometrial polyp in 13(22.8%) patients in postmenopausal period, whereas the most frequent diagnoses in reproductive period were reported as endometrial polyp in 18 (34.6%) and secretory endometrium in 12(23.1%) patients.*

When the full curettage was considered as golden standard method with respect to sample sufficiency; the sensitivity of endometrial cytologic evaluation in postmenopausal patients with regard to sample sufficiency was found as 36%, spesificity 81.3%, positive predictive value 60.0%, negative predictive value 61.9%; the values were found as 44.7%, 40.0%, 87.5%, 7.1%, respectively, in reproductive period patients.

Conclusions: *In both reproductive and postmenopausal period patients; endometrial cytology does not appear as a method which can be used alone for detection of premalignant or malignant lesions of endometrium, due to high rate of material inadequacy obtained by it compared to endometrial full curettage biopsy.*

Key words: *abnormal uterine bleeding, endometrial cytology, endometrial full curettage*

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Address for Correspondence: Mehmet Sakıncı. Akdeniz Üniversitesi Hastanesi, Kadın Hastalıkları ve Doğum Anabilim Dalı, 07059 Antalya
Phone: + 90 (535) 475 01 86
e-mail: mehmetsakinci@hotmail.com
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ENDOMETRİAL FIRÇA SİTOLOJİSİNİN ANORMAL UTERİN KANAMA VE POSTMENOPOZAL KANAMA ETİYOLOJİSİNİ SAPTAMADA GÜVENİLİRLİĞİNİN DEĞERLENDİRİLMESİ

ÖZET

Amaç: *Anormal uterin kanamalı hastalarda yapılmış endometrial full küretaj ve endometrial yayma sonuçlarını karşılaştırarak, endometrial sitolojik örneklemenin endometrial patolojileri (endometrial hiperplaziler ve kanserler) saptamada tanısal etkinliğini ortaya koymaktır.*

Gereç ve yöntemler: *Çalışmaya Ocak 2005- Haziran 2010 tarihleri arasında kliniğimize anormal uterin kanama nedeniyle başvuran reprodüktif ve postmenopozal dönemdeki toplam 109 hasta dahil edilmiştir. Transvajinal ultrasonografi ile endometrial kalınlıkları ölçüldükten sonra, önce endometrial fırça ile endometrial sitolojik örnekleme ardından keskin küretle endometrial full küretaj yapılan hastaların patoloji ve sitoloji sonuçları retrospektif dosya taraması yapılarak değerlendirilmiştir.*

Bulgular: *Endometrial fırça ile alınan endometrial sitolojik örneklerde en sık tanılar postmenopozal ve reprodüktif dönemde sırasıyla %73.7 (n:42) ve %53.8 (n:28) ile non-diagnostik'ti. Tüm hastalar bir arada incelendiğinde endometrial sitolojik örneklerin %64.2'sinde (n:70) (%38.5 postmenopozal, %25.7 premenopozal) tanı non-diagnostik idi. Sitolojik inceleme olguların sadece %35,8'inde (n:39) yeterli olarak sonuçlandı. Endometrial full küretaj patoloji tanıları postmenopozal dönem olgularının %56,1 (n:32)'inde, reprodüktif dönem olgularının ise %9.6 (n:5)'sında non-diagnostik olarak sonuçlandı. Postmenopozal dönemde diğer en sık tanı 13 (%22.8) hastada endometrial polip iken, reprodüktif dönemde en sık tanılar 18 (%34.6) hastada endometrial polip, 12 (%23.1) hastada sekretuar endometrium olarak rapor edilmiştir.*

Hastalara tanı verebilme açısından diğer bir deyişle yeterlilik durumuna göre full küretaj altın standart yöntem olarak ele alındığında; postmenopozal dönemdeki hastalarda, endometrial sitolojik değerlendirmenin, yeterli gelme durumuna göre, sensitivitesi %36.0, spesifitesi %81.3, pozitif prediktif değeri %60.0, negatif prediktif değeri %61.9 olarak saptandı. Reprodüktif dönem hastalarında ise yeterli gelme durumuna göre sensitivite %44.7, spesifitesi %40.0, pozitif prediktif değer %87.5, negatif prediktif değer %7.1 olarak saptandı.

Sonuçlar: *Hem reprodüktif dönem, hem de postmenopozal dönem hastalarında endometrial full küretajla alınan biyopsiye göre yetersiz materyal oranı yüksekliği nedeniyle endometrial sitoloji, endometriumun premalign veya malign lezyonlarını saptamada tek başına kullanılabilecek bir yöntem olarak görünmemektedir.*

Anahtar kelimeler: *anormal uterin kanamalar, endometrial full küretaj, endometrial sitoloji*

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INTRODUCTION

One of the leading causes of applications to gynecology clinics is abnormal uterin bleeding and often based on pregnancy and anovulation in young women, whereas it occurs mostly due to the pathological causes like myoma, polyps, endometrial hyperplasia and cancer at perimenopausal and postmenopausal period[1].

In spite of the complications such as uterine perforation, intrauterine adhesions, cervical laceration, intense bleeding and peritonitis; dilatation and curettage (D&C) is used as the gold standard for investigations of abnormal uterine bleeding (AUB)[2]. The high prevalance of AUB makes it essential to investigate the methods which are less invasive, more economical, more easily performed and have better patient comfort.

When the literature is inspected, a few studies are drawing attention that emphasize endometrial cytological sampling as an easily practicable and inexpensive method which has a lower risk of complications such as perforation or infection and does not require general anesthesia or cervical dilatation, patient conformity is higher and provides a possibility of taking results in short time by faster examining facility[3].

The primary aim of this study is to determine the diagnostic efficacy of the endometrial cytological sampling for detection of endometrial pathologies

(endometrial hyperplasia and cancer) by comparing the results of endometrial full curettage and endometrial smear via retrospective file review. The secondary aim of this study is to evaluate the correlation between endometrial thickness measured by transvaginal ultrasound and specimen adequacy in cytological sampling and full curettage procedures.

MATERIALS AND METHODS

Patients with the chief complaint of abnormal uterine bleeding at reproductive and postmenopausal period who applied to Ondokuz Mayıs University Medical Faculty, Department of Obstetrics and Gynecology between the dates January 1, 2005 and June 1, 2010 were included to the study. The study was approved by the local ethics committee. Written informed consent was taken from all the patients included in the study after being informed about the surgical procedures.

Patients who were operated and/or using tamoxifen for breast cancer, have intrauterine device, taking oral contraceptives or hormone replacement therapy, have evidence of upper or lower genital tract infection and were detected to have pregnancy and/or coagulation abnormalities were excluded from the study.

Cytology and pathology results of the patients who had undergone endometrial cytologic sampling and then full curettage were evaluated by retrospective chart review. Study forms containing menopausal status, obstetric history, past medical history, family history, body mass index, endometrial thickness measured by transvaginal ultrasound, biopsy and cytology results, categorized biopsy and cytology results were filled in for each patient.

Endometrial cytological samples of the patients were obtained with endometrial brush (endobrush). The specimen were spreaded on a glass slide then fixed with a sprey containing alcohol. Right after the cytological sampling, full curettage was performed with a sharp curette. Cytological and histological specimens were evaluated by a pathologist who was expert on endometrial cytology and histology.

Diagnosis specified in cytology and pathology reports were sorted into three groups as inadequate, normal or benign findings and pathological findings by virtue of the limited number of the study group. While results of endometrial full curettage were categorized as inadequate for the non-diagnostic ones; normal or benign findings for proliferative endometrium, secretory endometrium, atrophic endometrium, disordered endometrium, senile cystic endometrium, menstrual phase endometrium, inflamed endometrial tissue, endometrium under the influence of prolonged estrogen, endometrial polyps or endometritis and pathological findings for simple / complex endometrial hyperplasia without atypia, simple / complex atypical endometrial hyperplasia, high-grade mixed epithelial tumor, endometrial adenocarcinoma; the cytology results were categorized as inadequate for the non-diagnostic ones, normal or benign findings for the malignancy negative ones and pathological findings for the ones which were non-categorized, suspicious for malignancy or malignancy positive.

For cytological assessments the criteria defined by Buccoliero AM et al. were taken into the consideration and the cases identified as atrophic, secretory and proliferative endometrium were classified as 'malignancy negative', the cases identified as hyperplasia without atypia were classified as 'non-categorized', the cases identified as atypical hyperplasia as 'suspicious for malignancy' and finally the cases identified as carcinoma were classified as 'malignancy positive'. During the cytologic work-up, observation of at least five endometrial cell clusters was accepted as sufficient, the slides were considered inadequate when there were less than five evaluable endometrial clusters or excessive fragmantation[4].

After the evaluation of transvaginal ultrasonography results, the patients were grouped as 0-5 mm, 6-10 mm, 11-15 mm, 15-20 mm and 21-25 mm according to the endometrial thickness.

Statistical analyses were performed using Statistics Package for Social Sciences Version 15 (SPSS, Chicago, IL, USA) program. All values of continuous variables were expressed as mean ± standard deviation unless otherwise specified. Pearson chi-square test was used for the comparison of rates between independent groups and McNemar test between dependent groups. The degree of agreement between adequacy of cytology and biopsy was determined by Kappa analysis. Data in Table IVa, IVb and V were used for the calculations of sensitivity, specificity, positive predictive value and negative predictive value and the following formulae were utilized; Sensitivity TP / (TP + FN), specificity TN / (TN + FP), positive predictive value, TP / (TP +

FP), negative predictive value of TN / (TN + FN); TP: true positive, TN: true negative, FN: false negative, FP: false positive. Spearman nonparametric correlation analysis was used to evaluate the correlation between endometrial thickness and adequacy of full curettage biopsy and cytology. A p-value <0.05 was considered statistically significant.

RESULTS

57 (52.3%) of the 109 patients included to the study were at postmenopausal and 52 (47.7%) of them were at reproductive period. The mean age was 52.3 ± 12.6. Demographic information of patients such as age, parity, body mass index, menopausal status were summarized in Table I.

Table I: *Demographic properties of the patients.*

	Postmenopausal Group	Reproductive Group
Patient number (n)	57 (%52.3)	52 (%47.7)
Age	60.6±10.1	42.6±7.2
Parity	4.0±2.1	3,1±1.9
Body mass index (kg/m^2)*	31.2±4.7	27.6±6.3

** Body weight (kg)/square of height (m2)*

The most frequent diagnoses in endometrial cytologic specimens obtained by endometrial brush was nondiagnostic with a rate of 73.7%(n: 42) and 53.8%(n: 28) in postmenopausal women and reproductive period women, respectively. When all patients were analysed together, diagnosis was nondiagnostic in 64.2% (n: 70) (38.5% postmenopausal,25.7% premenopausal) of endometrial cytologic samples. Cytologic assessment was resulted as sufficient in only 35.8% (n: 39) of cases. Additionaly, 60% of the results attained as insufficient were belonged to postmenopausal patients and 40% were belonged to patients at reproductive period. On the other hand 38.5% of the results attained as sufficient were belonged to postmenopausal and 61.5% were belonged to the patients at reproductive period. Table II shows the original (real) and categorized cytology results of the patients.

When all patients were considered, endometrial biopsies obtained with full curettage were resulted as sufficient in 66.1% (n=72) and insufficient in 33.9% (n=37). Biopsy results were culminated in sufficient and insufficient in 43.9 % (n=25) and 56.1% (n=32) of patients at postmenopausal period; 90.4% (n=47) and 9.6% (n=5) of patients at reproductive period, respectively. Whereas the most frequent diagnoses in reproductive period were reported as endometrial polyp in 18 (34.6%) and secretory endometrium in 12 (23.1%) patients, the other most frequent diagnosis was endometrial polyp in 13 (22.8%) patients in postmenopausal period. The original and categorized biopsy results of the patients were summarized in Table III.

The results which were belonged to the endometrial full curettage biopsy were sufficient with a statistically significantly higher rate compared to the results of cytology in the whole study population (p<0.001). Kappa analysis showed that there was a weak concordance between cytology and full-curettage biopsy results (kappa:0.143; p=0.074). When the sufficiency of cytology and biopsy at postmenopausal and reproductive periods were compared; insufficient detection rate for both cytology and biopsy results at postmenopausal period were significantly higher than the reproductive period (p=0,031; p<0,001, respectively).

When full curettage was considered as golden standard method in terms of diagnosing the condition, in other

Table II: *Real and categorized cytology results of menopausal and reproductive period patients and percentages in study population.*

Real Diagnosis	Categorized Diagnosis	Menopausal Patients (n:57)*	Total	Reproductive Period Patients (n:52)*	Total
Insufficient	Insufficient	42	42 (%73.7)	28	28 (%53.8)
Malignity negative	Normal or benign findings	7	7 (%12.3)	19	19 (%36.6)
Non-categorized Suspicious malignancy Malignity positive	Pathologogical findings	5 (%8.8) 1 (%1.8) 2 (%3.5)	8 (%14.0)	4 (%7.7) 1(%1.9) 0	5 (%9.6)

** Rates are expressed within each group.*

words, with respect to sample sufficiency; the sensitivity of endometrial cytologic evaluation in postmenopausal patients with regard to sample sufficiency was found as 36%, spesificity 81.3%, positive predictive value 60.0%, negative predictive value 61.9% (Table IVa). According to the sample sufficiency; the sensitivity in reproductive period patients was found as 44.7%, spesificity 40.0%, positive predictive value 87.5%, negative predictive value 7.1% (Table IVb).

When the full-curettage is considered as gold standart in terms of detecting the pathologic condition (premalignant or malignant), and the patients whose biopsy and cytology results were insufficient were excluded from the analysis, in the whole study population, the sensitivity of endometrial cytologic evaluation with regard to determination of endometrial pathology was found as 100%, spesificity 77.8%, positive predictive value 33.3%, negative predictive value 100% (Table V).

When the cytological diagnoses and full curettage biopsy diagnoses of patients at postmenopausal period were compared, biopsy diagnoses of 42 patients whose cytological diagnosis were non-diagnostic were like following; non diagnostic in 26 patients, simple endometrial hyperplasia without atypia in one patient, benign or normal findings in 15 patients. Biopsy results of 7 patients whose cytology results were negative for malignency; non diagnostic in 4 patients, normal findings in 3 patients. Biopsy results of 5 patients who have non-categorized cytology results; non-diagnostic in two patients, endometrial polyps in 3 patients. Biopsy result of one patient with a suspected malignancy cytology result was diagnosed with endometrial adenocarcinoma. Biopsy results of two patients whose cytology results were positive for malignancy was reported as endometrial adenocarcinoma in one and high-grade mixed epitelial tumor in the other one.

Table IVa: *Comparison of Cytology and Biopsy Adequacy in Postmenopausal Period.*

Cytology Adequacy	**Biopsy Adequacy** Sufficient	Insufficient	**Total**
Sufficient	0	6	15
Insufficient	16	26	42
Total	25	32	57

Table IVb: *Comparison of Cytology and Biopsy Adequacy in Reproductive Period.*

Cytology Adequacy	**Biopsy Adequacy** Sufficient	Insufficient	**Total**
Sufficient	21	3	24
Insufficient	26	2	28
Total	47	5	52

Table V: *Comparison of cytology and biopsy results in whole study population in case of adequate specimen.*

Cytology Result	**Biopsy Result** Pathologic	Normal or Benign	**Total**
Pathologic	3	6	9
Normal ve Benign	0	21	21
Total	3	27	30

Table III: *Real and categorized biopsy results of postmenopausal and reproductive period patients and percentages in the study population.*

Real Diagnosis	**Categorized Diagnosis**	**Menopausal patients (n:57)***	**Total**	**Reproductive period patients (n: 52)***	**Total**
Insufficient	Insufficient	32	32 (%56.2)	5	5 (%9.6)
Proliferative endometrium	Normal or benign findings	1	21 (%36.8)	6	47 (%90.4)
Secretory endometrium		1		12 (%23.1)	
Atrophic endometrium		2		1	
Disordered endometrium		2		1	
Senile cystic endometrium		1		0	
Menstrual phase endometrium		0		2	
Endometrium under the influence of prolonged estrogen		0		2	
Endometrial polyp		13 (%22.8)		18 (%34.6)	
Endometritis		1		5	
Simple endometrial hyperplasia without atypia	Pathological Findings	1	4 (%7.0)	0	0
Endometrial adenocarcinoma		2		0	
High grade mixed epithelial tumor		1		0	

** Rates are expressed within each group.*

When the cytological diagnoses and full curettage biopsy diagnoses of patients at reproductive period were compared; biopsy diagnoses of 28 patients whose cytological diagnosis were non-diagnostic were like following; non-diagnostic in two patients, normal or benign findings in 26 patients. Biopsy results of 19 patients whose cytology results were negative for malignency; non diagnostic in one patient and normal or benign findings in 18 patients. Biopsy results of 4 patients who have non-categorized cytology results were reported as non diagnostic in two patients and normal or benign findings in two patients. Biopsy result of one patient with a suspected malignancy cytology result was reported as endometrial polyp. There were no patients in reproductive period whose cytology result was positive for malignancy.

Endometrial thickness measured by transvaginal ultrasound was 6-10 mm in 27 patients (47.4%) at postmenopausal period and 11-15 mm in 21 patients (40.4%) in reproductive period with the greatest number of patients. The distribution of patients with respect to endometrial thickness and the biopsy insufficiency rates were summarized in Table VI. The insufficiency rate of biopsy was 50% in cases with endometrial thickness of 0-5 mm and 11.1% in cases with endometrial thickness of 11-15 mm in the whole study population. There was statistically significant difference between postmenopausal and reproductive period groups according to the endometrial thickness (p=0.001). The insufficiency rates of biopsy showed statistically significant differences among 5 endometrial thickness groups in the entire study population (p=0.019). There was a statistically significant correlation between the increase in endometrial thickness and the sufficiency of full curettage biopsy results (rho=0.292, p=0.002). No statistically significant correlation could be found between the increase in endometrial thickness and the sufficiency of cytology results and the biposy sufficiency and cytology sufficiency (rho=0.111, p=0.25; rho=0.171, p=0.075 respectively).

DISCUSSION AND CONCLUSION

Abnormal uterine bleedings constituting an important part of the applications to gynecology clinics can be classified as dysfunctional uterine bleedings (anovulatory, ovulatory) and uterine bleedings due to an organic cause (pregnancy, infections, tumoral formations and malignancy, systemic diseases, etc.)[5]. Endometrial sampling is performed to rule out the premalignant or malignant pathologies of endometrium in patients with abnormal uterine bleeding.

Wide variety of techniques were used for endometrial sampling. Among these methods, cervical dilatation and endometrial full curettage (D&C) has the most common application area and is accepted as the gold standard. The first symptom is abnormal uterine bleeding in 80-95% of patients who underwent endometrial biopsy. Unless there is bleeding, invasive histopathological studies such as endometrial biopsy or D&C is not undertaken most of the time. Because these methods are invasive and performed in symptomatic patients, they are hardly ever used for screening[6].

Less than half of the uterine cavity is curetted during dilatation and curettage in most patients, and therefore false negative rate of D&C in the diagnosis of endometrial cancer is as high as 2-6%[7]. Twu et al. have identified endometrial cancer in 20% of the patients with postmenopausal bleeding whose D&C results were negative[8]. However, there are also some authors supporting the absolute requirement of D&C

Table VI: *Distribution of patients according to endometrial thickness and biopsy insufficiency rates.*

	Endometrial Thickness (mm)*				
	0-5	6-10	11-15	16-20	21-25
Postmenopausal Group (n ve %)	18 (%31.6)	27 (%47.4)	6 (%10.5)	3 (%5.3)	3 (%5.3)
Reproductive Group (n ve %)	8 (%15.4)	15 (%28.8)	21 (%40.4)	5 (%9.6)	3 (%5.8)
Biyopsy Insufficiency Rates**	%50	%42.9	%11.1	%25.0	%16,7

** Percentages of endometrial thickness are expressed within each group.*

*** Biopsy insufficiency rates are expressed in the entire study population and are given separately for each endometrial thickness group.*

if the material is insufficient taken by endometrial biopsy in symptomatic patients. Farrell et al. have detected pathologies including endometrial cancer in 20% of the cases with insufficient material obteined by endometrial biopsy[9]. Therefore any cytological and histological abnormality except invasive cancer makes the D&C mandatory no to skip a small invasive focus. Furthermore, if the symptoms continue or recur in patients with normal cytology or biopsy result, D&C must be performed[10].

Cytological sampling directly from endometrial cavity is another method which is used to diagnose the endometrial pathologies. However, this method had been used as a screening method instead of a diagnostic modality for endometrium cancer because it required special equipment and skill for cytological evaluation. Endobrush cytologic sampler that is developed for routine screening of endometrial cancer is recommended because it is a cheap and simple device besides the user-friendliness with conformity of patient and small number of complications[11].

Wu et al. have advocated that the endometrial brush biopsy could make a diagnosis in 90% of the patients treated as outpatients (could provide sufficient specimen) and have revealed 100% sensitivity and 96% specificity in cases with a sufficient specimen, and also championed that this method was quite valid. They have also emphasized the importance of specimen's sufficiency obtained by endometrial brush for the pathologist who was going to make the assesment by explaining endometrial cancer had developed during the follow up of patients whose endometrial brush cytology had been nondiagnostic before[12]. Klemi et al. have demonstrated the diagnostic adequacy of this method varied between 92.3% and 97.8% in their study performed over 1042 symptomatic patients and stated that curettage was indicated if the bleeding persisted in a postmenopausal woman even the cytology was normal[13]. In the other three studies related with conventional endometrial cytology although sensitivity and specificity up to 96% was reported, the use of this method was not gained acceptance due to the technical and diagnostic difficulties[14-16]. Caubel et al. have emphasized that it would be suitable to confirm the endometrial cytological diagnosis with histological diagnosis routinely, in the study which they pointed out to the dangers in the use of endometrial cytology in 1990[17]. Milojkovic et al. have compared endometrial brushing, D&C and pap smear, and found the diagnostic accuracy of endometrial brush method as 56% in patients with endometrial cancer and reported that the realiability of the samples obtained by endometrial brushing was not sufficient in the study performed on patients with late postmenopausal bleeding[18].

In our study, the result was reported as insufficient (non-diagnostic) (64.2%) in the majority of the patients who endometrial cytologic examination was performed. The majority of the patients with insufficient sample (60%) were of postmenopausal patient group. Results of endometrial full curettage were insufficient in 33.9% of the patients. In the present study, when full curettage was considered as golden standard method in terms of making a diagnosis, in other words, with respect to sample sufficiency; the sensitivity of endometrial cytologic evaluation in postmenopausal patients with regard to sample sufficiency was found as 36%, spesificity 81.3%, positive predictive value 60.0%, negative predictive value 61.9% (Table IVa). In reproductive period patients; the sensitivity with regard to the sample sufficiency was found as 44.7%, spesificity 40.0%, positive predictive value 87.5%, negative predictive value 7.1% (Table IVb). In the light of this result, hence sensitivity and specificity of the conventional endometrial cytologic examination in terms of detecting sufficient specimen is rather lower compared to the biopsy obtained by endometrial full-curettage, we think use of this method in routine practice is not safe or efficient.

Endometrial cytologic assessment may also be performed by using liquid-based cytological examination which is a relatively newer method in which a special container containing a protective liquid is used rather than a glass slide. This method provides a reduction of drying artifacts and vanishing of majority of blood cells. Inflammatory cells reduce by forming clusters and are differentiated from epitelial cells facilitating the diagnosis. In some studies, the diagnostic value of liquid-based endometrial cytology is especially emphasized. Specificity, sensitivity and insufficiency rates were reported as 96%, 78% and 15%, respectively, in a study enrolling 103 symptomatic patients by Garcia et al[19].

In a study performed by Buccoliero et al including 320 asymptomatic postmenopausal women, in which hysteroscopy before the liquid-based endometrial

cytology and biopsy was undertaken; it was found that obtaining sufficient material by endometrial cytology was significantly higher than biopsy. It was determined that 69% of biopsy and 5% of cytology materials were insufficient. Sensitivity of endometrial cytology was reported as 94%, specificity 95%, positive predictive value 80%, negative predictive value 99%. As a result, it was stated that; if the use of liquid-based endometrial cytology was combined with transvaginal ultrasonography, accuracy of diagnosis might increase and more invasive and expensive procedures could be reduced[20].

In our study, insufficiency rates of endometrial cytological samples were higher than the literature. The reasons of this may be due to endometrial sampling process was applied by different individuals, using conventional smear method instead of thin layer liquid-based cytology or endometrial brush model which was used in the study.

The limitation of this study was a relatively small number of the study group. When the patients with insufficient results of cytology and biopsy were excluded, sensitivity and specificity of endometrial cytology in determining the endometrial pathology was calculated with limited number of patients (Table V).

Although D&C is a definitive test, it has some disadvantages due to the invasive nature and high risk of complications. Additionally, sufficient material can not be obtained due to the thin layer of endometrium in postmenopausal women. In a study carried out by Buccoliero et al. the rate of obtaining sufficient material from postmenopausal endometrium under 4 mm was found as 24%[4]. In our study, we found that biopsy insufficiency rate was 50% in cases with 0-5 mm endometrial thickness and demonstrated that there was a positive correlation between the increase in endometrial thickness and the rates of obtaining sufficient material by biopsy (rho=0.292, p=0.002). We did not find any correlation between the increase in endometrial thickness and cytologic sufficiency. Examination of endometrial cavity with hysteroscopy before the biopsy may be an approach that can reduce the biopsy insufficiency rates in the group of patients with thin endometrium.

In conclusion, in both reproductive and postmenopausal period patients;endometrial cytology does not appear as a method which can be used alone for detection of pathologic lesions of endometrium (premalignant or malignant), due to high rate of material inadequacy obtained by it compared to endometrial full curettage biopsy.

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