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Factors Affecting the Diagnostic Accuracy of Endometrial Pipelle® Biopsy

Pipelle® Biyopsinin Tanısal Doğruluğunu Etkileyen Faktörler

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Abstract

Objective: In this study, we aimed to compare the endometrial suction biopsy (ESB) with Pipelle® and endometrial curettage (D&C) findings from patients with abnormal uterine bleeding and/or endometrial thickness to observe the possible influencing factors on ESB's diagnostic value.

Method: In Tekirdağ Community Hospital and Gynecology Clinic, data were retrospectively collected from hospital registry. 122 patients who had abnormal uterine bleeding and/or endometrial thickness were selected and from all cases, endometrial biopsies were taken with Pipelle® and D&C methods at the same time. In conclusion, pathologic results of two methods were compared.

Results: Pathology results were as follows: By Pipelle®, 44 patients (36.1%) were found with endometrial polyps, 26 patients (21.3%) with endometrial atrophy, 31 patients (25.4%) with proliferative endometrium, 11 patients (9%) with secretory endometrium, 4 patients (3.3%) with endometrial carcinoma, 1 patient (0.8%) with hyperplasia without atypia, 2 patients (1.6%) with inflammation; by D&C, 55 patients (45.1%) were found with polyp, 20 patients (16.4%) with endometrial atrophy, 34 patients (27.9%) with proliferative endometrium, 9 patients (7.4%) with secretory endometrium, 4 patients (3.3%) with endometrial carcinoma, 1 patient (0.8%) with hyperplasia without atypia, 2 patients (1.6%) with inflammation. Correlations between two methods were found as 97.6%, 95.3%, 91.7%, 98.3%, 100%, 100%, and 100% for proliferative endometrium, atrophy, polyp, secretory endometrium, endometrial cancer, hyperplasia without atypia and inflammation, respectively. Discorrelations between two diagnostic methods were more commonly seen in endometrial polyp pathology.

Conclusion: Our study findings revealed very high correlations between the pathology results of Pipelle® and D&C procedures. Pipelle®, with the advantages of being a simple outpatient procedure and having less complication rates, can be preferred over D&C reliably in most clinic situations. On the other hand, D&C method should be preferred in cases of endometrial polyp pathologies due to increased discorrelation rates and biopsy failures in Pipelle® biopsy.

Keywords: Dilatation and curettage, endometrial thickness, Pipelle® biopsy, uterine bleeding

Öz

Amaç: Anormal uterin kanama ve endometrial kalınlık artışı nedeniyle endometrial örnekleme yapılan hastaların Pipelle® biyopsi ve dilatasyon & küretaj (D&C) sonuçlarının karşılaştırılması ve Pipelle® biyopsinin tanısal doğruluğunu etkileyen faktörlerin araştırılması amaçlandı.

Yöntem: Tekirdağ Devlet Hastanesi, Kadın Hastalıkları ve Doğum Kliniği'ne anormal uterin kanama ve/veya endometrial kalınlık nedeniyle başvurup, aynı seansta Pipelle® D&C ile endometrial örnekleme yapılmış 122 olgunun retrospektif olarak dosya taraması ile sonuçları karşılaştırıldı.

Bulgular: Pipelle® yöntemi ile yapılan biyopsilerin sonuçlarında 44 (%36,1) polip, 26 (%21,3) atrofi, 34 (%27,9) proliferatif endometrium, 11 (%9,0) sekretuvar endometrium, 4 (%3,3) karsinom, 1 (%0,8) atipisiz hiperplazi, 2 (%1,6) enflamasyon bildirildi. D&C yöntemi ile yapılan biyopsilerde 55 (%45,1) polip, 20 (%16,4) atrofi, 31 (%25,4) proliferatif endometrium, 9 (%7,4) sekretuvar endometrium, 4 (%3,3) karsinom, 1 (%0,8) atipisiz hiperplazi, 2 (%1,6) enflamasyon saptandı. Her iki yöntemin uyum oranları proliferatif endometrium, atrofi, polip, sekretuar endometrium, endometrium kanseri, atipisiz hiperplazi ve enflamasyon için sırasıyla %97,6, %95,3, %91,7, %98,3, %100, %100 ve %100 olarak saptandı. İki tanısal yöntem arasında uyumsuzluk en fazla endometrial polip patolojisinde görüldü.

Sonuç: Sonuçlarımıza göre; Pipelle® biyopsi ve D&C prosedürü arasında patoloji sonuçları yönünden çok yüksek korelasyon olduğu görülmüştür. Pipelle® biyopsi; anestezi gerektirmemesi, ağrı miktarının az olması ve postoperatif komplikasyon riski azlığı nedeniyle endometrial patolojilerin teşhisi için D&C prosedürünün yerine güvenle tercih edilebilir. Diğer yandan, iki yöntem arasında en fazla uyumsuzluk görülen ve Pipelle® Biopside yetersizliğe yol açabilen endometrial polip olgularında D&C örneklemenin tercih edilmesi kanaatindeyiz.

Anahtar kelimeler: Dilatasyon ve küretaj, endometrial kalınlık, Pipelle® biyopsi, uterin kanama

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Introduction

Endometrial sampling is a valuable procedure in routine gynecology practice with its diverse advantages in differentiating malign-premalignant lesions, excision of certain lesions, observing the cyclic hormonal effects and being simple feasible method. Sampling can be achieved by endometrial suction biopsy (ESB), dilatation and curettage (D&C) and hysteroscopic biopsies.

Ultrasonography and hysteroscopy are among valuable imaging methods for diagnosing uterine and endometrial pathologies. Endometrium, cervix, uterus and adnexa can easily be evaluated by transvaginal ultrasonography, which is a frequently preferred non-invasive method. On the other hand, the minimally invasive method, saline infusion sonography is superior to traditional ultrasonography in detecting small focal endometrial lesions (1).

Hysteroscopy is the gold standard method for visualizing focal intrauterine lesions. Diagnostic accuracy of endometrial biopsies is increased when performed during hysteroscopy (2). Not requiring anesthesia, diagnostic hysteroscopies became a practical and reliable outpatient office procedure.

Endometrial sampling is the gold standard diagnostic method for the most patients with abnormal uterine bleeding complaint (3). The most common such clinical scenarios are postmenopausal bleeding, postmenopausal endometrial thickening, and perimenopausal menometrorrhagia (>45 years of age). Endometrial polyps, atrophy, hormonal, inflammatory, premalignant and malignant differentiations are among the important pathological findings that can be reported. Dilatation and curettage (D&C) is an invaluable diagnostic method for endometrial pathologies. However, due to its need for anesthesia, risk for uterine perforation and post-procedure adhesions, ESB is commonly preferred over D&C in routine gynecology practice (4).

A diagnostic method's accuracy is measured by comparing its correct diagnoses by those of gold standard method, which sometimes can depend on different target group characteristics. In addition, practicality and cost-effectivity are important aspects of a diagnostic method on the way of being "gold standard". ESB by Pipelle® has been shown to be cost-effective in diagnosing endometrial cancer among patients with postmenopausal bleeding (5).

In this study, because it has been suggested as practical and cost-effective method, we aimed to evaluate diagnostic reliability of Pipelle® biopsy, and to further delineate the possible factors causing inconsistent results when compared to D&C method.

Materials and Methods

Prior to the study, Namık Kemal University Faculty of Medicine Clinical Research Ethical Board approval was obtained (Document number 2020.87.04.11, April 30th, 2020). One hundred and twenty-two patients' pathology reports of endometrial samplings done via concurrent Pipelle® biopsy and D&C methods were retrospectively collected from medical records of Department of Obstetrics and Gynecology at Namık Kemal Community Hospital.

Statistical Analysis

Statistical analyses were performed by using SPSS-20 software. Demographic characteristics and endometrial thickness values were analyzed. Categorical variables were given as numeric and percentages. By calculating consistency rates for sensitivity, specificity, negative and positive predictive values, Pipelle® biopsy's diagnostic accuracy was determined in this cohort.

Prior to the procedures, routine gynecologic evaluation by speculum, bimanual exam and transvaginal ultrasonography was completed. Also, complete blood count, liver and renal function tests, serum β-hCG, basic coagulation tests, and serum work-up for hepatitis B, C, and HIV were done. Inclusion criteria were postmenopausal bleeding, postmenopausal endometrial thickening (>5 mm), menorrhagia, metrorrhagia and focal endometrial lesion on a transvaginal ultrasonography. Exclusion criteria were history of previous hormonal therapy or intrauterine surgery. Since general anesthesia is not given in endometrial biopsy procedures in our clinic, in order to evaluate the pain tolerance and cervical stenosis condition during the procedure, it is a long-standing method in our clinic to perform the endometrial biopsy procedures with Pipelle® or a 4.5 mm 00 number sharp curette before the D&C procedure. Only cases whose Pipelle® biopsy and D&C samples were evaluated by the same gyneco-pathologist were included in this study. Pipelle® biopsy's competency was decided by comparing its results to that of standard D&C method.

Results

After applying the inclusion and exclusion criteria, the data from the cohort of 122 patients were reviewed. The median age was 48.3±8.7 years. There were 80 (65.6%) premenopausal and 42 (34.4%) postmenopausal patients. The median values were 3.2±2.2 for gravida and 2.5±1.4 for parity. The mean body mass index (BMI) was calculated as

29.6±6.1 (Table 1). Pipelle® biopsy results were as follows: 44 cases with polyps (36.1%), 26 with atrophy (21.3%), 34 with proliferative endometrium (27.9%), 11 with secretory endometrium (9.0%), 4 with carcinoma (3.3%), 1 with hyperplasia without atypia (0.8%), and 2 with inflammation result (1.6%) (Table 2).

D&C results were as follows: 55 cases with polyps (45.1%), 20 with atrophy (16.4%), 31 with proliferative endometrium (25.4%), 9 with secretory endometrium (7.4%), 4 with carcinoma (3.3%), 1 with hyperplasia without atypia (0.8%), 2 with inflammation result (1.6%) (Table 2). Sensitivity, specificity, positive and negative predictive value of tests were measured, concordance rate was calculated for proliferative endometrium, atrophy, polyp, secretory endometrium, endometrial cancer, non-atypical hyperplasia and inflammation at the rates of 97.6%, 95.3%, 91.7%, 98.3%, 100%, 100%, and 100%, respectively (Table 3).

Discussions

In this study, our findings supported that, instead of D&C, a practical endometrial biopsy method Pipelle®s can be utilized in many clinical situations where uterine pathologies are searched for. In endometrial polyps and atrophies, acceptable inconsistency rates were observed while remarkably high consistency rates were found with the rest of the compared uterine pathologies.

Table 1. Demographic characteristics of the patients (n=122)

Age (median ± SD)	48.3±8.7
Gravida (median ± SD)	3.2±2.2
Parity (median ± SD)	2.5±1.4
Endometrial thickness (median ± SD)	10.7±5.1
Menopause n (%)	42 (34.4)
Body mass index (median ± SD)	29.6±6.1

SD: Standard deviation

Table 2. Pipelle® EMB and D&C results

Pathology	D&C, n (%)	Pipelle® EMB, n (%)
Proliferative endometrium	31 (25.4)	34 (27.9)
Atrophy	20 (16.4)	26 (21.3)
Polyp	55 (45.1)	44 (36.1)
Secretory endometrium	9 (7.4)	11 (9.0)
Endometrial cancer	4 (3.3)	4 (3.3)
Hyperplasia without atypia	1 (0.8)	1 (0.8)
Inflammation	2 (1.6)	2 (1.6)

D&C: Dilatation and curettage

Pipelle® biopsy is a valuable method that provides low false negative results especially in cases with endometrial cancer and atrophy (6). On the other hand, some factors can cause failures such as less than 4 mm endometrial thickness, inflammation, polyps, and submucous myomas (7). In some reports, hysteroscopic sampling was found to have lower sensitivity than Pipelle® biopsy and D&C methods, implying the leakage of endometrial cells along with hysteroscopic media (8).

D&C is the gold standard for diagnosing endometrial tissue pathologies (9). However, due the need for anesthesia, postoperative pain and relatively higher rate of complications, alternative diagnostic methods have been developed.

Pipelle® biopsy is an invaluable minimally invasive diagnostic method which provides sampling adequacy over 98% when endometrial thickness is over 5 mm (10). Interestingly none of our 12 cases with less than 5 mm endometrial thickness had result failure.

Piatek et al. (11) reported the sampling adequacy as 82.3% and 84.1% for Pipelle® biopsy and D&C methods, respectively. They observed that the highest sampling adequacy was in patients with abnormal uterine bleeding (88.8%) and lowest in patients with "abnormal endometrial imaging" indications (37%).

The most frequent factors associated with failure to report in D&C specimens were reported as menopausal status (25.4%) and BMI (11). At the same study, operator experience, whether performed by resident physician in training or by specialist in gynecology, was not associated with specimen adequacy. Although collection of all samples in this study by a single gynecologic oncologist was an advantage, limited number of patients could be considered as a disadvantage.

In endometrial sampling, both the diagnosis and exclusion of malignancy are important tasks. In this study, specimen inadequacy was not encountered whether specimens were obtained by Pipelle® biopsy or D&C in cases with endometrial hyperplasia or endometrial carcinoma. Regarding pathology results, diagnostic consistency of the two methods was 100% (Table 3). Amant et al. (12) reported that malignancy diagnosis was ruled out in 96% by using the postmenopausal endometrial thickness >4 mm as cut-off value.

However, in exclusion of malignancy, regularity of the entire endometrial cavity is an important factor. In 3 of our endometrial carcinoma cases, endometrial irregularities

Table 3. Diagnostic consistency rates between methods

Diagnosis	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Consistency rate
Proliferation	100%	96.8%	91.1%	100%	97.6%
Atrophy	100%	94.4%	76.9%	100%	95.3%
Polyp	83.3%	100%	100%	85.8%	91.7%
Secretory endometrium	100%	98.2%	81.8%	100%	98.3%
Endometrial cancer	100%	100%	100%	100%	100%
Hyperplasia without atypia	100%	100%	100%	100%	100%
Inflammation	100%	100%	100%	100%	100%

were noticed as invasions into the myometrium. In this study, we diagnosed 3 endometrial cancers, these cases had >7 mm endometrial thickness. Behnamfar and Arshad (13) reported the sensitivity and specificity of Pipelle® biopsy as 94.1% and 100%, respectively. The one leiomyosarcoma case was diagnosed only with D&C method.

In a cohort of 1.535 cases, Machado et al. (14) Pipelle® biopsy's sensitivity and specificity in atypic hyperplasia and endometrial carcinoma diagnoses were reported as 84% and 99%, respectively. In another study, diagnostic accuracy for high grade endometrial cancer was higher than that of low-grade endometrial cancer by Pipelle® biopsy (15). Antoni et al. (16) observed 71% sensitivity and 60% specificity in endometrial hyperplasia and endometrial cancer diagnoses. The latter percentages are lower than our findings. However, there was not any atypical hyperplasia case, which was a limitation in our study.

In this study of Pipelle®, in biopsy and D&C comparison, very consistent results were observed except for endometrial polyp diagnosis. In detail, 13 inconsistent cases out of 14 (92.8%) had endometrial polyps (Table 4).

In their study, while Xie et al. (17) were able to diagnose all off the endometrial cancer cases by Pipelle® biopsy, the most common reasons for inconsistent results were endometrial polyp and atypical hyperplasia diagnoses. In diagnosing atypical hyperplasia and endometrial polyps, they reported the sensitivity and specificity of Pipelle® biopsy as 50% and 26.4%, respectively (17).

In their study, Dijkhuijen et al. (18) reported that in cases with endometrial polyps and endometritis, the sensitivity was 60% for Pipelle® biopsy and was 88.9% for D&C, with the accuracy rates of 98.6% and 99.3%, respectively. The possible reason for the relatively lower sensitivity of these two methods on certain diagnoses such as endometritis and polyps is inadequate sampling.

Chaudry and Javaid (19) observed high accuracy and consistency rates on histopathologic diagnosis results between Pipelle® biopsy and D&C, and they found Pipelle® biopsy method more advantageous since it is less invasive. However, Clark et al. (20), suggested that the Pipelle® biopsy accuracy rates might be lower and therefore additional diagnostic procedures would be recommended in cases with ongoing symptoms.

Several complications can be encountered during an endometrial sampling procedure, uterine perforation is the most bothersome. Seamark (21) reported 1% perforation rate during D&C procedures (21). In a study of Piatek et al. (11), D&C related uterine perforation rate was 0.5% and no complication was observed during Pipelle® biopsy procedures. In our current study, neither perforation nor other complications were occurred in either Pipelle® biopsy or in D&C groups.

Study Limitations

Finally, we mentioned some limitations and strengths of this study. Collection of all samples by experienced gynecologic oncologist and analysis of all samples by the same gyneco-pathologist were the strengths of the study, while presence of a single pathologist in analyzing process, absence of hysterectomy specimens as a definitive pathology results and low number of patients were among its limitations.

Conclusions

In this study, final pathology results were highly correlated between Pipelle® biopsy and D&C procedures. Pipelle®biopsy has lower complication rates, it is less painful and it does not require anesthesia. It can be reliably preferred over D&C in the diagnosis of endometrial pathologies with its comparable consistency rates. Future prospectively designed and larger studies would contribute more on this important subject.

Ethics

Ethics Committee Approval: Namık Kemal University Faculty of Medicine Clinical Research Ethical Board

Table 4. Inconsistent results between Pipelle® EMB and D&C samplings

	Age	Gravida/ parity	BMI	Menopause duration	Endometrial thickness	Biopsy indication	Pipelle® EMB result	D&C result
Case 1	45	2/1	28.6	-	4 mm	Menorrhagia	Endometrial polyp	Atrophy
Case 2	56	3/2	31.25	8 yrs	6 mm	Endometrial thickness	Atrophy	Polyp
Case 3	67	2/2	33.09	20 yrs	9 mm	Endometrial thickness	Atrophy	Polyp
Case 4	44	2/2	19.5	-	10 mm	Intracavitary lesion	Atrophy	Polyp
Case 5	48	7/5	24.8	1 year	13 mm	Endometrial thickness	Proliferative endometrium	Polyp
Case 6	31	1/1	21.4	-	14 mm	Menorrhagia	Atrophy	Polyp
Case 7	49	1/1	24.2	1 year	3 mm	Postmenopausal bleeding	Secretory endometrium	Polyp
Case 8	42	3/3	26.5	-	22 mm	Endometrial thickness and Intracavitary lesion	Proliferative endometrium	Polyp
Case 9	54	2/2	32.1	4 yrs	14 mm	Endometrial thickness and bleeding	Atrophy	Proliferative endometrium
Case 10	53	0/0	29.2	2 yrs	10 mm	Endometrial thickness	Atrophy	Polyp
Case 11	60	3/2	28.5	15 yrs	9 mm	Endometrial thickness and bleeding	Atrophy	Polyp
Case 12	39	5/2	32.8	-	14 mm	Menorrhagia	Secretory endometrium	Polyp
Case 13	49	2/2	26.8	-	13 mm	Menorrhagia	Proliferative endometrium	Polyp
Case 14	51	10/5	27.1	-	14 mm	Menorrhagia	Polyp	Atrophy

BMI: Body mass index, D&C: Dilatation and curettage

approval was obtained (document number 2020.87.04.11, April 30th, 2020).

Informed Consent: This study were designed as hospital data research retrospectively.

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