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Comparison of the Quality of Taking and the Efficiency of Histological Examination of Tissue Samples Obtained Using a Pipette (Pippele (Pipelle) Method) and Methods of Classical Dilation and Curettage

Conflict of interest: nothing to declare.
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Abstract

Introduction. Many methods were invented to obtain endometrial tissue samples to evaluate and realize the reason for abnormal vaginal bleeding.
Purpose. To compare endometrial histology of the sampling specimen by Pipelle with hysterectomy specimens, and D&C biopsy.
Materials and methods. A total of 50 premenopausal and postmenopausal women were prospectively included in this study and were scheduled for hysterectomy, two samples from each patient were taken one by Pipelle device and the other after the hysterectomy. Both were analyzed at the same pathology laboratory.
Results. The patient's mean age was 51.2±7.7 years. Endometrial thickness was more than normal in 37.5% of premenopausal women (>10 mm) and in 83.3% of postmenopausal women (>5 mm). The final histopathology reports were the same in women who had D&C biopsy followed by hysterectomy. Pipelle endometrial histopathology results were in agreement with Hysterectomy histopathology results in 48 patients out of 50 patients, this yielded 96% sensitivity for the Pipelle endometrial sampling device. Invasive well-differentiated endometrial adenocarcinoma was found in 2 cases, they were identical in both, thus this study yielded 100% sensitivity for the Pipelle sampling device in confirming endometrial cancer. Pipelle sampling failed to get adequate samples for histopathology in two samples, which gave 96% adequacy for histopathology.
Conclusions. Pipelle endometrial sampling is an accurate and cost-effective method in diagnosing patients with endometrial disease.
Keywords: Pipelle Endometrial Sampling, Dilatation and Curettage, Endometrial thickness, hysterectomy

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Сравнение качества взятия и эффективности гистологического исследования образцов ткани, полученных с использованием пипетки (способом Пиппеле) и методами классической дилатации и кюретажа

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Резюме

Введение. Существует множество методов для получения образцов ткани эндометрия, чтобы понять и оценить причину аномального вагинального кровотечения.
Цель. Сравнить гистологию эндометрия в образце, взятом способом Пиппеле, с образцами, полученными после гистерэктомии и биопсией D&C (дилатация и кюретаж).
Материалы и методы. В общей сложности 50 женщин в пременопаузе и постменопаузе были проспективно включены в это исследование, и им была назначена гистерэктомия, было взято по два образца от каждой пациентки, один с помощью пипетки, а другой после гистерэктомии. Оба были проанализированы в одной и той же лаборатории.
Результаты. Средний возраст составил 51,2±7,7 года. Толщина эндометрия была больше нормы у 37,5% женщин в пременопаузе (>10 мм) и у 83,3% женщин в постменопаузе (>5 мм). Окончательные гистопатологические отчеты были одинаковыми у женщин, которым была проведена биопсия D&C с последующей гистерэктомией. Результаты гистопатологии эндометрия способом Пиппеле совпали с результатами гистопатологии гистерэктомии у 48 пациенток из 50, что продемонстрировало 96%-ю чувствительность устройства для взятия проб эндометрия способом Пиппеле. Инвазивная высокодифференцированная аденокарцинома эндометрия была обнаружена в 2 случаях, они были идентичными; таким образом, это исследование продемонстрировало 100%-ю чувствительность устройства для отбора проб способом Пиппеле в подтверждении рака эндометрия. В двух образцах способом Пиппеле не удалось получить адекватные образцы для гистопатологии.
Выводы. Забор эндометрия способом Пиппеле является точным и экономически эффективным методом диагностики у пациенток с заболеванием эндометрия.
Ключевые слова: забор эндометрия способом Пиппеле, дилатация и кюретаж, толщина эндометрия, гистерэктомия

■ INTRODUCTION

Endometrial hyperplasia relates to excessive cellular proliferation leading to a rising volume of endometrial tissues. Endometrial hyperplasia is further classified based on the complexity of endometrial glands and cytological atypia, resulting in a classification system of simple or complex hyperplasia, with or without atypia. The most common presentation of endometrial hyperplasia is abnormal uterine bleeding, including menorrhagia, and inter-menstrual bleeding [1, 2].

The WHO classified glandular/stroma architectural patterns, which are either simple or complex. The presence or absence of nuclear atypia is classified into simple atypical hyperplasia and complex atypical hyperplasia [2–5].

Simple hyperplasia represents a very low risk of cancer progression. It is reported that the majority spontaneously regress [2, 4], 18% persist [2], 3% progress to complex atypical hyperplasia [5], and 1% progress to endometrial adenocarcinoma [4, 5]. Complex hyperplasia is reported to regress in the majority of cases, with 22% persisting and 4% progressing to endometrial carcinoma, with a mean duration to progression of approximately 10 years. Both simple and complex hyperplasia is, therefore, not considered pre-neoplastic forms [3].

Complex atypical hyperplasia has been reported to progress in 29% of cases, with a mean duration to progression of 4.1 years [2]. Endometrial hyperplasia with cytological atypia may carry a higher risk of coexistent invasive carcinoma than previously believed 14 with recent studies showing up to 50% of women with atypia having an endometrial carcinoma in subsequent hysterectomy specimens [5–7].

Screening for endometrial hyperplasia and cancer is generally not warranted in asymptomatic women, except those with hereditary nonpolyposis colorectal cancer Women taking tamoxifen are at increased risk of developing endometrial hyperplasia, endometrial polyps, and endometrial cancer and sarcoma although the risk increases are statistically significant only in postmenopausal women [8, 9]. An endometrial biopsy should be performed in all women with abnormal uterine bleeding in whom endometrial hyperplasia or carcinoma is a possibility [9].

Asymptomatic women with benign-appearing endometrial cells noted on cervical cytology should undergo endometrial biopsy if they are at increased risk of endometrial cancer (e.g. postmenopausal, family or personal history of ovarian, breast, colon, or endometrial cancer; tamoxifen use; chronic anovulation; obesity; estrogen therapy; prior endometrial hyperplasia; diabetes) [10–12].

In the UK, hysteroscopy remains the gold standard investigation for abnormal uterine bleeding. Other techniques include blind endometrial biopsy, directed biopsy, dilation and curettage, transvaginal ultrasound, and sono-hysterography. Blind endometrial biopsy techniques are commonly performed using the Pipelle and endometrial lavage. Meta-analysis of 28 of 7914 women has shown Pipelle biopsy to have the highest sensitivity (81%) for the overall detection of atypical endometrial hyperplasia [13–16].

A prospective randomized control trial of Pipelle versus curettage in women with abnormal uterine bleeding revealed a 96% agreement between biopsy pathology and final diagnosis for both procedures [17]. The combination of hysteroscopy with dilatation and curettage or endometrial biopsy, therefore, appears to be a superior diagnostic tool compared with hysteroscopy, dilatation, and curettage or endometrial biopsy performed alone [18, 19].

Transvaginal ultrasound assessment of endometrial thickness is of proven value in the investigation of abnormal uterine bleeding. When considering an endometrial thickness of >5 mm, a meta-analysis of 33 of 35 studies revealed high sensitivity and specificity for detecting endometrial disease. Studies on sono-hysterography and Pipelle biopsy have shown high sensitivity (94%) comparable to that for hysteroscopy and dilatation and curettage in detecting endometrial pathology. Both transvaginal ultrasound and sono-hysterography should be performed in conjunction with endometrial biopsy [20, 21].

■ PURPOSE OF THE STUDY

To compare endometrial histology of the sampling specimen by Pipelle with hysterectomy specimens and D&C biopsy.

■ MATERIALS AND METHODS

Study design and setting

A total of 50 women presented with abnormal uterine bleeding were prospectively included in this study. They were scheduled for a hysterectomy. D&C biopsy was done Full history was taken, and full examination was done. A pelvic ultrasound scan is done on all of them to assess the endometrial thickness, uterine shape, and position and to screen for any abnormality in the ovaries and adnexia. Endometrial samples were taken from each patient by Pipelle sampling instrument preoperatively and sent for histological examination. The histology results of Pipelle endometrial sampling were compared with the histology results of the preoperative D&C biopsy and postoperative hysterectomy results and all were done in the same laboratory.

Inclusion criteria

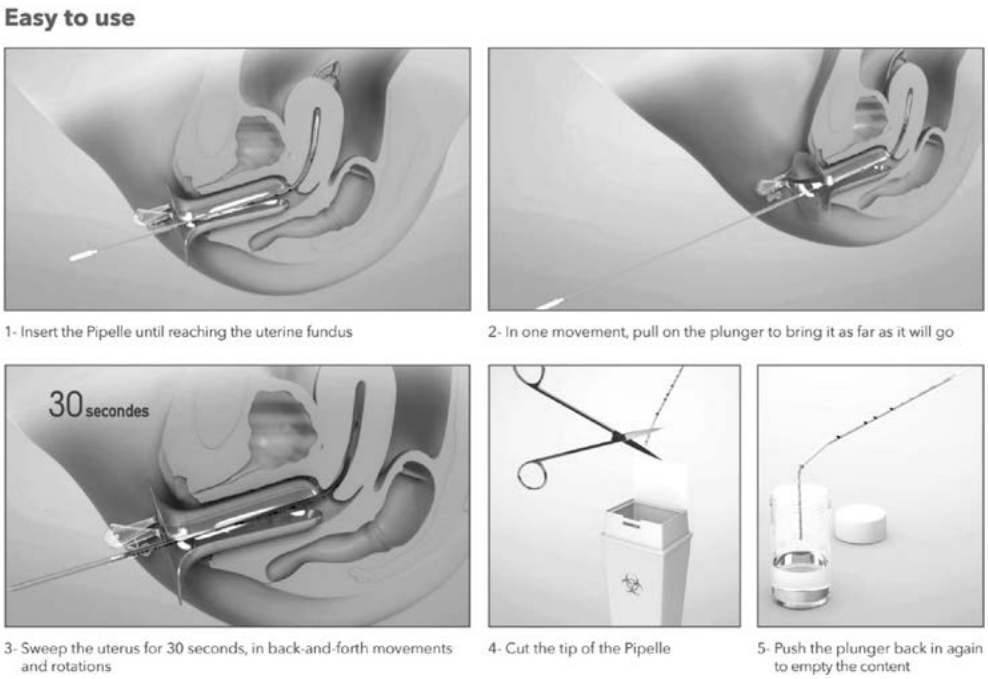
50 patients were diagnosed previously by D&C biopsy due to abnormal uterine bleeding for which a hysterectomy was planned.

Exclusion criteria

Women planned for hysterectomy due to cervical cancer, uterine fibroids, ovarian tumors, or prolepses.

Procedures

A woman is placed in a lithotomy position and a bimanual examination is performed to determine the uterine size and position. Then pick up a sterile speculum from the sterile tray and place it in the vagina. The cervix was anesthetized and then cleaned with a povidone-iodine solution. The cervix was gently probed with the sterile sound after stabilizing the cervix with a tenaculum placed on the anterior lip of the cervix grabbing enough tissue to avoid laceration of the cervix. The endometrial catheter was inserted into the cervix, avoiding contamination from nearby tissue up to the fundus of the uterus until resistance was felt, then the internal piston of the catheter was fully withdrawn, creating suction at the catheter tip. The catheter was moved with an in-and-out motion taking care not to exit the internal os of the cervix, which maintains the vacuum effect than a 360-degree twisting motion was done to move the catheter between the uterine fundus and the internal os. At least four up and down motions were done to ensure that adequate tissues are obtained in the catheter, once the catheter was filled with tissues, the catheter



Pipelle method of sampling [https://www.eurosurgical.co.uk/gynaecology/1997-2/]

was withdrawn, and the sample was placed in a formalin container. The tenaculum was gently removed (Figure).

Statistical analysis

Data were entered into SPSS version 20, descriptive statistics were applied as mean, SD, frequencies, and percentage.

■ RESULTS

Fifty patients with a history vaginal bleeding were recruited for the study. Their mean age of (51.2±7.7 years), with a range of 30 years minimum age years and maximum age of 70 years. Eighty-eight percent of patients were housewives and 94% of them were Iraqi. Eighty-six percent of patients were from urban, while 14% were from rural. According to marital status, 72% were married and 20% were widows. Family history of cancer was positive in 6 (12%) women, HT in 12%, asthma in 4% and DM in 6%. Surgical history was positive in 33 (66%) patients, 26% had D &C. and 20% had CS in the past (Table 1).

The mean age of menarche was (12.7±0.60 years). The mean duration of the menstrual cycle was (5.7±1.9 days), with a minimum of 2 days and a maximum of 10 days. Length of menstrual period range between 15 days to 32 days, with a mean equal to (28.5±2.7 days). Regular menstrual periods were recorded in 84% and a normal amount of blood

Table 1
The demographic of the study

Variables		No.	%
Age (years)	40–49	24	48
	50–59	17	34
	60–69	6	12
	≥70	3	6
Job	Housewife	44	88
	Teacher	4	8
	Nurse	1	2
	Lawyer	1	2
Nationality	Iraqi	47	94
	Non	3	6
Residency	Urban	43	86
	Rural	7	14
Marital status	Married	36	72
	Divorce	4	8
	Widow	10	20
History of cancer	Yes	3	6
	No	47	94
DM	Yes	3	6
	No	47	94
HT	Yes	6	12
	No	44	88
Bronchial asthma	Yes	2	4
	No	48	96
Surgical history	CS	10	20
	Appendectomy	3	6
	D&C	13	26
	Cholecystectomy	5	10
	Polypectomy	1	2
	Thyroidectomy	1	2
	No	17	34

loss in 62%, while 38% mentioned that their cycles were heavy. Eighteen (36%) of patients were postmenopausal. The median duration of menopause was 5.5 years with a minimum of one year and a maximum of 20 years. Nulliparity was recorded in one (2%) patient only, and gravida 6 or more in 60%. A parity of 6 and more was recorded in 36%, with a mean parity of (5.1±2 children), with a range equal to 9 children. Abnormal bleeding was the main complaint of the patients in 40%, menorrhagia in 38%, postcoital bleeding in 6%, postmenopausal bleeding in 34%, dysmenorrhoea in 28%, and others complained of vaginal discharge and lower abdominal pain in 20% of cases. History of ever using contraceptives was positive in 22 (44%), 24% of them used combined oral contraceptive pills and 20% did use an IUC device. The mean duration of oral contraceptive use was (2.14±1.3 years) with a range of 5.6 years, while the mean duration of using the intrauterine contraceptive device was (3.4±1.13 years) with a range of 6 years (Table 2).

Table 2
Gynecologic and obstetric history of women

Variables		No.	%
Age at menarche (years)	12	16	32
	13	23	46
	14	3	6
	Un-identify	8	16
Duration of menstrual period (days)	2–7	40	80
	>7	10	20
Length of menstrual period (days)	15–24	2	4
	25–34	48	96
Regularity of cycle	Regular	42	84
	Irregular	8	16
Blood loss amount	Normal	31	62
	Heavy	19	38
Menopause duration (years)	1–5	9	50
	6–10	2	11.1
	11–15	6	33.3
	16–20	1	5.6
Gravidity	Nulliparous	1	2
	1–5	19	38
	6–10	28	56
	>10	2	4
Parity	Nulliparous	1	2
	1–5	31	62
	6–10	16	32
	>10	2	4
Abortion	1	10	20
	2	12	24
	3	3	6
	Non	25	50
Chief complain	Menorrhagia	19	38
	Intermenstrual bleeding	20	40
	Post-coital bleeding	3	6
	Postmenopausal bleeding	17	34
	Dysmenorrhea	14	28
	Other: VD and pain	10	20
Contraceptive	CCP (Oral)	12	24
	Intrauterine device	10	20
	No	28	56

About 58% of the patient's blood group was O+. Systolic blood pressure was high in 27 (54%) of the patient 140 mmHg, normal in 23 (46%). The mean systolic blood pressure was (136.6±12.87 mmHg). Diastolic blood pressure was ≥90 mmHg in 19 (38%) of the patients with a mean of (83.7±7.8 mmHg). Speculum examination identifies bleeding in 10% and abnormal vaginal discharge in 20%. Ultrasound findings were abnormal in 40%

of patients (polycystic ovarian, bulky uterus, and small-size uterus). Hemoglobin level was <11 in 20% of patients, with a mean of (8.7±4.8 g/dl), minimum hemoglobin level was 8.5g/dl and maximum level was 13.2g/dl. Endometrial thickness was more than normal in 37.5% of premenopausal women and 83.3% in postmenopausal women (Table 3).

The histopathology results of the endometrial tissues obtained by D&C were completely the same as those endometrial tissues obtained by hysterectomy and the Pipple endometrial samples.

The Pipelle endometrial histological results were in agreement with Hysterectomy histology results in 48 patients out of 50 patients, there for this study yielded 96% sensitivity for the Pipelle endometrial sampling device. In two patients the Pipelle failed to get an adequate sample. Comparing Pipelle and hysterectomy histology for individual patients. Simple glandular endometrial hyperplasia without atypia was identical in 10 patients, but in two patients the Pipelle failed to detect polyps, while by hysterectomy sample both were identified.

Complex endometrial hyperplasia with mild atypia was found in 9 patients, and the results were identical in both groups. Complex endometrial hyperplasia with ever atypia was identified in 4 patients and was reported in both groups, Simple and complex endometrial hyperplasia without atypia, were identified in 14 samples of hysterectomy, while detected in 13 samples of Pipelle, because one sample of Pipelle was not adequate for histology. Simple complex endometrial hyperplasia with reactive atypia was present in 5 samples and was identical in both groups.

Table 3
Examination and investigation of women

Variables		No.	%
Blood group	O+	29	58
	A+	11	22
	B+	7	14
	O–	3	6
Systolic BP (mmHg)	<140	23	46
	≥140	27	54
Diastolic BP (mmHg)	<90	31	62
	≥90	19	38
US	Abnormal	20	40
	Normal	30	60
Speculum examination	Normal	35	70
	Bleeding	5	10
	Discharge	10	20
Hb (g/dl)	<11	10	20
	≥11	40	80
Endometrium thickness (n=32) premenopause	<10 mm	20	62.5
	≥10 mm	12	37.5
Endometrium thickness (n=18) postmenopause	<5 mm	3	16.7
	≥5 mm	15	83.3

Table 4
Histopathology distribution

Histopathology	Pipelle	D&C	Hysterectomy	Accuracy (%)
Simple glandular endometrial hyperplasia without atypia	10	10	10	100
Complex endometrial hyperplasia with mild atypia	9	9	9	100
Complex endometrial hyperplasia with severe atypia	4	4	4	100
Simple and complex endometrial hyperplasia without atypia	13	14	14	93
Simple and complex endometrial hyperplasia with reactive atypia	5	5	5	100
Acute on (and) chronic endometritis	1	1	1	100
Hypersecretory endometrial with mild atypia	1	1	1	100
Cystic atrophic endometrial with degeneration	2	3	3	66.7
Invasive well-differentiation endometrial carcinoma	2	2	2	100
Proliferative endometrium gland no atypia	1	1	1	100
Inadequate sample	2	0	0	0

■ DISCUSSION

A population-based study in Finland by Hinkula M. et al reported that a high number of birth, older age of first birth, long birth period, and a short premenopausal delivery-free period reduces the risk of endometrial hyperplasia and cancer in grand-multiparous women 46, history of abortion was positive in 50% of the patients, 24% had 2 abortion, with a mean (1.7±0.68 abortion) [22].

Kurman and colleagues retrospectively studied endometrial samples from 170 patients with untreated endometrial hyperplasia followed by a mean of 14.3 years. They found that progression to carcinoma occurred in 1% of patients with simple hyperplasia, 3% in patients with complex hyperplasia, 8% in patients with simple atypical hyperplasia, and 29% in patients with complex atypical hyperplasia [2]. Acute on (and) chronic endometritis, hypersecretory endometrium with mild atypia, and proliferative endometrium gland no atypia was found in one sample and were reported in both groups [13].

Well-differentiated endometrial adenocarcinomas were found in 2 samples, there were identical in both groups. This confirmed the 100% sensitivity of the Pipelle sampling device in detecting endometrial cancer. Thomas G. et al study found that the sensitivity of the device in detecting endometrial carcinoma was 97.5% 42, and Schneider J., et al, gave a 100% sensitivity result for cancer diagnosis [23].

Invasive cystic atrophic endometrium with degenerative changes was found in 3 samples of hysterectomy, while found in two samples of the Pipelle group. It was due to the inadequacy of the sample. Pipelle sampling failed to get adequate tissue in two samples, which gave it 96% adequacy for histological evaluation [24, 25].

■ CONCLUSIONS

Adequate preoperative histological assessment of the endometrium is feasible with Pipelle biopsies and they are highly accurate in detecting endometrial malignancy,

with 100% sensitivity. The only disadvantage of this study for Pipelle, it failed to get an adequate sample in two patients and failed to detect polyps The cost of D&C was 6 times the cost of Pipelle.

We recommend the use of Pipelle endometrial sampling when we suspect endometrial pathology through careful assessment of the patient by history and examination as an alternative method to D&C biopsy, aiming to reduce the cost and overcome some problems related to D&C biopsy, such as the risk of general anesthesia, uterine perforation, and others.

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