

A Comparative Evaluation of the Three Different Methods of Endometrial Sampling in the Diagnosis of Perimenopausal Bleeding

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Abstract

Background: The aim of the study was to compare the efficacy of three different methods of endometrial sampling (endometrial cytology using nasogastric tube no. 10, endometrial aspiration biopsy using pipelle, and traditional dilatation and curettage) in diagnosis of perimenopausal bleeding.

Methods: This study was conducted on patients with perimenopausal bleeding in the Department of Obstetrics and Gynaecology at R.L. Jalappa Hospital and Research Centre, Tamaka, Kolar, from January 2012 to June 2013. A total of 100 women with perimenopausal bleeding were evaluated using the three different methods of endometrial sampling. After detailed history, examination and relevant investigations, each patient was subjected firstly to endometrial aspiration cytology using nasogastric tube, followed by pipelle aspiration biopsy and lastly traditional dilatation and curettage. Samples collected were sent for cytohistopathological assessment and the results were compared with dilatation and curettage method of sampling.

Results: Data were analyzed using Chi-squared test. There were 91 women with perimenopausal bleeding and nine women had postmenopausal bleeding. Endometrial aspiration cytology could detect benign endometrial pathologies in 44% and premalignant lesions in 19%. Pipelle biopsy detected benign pathologies in 49% and premalignant pathology in 45%. Dilatation and curettage detected benign pathology in 50% and premalignant lesions in 44%. About 37% of endometrial samples by aspiration cytology were found to be inadequate in comparison to 4% of endometrial samples by both pipelle biopsy and dilatation and curettage methods. The sensitivity, specificity and diagnostic accuracy of endometrial aspiration cytology were 29.09%, 87.04% and 59% ($P = 0.095$) respectively. Pipelle biopsy had 100% sensitivity and 98.15% specificity with diagnostic accuracy of

99% ($P < 0.001$).

Conclusion: Pipelle biopsy and dilatation and curettage showed almost equal success rate in the diagnosis of endometrial pathologies. Pipelle biopsy preserves stromal architecture better and takes shorter time compared to dilatation and curettage. Hence, it can be used as an initial screening procedure.

Keywords: Aspiration cytology; Dilatation and curettage; Perimenopausal bleeding; Pipelle biopsy

Introduction

Perimenopausal bleeding is related to unstable and reducing ovarian function. As women approach menopause, an increasing variability of the menstrual pattern is observed. This may make the detection of underlying endometrial pathology particularly challenging in this age group. Endometrial assessment is indicated above the age of 40 years to exclude endometrial hyperplasia or carcinoma [1-3]. Less than 1% of endometrial carcinomas occur under 35 years of age and 6% in those 45 years or less [4].

Besides systemic, iatrogenic and hormonal causes, an endometrial pathology (polypi, submucous myomas, endometrial hyperplasia and endometrial carcinoma) should always be suspected and evaluation is mandatory [5]. The earlier the diagnosis of endometrial carcinoma is made, the better the survival rate. The presentation of the disease is usually by abnormal vaginal bleeding. Diagnosis comprises of well-established techniques ranging from clinical examination to transvaginal scan, traditional dilatation and curettage, endometrial aspiration cytology, and office-based endometrial biopsy [5]. The main reason for performing endometrial biopsy in women with perimenopausal bleeding is to diagnose benign and malignant pathology, so that the necessary treatment can be planned [6, 7].

Various methods of endometrial sampling are used in practice including invasive and non-invasive methods at either inpatient or outpatient basis. The present study was carried out to obtain endometrial sampling by three different methods: endometrial cytology using nasogastric tube, endometrial as-

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Table 1. Age Distribution of Patients

Age in years	No. of patients (n)	%
40 - 44	46	46.0
45 - 49	34	34.0
50 - 54	11	11.0
55 - 59	6	6.0
60 - 64	3	3.0
Total	100	100.0

piration biopsy using pipelle, and conventional dilatation and curettage and to compare the efficacy of these three different methods in obtaining satisfactory samples for endometrial evaluation by pathologists. The study of available literature shows that all the three different methods of endometrial sampling have not been compared to each other.

Materials and Methods

This was a hospital-based comparative study conducted on patients with perimenopausal bleeding in the Department of Obstetrics and Gynaecology at R.L. Jalappa Hospital and Research Centre, Tamaka, Kolar, from January 2012 to June 2013. A total of 100 women with perimenopausal bleeding were evaluated. Each woman was subjected to the three different methods of endometrial sampling (endometrial aspiration cytology using nasogastric tube, pipelle aspiration biopsy and dilatation and curettage). Patients aged above 40 years were included in our study. Patients with adenomyosis, cervical stenosis, bleeding disorders, history of hormonal intake or IUCD, and lower genital tract infections were excluded from the study.

Patients were counseled about all three procedures and informed written consent was taken. After detailed history and examination, pelvic ultrasound was performed. Patients were asked to evacuate their bladder. With patient in dorsal position, Sim's speculum was inserted into vagina to retract posterior vaginal wall, and anterior lip of cervix was held with vulsellum. Firstly an infant nasogastric tube no. 10 was introduced into endometrial cavity without anesthesia or analgesia. Five milliliters of normal saline was injected with the help of syringe, followed by suction of uterine cavity material through nasogastric tube using the syringe. Material aspirated was collected in a bottle containing normal saline. Sample was labeled

as A.

Secondly, the pipelle was introduced into uterine cavity without performing cervical dilatation and then withdrawn outside by rotatory movements to get a sample which was collected in a bottle containing formalin and was labeled as sample B. The pipelle biopsy was followed by standard dilatation and curettage procedure and sample was collected in bottle containing formalin and labeled as sample C. All three samples were examined by pathologist for cytohistopathology assessment. Data were analyzed using Chi-squared test. The sensitivity, specificity, positive predictive value, negative predictive value and the accuracy of the both endometrial aspiration cytology and pipelle biopsy were calculated taking the result of dilatation and curettage method as the reference.

Results

In our study as shown in Table 1, the mean age of patients was 45 years. About 56% were above para 3, 39% were para 2, 3% were primiparous and 2% were nulliparous women. Among 100 women, 91 women presented with perimenopausal bleeding and nine women presented with post-menopausal bleeding. Menorrhagia was the most common bleeding pattern seen in 50% women with perimenopausal bleeding. In Table 2, benign cytomorphology was seen in 42%, endometrial hyperplasia was seen in 19%, and smear was inadequate to comment in 37%.

In Table 3, there was 100% correlation between pipelle biopsy and dilatation and curettage in detecting simple hyperplasia without atypia, secretory endometrium, complex hyperplasia without atypia, irregular endometrium, and complex hyperplasia with atypia by both methods (pipelle biopsy and dilatation and curettage). Carcinoma was detected by both methods. Among the two cases which were reported inadequate by pipelle biopsy, endometrial sampling by dilatation and curettage reported proliferative endometrium in one and inactive endometrium in the other. In contrast, in two cases where samples by dilatation and curettage were inadequate, pipelle biopsy could detect disordered proliferative endometrium in one and simple hyperplasia with atypia in the other.

In Table 4, 37% of endometrial samples were found to be inadequate by endometrial aspiration cytology method when compared to 4% by both pipelle and dilatation and curettage methods. In Table 5, on endometrial aspiration cytology, benign pathology was detected in 44%, and premalignant pathologies in 19%. In 37%, it failed to detect pathology. It could

Table 2. Endometrial Aspiration Cytology Report

Endometrial cytology report	No. of patients (n)	%
Benign cytomorphology (BCM)	42	42
Endometrial hyperplasia (EH)	19	19
Disordered proliferative endometrium (DPE)	1	1
Inflammatory smear (IS)	1	1
Inadequate (IA)	37	37
Total	100	100.0

Table 3. Endometrial Histopathology Report by Pipelle and Dilatation and Curettage

Endometrial histopathology report	Pipelle biopsy no. (%)	Dilatation and curettage no. (%)
Simple hyperplasia without atypia (SHWOA)	28 (28%)	28 (28%)
Secretory endometrium (SE)	19 (19%)	19 (19%)
Proliferative endometrium (PE)	15 (15%)	16 (16%)
Complex hyperplasia without atypia (CHWOA)	9 (9%)	9 (9%)
Disordered proliferative endometrium (DPE)	9 (9%)	8 (8%)
Simple hyperplasia with atypia (SHWA)	5 (5%)	4 (4%)
Irregular endometrium (IRE)	5 (5%)	5 (5%)
Complex hyperplasia with atypia (CHWA)	3 (3%)	3 (3%)
Inadequate (IA)	4 (4%)	4 (4%)
Carcinoma (CA)	2 (2%)	2 (2%)
Inactive endometrium (IE)	1 (1%)	2 (2%)
Total	100 (100%)	100 (100%)

Table 4. Comparison of Adequacy of Endometrial Sampling by Different Methods

Endometrial sampling	Adequate (n = 100)	Inadequate (n = 100)
Endometrial aspiration cytology	63 (63.0%)	37 (37.0%)
Pipelle biopsy	96 (96.0%)	4 (4.0%)
Dilatation and curettage	96 (96.0%)	4 (4.0%)

not detect malignancy. On pipelle biopsy, benign pathologies were detected in 49%, premalignant pathology in 45%, carcinoma in 2% and sample was found to be inadequate in 4%. On dilatation and curettage, benign pathologies were detected in 50%, premalignant pathologies in 44%, carcinoma in 2% and sample was found to be inadequate in 4%.

Discussion

Endometrial sampling for histopathology is very important in evaluation of perimenopausal bleeding. Until recently, the standard method of endometrial assessment was by dilatation and curettage. It requires general anesthesia and has complications such as uterine perforation, hemorrhage and infection. It obtains tissue from less than 50% of the uterine cavity in 60% of procedures [2, 5, 8]. The concept of office endometrial sampling has gained wide acceptance as there is no need for general anesthesia or elaborate equipment.

In 2010, Bhosale and Fonseca conducted a retrospective study of 112 perimenopausal women with abnormal uterine bleeding in the age group of 40 - 52 years for a period of 6 months and reported that 78.6% belonged to age group of 40 - 49 years [9]. In our study, 80% of women belonged to age group of 40 - 49 years which correlates with other studies. An increased number of cases in age group of 40 - 49 years could be due to the fact that as menopause approaches, there is decrease in number of ovarian follicles with increasing resistance to gonadotrophic stimulation resulting in a low level of estrogen which cannot keep the normal endometrium growing.

The most common endometrial pathology in our study was simple hyperplasia without atypia (28%) followed by secretory endometrium (19%) and proliferative endometrium (16%). The incidence of endometrial carcinoma in our study was 2%. Both these women were aged more than 60 years and presented with post-menopausal bleeding. One of them was a known diabetic and on regular oral hypoglycemic agents and the other was detected hypertensive at the time of admission to our hospital and was started on antihypertensives. Endome-

Table 5. Correlation of Detection of Endometrial Pathologies by Three Different Methods

Endometrial pathology	Methods of endometrial sampling		
	Aspiration cytology (%)	Pipelle biopsy (%)	Dilatation and curettage (%)
Benign pathology	44	49	50
Premalignant pathology	19	45	44
Carcinoma	0	2	2
Inadequate	37	4	4

triod adenocarcinoma was reported in both cases.

Muzzafar et al [10] in 2005 conducted a retrospective analysis of 260 endometrial curettings to study various histopathological features in women aged 21 - 50 years with excessive blood loss and correlate them with clinical presentations. He found majority of them (48.1%) belonged to 41 - 50 years and the most common endometrial pathology detected was endometrial hyperplasia (24.7%). Sarwar and Haque [11] in 2005 studied 50 women with abnormal uterine bleeding to compare the type and frequencies of pathologies in endometrial curettings and reported 2% incidence of endometrial carcinoma. The frequency of most of endometrial pathology in our study closely correlates with other studies [10-14].

Endometrial hyperplasia is a common diagnosis especially in perimenopausal women causing irregular or prolonged bleeding due to anovulatory cycles. Heavy bleeding is due to sustained levels of estrogens. The importance of histopathological evaluation of the endometrium in women with perimenopausal bleeding should not be underestimated as it could be due to an underlying malignancy.

Cytology failed to detect benign endometrial pathologies in 20% and endometrial hyperplasia in 14% in women with perimenopausal bleeding. Among nine women who presented with post-menopausal bleeding, endometrial aspiration cytology could detect pathologies in only six of them. It missed one case of proliferative endometrium and one case of endometrial hyperplasia in women with post-menopausal bleeding. In one case of post-menopausal bleeding where both pipelle biopsy and dilatation and curettage reported sample to be inadequate, cytology could detect benign pathology in that patient. This is the only instance where endometrial cytology has proved to be superior to other two methods of sampling. Cytology failed to detect malignancy in both patients.

In our study, the adequacy of sample by pipelle biopsy was 96% and by dilatation and curettage was 96%. Both the methods were comparable. Of the four inadequate endometrial samples obtained by pipelle biopsy, two were from women with perimenopausal bleeding where in one woman, cytology reported endometrial hyperplasia and dilatation and curettage method reported inactive endometrium. In the other woman, dilatation and curettage method reported proliferative endometrium which was missed by other two methods of sampling. Rest two inadequate samples were from women with post-menopausal bleeding of whom all the three methods of endometrial sampling were insufficient in one woman and in the other woman benign pathology was detected on endometrial aspiration cytology.

Dilatation and curettage reported four endometrial samples as inadequate. It failed to detect one case of simple hyperplasia with atypia and one case of disordered proliferative endometrium in women with perimenopausal bleeding which were detected by pipelle endometrial sampling. Other two cases were in women with post-menopausal bleeding where all three methods failed to detect any pathologies in one woman and in the other woman benign pathology was detected by cytology alone.

Very limited literature is available regarding the criteria for considering an endometrial specimen as adequate or inadequate.

In our study the endometrial samples showing only large areas of hemorrhage and scanty glands or stroma were labeled unsatisfactory to report and the clinician was advised to repeat biopsy if clinically indicated. After menopause, there is lack of estrogen stimulation, resulting in atrophic endometrium which may yield inadequate sample during endometrial biopsy. Large dilated venules situated superficially under a thin endometrium may rupture causing excessive uterine bleeding.

Baral and Pudasaini [12] reported 8% samples to be inadequate. Jairajpuri et al [15] found 2.6% and Shams [16] found 2% samples to be inadequate in women with perimenopausal bleeding.

We found that endometrial aspiration cytology has a very low sensitivity of 26.09% with specificity of 87.04% and positive predictive value of 83.16%. It had accuracy of 59% in detecting premalignant and malignant endometrial pathologies ($P = 0.095$). In contrast, Malik et al [17] reported sensitivity of 83.3% and specificity of 95.4% using insemination cannula. Hemalatha et al [18] found that the diagnostic accuracy was greater in aspiration cytology than dilatation and curettage since two cases of endometrial hyperplasia were missed on dilatation and curettage but were diagnosed on aspiration cytology and confirmed on hysterectomy. Correlation of aspiration cytology with dilatation and curettage was reported to be 94%. Roger et al have reported 98% and Murice et al have reported 93.75% correlation of cytology with dilatation and curettage reports [18].

In our study pipelle endometrial biopsy showed sensitivity of 100% and specificity of 98.15% for detecting premalignant and malignant endometrial pathologies. It has a very high accuracy of 99% in detecting premalignant and malignant endometrial pathologies ($P < 0.001$). Fakhar et al [6] compared endometrial sampling by pipelle curette with dilatation and curettage and reported high sensitivity of 100% and specificity of 98% for detecting hyperplasias with atypia and 100% sensitivity and specificity for detecting malignancy. In another study by Bunyavejchevin et al [19], the sensitivity and specificity of pipelle in endometrial tissue sampling compared to fractional curettage were 87.5% and 100% respectively.

Conclusion

Endometrial aspiration cytology had sample adequacy of 63% compared to pipelle biopsy (96%) and dilatation and curettage (96%). Pipelle biopsy has 100% sensitivity and 98.15% specificity in detecting premalignant and malignant endometrial pathologies compared to dilatation and curettage method of endometrial sampling. Pipelle biopsy has very high accuracy of 99% in detecting premalignant and malignant pathologies of endometrium. Pipelle biopsy and dilatation and curettage showed almost equal success rate in the diagnosis of endometrial pathologies. Pipelle sampling of endometrium preserves stromal architecture better and takes shorter time compared to dilatation and curettage. Pipelle biopsy is a rapid outpatient procedure, less painful and cost effective. It does not require anesthesia or cervical dilatation and has fewer complications. Hence, it can be used as an initial screening procedure in low

resource settings.

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