Original Research Article

Pipelle endometrial sampling vs dilatation and curettage in abnormal uterine bleeding

Harpreet Kaur[1],*, Priyanka Mukherjee[1], Ritika Gupta[1], Esha Patel[1]

[1]Dept. of Obstetrics and Gynaecology, Tata Main Hospital, Jamshedpur, Jharkhand, India

A B S T R A C T

Aim to ascertain if aspiration endometrial sampling can replace conventional dilatation and curettage for histopathological evaluation in abnormal uterine bleeding.

Materials and Methods: The present study was a prospective, observational, comparative study conducted at Tata Main Hospital from 1st November 2015 to 31st October 2016. Sample size was calculated as 200. Data was analyzed using SPSS 22 version software. Sensitivity, pecificity, NPV, PPV and accuracy of histopathological diagnosis of pipelle will be computed taking DNC as the standard.

Result: The global sensitivity of pipelle endometrial biopsy is 90.72%, specificity is 100%, NPV is 25%, 100% is PPV.

Conclusion: The accuracy for histopathological diagnosis is good if sample is adequate, hence it can be used as a first line method for endometrial sampling. Additional diagnostic methods need to be applied if sample obtained is inadequate for histological examination or if insertion fails.

1. Introduction

Abnormal uterine bleeding (AUB) is a common gynaecologic complaint, affecting 10 to 30% reproductive age women and 50% premenopausal women. Factors that impact the incidence most greatly are age and reproductive status. Menorrhagia is a frequent problem in reproductive aged women. It is estimated that a woman has a 1 in 20 lifetime chance of consulting her primary physician because of menorrhagia.[1] With increasing age in premenopausal and postmenopausal women there is a greater risk of neoplastic growths. The diagnostic goal with AUB is to exclude cancer and to identify the underlying pathology to allow optimal treatment.

Endometrial sampling should be performed to evaluate AUB in women who are at risk of endometrial pathology including polyps, hyperplasia and carcinoma. Such sampling is advisable in evaluation of anovulatory bleeding in women older than 35 to 40yrs of age and in younger women who are obese, have history of prolonged anovulation and in those who do not respond to medical therapy.[2]

Hysteroscopic biopsy is the gold standard technique for endometrial evaluation, however it is not widely available in developing countries. In primary care settings, the most frequently used method for endometrial evaluation is sonography with conventional dilatation and curettage (D&C). In comparison to dilatation and curettage office endometrial biopsy is less invasive, can be performed without need of anaesthesia and can expedite appropriate evaluation and therapy.

This study is designed to ascertain if aspiration endometrial sampling with pipelle can replace conventional dilatation and curettage for histopathological evaluation in abnormal uterine bleeding.

2. Aim and Objectives

To compare diagnostic accuracy and efficacy of pipelle endometrial sampling with conventional dilatation and

* Corresponding author.
E-mail address: portnewrg@gmail.com (H. Kaur).

curettage and to determine the factors which may impact it's effectiveness.

3. Materials and Methods

The present study was a prospective, observational, comparative study conducted from 1st November 2015 to 31st October 2016. Sample size was 200.

3.1. Inclusion criteria

1. Patients aged 35yrs and above presenting with AUB
2. Patients less than 35yrs with risk factors of endometrial cancer (obese, hypertension, diabetic, chronic an ovulation).
3. Postmenopausal bleeding of any amount.

3.2. Exclusion criteria

1. Pregnancy associated bleeding.
2. Local gynecologic causes of bleeding.
3. Endometrial thickness of less than 4mm.
4. Infection of the genital tract.

3.3. Methodology

Patients were enrolled in the study after providing a written informed consent. Detailed history was taken. A general physical, abdominal and pelvis examination was performed and findings noted. Transvaginal sonography was performed to detect uterine size, endometrial thickness and uterine/ adnexal pathology. Patients with local causes like myomas and polyps were excluded from the study. Routine pre-operative investigations for minor procedures were performed on outpatient basis.

Endometrial sampling was done in the last week of menstrual cycle for women with regular periods and in those with irregular cycles it was done when she was not having bleeding. Endometrial sampling with pipelle and by dilatation and curettage was done at the same time to maintain synchronicity. Pipelle sampling was done prior to anaesthesia for dilatation and curettage.

Both the samples were sent to the pathologist who was blinded as to the method of sample collection. All samples were graded as adequate /inadequate. The histopathology reports of the pipelle sample were compared with that of D&C sample.

Factors affecting insertion of pipelle (parity, menopausal status, BMI) and adequacy of samples obtained by pipelle were analysed and complications of both the procedures were noted.

Data was analyzed using SPSS 22 version software. Categorical data was represented in the form of frequencies and proportions. Continuous data was represented as mean and standard deviation Chi-square and t test was used to significance. Sensitivity, specificity, NPV, PPV and accuracy of histopathological diagnosis of pipelle was computed taking D&C as the standard. The significance level adopted in all analyses was 0.05.

4. Results

The demographic characteristics of the patient population are listed in Table 1. Most of the patients (40.5%) belonged to the perimenopausal age group of 46 to 50 yrs. Two percent of subjects were nulliparous and 98% multiparous. Majority of subjects were para 2. Out of 200 subjects, 112 were Obese class 1 with a BMI ranging between 30 to 34.99kg/m^2. None of the subjects were morbidly obese or underweight.

Table 2 describes the outcome of pipelle and D&C. In 6 (3%) of the subjects pipelle could not be inserted through the cervical os. Uterine curettage procedure failure occurred in 2 subjects with a very fibrous and hypertrophied cervix, where the pipelle obtained adequate sample for examination. There was no significant difference between the two techniques with regard to insertion failure (p = 0.2888).

Following insertion the sample attained was subjected to histopathological examination. Inadequate samples were defined as consisting of only blood, cervical mucus and stromal fragments inadequate for histopathological assessment and diagnosis. In 18 cases (9%), after being correctly introduced in the uterine cavity, the pipelle technique failed to obtain sufficient material for histopathological examination, while uterine curettage was unable to obtain adequate material in 4 cases (2%). The proportion of inadequate samples were higher in the pipelle group and the results were statistically significant (p= 0.0056).

We evaluated the affect of parity, menopausal status (Table 3) and BMI (Table 4) on procedural success of pipelle endometrial sampling. Percentage of insertion failure of pipelle in nulliparous subjects was 50% (2 out of 4 women), while in parous subjects it was only 2.04%. The procedural success of pipelle is better in parous than nulliparous subjects and this result is statisically significant (p<0.0001). Insertion failure of pipelle in postmenopausal women was 8.7% (2 out of 23 postmenopausal women), while in premenopausal women it was only 2.25%., however the difference was not statistically significant(p = 0.2921).

Another factor of significant consequence for the diagnostic effectiveness of pipelle biopsy is BMI (Table 4). We registered the highest percentage of insertion failure in obese class II patients. This can be explained in terms of technical difficulties with performing the procedure, however the results were not statistically significant (p = 0.1080).

Table 5 shows the corelation between endometrial thickness (ET) and adequacy of samples obtained by pipelle and D&C along with p value. Individually it is seen that

Table 1: Demographic characteristics

		No. of subjects(n)	Percentage(%)
Age(in years)	35 – 40	16	8
	41 – 45	69	34.5
	46 – 50	81	40.5
	>50 year	34	17
Menopausal Status	Premenopausal	177	88.5
	Postmenopausal	3	11.5
Parity	0	4	2
	1	23	14
	2	77	36.5
	3	53	28.5
	≥ 4	38	19
BMI	Normal {18.5 – 24.99}	5	2.5
	Preobese {25 – 29.99}	67	33.5
	Obese class –I {30 – 34.99}	112	56
	Obese class –II{35 – 39.99}	6	8
	Obese class –III {≥ 40}	0	0

Table 2: Outcome of pipelle and D&C among the subjects

Tissue adequacy	Pipelle(n=200)		D&C(n=200)		p value
	No.	Percentage	No.	Percentage	
Adequate	176	88%	194	97%	0.3768
Inadequate	18	9%	4	2%	0.0056
Failed to perform procedure	6	3%	2	1%	0.2888

Table 3: Correlation between parity and menopausal status on insertion failure by Pipelle

Parity	Pipelle(n =200)				
	Sample obtained		Insertion failure		
Nulliparous	2	50%	2	50%	p<0.0001
Parous	192	97.96%	4	2.04%	
Premenopausal	173	97.74%	4	2.25%	p 0.2921
Postmenopausal	21	91.3%	2	8.7%	

Table 4: Correlation between BMI and adequacy of sample in study population

BMI (in kg/m^2)	Pipelle(n = 200)				
	Sample obtained		Insertion failure		
Normal {18.5 – 24.99}	5	100%	0	100%	
Preobese {25 – 29.99}	66	98.5%	1	1.5%	
Obese class –I {30 – 34.99}	109	97.32%	3	2.68%	p-value 0.1080
Obese class –II{35 – 39.99}	14	87.5%	2	12.5%	
Obese class –III {≥ 40}	0		0		

when segregated according to endometrial thickness, D&C is considered superior for collection of an adequate sample at an ET between 5 to 8mm, and the result is statistically significant (p 0.0368). At Endometrial thickness of 4mm and $\geq$16mm both pipelle and D&C collected 100% samples. At ET between 9 to 12mm and 13 to 15mm the proportion of samples collected is higher in D&C but the results are not statistically significant.(p = 0.1433 and p = 1 respectively).

The comparison of histopathology of pipelle and D&C is shown in Table 6 and the diagnostic efficiency of pipelle biopsy in our study is summarised in Table 7. For computing the sensitivity and specificity of pipelle biopsy in comparison with D&C, we excluded 6 patients in whom pipelle could not be inserted.

Table 5: Correlation between endometrial thickness and adequacy of sample in the study population

Endometrial thickness (mm)	Pipelle (n= 194)			D&C(n=198)			
	Adequate	Inadequate	% of adequate	Adequate	Inadequate	% of adequate	P value
4.0	1	0	100%	1	0	100%	0.4795
5 - 8	85	10	89.5%	93	2	97.9%	0.0368
9 - 12	63	7	90%	72	2	97.3%	0.1433
13 - 15	26	1	96.3%	27	0	100%	1
$\geq$ 16	1	0	100%	1	0	100%	0.4795

Table 6: Outcome and HPE of pipelle vs D&C in the study population

	D&C (n = 198)		Pipelle (n = 194)		
HPE	No. of patients	Percentage	No. of patients	Percentage	p value
Atropic endometrium	6	3.03%	4	2.06%	0.7728
Proliferative endometrium	106	53.53%	96	49.48%	0.4832
Secretory endometrium	53	26.76%	50	25.77%	0.9141
Hyperplasia without atypia	16	8.07%	14	7.21%	0.8754
Hyperplasia with atypia	5	2.52%	4	2.06%	0.9735
Endometrial polyp	3	1.51%	2	1.03%	0.9787
Adenocarcinoma endometrium	5	2.52%	5	2.57%	0.7723
Not Reported(Sample inadequate)	4	2.02%	18	9.27%	0.0056

Table 7: Accuracy of pipelle biopsy in determining endometrial histopathology

Diagnosis	Sensitivity	Specificity	PPV	NPV	Accuracy
Proliferative endometrium	93.40%	100%	100%	92.63%	98%
Secretory endometrium	96.23%	100%	100%	98.60%	98%
Hyperplasia without atypia	92%	100%	100%	99.48%	99%
Hyperplasia with atypia	80%	100%	100%	99.47%	99%
Endometrial polyp	66.67%	100%	100%	99.48%	99%
Adenocarcinoma endometrium	100%	100%	100%	100%	100%
Atrophic	66.66%	100%	100%	99.47%	97%

5. Discussion

The main reason to perform endometrial biopsy in patients with abnormal uterine bleeding is to exclude cancer and confirm benign nature of the disease. The traditional "gold standard" method of endometrial evaluation represented by dilatation and uterine curettage, is one of the most frequent interventions performed in gynecology.[3] Widespread use of this technique was criticisedfor many years, leading to the introduction of many alternative sampling techniques for detection of endometrial pathology, the most popular of these being the cornier pipelle. Lack of need for general anaesthesia, reduced duration of the diagnostic procedure, cost reduction and decrease in the number and incidence of complications constitute significant advantage of this procedure compared with dilatation and curettage.[4]

Pipelle is a flexible device with a smooth rounded distal tip and tissue collection through side perforations. In order to minimize patient comfort we performed sampling without stablising cervix with a tenaculum. The insertion failure rate in our study was 3% and in 9% of subjects we failed to obtain a sample adequate for histopathological analysis. Toma Aron et al[5] had insertion failure in 8.6% subjects and inadequate sample in 6.7% cases. Szymon Piatek et al[6] had adequate sample in 259 out of 312 women(83.01%) in whom pipelle biopsy was performed. These results are comparable with my study. A recent study by Illavarasi et al. have reported a higher percentage of sample inadequacy

(22.1%).

Factor having potential effect of on insertion of pipelle sampler were analysed and we found that nulliparity adversely afftected insertion while the affect of BMI and postmenopausal was not statistically significant.

We analyzed the effect of endometrial thickness on adequacy of sample obtained and found a higher rate of inadequacy (10.5%) when endometrium was thinner (5 to 8mm), however we had only 1 patient with an ET of 4mm in whom both pipelle and DnC obtained an adequate sample reported as atrophic endometrium. Elsandabesee D and Greenwood P[7] have shown that there is only 27% probability of obtaining an adequate endometrial sample if the central endometrial thickness is less than 5mm. Bakour et al. reported that atropic endometrium on hysteroscopy and ultrasonographic endometrial measurement of less than 5mm decreased the odds of obtaining an adequate sample.

For computing the sensitivity and specificity of pipelle biopsy in comparison with DnC, we excluded 6 patients in whom pipelle could not be inserted.

Proliferative and secrectory histology the sensitivity is 93.4% and 96.23% respectively and accuracy was 98% in both the cases. The specificity and PPV is 100% since there was no discordance between biopsy by pipelle and DnC if the sample collected by pipelle was adequate.

Pipelle detected 14 out of 16 cases of hyperplasia without atypia, sensitivity being 92% and NPV of 99.48%.

In the study by Mona Al Sayed Elkafrawy et al[8] Pipelle had a 100% sensitivity, specificity, PPV and NPV for diagnosing endometrial cancer, hyperplasia and secretory endometrium. For proliferative endometrium the 94% sensitivity and 93% specificity for endometritis the sensitivity was low (57%) while specificity and NPV were high. Only one case of endometrial polyp was present in this study which was missed by pipelle sampler. Sensitivity of 90% for detection of proliferative endometrium, secretory endometrium, hyperplasia without atypia was also reported by Sanam et al.[9] These results are in line with my study. There were no cases of endometritis in my study.

In 1 out of 3 cases of endometrial polyp in my study, the sample obtained by pipelle was inadequate. The sensitivity for this focal lesion is 66.67% being the lowest of all histopathology reports.

The cornier pipelle had a modest sensitivity(66.67%) for detecting endometrial polyp in my study this result was in line with that of Toma Aron et al[5] (Sensitivity 61.5%) and Ibrahim Anwar et al[10] (Sensitivity 60%). Kazandi M et al[11] diagnosed only one case of endometrial polyp from 13 cases.

The sensitivity of detecting is significantly higher in my study compared to 37.5% in the study of Gungorduk et al[12] and 50% in Sanam et al.[9]

For hyperplasia with atypia 4 out of 5 cases were picked up by pipelle, sensitivity being 80% and a NPV of 99.47%.

All cases of adenocarcinoma of endometrium could be diagnosed by pipelle biopsy showing 100% sensitivity.

Bunyavejchevin S et al.in their cross over study on postmenopausal women with bleeding reported 100% specificity and 87% sensitivity of pipelle in relation to fractional curettage, however 1 out of the 3 cases of endometrial cancer was missed. Schnieder J et al[13] showed 100% sensitivity in the 56 cases of endometrial cancer, however the histological subtype differed. In the meta analysis by Dijkhuizen et al[14] 39 studies were analysed which included both premenopausal and postmenopausal women, overall sensitivity for endometrial carcinoma was 99.6% and specificity was 91%. Sensitivity for atypical hyperplasia was 81% with a specificity exceeding 98%. A similar systematic review by Clark et al[3] involving 1013 patients from 11 primary studies concluded that when a biopsy was positive for cancer, the post biopsy probability of endometrial cancer was 81.7% and the pooled probability that a negative biopsy missed an endometrial cancer was 0.95%.

Yasmin et al[15] reported an overall sensitivity of 75%, specificity of 100%, accuracy of 98%, PPV of 100% and NPV of 97.9%. In my study the global sensitivity of pipelle endometrial biopsy is 90.72%, specificity is 100%, NPV is 25%, 100% is PPV. Here we note that when pipelle collects an adequate specimen the NPV varies between 92.63% to 100% but the global NPV is 25%. Hence if the sample collected is inadequate, additional diagnostic measures need to be applied before ruling out disease.

6. Conclusion

The following conclusions are drawn from this study-

1. Endometrial biopsy with pipelle as an outpatient procedure, is a safe and efficient method for evaluating AUB with good patient compliance.
2. The accuracy for histopathological diagnosis is good if sample is adequate, hence it can be used as a first line method for endometrial sampling.
3. Additional diagnostic methods need to be applied if sample obtained is inadequate for histological examination or if insertion fails.
4. Nulliparity adversely affects the procedural success of pipelle sampling which is statistically significant and B.M.I, menopausal status and endometrial thickness have an effect but the results are not statistically significant.

7. Limitations

1. In this study diagnostic accuracy of histopathology of pipelle was compared with D&C only, however focal lesions will be missed by pipelle and hysteroscopic directed biopsy is the gold standard for endometrial evaluation.

2. This study was done with a sample size of 200 women with AUB, however only one patient had an ET of 4mm, hence the comparison of D&C and pipelle in postmenopausal patients requiring endometrial evaluation at ET 4mm was limited.

8. Source of Funding

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9. Conflict of Interest

There is no conflict of interest among authors.

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Author biography

Harpreet Kaur, DNB Resident

Priyanka Mukherjee, Associate Consultant

Ritika Gupta, DNB Resident

Esha Patel, DNB Resident