A Comparison of Pipelle Endometrial Biopsy with Dilatation and Curettage for Evaluation of Endometrial Pathology in Abnormal Uterine Bleeding

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ABSTRACT

BACKGROUND

Histopathological assessment of endometrium is recommended in cases of AUB to rule out premalignant conditions and malignancy. Endometrial sampling can be done by Pipelle biopsy in outpatient units as well as by conventional Dilatation and Curettage in an operation theatre setup. Our study aims to compare the efficacy of office endometrial biopsy with D and C in terms of its sample adequacy and diagnostic accuracy

METHODS

This prospective study was conducted in a tertiary care centre over a period of 2 year follow up. 150 women presenting with abnormal uterine bleeding were included. A detailed history along with clinical examination findings and ultrasound report showing pelvic pathology and endometrial thickness were entered in the proforma. They were then randomly allotted into 2 groups, group A (n=75) had D and C under anaesthesia and group B (n=75) underwent Pipelle endometrial sampling. Histopathology reports are collected and sample adequacy and histopathology pattern were analysed. Patients are subsequently followed up for a period up to two years. Those who underwent subsequent hysterectomy are analysed for the endometrial pathology in hysterectomy specimen which is used as gold standard to compare endometrial pathology.

RESULTS

Sample accuracy for D and C is 93% and for Pipelle biopsy it was 92%. Inadequate specimens by both methods were mostly focal lesions. Diagnostic accuracy for atypical hyperplasia and adenocarcinoma by D and C is 97.6% and by Pipelle biopsy is 95.7%.

CONCLUSIONS

Thus, focal lesions can be missed by Pipelle endometrial biopsy as well as by D and C. 33.3% of atypical hyperplasia diagnosed by both D and C and Pipelle biopsy had coexisting adenocarcinoma in hysterectomy specimen. Pipelle biopsy is a cost effective method for endometrial sampling when compared with D and C.

KEYWORDS

Abnormal Uterine Bleeding, Dilatation and Curettage, Pipelle Endometrial Biopsy, Atypical Hyperplasia, Endometrial Carcinoma

BACKGROUND

Abnormal Uterine Bleeding (AUB) has a huge impact on women's quality of life with a reported incidence of up to 30% among women of reproductive age group.[1] FIGO has classified AUB according to the aetiology by PALM-COEIN classification. Descriptive terms used to categorise AUB pattern include Heavy Menstrual Bleeding, Intermenstrual bleeding, Post-menopausal bleeding, Polymenorrhoea and irregular bleeding pattern. ACOG recommends endometrial biopsy for women with AUB older than 45 year as first line test and in younger women with history of unopposed oestrogen exposure (such as obesity, and PCOS) and persistent AUB.[2]

Endometrial sampling can be done either by conventional Dilatation and Curettage or by office endometrial biopsy devices like Pipelle, Vabra aspirator etc. The latter can be done in outpatient department without any anaesthesia and at a comparatively lower cost. The literatures show a sample adequacy rate of 89.74% to 97% for Pipelle biopsy when compared with D & C.[3] Moreover in 60% of D&C less than half of the endometrium is curetted with added risk of anaesthesia complications, perforation and infections. The incidence of endometrial carcinoma is increasing along with its risk factors like obesity, diabetes and PCOS. Thus diagnosing endometrial hyperplasia, a premalignant condition for carcinoma endometrium helps to reduce the morbidity of carcinoma endometrium.

The study aims at assessing the efficacy of Pipelle biopsy as still many clinicians rely on Dilatation and Curettage doubting sample adequacy of Pipelle endometrial biopsy. The study population was randomised into 2 groups because the literature shows many studies with both procedure done on same group of patients and also considering the excessive cost when both procedures are done on the same patient. In this study the sampling accuracy of Pipelle endometrial biopsy and D and C are compared with the gold standard which is the hysterectomy specimen.

METHODS

This prospective cohort study was conducted at Believers Church Medical College Hospital, Thiruvalla, Kerala with due ethical permission from Institutional Ethical Committee. Women (n=150) who presented to our gynaecology OPD during the period July 2017 to December 2019 with AUB were included in this study after obtaining the written informed consent. They were then randomly allotted into 2 groups, group A (n=75) had D and C under anaesthesia and group B (n=75) had Pipelle biopsy in Out Patient Clinics. The proforma included details like age, parity, mode of delivery, bleeding pattern, examination findings and Ultrasound report with endometrial thickness. Patient selected in group A had D and C under short anaesthesia after getting their informed consent. Group B underwent Pipelle biopsy in the Outpatient Clinic 1 to 2 hour after taking oral analgesics.[4]

Endometrial sampling was done with Pipelle without anaesthesia and after explaining the procedure. An Endometrial cannula with a length of 23 cm, inner diameter of 2.6 mm and outer diameter of 3.1 mm and with a blunt distal tip is used for this procedure. The endometrial tissue is obtained by suction aspiration from all walls of uterus by rotating the device 3 to 4 times to ensure adequate specimen collection. Both specimens are sent in formalin bottles to pathology department. The pathologist is kept blinded about which procedure was done to reduce bias. Histopathology report is collected and sample size, adequacy and histologic patterns are evaluated. Patients are subsequently followed up for a period of up to two year. Those who underwent hysterectomy are further analysed for the endometrial pathology in hysterectomy specimen which is compared with their prior endometrial sampling report. 42 out of 75 patients in Group A (D and C) and 47 out of 75 in Group B (Pipelle) underwent subsequent hysterectomy for AUB during the follow-up period.

Inclusion Criteria
- Woman above 35 years with AUB.
- Ultrasound findings suggestive of fibroids, adenomyosis, endometriosis and malignancy.
- All postmenopausal bleeding irrespective of endometrial thickness.
- Endometrial thickness above 12 mm in perimenopausal if there is no other pelvic pathology in USG.

Exclusion Criteria
- AUB due to coagulopathy, drugs and endocrine causes.
- Pregnancy.
- Cervical stenosis.
- Bleeding due to cervical or vaginal pathology.
- Genital tract infections and PID.

Statistical Analysis
Histopathological report of endometrium by D and C, Pipelle biopsy and subsequent hysterectomy were analysed using Fisher's exact test and Chi Square test, as appropriate. The accuracy was calculated and expressed as percentage with 95% confidence interval. SPSS version 20 was used for statistical analysis. A p- value less than 0.05 was considered as significant.

RESULTS

In both groups the majority of the women were of the age group 45-49 years i.e., 31.3% (47 patients of 150) belonged to this age group. This was followed by the group 40-44 years with 22.6% incidence. Thus 54% of women belongs to the age group of 40-49 years. 12.6% of women were above 60 years. Oldest being a 78-year-old lady with recurrent Postmenopausal bleeding and negative Pipelle

biopsy and it was a benign submucosal fibroid in subsequent hysterectomy.

Age in Years	D & C (%)	Pipelle (%)	Total (n=150)
35-39	5(6.6%)	4(5.3%)	9(6%)
40-44	15(20%)	19(25%)	34(22.6%)
45-49	21(28%)	26(34%)	47(31.3%)
50-54	16(21.3%)	12(15%)	28(18.6%)
>55-59	8(10.6%)	5(6.6%)	13(8.6%)
>60	10(13.3%)	9(12.5%)	19(12.6%)
Table 1. Age Distribution of Study Population in the Two Groups			

Bleeding Pattern in AUB

Heavy Menstrual Bleeding (HMB) was the most common bleeding pattern with an incidence of 66% in D and C group and 64% in Pipelle group, followed by postmenopausal bleeding (PMB) with incidence of 18% in group A and 21% in group B. Polymenorrhagia was seen among 5% of women.

Figure 1. Bleeding Pattern of AUB

*HMB-Heavy Menstrual Bleeding, IMB-Inter Menstrual Bleeding, PMB- Post Menopausal Bleeding
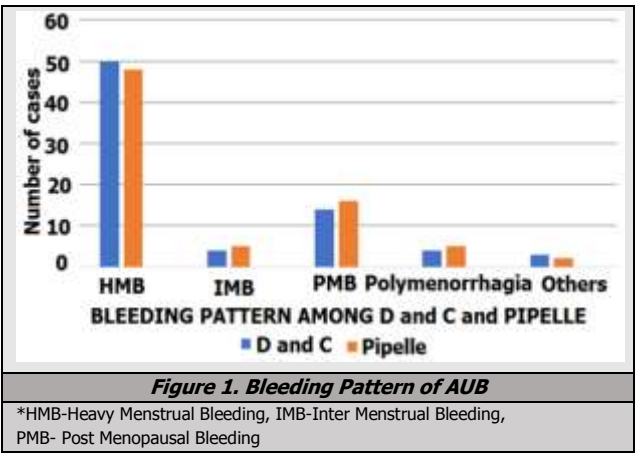
Sample Adequacy

The sample adequacy by D and C was 93% and by Pipelle biopsy was 92%. 7% (5 cases) in group A had inadequate samples. On analysing these inadequate samples, two were taken from thin endometrium in postmenopausal bleeding and histopathological report were just blood clots with fragmented scanty glands and senile cystic atrophic changes respectively. Two cases of recurrent postmenopausal bleeding with negative Pipelle biopsy (inadequate samples) were found to have endometrial polyp and remaining one had sub mucous fibroid and proliferative endometrium in their subsequent hysterectomy specimen. In Pipelle group there were 6 inadequate samples (8%) and all underwent subsequent hysterectomy due to recurrent PMB. There were 2 cases of endometrial polyp, one atrophic endometrium, and 3 had proliferative endometrium with submucous endometrial polyp. Thus, focal lesions can be missed by both methods.

The most common histopathological pattern in both groups was proliferative endometrium (30.6% in group A and 28% in group B). This was followed by secretory endometrium and disordered proliferative endometrium. There was concordance for Hyperplasia without atypia diagnosed by both methods when compared with final

hysterectomy specimens but not for atypical hyperplasia. 1 out of 3 in the D and C group and 2 out of 6 cases in the Pipelle biopsy group showed carcinoma endometrium in hysterectomy specimens, thus 33.3% of atypical hyperplasia had coexisting carcinoma endometrium in the hysterectomy sample.

The incidence of endometrial polyp in D and C group was 4% but in subsequent hysterectomy it was 11.9%. Similarly, the incidence of endometrial polyp in Pipelle group was 1.3% and in the follow-up hysterectomy it was 6.3%.

Figure 2. Sample Adequacy of D and C and Pipelle Biopsy Specimens
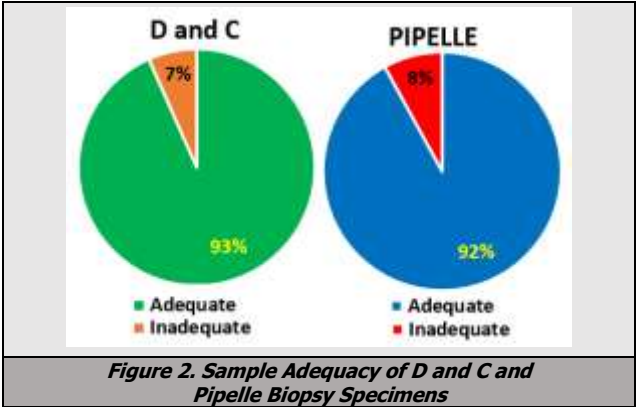
HPE Report	D and C (n=75), n(%)	Hysterectomy (n=42), n(%)
Proliferative endometrium	23(30.6%)	10(23.8%)
Secretory endometrium	16(21.3%)	8(19%)
Hormonally modified endometrium	5(6.6%)	3(7.1%)
Disordered Proliferative Endometrium	12(16%)	4(9.5%)
Hyperplasia without atypia	4(5.3%)	3(7.1%)
Atypical hyperplasia	3(4%)	2(4.7%)
Atrophic endometrium	1(1.3%)	3(7.1%)
Carcinoma Endometrium	3(4%)	4(9.5%)
Endometrial polyp	3(4%)	5(11.9%)
Inadequate biopsy	5(6.6%)	-
Total	75(100)	42(100)
Table 2. Comparison of Histopathological Report of D and C and Hysterectomy		

HPE Report	Pipelle Biopsy (n=75), n(%)	Hysterectomy (n=47), n(%)
Proliferative endometrium	21(28%)	10(21.2%)
Secretory endometrium	15(20%)	12(25.5%)
Hormonally modified endometrium	5(6.6%)	3(6.4%)
Disordered Proliferative Endometrium	12(16%)	5(10.6%)
Hyperplasia without atypia	7(9.3%)	5(10.6%)
Atypical hyperplasia	6(8%)	4(8.5%)
Atrophic endometrium	-	1(2.1%)
Carcinoma Endometrium	2(2.6%)	4(8.5%)
Endometrial polyp	1(1.3%)	3(6.3%)
Inadequate biopsy	6(8%)	-
Total	75(100)	47(100)
Table 3. Comparison of Histopathological Report of Pipelle Biopsy and Hysterectomy		

Statistical Analysis of Endometrial Histopathology Report by D and C Pipelle Biopsy

D and C had 100% sensitivity and negative predictive value and 97.5% specificity for atypical hyperplasia .For endometrial carcinoma it was 75% sensitive but with 100% specificity and positive predictive value. The accuracy to diagnose both pathology by D and C was 97.62% (95% CI-87.43% to 99.94%). On analysis by Fisher's Exact test the P value was 0.0035 for atypical hyperplasia and 0.0003 for carcinoma endometrium and both were significant.

Pipelle biopsy had 100% sensitivity and Negative predictive value and 95.35% specificity for diagnosing atypical hyperplasia. The P value was .0001 and significant. For diagnosing endometrial adenocarcinoma Pipelle biopsy had sensitivity of 50%, but had 100% specificity and positive predictive value. P value being 0.0056 and significant. Pipelle was 95.74% accurate (95% CI- 85.46% to 99.48%). in diagnosing both atypical hyperplasia and adenocarcinoma.

Variable	D and C		Pipelle	
	Atypical Hyperplasia	Carcinoma Endometrium	Atypical Hyperplasia	Carcinoma Endometrium
Sensitivity (%)	100	75	100	50
Specificity (%)	97.5	100	95.35	100
Positive Predictive value (%)	66.6	100	66.6	100
Negative Predictive Value (%)	100	97.44	100	95.56
Accuracy rate (%)	97.62	97.62	95.74	95.74
P-value	0.0035	0.0003	0.0001	0.0056

Table 4. Validity of D and C and Pipelle Biopsy for Atypical Hyperplasia and Carcinoma Endometrium

DISCUSSION

Majority of the women in our study were of the age group 45-49 year (47 cases, 31.3%)) followed by the group 40-44 years (22.4%). 54% of women (n=81) belonged to age 40-49 years .This goes in accordance with the study by Gopalan U et al with 54.7% incidence in this age group.[5]

Descriptive terms used to categorise AUB pattern include Heavy Menstrual Bleeding, Intermenstrual bleeding, Post-menopausal bleeding (PMB), Polymenorrhoea and irregular bleeding pattern. Heavy Menstrual Bleeding was the most common bleeding pattern with incidence of 65% in our study**.** Jetley S et al also have reported this as the most common clinical presentation.[6] 18% of patient in D and C group and 21% in Pipelle group had post-menopausal bleeding .In a similar study by Singh et al in 2018 the incidence of PMB was 14.8%.[7] In more than 90% of postmenopausal women with endometrial carcinoma, PMB is the presenting symptom.[8] Thus all cases of postmenopausal bleeding must be promptly evaluated.

The sample adequacy in our study was 93% for D and C and 92% for Pipelle biopsy. This goes in concordance with a recent study in 2019 by Tumrongkunagon S et al who reported accuracy rate of 91.76% for Fractional Curettage and 89.41% for Pipelle endometrial sampling.[9] The inadequate samples in both groups were endometrial polyps, atrophic endometrium and scanty curetting with sub mucosal fibroid polyp in the final hysterectomy specimens. Thus focal lesions can be missed by both methods.[10]

On analysing the hysterectomy specimens, the incidence of endometrial polyp was 6.3% in the Pipelle group and 11.9% in the D and C group. This was similar to a study by Abid M et al.[11] The incidence of carcinoma endometrium detected by Pipelle biopsy was 2.6% which shows concordance with a study by Singh P et al (2.6%) conducted

at AIIMS Jodhpur.[7] Among D and C group it was 4%. But the incidence in subsequent hysterectomy was 8.5% to 9.5%.

This higher incidence of carcinoma in the hysterectomy specimens was due to the high incidence of coexisting atypical hyperplasia and early stage carcinoma endometrium. 33.3% of atypical hyperplasia diagnosed by both methods had coexisting carcinoma in the subsequent hysterectomy specimen which was similar to studies by Rakha E et al which reported 37%.[12] In a study by Byun JM etal the rate of coexisting carcinoma endometrium in patients with atypical hyperplasia is 30.8%.[13] Majority of these patients had grade 1 stage 1 carcinoma endometrium and they did not need any subsequent treatment. Thus surgical intervention is preferable for women with atypical hyperplasia rather than conservative management.

D and C had 100% sensitivity for detecting atypical hyperplasia and 75% sensitivity for carcinoma endometrium in our study. A study by Moradan S et al showed similar results for atypical hyperplasia and 83.3% sensitivity for endometrial cancer.[14] Pipelle endometrial biopsy had 100% sensitivity, 95.3% specificity and 100% negative predictive value for detecting atypical hyperplasia which showed concordance with study by Fakhar S et al with 100% sensitivity and negative predictive value and 98% specificity.[15]

The accuracy of D and C for detecting atypical hyperplasia and carcinoma endometrium is 97.62%. Pipelle endometrial biopsy had 95.74% accuracy for both these pathologies. These are comparable with study by Narice BF et al.[16] Thus Pipelle biopsy is a suitable cost-effective method for diagnosing endometrial pathology when combined with proper history and ultrasound examination.

CONCLUSIONS

Sample adequacy obtained by D and C and Pipelle biopsy were similar (93% vs 92%). Accuracy for detecting atypical hyperplasia and carcinoma endometrium by both methods were also similar (97.6% vs. 95.7%). Due to high incidence of coexisting carcinoma endometrium in atypical hyperplasia surgical treatment is recommended. Thus, Pipelle endometrial biopsy is a cost-effective method for endometrial sampling except for focal lesions.

ACKNOWLEDGEMENTS

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