Original Research Paper

Volume - 11 | Issue - 02 | February - 2021 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Gynaecology

A STUDY ON CORRELATION BETWEEN ENDOMETRIAL ASPIRATION CYTOLOGY AND HISTOPATHOLOGY IN WOMAN WITH AUB.

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ABSTRACT **Aims and objectives:** To study the effectiveness of Endometrial aspiration in the evaluation of AUB and to compare with conventional D&C in order to assess the value and shortcomings of former, thus assessing its role as routine office based endometrial sampling technique for evaluating AUB and to encourage the same. **Materials and methods:** This was a hospital based cross section descriptive study conducted over a period of 12 months from June 2019 to May 2020 amongst 100 married women of reproductive age group attending department of Obstetrics and Gynaecology, Gauhati Medical College with AUB. Endometrial aspiration was done using Pipelle cannula following which every patient was subjected to conventional D&C and the results were compared. **RESULTS:** In Pipelle sampling, out of 100 cases, one was failure. Sample adequacy was 89% and hence HPE report was available in 89% cases with p value of 0.003. 10 samples were reported inadequate on Pipelle sampling. In D&C, HPE report was available in 100% cases. Diagnostic accuracy of Pipelle endometrial sampling was found to be 86%. For carcinoma endometrium and endometrial hyperplasia with and without atypia, Pipelle showed 100% diagnostic accuracy with 100% sensitivity and specificity. For generalised endometrial pathology like proliferative endometrium, secretory endometrium Pipelle aspiration showed good results however for focal endometrial pathology like endometrial polyps Pipelle had sensitivity of only 14.29%. No complications were seen in Pipelle aspiration. Patient's acceptibilty was good with lesser pain and discomfort. Endometrial thickness was found to be related to the sample adequacy. Chances of sample insufficiency is more when ET is less. Cut off value of 5.5 mm ET was found to get adequate sample in our study with p value 0.0480. **CONCLUSION:** Pipelle endometrial aspiration is a simple, effective and minimally invasive procedure of endometrium sampling and results are comparable with D&C. With an experienced cytologist, it can be used routinely as office based procedure for the primary investigation of women with AUB.

KEYWORDS : Endometrial aspiration, Pipelle cannula, D&C, sample adequacy, diagnostic accuracy.

INTRODUCTION

Abnormal uterine bleeding is very common gynaecological problem affecting females of all age groups accounting for one-third of outpatients visitings to the gynaecologists[1]. It can be caused by varieties of local and systemic causes or can be related to medications[2]. The world wide impact of AUB in the reproductive years is substantial with prevalence of approximately 3% to 30% amongst reproductive age women, being higher in adolescents and in the fifth decade of life and vary somewhat with the country of origin as well[3-11] . The main aim of investigating abnormal uterine bleeding is to exclude endometrial pathology, particularly malignant conditions. Dilatation and curettage remains the most common and has been considered for long as the 'gold standard' in the diagnosis of endometrial pathology but carries risk of anaesthesia, infection and complications with post procedure pain and discomfort as well. Hence there is a need for simple, safe, cost-effective, patient friendly out-patient department procedure as an alternative to D&C for endometrial sampling. Endometrial aspiration cytology can be used as routine office based endometrial sampling technique. Introduced by Cornier in 1984, the Pipelle is the most studied biopsy device, is a thin, flexible, plastic tube and is very much convenient, best tolerated and least expensive outpatient endometrial cell sampler which needs no cervical dilatation and can be used for the detection of a wide varieties of benign lesions of endometrium and screening of malignancy. Thus the study was done with the objective to correlate the findings of endometrial aspiration with the subsequent histopathology obtained from conventional D&C in women suffering from AUB in order to assess the value of former in terms of sample adequacy, reliability, diagnostic accuracy, cost effectiveness, pain and discomfort, patient's acceptability and its shortcomings.

MATERIALS AND METHODS:

It was a hospital based cross sectional descriptive study conducted from June 2019 to May 2020 amongst 100 married women of reproductive age group with AUB attending department of Obstetrics and Gynaecology, Gauhati medical college.

INCLUSION CRITERIA:

1. Married women of reproductive age group with AUB.

EXCLUSION CRITERIA:

1. Unwilling Patients.
2. Any suspected underlying pelvic infections or any acute conditions.
3. Any obvious genital trauma or infections.
4. Profusely bleeding patients requiring therapeutic curettage or immediate intervention.
5. Women on hormonal treatment.
6. Evidence of any haematological intervention.
7. Patients with any local cause of bleeding per vaginum.

A detailed clinical history was taken and general physical, systemic and local examination of pelvis was done and all the relevant investigations were done including ultrasonography. After taking proper written consent, under all aseptic and antiseptic conditions endometrial aspiration using Pipelle cannula was done and subsequently patients were taken for D&C at the same sitting. Both the samples were sent separately to pathology department in Gauhati Medical College separately for analysis. In Pipelle aspiration, the aspirate contained both cells and tissues, so we used both the components. The tissues were sent for the histopathological study in 10% formalin and remaining components were used to make smears which were then air dried, fixed in 95% ethyl alcohol and stained with PAP stain and Leishman stain and reporting was done by pathologists. The materials obtained from D&C were collected in a sterile container containing 10% formalin which was then sent for histopathological reporting. Experience regarding the procedure was asked from the patients and was categorised as poor, satisfactory, good and excellent. Acceptability of the procedure was mainly referred whether the patients would recommend this procedure to others or not and it was asked simply as yes or no. Pain and discomfort during the procedure was asked from the patients on simple visual analogue scale graded from 0-10 for both the procedure separately. After the reports arrived, findings of both were correlated and presented in forms of tables and graphs. Collected data was entered in MS excel spread sheet and data

was analysed using statistical analysis software SPSS VERSION 21 (Statistical Package for Social Science). Results and observations were analysed using chi square test and p value. P value < 0.005 was considered statistically significant. Endometrial sampling using Pipelle cannula was compared with the conventional D&C in terms of patient's acceptability, pain score, need for analgesia, complications, reliability and diagnostic accuracy. Both the patients and pathologists were blind about the sequence of sampling and the techniques of sampling.

RESULTS AND OBSERVATION:

In our study, maximum (38%) cases were in the age group of 41 to 45 years. The minimum age was 22 years and the maximum age was 45 years. The mean age was 37.7 years. The chief pattern of AUB was HMB and it was found in 37% of cases. Sample adequacy was 100% in D&C and hence the HPE report was available in 100% cases. In Pipelle endometrial aspiration, 10 samples were reported as insufficient and 1 was failure. Sample adequacy in Pipelle endometrial aspiration was 89% and hence HPE report was available in 89% of cases. 10 samples were reported to be inadequate on Pipelle aspiration. But the conventional D&C could yield adequate tissues in those cases and subsequent HPE report showed 2 cases had anovulatory endometrium, 3 had endometrial polyp, 3 were endometritis, 1 was proliferative endometrium and 1 was secretory endometrium.

The various histopathological conditions as reported on D&C were proliferative endometrium (28%), secretory endometrium (12%), anovulatory endometrium (17%), endometrial hyperplasia with atypia (6%) , endometrial hyperplasia without atypia (20%), endometrial polyp (7%), endometritis (7%) and endometrial carcinoma (3%). Findings of D&C and EAC when compared showed the following result as shown in the table below:

Table:1 showing specific HPE report on D&C and Pipelle sampling .

	D&C	PIPELLE
Anovulatory endometrium	17(17%)	15(15%)
Carcinoma endometrium	3(3%)	3(3%)
Endometrium hyperplasia with atypia	6(6%)	6(6%)
Endometrium hyperplasia without atypia	20(20%)	20(%)
Endometrial polyp	7(7%)	1(1%)
Endometritis	7(7%)	4(4%)
Inadequate	--	10(10%)
Failed	--	1(1%)
Proliferative endometrium	28(28%)	27(27%)
Secretory endometrium	12(12%)	13(13%)
Total	100(100%)	100(100%)

No cases of carcinoma endometrium and endometrial hyperplasia were missed on EAC. The sensitivity, specificity, PPV and NPV of EAC in various endometrial conditions has been shown in the table below:

Table:2 showing validity of Pipelle sampling in various endometrial conditions.

	Sensitivity	Specificity	Positive Predictive Value [PPV]	Negative Predictive Value [NPV]
Anovulatory endometrium	88.24%	100.00%	100.00%	97.65%
Carcinoma endometrium	100.00%	100.00%	100.00%	100.00%
Endometrial hyperplasia with atypia	100.00%	100.00%	100.00%	100.00%
Endometrial hyperplasia without atypia	100.00%	100.00%	100.00%	100.00%
Endometrial polyp	14.29%	100.00%	100.00%	93.94%
Endometritis	57.14%	100.00%	100.00%	96.88%
Proliferative endometrium	96.43%	100.00%	100.00%	98.63%
Secretory endometrium	83.33%	100.00%	100.00%	97.78%

Pipelle sampling showed 100% sensitivity and specificity for carcinoma endometrium, Endometrial hyperplasia with and without atypia with 100% PPV and NPV. For proliferative endometrium, Pipelle showed sensitivity of 96.43%, specificity of 100%, NPV of 98.63% and PPV of 100%. For secretory endometrium, Pipelle had sensitivity of 83.33%, specificity of 100%, NPV to be 97.78% and PPV to be 100%. For Endometrial Polyp, Pipelle showed sensitivity of 14.29%, specificity of 100%. The NPV was 93.94% and PPV was 100%. For Endometritis, it showed sensitivity of 57.14%, specificity was 100%. The PPV was 100% and NPV was 96.88%. For anovulatory endometrium, Pipelle showed sensitivity of 88.24%, specificity of 100%. The PPV was 100% and NPV was 97.65%. Overall diagnostic accuracy of EAC was 86%.

Endometrial aspiration showed no complications. Pipelle aspiration caused less pain and discomfort than D&C and it was found statistically significant with p value <0.0001. Most of the patients accepted it well. Mode of delivery and parity had no statistically proven role in sample adequacy however they have role in ease of procedure. ROC curve was plotted to define the cut-off values for the endometrial thickness which would enable successful histopathology reporting in Pipelle sampling. In our study, the best cut-off value to predict the successful histopathology reporting of sample was found to be 5.5 mm. For adequate Pipelle sampling, the mean ET was found to be 7.17 with standard deviation of 3.36. In inadequate samples, the mean ET was found to be 3.8 with standard deviation of 1.7 with p value 0.003 which is statistically significant. Thus ET was found to be related to sample adequacy, the chances of which increases with increase in ET.

DISCUSSION :

Endometrial sampling by means of Pipelle biopsy is minimally invasive, cost efficient with lesser discomfort and with better patient's acceptability along with good diagnostic accuracy and an alternative to the commonly performed conventional dilatation and curettage or hysteroscopy and curettage. When analysing the various studies which compared the results of both D&C and Pipelle sampling, the Pipelle sampling was found to be as effective and safe in diagnosing the endometrial lesions including hyperplasia and malignancy as was the D&C. It has good sample adequacy and in case of insufficient samples, it can be repeated without much inconvenience to the patients.

Table 3: showing sample adequacy and the diagnostic accuracy of endometrial aspiration.

YEAR	REFERENCE	CASES	D&C	PIPELLE	ADEQUACY [%]	ACCURACY[%]
2015	Sanam and Majid	130	130	130	88	94
2014	Rauf et al.	203	203	102	98	-
2014	Gungorduk et al.	267	189	78	93	62
2013	Leng et al.	200	200	200	93	85
2008	Fakhar et al.	100	100	100	98	94
2018	Handa, Uma, et al	100	100	100	89%	-
2019	Dr Neena Agarwal et al	200	200	200	88%	Endometrial cancer (100%)
2014	Kaur, Navjot et al	100	100	100	100%	Malignancy (96.8%) Benign (93.8%)
2012	Kazandi et al.	82	82	82	93	66
2019	Present study	100	100	100	89	86

It can be seen from the above table that the sample adequacy rate of Pipelle, according to these studies, ranged from 88% to 100%. In our study also the sample adequacy was 89%. In rest of the 11 cases, one was failure and 10 samples were reported inadequate for reporting. But the conventional D&C could yield adequate tissues in those cases and subsequent HPE report showed 2 anovulatory endometrium, 3 endometrial polyp, 3 endometritis, 1 proliferative endometrium and 1 secretory endometrium.

Bakour, Shagaf H, Khalid S and Janesh K. Gupta12 (2000) did

controlled analysis of factors associated with insufficient samples on outpatient endometrial biopsy and they concluded that endometrial thickness less than 5mm is a significant factor in predicting insufficient sample on outpatient endometrial biopsy. There was no association with patient's age, menopausal status, parity, mode of delivery and use of hormones. Pratibha singh from the Department of obstetrics and Gynaecology, All India Institute of Medical Science, Jodhpur, Rajasthan, India13 studied role of Endometrial Aspiration in the evaluation of AUB (2018) amongst 115 women and showed in her study that maximum cases of inadequate samples were having endometrial atrophy.

Table 4: showing correlation between Endometrial Aspiration Cytology and histology in various series.

DIAGNOSIS	Bhandari et al	Dr Neena Agarwal et al	Schachter et al	Kaur, Navjot et al	Fox et al	Demikaran et al	Present study
Proliferative endometrium	91.3%	92.05%	86.4%	93.8%	95%	-	96.4%
Secretory endometrium	91.3%	100%	78.5%	-	71%	-	83.3%
Endometrial hyperplasia without atypia	62.5%	91.75%	77%	-	79%	67%	100%
Endometrial hyperplasia with atypia	-	91.75%	-	-	-	75%	100%
Endometritis	100%	-	-	-	-	-	57.14%
Endometrial carcinoma	-	-	100%	96.84%	100%	-	100%
Endometrial polyp		100%	-	-	-	-	14.29%

In our study, the overall diagnostic accuracy of Pipelle endometrial sampling was found 86%. Above table shows the diagnostic accuracy of endometrial aspiration in various studies. If we see individually, Pipelle aspiration was found to be 100% accurate in diagnosing endometrial carcinoma, endometrial hyperplasia with atypia and without atypia as none of them were missed or wrongly diagnosed when compared with the conventional dilatation and curettage. For endometrial polyps: Studies have shown that Pipelle has poor diagnostic accuracy for focal endometrial pathologies like endometrial polyp. In our study, Pipelle showed sensitivity, specificity, PPV and NPV of 14.29%, 100%, 100% and 93.94% respectively. Kazandi, M. E. R. T., et al [14], Fakhar, Shazia, et al [15], and many more studies have shown the same result. For carcinoma endometrium and endometrium hyperplasia: Macahdo F et al, Stovall, Thomas G, et al, Kazandi, M. E. R. T, et al and many more studies are done in past and everywhere it has been shown that Pipelle sampling and D&C has equal level of diagnostic accuracy in generalised endometrial pathologies like carcinoma endometrium or endometrial hyperplasia.

Parity and previous mode of delivery is related to ease of delivery, however it has no specific relation with sample adequacy and diagnostic accuracy. It is acceptable to patients and it has no complications. There is no need of prior dilatation of cervical os, however patient's uncooperation and apprehension can lead to procedure failure sometimes.

Studies are there which have reported missing significant uterine pathologies including that of endometrial cancers in about 20% of insufficient samples [16]. This is not so surprising as these samplings are done blindly and hence are not fully representative due to variable portion of endometrial surface sampled and non sampling of focal intrauterine lesions . Upto 50% of insufficient samples are associated with endometrial polyp detected by uterine imaging [17]. Despite its advantages, there are some limitations to endometrial sampling with Pipelle device. First, a tissue sample that is inadequate for histologic evaluation such as from endometrial atrophy or cervical stenosis. Negative cytology or an inadequate sample in clinical background of endometrial atrophy or thinned endometrium does not need further investigation. But if AUB is continued or EAC finding does not correlate clinically, we need further investigations like D&C, hysteroscopy and other investigation as per need for better evaluation. Endometrial aspiration has very good sensitivity for endometrial carcinomas and can be used routinely for assessing the endometrium, however negative result does not always rule out its presence, especially if the lady is having persistent AUB and hence it needs to be evaluated further.

CONCLUSION:

Endometrial aspiration using Pipelle cannula is a simple, easy, office based and a minimally invasive method of endometrium sampling without any complications with almost as good diagnostic accuracy as conventional D&C, requires no anaesthesia, no prior dilatation of cervical os and with minimal discomfort making it more acceptable to patient. An important criterion in endometrial aspiration is the pathologist's ability to report the findings. With an experienced and a confident pathologist, it can be used as one of the primary tool in the investigation of AUB. Considering some of its drawbacks, Pipelle Endometrial aspiration can be looked forward as a simple routine method for assessing endometrium and one of the primary tool for investigating AUB.

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