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To evaluate the role of chromohysteroscopy in perimenopausal and postmenopausal bleeding

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Introduction

Abnormal uterine bleeding (AUB) refers to any change in the frequency of menstruation, duration of flow or amount of blood loss per vaginum. AUB is one of the most frequent gynecological problems.

The primary goal of evaluation of AUB is to establish a specific diagnosis in an efficient and least invasive manner possible. The ACOG Practice Bulletin[1] recommends endometrial sampling in all women above age 35 with abnormal uterine bleeding. Younger woman with a history of chronic anovulatory bleeding or with risk factor for endometrial carcinoma such as positive family history, hypertension, obesity, diabetes and unopposed estrogen therapy can be considered for endometrial sampling at any age.

Hysteroscopy guided biopsy has now become the gold standard for diagnosis of AUB[2-7]. Hysteroscopy allows direct visualization of the endometrial cavity and taking directed biopsies. Besides, giving adequate visualization of endometrial cavity, it provides accurate detection of intracavitary lesions like endometrial polyps, submucous myoma or uterine adhesions. However, accuracy of hysteroscopy in diagnosing diffuse endometrial pathologies like endometrial hyperplasia, endometritis and endometrial carcinoma is not well established. Even visually directed biopsy can miss atypical lesions.

Therefore, a specialized technique needs to be developed which can increase the efficacy of hysteroscopy in diagnosing endometrial pathologies. Chromo hysteroscopy is proposed to be one such modality that can accurately help in detecting endometrial pathologies and targeting biopsy from suspicious area thereafter.

Chromo hysteroscopy is a type of chromo endoscopy that involves a topical application of stains or pigments to improve endometrial tissue characterization and thereby helps in diagnosis of endometrial lesion. Differential type of staining can help in targeting biopsy and early detection of the endometrial pathology[8,9].It has potential to improve the efficacy and accuracy of conventional hysteroscopy by detecting missed endometrial pathologies. Hence the present study was undertaken to evaluate the role of chromo hysteroscopy in detecting endometrial pathologies in patients of AUB.

Material and Method

This comparative prospective study was conducted in Department of Obstetrics and Gynaecology at SMS Medical College, Jaipur. 88 women with complaint of perimenopausal and postmenopausal bleeding attending outpatient department who gave the informed written consent were enrolled for the study after application of exclusion criteria (Age less than 35, pregnancy, deranged thyroid profile, coagulopathy, abnormal liver function, pelvic infection, Carcinoma cervix).

Each study subject was subjected to a thorough history and clinical examination according to a prescribed proforma. Pelvic ultra-sonography was done in all patients. All women underwent diagnostic hysteroscopy. The hysteroscopic findings were recorded and any abnormal areas if detected were noted. Conventional hysteroscopy was followed by chromo hysteroscopy. 1% methylene blue dye was instilled, and endometrium was observed for uptake of dye, pattern of uptake whether diffuse or focal. Focal, dark blue staining regardless of size and number of stained areas, was considered positive finding. Diffuse light blue staining was considered as normal finding. These findings were compared with the previously noted findings (on conventional hysteron scopy). Biopsies were obtained from focal dark and diffuse light stained areas by hysteroscopic guided biopsy forceps followed by blind endometrial sampling.

Hysteroscopic, chromohysteroscopic and conventional endometrial biopsy findings were correlated with histopathology results.

Statistical Analysis

Continuous variables were presented as mean ± SD. Categorical variables were expressed as frequencies and percentages. Nominal categorical data between the groups were compared using Chi- square test or Fisher's exact test as appropriate. Sensitivity, specificity, NPV and PPV of chromo hysteroscopy and conventional hysteroscopy were also calculated in detection of endometrial pathologies in patients of AUB correlation their findings with Histopathology. $p<0.05$ was considered statistically significant.

Results and Observations

The study group ranged from 36-57 years. Majority of cases enrolled in the study were of the age group 40-44 years (51%). The mean age of study group was 41.88 ± 4.31 years. (Table 1).

Age Group (in yrs)	Frequency	%
35 – 39	29	24.00
40-44	45	51.00
45-49	20	23.00
>50	2	2.00
Total	88	
Mean ± SD	41.88 ±4.31	

Table 1: Distribution of Age (n=88)

Out of 88 patients, endo metrium got homogenously stained in 60 cases whereas 28 cases had focal dark blue staining. No pathology was detected on histology in 95% cases of homogenously stained endo metrium. Endometrial disease was diagnosed in 61% cases with focal blue stained endometrium. Chromo hysteroscopy detected 17 out of 20 (85.70%) cases with histopathologic ally confirmed endometrial disease. The diagnostic accuracy of chromo hysteroscopy in detecting endometrial disease was found to be high (Sensitivity - 85.00%, Specificity - 83.80%, Negative Predictive Value - 95.00%, Positive Predictive Value – 60.07%) (Table 2).

Table-2: Diagnostic Accuracy of Chromo Hysteroscopy

Chromo Staining Pattern	Total	HPE		p-value	Sensitivity	0.85
		Abnormal	Normal		Specificity	0.83
Focal	28.00	17.00	11.00	<0.001	PPV	0.60
HLS	60.00	3.00	57.00		NPV	0.95
Total	88.00	20.00	68.00		Accuracy	0.84

Table-3: Comparison of Conventional Hysteroscopy with Chromohysteroscopy and Blind endometrial sampling with findings on HPE

Blind endometrial sampling		Hysteroscopy findings endometrium	Total	Chromohysteroscopy staining pattern	Total	Hpe		P-value
						Abnormal	Normal	
Abnormal	12	Abnormal	23	Focal dark	9	6(100%)	3(17.6%)	<.001
				Diffuse light	14	0	14(82.3%)	
Normal	76	Normal	65	Focal dark	19	11(78.5%)	8(15.6%)	<.001
				Diffuse light	46	3(21.4%)	43(84.4%)	

Table3 compares the findings of conventional hysteroscopy, chromohysteroscopy and histopathology. Endometrium appeared normal in 65 cases in conventional hysteroscopy. 19 cases which were found to be normal on conventional hysteroscopy got differentially stained on chromo hysteroscopy and 11 of them (57.80%) had abnormal histopathology findings. Abnormal endometrial disease was suspected in 23 cases on conventional hysteroscopy. All 14 cases with diffuse light staining pattern of endometrium had normal histopathology. Out of the 9 cases with focal blue stained endometrium, disease was confirmed in 6 cases on histopathology. Blind endometrial biopsy identified disease in 12 cases.

It was thus found in our study that diagnostic efficacy of chromo hysteroscopy is much higher than conventional hysteroscopy in detecting the endometrial diseases. Chromo hysteroscopy detected 11 new endometrial pathologies which were missed on conventional hysteroscopy.

Discussion

Traditionally, abnormal uterine bleeding has been investigated with dilatation and curettage, but hysteroscopic guided biopsy has now become the gold

standard for diagnosis of AUB. However, there is a continuing debate about the accuracy of hysteroscopy in diagnosing diffuse endometrial diseases like endometrial hyperplasia and endometritis. A systematic quantitative review of 3486 articles and 65 primary studies on efficacy of conventional hysteroscopy by Clark et al (2002)[10], indicates that the accuracy of hysteroscopy in diagnosis or exclusion of endometrial disease is moderate.

Therefore, a technique that will increase the efficacy of hysteroscopy is needed. Chromo hysteroscopy appears to have a potential in improving the efficacy of conventional hysteroscopy. It has not been pursued much in the past. This study has therefore been undertaken to evaluate the role of chromo hysteroscopy in detecting the endometrial pathologies in patients with abnormal uterine bleeding.

The age of the study group ranged from 36 to 57 years. Majority of cases enrolled in the study were of the age group 40 to 44 years. The mean age among the cases was 41.88 years with standard deviation of ± 4.31 years. However, the pattern of distribution of the various chromo hysteroscopic staining patterns in different age groups did not attain any statistical significance ($p>0.001$).

Endo metrium got homogenously stained in 60 cases, whereas focal staining was observed in 28 cases. No pathology was detected on histopathological examination in 57 out of 60 cases that got homogenously stained. It can thus be concluded that endometrial disease is significantly less frequent($p<0.001$) in cases with homogenously stained endometrium. This is in accordance with the study by Gupta T et al[11], a prospective study done on 60 patients with AUB,39 cases showed light staining on chromohysteroscopy in which 94.8% (37/39) cases showed normal endometrium and 5.2% (2/39) showed endometrial pathology. Hoda Mansour et al[12] did a prospective study to evaluate the role of methylene blue dyeing in hysteroscopy for diagnosis of endometrial pathology. Only 3/41 (7.32%) had endometrial pathology with diffuse light blue staining.

Endometrial disease was diagnosed in 17 out of 28 cases (60.7%) with focal blue stained endometrium. Chromohysteroscopy detected 17 out of 20 cases (85%) with histopathologic ally confirmed endometrial disease. According to study by Gupta T et al[11], out of 21 cases that showed focal dark staining, endometrial pathology was found in 16 cases (76.1%) on HPE. According to study conducted by Vijay et al[13], out of 50 patients with AUB, endometrial pathology was found in 13 cases (26%) on HPE and 10 out of 13 cases (77%) showed focal dark staining on chromohysteroscopy. According to another study by Hoda Mansour et al[12], endometritis was diagnosed in 7/16 cases (43.7%) with focal dark staining. According to study by Singh and Singh[14],8/11 cases (72.7%) with endometrial pathology were picked up only in biopsy from stained area, so it can be concluded from the findings that in presence of focal dark staining, chances of endometrial disease is significantly increased($p<.05$).

During conventional hysteroscopy, normal endometrium was found in 65 cases (733.8%). Out of 65 cases,19 cases which were found to be normal on conventional hysteroscopy, got focal staining on chromohysteroscopy and 11 of them (57.8%) had abnormal histopathology findings. Chromohysteroscopy detected 11 more cases of endometrial pathologies (3 cases of chronic endometritis,5 cases of hyperplasia without atypia and 3 cases of hyperplasia with atypia) which were missed on

conventional hysteroscopy. Agarwal S et[15] al detected 2 more cases of chronic endometritis,4 cases of hyperplasia without atypia and 2 cases of hyperplasia with atypia which were missed on conventional hysteroscopy in a study of 60 patients with AUB. Deveci et al[9] detected two more cases of endometritis and one cases of hyperplasia in a study of 27 patients with postmenopausal bleeding to detect the role of endometrial dyeing in diagnostic hysteroscopy. Abd El-Moneim A Saleh et al[16] diagnosed 46 more new endometrial histopathologies otherwise missed on conventional hysteroscopy during chromo hysteroscopy while studying the role of chromo hysteroscopy in 100 perimenopausal women.

Blind endometrial sampling missed 8 cases of endometrial pathology. The cases that were missed on blind endometrial sampling included 4 cases of atypical hyperplasia that showed proliferative endometrium in one case which was diagnosed to have endometrial polyp on hysteroscopy and also took dark focal stain on CHPE. Other 3 cases of atypical hyperplasia which were identified as secretory endometrium were also darkly stained on CHPE. Blind endometrial biopsy failed to diagnose hyperplasia without atypia in 3 cases of which 1 had submucosal fibroid on hysteroscopy and was darkly stained on CHPE. The other 2 cases were identified as secretory and proliferative endometrium on blind endometrial sampling. Blind endometrial sampling also missed 1 case of chronic endometritis and was identified as secretory endometrium. In a study by Singh and Singh[14], out of 60 women complaining of AUB, non-hormonal pathology was found in 11 cases (18.3%) by CHPE while blind endometrial sampling picked up only 3 cases (5%). In a study by Haider et al[17], abnormal HPE results were obtained from 20 cases (90%) with dark stained areas on CHPE, while on Blind endometrial sampling only 13 cases (37.1%) had endometrial pathology.

The diagnostic accuracy of chromo hysteroscopy in detecting endometrial disease was found to be high (Sensitivity – 85.00%, specificity – 83.80%, negative predictive value - 95.00%, positive predictive value – 60.07%). This is in accordance with other studies. Safali Met al[18] (Sensitivity - 69.20%, specificity - 74.00%, positive predictive value - 40.90% and negative predictive value - 90.20%.) Abd El-Moneim A Saleh et al[16](sensitivity of 93.20%, specificity of 87.80%, a positive predictive value of 91.60% and a negative predictive value of 90.00%.) Hoda Mansour et al[12] (sensitivity 70.00%, specificity 80.80%, positive predictive value 43.70% and negative predictive value 92.60%) in detecting endometrial disease during chromo hysteroscopy.

It was therefore strongly concluded in our study that chromo hysteroscopy has definitely increased the efficacy of conventional hysteroscopy in diagnosing as well as excluding endometrial disease. Use of chromo hysteroscopy technique with methylene blue, a cost-effective and easily available dye with minimal side-effects, for staining the endometrium is therefore, worth consideration. We recommend that chromo hysteroscopy should routinely be used in the evaluation of women with abnormal uterine bleeding in addition to the conventional hysteroscopy technique.

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