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TO EVALUATE THE ROLE OF CHROMO HYSTEROSCOPY IN ABNORMAL UTERINE BLEEDING

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Conflicts of Interest: Nil

ABSTRACT:

Objective: To evaluate the role of chromohysteroscopy in improving diagnostic accuracy of endometrial biopsy in cases of AUB.

Design: This observational prospective study was conducted in 60 women with complaint of AUB attending, outpatient Department of Obstetrics and Gynaecology at SMS Medical College, Jaipur over a period of one year. Conventional hysteroscopy was followed by chromo hysteroscopy using 5 ml of 1% methylene blue. Differential patterns of staining noted. Focal staining was considered positive finding whereas diffuse light blue staining was considered as normal finding. These findings were compared with the previously noted findings (on conventional hysteroscopy).Biopsies were obtained from differentially stained areas. Hysteroscopic and chromo-hysteroscopic findings were correlated with histopathology results.

Result The diagnostic accuracy of chromo hysteroscopy in detecting endometrial disease was found to be high (Sensitivity - 85.70%, specificity - 84.80%, negative predictive value - 95.10%, positive predictive value - 63.20%). 2 cases of chronic endometritis, 4 cases of simple hyperplasia and 2 cases of complex hyperplasia were detected on chromo hysteroscopy which were missed on conventional hysteroscopy.

Conclusion: chromo hysteroscopy has definitely increased the efficacy of conventional hysteroscopy in diagnosing as well as excluding endometrial disease in AUB.

Keywords: Abnormal uterine bleeding, chromohysteroscopy, diffuse light blue staining, endometrial pathology, focal staining.

1. 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.

Hysteroscopic guided biopsy has now become the gold standard for diagnosis of AUB. Hysteroscopy allows direct visualization of the endometrial cavity and taking directed biopsies.

Besides giving adequate visualization of endometrial cavity, it provides accurate detection of intracavitory 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.

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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. Endometrial dyeing using 1% methylene blue can help in enhancement and detection of subtle endometrial changes otherwise not detected by the naked eye during conventional hysteroscopy. Differential patterns of staining like homogenous light blue staining/dark blue staining/partial staining/and unstained areas were seen. Diffuse light blue staining was considered as normal. Focal staining, dark blue staining denotes endometrial lesions like endometritis, endometrial hyperplasia. This differential type of staining can help in targeting biopsy and early detection of the endometrial pathology.[2_3]

Chromo hysteroscopy 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 observational prospective study was conducted in Department of Obstetrics and Gynaecology at SMS Medical College, Jaipur. 60 women with complaint of AUB 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 ultrasonography was done in all patients. All women underwent diagnostic hysteroscopy using Karl Storz 4-mm rigid diagnostic telescope with a 5.5 mm, outer sheath.. The hysteroscopic findings were recorded and any abnormal areas if detected were noted. Conventional hysteroscopy was followed by chromo hysteroscopy. 5 ml of 1% methylene blue was introduced through the hysteroscopic inlet. After 3 minutes (staining time) distending medium (0.9% sodium chloride solution) flow was started again to let wash the endometrium. The fully assembled hysteroscope was then reintroduced and the uterine cavity was then visualized for staining pattern. 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 hysteroscopy).Biopsies were obtained from focal dark stained areas by hysteroscopic guided biopsy forceps. When no specific staining pattern was seen, biopsy was taken from all four walls and the posterior fundal region of endometrium. Hysteroscopic and chromo-hysteroscopic 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 35-45 years. The mean age of study group was 42.90 ± 6.34 years. (Table 1)

Table-1 Distribution of Age (n=60)

Age Group (in yrs)	Frequency	%
35 – 40	27	45.00
41 – 45	13	21.70
46 – 50	15	25.00
>50	5	8.30
Total	**5**	**8.30**
Mean ± SD	**42.90 ± 6.34**	

Out of 60 patients endometrium got homogenously stained in 41 cases whereas 19 cases had focal dark blue staining. No pathology was detected on histology in 95% cases of homogenously stained endometrium. Endometrial disease was diagnosed in 63% cases with focal blue stained endometrium. Chromo hysteroscopy detected 12 out of 14 (85.70%) cases with histopathologically confirmed endometrial disease. The diagnostic accuracy of chromo hysteroscopy in detecting endometrial disease was found to be high (Sensitivity - 85.70%, Specificity - 84.80%, Negative Predictive Value - 95.10%, Positive Predictive Value - 63.20%). (Table 2)

Table-2 *Diagnostic Accuracy of Chromo Hysteroscopy*

Chromo Staining Pattern	Total	HPE				p-value	Sensitivity	0.86
		Abnormal	%	Normal	%		Specificity	0.85
Focal	19.00	12.00	0.86	7.00	0.15	<0.001*	PPV	0.63
HLS	41.00	2.00	0.14	39.00	0.85		NPV	0.95
Total	60.00	14.00	1.00	46.00	1.00		Accuracy	0.85

Table 3: *Comparison of Conventional Hysteroscopy with Chromohysteroscopy and HPE*

Hysteroscopic Findings Endometrium	Total	Chromohysteroscopy Staining Pattern	Total	HPE				p-value
				Abnormal	%	Normal	%	
HE	16	FDS	6	4	100	2	16.7	<0.001
		HLS	10	0	0	10	83.3	
Normal	44	FDS	13	8	80	5	14.7	<0.001
		HLS	31	2	20	29	85.30	

Table3 compares the findings of conventional hysteroscopy, chromohysteroscopy and histopathology. Endometrium appeared normal in 44 cases in conventional hysteroscopy. 13 cases which were found to be normal on conventional hysteroscopy got differentially stained on chromo hysteroscopy and 8 of them (61.50%) had abnormal histopathology findings.

Abnormal endometrial disease was suspected in 16 cases on conventional hysteroscopy. All 10 cases with HLS pattern of endometrium had normal histopathology. Out of the 6 cases with focal blue stained endometrium, disease was confirmed in 4 cases on histopathology.

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 8 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.[4-15] However, there is a continuing debate about the accuracy of hysteroscopy in diagnosing diffuse endometrial

diseases like endometrial hyperplasia and endometritis.[16-19.] A systematic quantitative review of 3486 articles and 65 primary studies on efficacy of conventional hysteroscopy by Clark et al (2002)[16], 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 35 to 45 years. The mean age among the cases was 42.90 years with standard deviation of ± 6.34 years. However, the pattern of distribution of the various chromo hysteroscopic staining patterns in different age groups did not attain any statistical significance.

Endometrium got homogenously stained in 41 cases whereas focal staining was observed in 19 cases. No pathology was detected on histology in 39 out of 41 cases that got homogenously stained. It can thus be concluded that endometrial disease is significantly less frequent ($p<0.001$), in cases with homogenously staining endometrium. This finding is in accordance with the studies by Safali et al[20]who studied the role of chromohysteroscopy in recurrent IVF failure. He observed that diffuse light blue staining of endometrium strongly suggest a disease free endometrium. Hoda Mansour et al[21]did a prospective study to evaluate the role of methylene blue dyeing in hysteroscopy for diagnosis of endometrial pathology. Only 3/41(7.32%) cases had endometrial pathology with diffuse light blue staining.

Endometrial disease was diagnosed in 12 out of 19 cases with focal blue stained endometrium. Chromo hysteroscopy detected 12 out of 14 (85.70%) cases with histopathologically confirmed endometrial disease. Kucuk T et al[2] conducted a study wherein chromohysteroscopy was done in recurrent miscarriage patients with normal hysteroscopy.10/19 patients in whom focal dark staining was observed on chromo hysteroscopy had endometritis. Hoda Mansour et al[21], had endometritis in 7 / 16 patients with focal dark staining. According to study by Nisha Singh, Bharti Singh[22], 8/11 with endometrial pathology were picked up only in the biopsy from stained area. So it can be concluded from these findings that in presence of focal dark staining, chances of endometrial disease is significantly increased ($p<0.005$).

During conventional hysteroscopy, 44 cases were found to have normal endometrium . 13 cases which were found to be normal on conventional hysteroscopy got differentially stained on chromo hysteroscopy and 8 of them (61.50%) had abnormal histopathology findings. chromo hysteroscopy detected 8 more cases of endometrial pathologies which were missed on conventional hysteroscopy. Deveci et al[3]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[23] diagnosed 46 more new endometrial histopathologies otherwise missed on conventional hysteroscopy during chromohysteroscopy while studing the role of chromohysteroscopy in 100 perimenopausal women.

The diagnostic accuracy of chromo hysteroscopy in detecting endometrial disease was found to be high (Sensitivity - 85.70%, specificity - 84.80%, negative predictive value - 95.10%, positive predictive value - 63.20%). This is in accordance with other studies. Safali M et al[20] (Sensitivity - 69.20%, specificity - 74.00%, positive predictive value - 40.90% and negative predictive value - 90.20%.) Abd El-Moneim A Saleh et al[23](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[21] (sensitivity 70.00%, specificity 80.80%, positive predictive value 43.70% and negative predictive value 92.60%) in detecting endometrial disease during chromo hysteroscopy. Nisha Singh and Bharti Singh[22] stated that chromo hysteroscopy added diagnostic accuracy

of hysteroscopy in 45.50% cases which is a great advantage.

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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