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Gynaecology

CHROMOHYSTEROSCOPY ROLE IN EVALUATION OF INTRAUTERINE CAVITY LESIONS IN PERIMENOPAUSAL WOMEN OF AUB

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ABSTRACT **Aim:** To evaluate the role of chromohysteroscopy in detection of intracavitary lesions in perimenopausal women with abnormal uterine bleeding.

Methods: This was a prospective study conducted in 100 perimenopausal women with AUB who underwent transvaginal sonography, conventional hysteroscopy and chromohysteroscopy. A total of 34 cases in our study group underwent hysterectomy and specimens were sent for histopathology. Histopathological examination was carried out by a clinical pathologist who was blinded regarding hysteroscopic findings. Diagnostic accuracy of hysteroscopy and chromohysteroscopy in detection of intracavitary lesions was then studied keeping histopathology as the gold standard.

Results: Mean age of the study group was 43.49 ± 3.42yrs, average parity was 3 and mean BMI was 25.41± 3.41 Kg/m^2. 40% cases presented with menorrhagia, 38% with polymenorhagia, 9% with metrorrhagia and 4% with postmenopausal bleeding. Hysteroscopy revealed normal cavity in 59 cases, intracavitary lesions were detected in 26 cases (submucous fibroids in 14, endometrial polyps in 11, and growth with areas of necrosis in one case), synechiae in 2 cases and diffuse endometrial disease was suspected in 17 cases (hyperplastic in 13 cases and polypoidal in 4 cases. On chromohysteroscopy, most of the intracavitary lesions (72%) either did not stain or the uptake was very minimal giving an unstained appearance in comparison to the surrounding endometrium. The lesions thus got demarcated and separated from the surrounding endometrium. The conventional hysteroscopic, chromohysteroscopic and histopathologic findings were then compared with each other. The diagnostic accuracy of conventional hysteroscopy in detecting polyps was found to be high (Sensitivity-85.71 %, specificity- 92.59%, positive predictive value- 75.0%, negative predictive value- 96.15% ; *P<0.001)*. Its diagnostic accuracy in detecting submucous fibroids was also high (Sensitivity-92.31 %, specificity- 90.47%, positive predictive value 85.71%, negative predictive value- 95.00 %;*(P<0.001)*. The diagnostic accuracy of chromohysteroscopy in detecting intracavitary lesions as unstained areas was also found to be significantly high (Sensitivity-80.0 %, specificity-78.57%, positive predictive value- 84.2%, negative predictive value- 73.34% ; (P<0.01).

Conclusion: The diagnostic accuracy of both hysteroscopy and chromohysteroscopy in detecting intracavitary lesions is high. However, differential staining on chromohysteroscopy made these lesions look more prominent and easily identifiable to the observer.

KEYWORDS : perimenopausal, abnormal uterine bleeding, intrauterine cavity lesion staining, chromohysteroscopy

INTRODUCTION

Primary goal of clinical evaluation of abnormal uterine bleeding (AUB) is to establish a specific diagnosis in the most efficient and least invasive manner possible. AUB has been traditionally investigated with blind procedures like dilatation and curettage or office endometrial biopsy, but now with changing trends towards minimally invasive investigations, diagnostic hysteroscopy with directed biopsy has become the gold standard[1] in the AUB workup. Hysteroscopy technique facilitates adequate visualization of uterine cavity, accurate detection of intracavitary lesions, less hospitalization, reduced disability and rapid return to normal activity. However, eyes see only what their minds know. Lack of experience in hysteroscopy might lead to missing of pathological lesions. Thus, there is an urgent need to decrease inter-observer variations and for a technique that would increase the efficacy of hysteroscopy. Chromohysteroscopy is proposed to be one such novel chromoendoscopy technique. Hence, this study was undertaken to evaluate the role of chromohysteroscopy in detection of intracavitary lesions in perimenopausal women with abnormal uterine bleeding and to compare the hysteroscopic and chromohysteroscopic findings with the histopathologic diagnoses in these women.

Chromoendoscopy or tissue staining techniques like chromohysteroscopy involve application of stains or pigments to improve localization, characterization, or diagnosis of lesions[2]. It enables endoscopists to formulate a diagnosis and to direct biopsies based on a specific reaction or enhancement of surface morphology. In recent years, there has been a resurgence of interest in this technique because it is a simple, safe, quick, widely available, and an inexpensive diagnostic tool that has been extensively used in gastro-endoscopy[3-5]. Methylene blue is a water-soluble vital stain that is actively taken up by absorbing tissues. Though unlike gastrointestinal mucosa, endometrium is not an absorptive epithelium, it has been reported that endometrium can be stained with methylene blue in all phases except in the peri-ovulatory phase[6]. The reason for endometrial staining has been explained with theory of apoptosis and it has been stated that the apoptotic structural damage allows passage of the methylene blue dye into the cell. Mucosal staining by methylene blue has been comprehensively studied in gastroenterology and it has been found to be a safe, inexpensive, reproducible, and a highly accurate method[7] of diagnosing subtle mucosal changes. Inspired from wide success of chromoendoscopy in the field of gastroenterology, possibility of application of vital stains to endometrium came to the mind of gynaecologists and chromohysteroscopy technique came into existence.

MATERIAL METHODS

The subjects of the present prospective study were 100 perimenopausal women aged ≥40 years who presented with complaints of abnormal uterine bleeding and who met the inclusion criteria. The aim and procedures of the study were explained to each potential subject. Subjects who did not give informed consent and those with pelvic infection, pregnancy, pregnancy related complications, carcinoma cervix, deranged thyroid profile, abnormal liver functions and coagulopathy were excluded. The study protocol was approved by the Institute's Ethics Committee. A comprehensive history was taken and a clinical (general, systemic and pelvic) examination was done in all subjects. All cases were subjected to transvaginal sonography.

Following the necessary pre-operative preparation, all women underwent diagnostic hysteroscopy, chromohysteroscopy and targeted

biopsy of the endometrial tissue in the operation theatre. With patients under suitable anaesthesia, fully assembled hysteroscope i.e. attached to the fibreoptic light source, distending medium (0.9% sodium chloride solution) and video endocamera was introduced into the cervical os and the irrigating system was turned on. Adequate focussing of the image was done prior to insertion of the hysteroscope which was advanced slowly into the uterine cavity under direct vision. The cervical canal was visualised in its totality. Once the junction between cervix and uterus was crossed, the uterine cavity was first observed panoramically and then, bilateral tubal ostia were inspected. Following this, all portions of uterine wall: - fundus, anterior wall, left lateral wall, posterior wall and right lateral wall were systematically (clockwise) inspected. Slight rotation of the hysteroscope was needed to observe the utero-tubal regions, aided by its inbuilt fore-oblique view. The hysteroscopic findings were recorded and any abnormal areas if detected were noted.

This was followed by chromohysteroscopy. 5 ml of 1% methylene blue was introduced through the hysteroscopic inlet. After 3 minutes (staining time) distending medium flow was started again to wash the endometrium and the uterine cavity was then visualised for staining pattern. First the staining pattern over the intracavitary lesion (if present) was noted and then the adjacent endometrial staining patterns were studied. In cases without cavity lesions differential staining pattern of the endometrium was directly studied. Different patterns of staining observed were: homogenous light blue staining, dark blue staining, partial staining and unstained areas. Diffuse light blue staining was considered normal. Partial staining, dark blue staining or unstained areas above the internal cervical ostium regardless of size and number of stained areas were considered positive findings. These findings were compared with the diagnostic hysteroscopy findings. All the endometrial biopsy specimens were examined by the same pathologist who was blinded about the hysteroscopic findings. The hysteroscopic and chromohysteroscopy findings were then compared with the histopathology results and the diagnostic accuracy of both the techniques were calculated. The results were statistically analyzed using SPSS Software using T test, Chi square test and Mann Whitney tests. A total of 34 cases in our study group underwent hysterectomy and specimens sent for histopathology. Histopathological examination was carried out by a clinical pathologist who was blinded regarding hysteroscopic findings. Diagnostic accuracy of diagnostic hysteroscopy and chromohysteroscopy in detection of intracavitary lesions was then studied keeping the histopathology as the gold standard.

RESULTS

Mean age of the study group was 43.49 ± 3.42yrs, average parity was 3 and mean BMI was 25.41± 3.41 Kg/m^2. Forty percent cases presented with menorrhagia, 38% with polymenorhagia, 9% with metrorrhagia and 4% with postmenopausal bleeding.

Conventional hysteroscopy revealed normal cavity in 59 cases, intracavitary lesions were detected in 26 cases (submucous fibroids (Fig1) in 14, endometrial polyps (Fig2) in 11, and growth with areas of necrosis in one case), and synechiae in 2 cases, diffuse endometrial disease was suspected in 17 cases.

On chromohysteroscopy, most of the intracavitary lesions (72%) either did not stain or the uptake was very minimal giving an unstained appearance in comparison to the surrounding endometrium. The lesions thus got demarcated and separated from the surrounding endometrium and this facilitated their easy and quick detection.

A total of 34 cases in our study group underwent hysterectomy. In 23 of them intracavitary lesions (submucous fibroids in 14 cases, endometrial polyps in 8 cases and an abnormal growth in one cases) were detected on hysteroscopy. In the rest eleven cases, no intracavitary lesion was visualised on hysteroscopy. Histopathology findings of the hysterectomy specimens were noted and have been summarised in Table1.

Table 1: Histopathology Findings of Hysterectomy Specimens (n=34)

Findings	No of cases	Percent
Sub mucosal leiomyoma	15	44.12
Intramural leiomyoma	6	17.65
Endometrial polyps	7	20.59
Sub mucosal leiomyoma with degeneration	1	00.34
Myohyperplasia	5	14.70
Total cases	34	100.00

The conventional hysteroscopic, chromohysteroscopic and histopathologic findings were then compared with each other (Table2) and diagnostic accuracy of both the techniques was computed (Tables 3, 4). The diagnostic accuracy of conventional hysteroscopy in detecting polyps was found to be high (Sensitivity-85.71 %, specificity- 92.59%, positive predictive value- 75.0%, negative predictive value- 96.15% ; *P<0.001)*. Its diagnostic accuracy in detecting submucous fibroids was also high (Sensitivity-92.31 %, specificity- 90.47%, positive predictive value 85.71%, negative predictive value- 95.00%; *P<0.001)*. The diagnostic accuracy of chromohysteroscopy in detecting intracavitary lesions as unstained areas was also found to be significantly high (Sensitivity-80.0 %, specificity- 78.57%, positive predictive value- 84.2%, negative predictive value- 73.34% ; (P<0.01).

TABLE 2. COMPARISON OF CONVENTIONAL HYSTEROSCOPY AND CHROMO-HYSTEROSCOPY WITH HISTOPATHOLOGY OF HYSTERECTOMY SPECIMENS (n=34)

Conventional hysteroscopic Findings			Chromohysteroscopic Findings		Histopathologic diagnosis			
Intracavitary lesions	**No of cases**	**No of operated cases**		**No of cases**	**Histology of the lesion**	**No of cases**	**Histology of the endometrium**	**No of cases**
Submucosal fibroids	14	14	**Homogenously stained**	2	Intramural leiomyoma	2	Proliferative	2
			Unstained	12	Submucosal leiomyoma	12	Proliferative	9
							Disordered proliferative	2
							Simple hyperplasia	1
							Proliferative	9
			Partially stained	0	-		-	
Endometrial Polyps	11	8	**Homogenously stained**	0	-		-	
			Unstained	7	Benign Endometrial polyps	6	Proliferative	5
							Chronic Endometritis	1
					Submucosal leiomyoma	1	Proliferative	1
			Partially stained	1	Submucosal leiomyoma	1	Proliferative	1

Necrotic Growth			**Homogenously stained**	0	-	-	-	-
			Unstained	0	-	-	-	-
			Partially stained	1	Submucosal leiomyoma with degeneration	1	Proliferative	1
No Intracavitary lesion		11			Intramural leiomyoma	4	Proliferative	3
							Simple hyperplasia	1
					Submucosal leiomyoma	1	Proliferative	1
					Benign Endometrial polyps	1	Simple hyperplasia	1
					Myohyperplasia	5	Proliferative	3
							Secretary with Decidualisation	2
Total cases		34	34			34		34

TABLE 3: DIAGNOSTIC ACCURACY OF DIAGNOSTIC HYSTEROSCOPY IN DETECTION OF INTRACAVITARY LESION (n=34)

Diagnostic Hysteroscopic Diagnosis		Histopathologic Diagnosis of hysterectomy specimens			Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	P value
		Present	Absent	Total					
Polyps	Present	6	2	8	85.71	92.59	75.0	96.15	0.000*
	Absent	1	25	26					
	Total	7	27	34					
Submucos Fibroid	Present	12	2	14	92.30	90.47	85.7	95.00	0.000*
	Absent	1	19	20					
	Total	13	21	34					

TABLE 4: DIAGNOSTIC ACCURACY OF CHROMOHYSTEROSCOPY IN DETECTION OF INTRACAVITARY LESION (n=34)

Chromohysteroscopic Diagnosis		Histopathologic	Diagnosis of	Hysterectomy specimens	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	P value
		Present	Absent	Total					
Intracavitary lesions	Present	16	3	19	80.0	78.57	84.2	73.34	0.005*
	Absent	4	11	15					
	Total	20	14	34					

DISCUSSION

Uterine cavity was considered to be normal on hysteroscopy when all the following three criteria were met: good visualization of the entire uterine cavity, no structural abnormalities in the uterine cavity and a uniformly thin, homogenous-appearing endometrium without variations in thickness. Hysteroscopic detection of focal or extensive endometrial thickening, irregular vascularity or architectural distortion was considered endoscopic features consistent with diffuse endometrial disease. A note was made of the intracavitary lesion if detected..

The diagnostic accuracy of conventional hysteroscopy in detecting both polyps and submucosal fibroids is significantly high These findings are in accordance with a study by Angioni S et al [8] in which hysteroscopy demonstrated a sensitivity of 100% and a specificity of 97%, with an accuracy of 91% in diagnosing endometrial polyps, a sensitivity and specificity of 100% and 98%, respectively, with an accuracy of 99% for submucous myomas.

Chromohysteroscopy was done in all and it was found that the endometrium in majority cases, intracavitary lesions (72%) either did not stain or the uptake was very minimal giving an unstained appearance in comparison to homogenous staining of the surrounding endometrium. This resulted in better demarcation of these lesions which got separated from the surrounding endometrium and this facilitated their easy and quick detection.

In future, this feature may become useful in operative hysteroscopy as a well demarcated lesion will be technically much easier to approach and operate for the surgeon. In various studies [9-11] on chromohysteroscopy, cavities with intracavitary lesions were excluded from the study and staining was not done in them. Further, those cavities in which endometrium did stain were also not sampled. No study, in the reviewed literature, therefore has till date compared the histopathology findings with unstained areas found on chromohysteroscopy The diagnostic accuracy of chromohysteroscopy in detecting intracavitary lesions as unstained areas was found to be significant in our study (Sensitivity-80.0 %, specificity- 78.57%, positive predictive value- 84.2%, negative predictive value- 73.34% ; P<0.01). To the best of our knowledge no study has evaluated the efficacy of chromohysteroscopy in detection of intracavitary lesions.

It is therefore concluded that the diagnostic accuracy of both hysteroscopy and chromohysteroscopy in detecting intracavitary lesions is high. However, differential staining on chromohysteroscopy made these lesions look more prominent and easily identifiable to the observer, thereby minimising inter-observer variations. A well outlined lesion is difficult to miss and less likely to involve conflicting diagnoses. Inter-observer variations will decrease with chromohysteroscopy and it is thus a useful cost-effective adjunct to hysteroscopy. However, Studies with a larger sample size and studies to standardize the chromohysteroscopy technique needs to be undertaken to further explore the uses of chromohysteroscopy, to adequately study its clinical efficacy and work out its final indications.

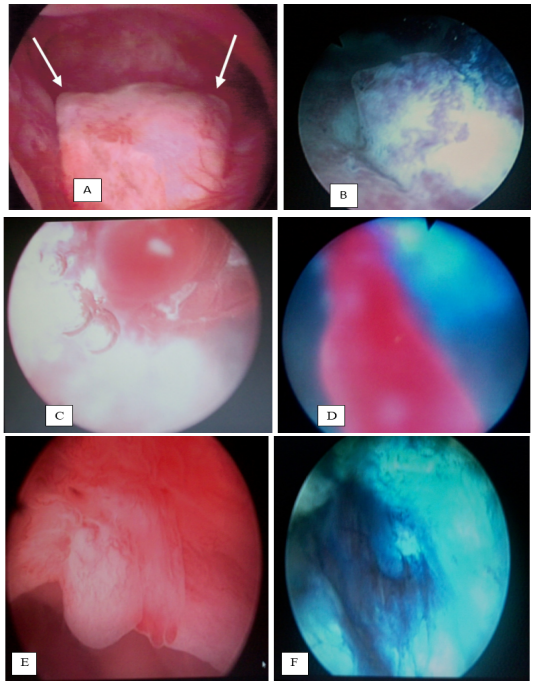

FIGURE: A,E show submocosal fibroids and C shows endometrial polyp on diagnostic hysteroscopy while B,D,F are corresponding pictures on chromohysteroscopy showing unstaine and partially stained intracavitary lesions.

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