Abstract:
The study was done to find out the role of saline infusion sonohysterography in the diagnosis of abnormal uterine bleeding. 50 patients in the perimenopausal and postmenopausal age group with abnormal uterine bleeding were subjected to saline infusion sonohysterography. The findings obtained were compared with histopathology of endometrium in all patients and hysterectomy specimens in 35 patients. When histopathologic examination was taken as confirmatory, SIS findings had 100% sensitivity and negative predictive value but specificity and positive predictive value were 42% and 37% respectively. When hysterectomy specimens were taken as gold standard, sensitivity and negative predictive value were each 100% and specificity was 97% for polyp, submucous fibroids and malignancy. The positive predictive value was 75% for both submucous fibroids and polyps and 66.6% for malignancy. SIS is a cost effective minimally invasive first line investigation in patients with abnormal uterine bleeding.

Key words: Sonohysterography, abnormal uterine bleeding, histopathology, hysterectomy specimen

Introduction:
Screening for gynaecological malignancies and early diagnosis is gaining more importance in peri and postmenopausal women. New innovations are coming up to provide the best management option with minimum morbidity to women with abnormal uterine bleeding who are scared by taboos about malignancies of the genital tract.

1 in 20 women of 40 – 49 years, consult their gynaecologist with history of abnormal uterine bleeding at least once in their lifetime. 1 in 10 women are undergoing hysterectomy before 60 years. Out of them 50 percent women undergo hysterectomy for abnormal uterine bleeding. In 50% of hysterectomies the uterus removed has no local pathology. Uterus is just the target organ responding to the variations in hypothalamo pituitary ovarian axis. But before we conclude the uterus to be an innocent target organ, there should be a confirmatory evidence. A step towards such a conclusion should be cost effective, easily available and safe.

The idea of fractional curettage for all patients with perimenopausal and post menopausal abnormal uterine bleeding is now shifting towards
hysteroscopic guided biopsy. Such sophisticated investigations demand greater technical skill and expertise which is not within the reach of most patients. Plain transvaginal sonography can miss early malignancies and polyps. A simple modification by saline infusion sonohysterography (SIS), has become a less invasive alternative to hysteroscopy in the evaluation of abnormal uterine bleeding [1].

SIS can rule out malignancy with 100% sensitivity, but to confirm malignancy, further biopsy and histopathology are mandatory. The combination of sonohysterography and endometrial biopsy offers high sensitivity and negative predictive values for detection of endometrial and uterine pathology in patients with abnormal uterine bleeding [2,3]. The use of saline infusion sonohysterography reduces the need for unnecessary surgical interventions [4]. It helps to differentiate endometrial, submucous and intracavitary lesions without using contrast agents [5].

Materials and Methods

This is a prospective cohort study done in 50 women in peri and postmenopausal age group between 40 to 55 years who attended the gynaecological OPD with abnormal uterine bleeding. Patients who were suspected to have pelvic infection, pre malignant and malignant lesions of the cervix, cervical stenosis and those with profuse bleeding requiring therapeutic endometrial curettage were excluded from the study.

After detailed history, medical and gynaecological examination were done. Informed consent obtained. The procedure was done in the post menstrual phase. All patients were subjected to transvaginal scan with empty bladder. The TVS probe was removed and Sims speculum was inserted to visualize the cervix and the anterior lip was held with a vulsellum. Cervix was cleaned with povidone iodine and 8 size infant feeding tube was slowly introduced into the uterine cavity. The probe was re introduced into the vagina with the tube in situ. Sterile saline about 10 ml was slowly instilled through the tube and cavity distended. The uterus was scanned in longitudinal axis from one corner to another and in transverse direction from fundus to cervix. Those who complained of abdominal pain were given a single tablet of mefenamic acid 500mg.

All 50 patients were subjected to fractional curettage in the premenstrual phase and histopathological examination of endometrium was done. Correlation between SIS findings and HPE studied. 35 patients underwent hysterectomy for various reasons like fibroid uterus, adenomyosis, endometrial hyperplasia, endometrial polyps. Correlation between SIS findings and cavities of uterine specimens studied.

Results

Among 50 patients studied 44(88%) belonged to 40 – 50 years age group, 6 (12%) were above 50 years. One (2%) patient was a nullipara. Most of them 40(80%) belonged to low socioeconomic status. 41(82%) patients included in the study had perimenopausal abnormal uterine bleeding. 9(18%) had postmenopausal bleeding. Out of the perimenopausal patients 19(46.3%) presented with menorrhagia, 4 (9.8%) had polymenorrhea, 12(29.2%) presented with polymenorrhagia, 6(14.6%) had menometorrhagia. 31(75%) patients reported to the hospital within 1 year of onset of symptoms, 8(19.5%) reported within 1-2 years of symptom onset. In post menopausal age group 7(77%) patients reported within 1 month of symptom onset and only 2(22%) reported late within 6 months. 7(14%) patients were diabetic, 11(22%) had hypertension, 13(26%) had BMI >25.12(24%) patients were severely anemic requiring blood transfusions.

On clinical examination, 3(6%) patients had cervical polyp, out of which 2 (4%) were mucous polypi and 1(2%) was a myomatous polyp. All 3 underwent polypectomy. The 3(6%) adnexal masses were functional ovarian cysts, 39(78%) patients were clinically diagnosed to have dysfunctional uterine bleeding. Transvaginal scan showed that fibroids were present in 10(20%). 7(14%) had adenomyosis. Endometrial thickness in saline infusion sonohysterography is the sum of thickness of anterior and posterior endometrium at the thickest portion after distension of cavity. It was uniformly equal in 31(62%) patients except 4 (8%) who had focal thickening of endometrium in one wall. Thickness >5 mm is considered hyperplasia in the post menstrual phase. 35(70%) patients had hyperplasia according to SIS. 4(8%) patients had endometrial polyp, 4(8%) patients had submucous fibroids, 5(10%) patients had intramural fibroids distorting the cavity. 2 patients, one with focal hyperplasia and another with a polyp were both suspicious of malignancy.

The histopathological examination of endometrium showed atrophic endometrium in
5(10%), 13(26%) had secretory endometrium, 18(36%) had proliferative endometrium. Endometrial hyperplasia was seen in 12(24%) patients out of which 10(20%) had cystoglandular hyperplasia, 1(2%) simple adenomatous hyperplasia, 1(2%) had atypical adenomatous hyperplasia Adenocarcinoma was seen in 1(2%) patient. Out of 31(62%) cases with globally thickened endometrium, 32.3% had proliferation, 35.5% had secretory endometrium, 29% had cystoglandular hyperplasia. Out of 4(8%) patients with focal thickening of endometrium, atypical adenomatous hyperplasia, adenocarcinoma were equally distributed in 1(25%) each.

Out of 50 cases, 35 (70%) underwent hysterectomy for fibroid, adenomyosis, endometrial hyperplasia, endometrial polyps and carcinoma endometrium. 21(60%) patients had normal cavity on cut section. 3(8.6%) polyps were identified, 3(8.6%) submucous fibroids, 6 (17%) specimens showed distortion of cavity by intramural fibroids, 1(2.9%) had lippes loop, 1(2.9%) showed features of carcinoma endometrium – a friable proliferative growth with necrosis filling the cavity.

Out of 35 patients who underwent hysterectomy, cavity was normal in 21(60%) in both SIS and actual specimen. Polyps were found in 4(11.4%) in SIS, 3(8.5%) benign and 1(2.8%) suspected malignant. But in the specimen only 3(8.5%) benign polyps were identified. The suspected malignant polypl was a foreign body, a forgotten lippes loop partially embedded in the myometrium. Diagnosis of submucous fibroids were 4(11.4%) by SIS but only 3(8.5%) were submucosal in specimens. The other case of suspected malignancy with focal irregular polypoid projections showed features of carcinoma endometrium in actual specimen also. Only 4% patients complained of abdominal pain after the procedure. There was no other complication.

When findings of histopathologic examination of endometrium were taken as confirmatory, SIS findings had 22(44%) false positives and no false negatives. There were 13(26%) true positives and 15(30%) true negatives. Sensitivity and negative predictive value were 100% but specificity and positive predictive value were 42% and 37% respectively. Taking the findings of hysterectomy specimens on cut sections as the gold standard SIS findings were compared. There was 1 false positive (2.8%) in diagnosis each of polyp, submucosal fibroid and malignancy. There was 1(2.8%) negative in the diagnosis of intramural fibroid distorting the cavity. Sensitivity and negative predictive value were each 100% for polyps, submucous fibroids and malignancy. But for intramural fibroid distorting cavity, sensitivity was 83.3% and negative predictive value was 96.7% while specificity and positive predictive value were 100%. For polyps, submucous fibroid, malignancy, specificity and positive predictive value were 96.8%, 96.8%, 97% and 75%, 75%, 66.6% respectively.

**Discussion**

Abnormal uterine bleeding is common in the peri and post menopausal women. The etiology varies from dysfunctional uterine bleeding to lesions like polyps, fibroids and malignancies. Apart from the clinical examination, various diagnostic modalities are available to confirm the diagnosis. Sonohysterography has a significant role in diagnosing these abnormalities [6]. In our study, the efficacy of saline infusion sonohysterography in diagnosing abnormal uterine bleeding and its correlation with histopathology of endometrium by fractional curettage and hysterecomy specimens was studied. In our study 88% patients belonged to 40 – 50 years. Only 12% were in 51-55 years age group. In a study by valenzano, 64% were of median age 38.9 years, 35.6 % were in median age of 60.5 years. A few postmenopausal women had to be excluded because of cervical stenosis which prevented effective intra uterine catheterization.

In our study taking more than 5mm as the cut off value for the sum of anterior and posterior wall thickness, 70% patients had endometrial thickening. Out of which, 62% had generalized thickening and 8% had focal thickening. In a study by Goldstein SR 23% had generalized hyperplasia and 1% had focal hyperplasia. In our study out of 31 cases of globally thickened endometrium 38.7% had proliferative endometrium, 32.2% had secretory endometrium and 29% had cystoglandular hyperplasia, 3.2% had adenomatous hyperplasia. In Goldstein’s study, 50% had proliferative endometrium and 50% had hyperplasia [7,8].

According to Descargues, while comparing the results of sonohysterography and histopathological examination, the positive and negative predictive values were 83% and 100% respectively [9]. In our study negative predictive value was 100% but positive predictive value was low 37%. This may be due to interpretation errors associated with simple mucous hypertrophy as hyperplasia. Also in patients with irregular cycles,
the timing of the procedure could not be made exactly at the early proliferative phase and quite a number of patients around 26% had secretory endometrium in HPE. In few cases with suspected hyperplasia, when cavity was forcibly distended with saline, there was a decrease in the thickness of endometrium by 1-2 mm with SIS compared to TVS.

In our study, clinical diagnosis of fibroids was made in 10%. This increased to 20% with TVS. With saline instillation diagnosis of fibroids increased to 22% since a submucous fibroid came into view only after saline instillation. Among findings exclusively diagnosed by SIS, endometrial polyps were found in 8.5%, submucous fibroids in 8.5%, intramural fibroid distorting cavity in 12% malignancy in 2.8%. In study by Pasrija, 3.4% had submucous fibroids, 6.8% had polyps and 3.4% had suspected carcinoma thus almost correlating with our study. In our study the sensitivity of SIS in comparison with hysterectomy specimens was 100% for polyp, submucous fibroids, intramural fibroids distorting the cavity and malignancy. Conventional TVS missed polyps and suspected only 4% submucous fibroids. The sensitivity of SIS in the study by Dodero D is also high in perimenopausal women [10]. In postmenopausal women the sensitivity of SIS was 100% for hyperplasia, 93.8% for polyps and 75% for submucous fibroids [11].

Diagnosis of polyps were 8% in our study by SIS. In the actual specimens only 6% polyps were identified. One suspected malignant polyp was a foreign body, a forgotten lippe's loop partially embedded in the myometrium. Diagnosis of submucous fibroids were 8 % by SIS but only 6% were submucosal in actual specimen. An intramural fibroid distorting the cavity was mistaken for submucosal in SIS. In our study the specificity for diagnosing polyps, submucous fibroids, intramural fibroids distorting cavity and malignancy are 96.85%, 96.6% and 97% respectively. According to Pasrija and others, specificity was 88.5% on the whole(less than our study). Negative predictive value overall was 100% in our study. Positive predictive value for polyps submucous fibroids, intramural fibroids distorting cavity and malignancy are 75%, 75%, 83.3%, 66.6% respectively [12].

In Deuholm, Forman and colleagues 2001 study, negative predictive value was 85% thus correlating with our study [13].

According to Nanda S, Chanda N and colleagues, in whose study hysterectomy findings were kept as the gold standard, the sensitivity and specificity were kept as gold standard, the sensitivity and specificity for polyps was 100% and 97.8% respectively comparable to our study [14]. For submucous fibroids, sensitivity was 89.5%, specificity was 100% where as our study had 100% sensitivity

Detection of focal hyperplasia is significant as 75% with focal hyperplasia had abnormal histopathology of endometrium requiring surgical interventions. In our study only 2% patients complained of abdominal pain after the procedure. There was no other complications. In a study by Bonnamy, Marret H and others, out of 81% patients, the incidence of pelvic pain was 1.2% and endometritis was 1.2% [15].

Conclusion

Saline infusion sonohysteroegraphy is an ideal cost effective minimally invasive investigation to be done as the first step in the evaluation of abnormal uterine bleeding in perimenopausal and post menopausal patients. This alone will be sufficient in most patients except very few who will require subsequent sophisticated investigation like hysteroscopy. SIS has an overall sensitivity and negative predictive value of 100% but positive predictive value and specificity are less, but it is still high for detecting focal endometrial abnormalities. Combined with histopathology, the specificity and positive predictive value can be increased further and false positives can be reduced.

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