Comparison of Diagnostic Hysteroscopy and Saline Infusion Sonography in Abnormal Uterine Bleeding

Dr. Pallavi patil[1], Dr. Sanjay Patil[2], Dr.N S kshirsagar[2*]
[1]Postgraduate student, Department of obstetrics and gynaecology, Krishna Institute of Medical Sciences (Deemed to be University), Karad – 415110, Maharashtra, India
[2]Professor, Department of obstetrics and gynaecology, Krishna Institute of Medical Sciences (Deemed to be University), Karad – 415110, Maharashtra, India

Abstract

Background

Abnormal uterine bleeding (AUB) is a common symptom in postmenopausal women and its association with endometrial cancer in this group warrants investigation.Recently, saline infusion sonography (SIS) hasbecome a fetching alternative to hysteroscopy. However, its diagnostic accuracy is not well established.

Objective

To evaluate and compare the diagnostic accuracy of SIS and hysteroscopy for diagnosing AUB.

Material and Methods

This cross-sectional, observational study was conducted in 35 randomly selected pre- and peri-menopausal patients with AUB. SIS was performed one day before surgery, after distension of the uterine cavity with 15-30 mL of saline. On the same day hysteroscopy was also performed. After the hysterectomy was performed, findings from histological examination of the hysterectomy specimen were compared with those from SIS. Sensitivity, specificity, positive predictive value, and negative predictive value were calculated for SIS and hysteroscopy. Cohen's kappa was used to show the diagnostic agreement between histopathology, SIS, and hysteroscopy.

Results

The maximum number of cases were in the age group of 41 to 45 years (40%) and 36 to 40 years (37.1%). The most common presenting complaint was menorrhagia (57.14%). The sensitivity of SIS was 92.86% and specificity was 85.71% with an accuracy of 88.57%, whereas the sensitivity of hysteroscopy was 100%, specificity was 95.24%,and accuracy was97.14% compared to those of histopathological findings. The kappa coefficient (0.9412) indicated an almost perfect agreement between histopathology and hysteroscopy and substantial agreement between SIS and histopathology (0.7674).

Conclusion

Although hysteroscopy has better diagnostic accuracy for patients with AUB, SIS can be used as a first-line diagnostic measure due to its non-invasive nature and cost-effectiveness.

Keywords: Hysteroscopy, polyps, uterine hemorrhage, uterine neoplasms, uterine perforation

Introduction

Abnormal uterine bleeding (AUB) is one of the most common gynaecological problems faced by women,whichaccounts for more than 70% of all gynecological consultations in the peri- and post-menopausal age group.[1]Forty percent of these affected women have intrauterine abnormalities.[2,3] The most common intrauterine abnormalities in women are submucosal fibroids, endometrial polyps, and endometrial hyperplasia. The early and accurate diagnosis of AUB becomes vital as 10% to 15% of menopausalAUB is due to endometrial cancer.[4]

Ultrasonography (2D or 3D) is a common diagnostic procedure performed on women with AUB.[5] Transvaginal sonography (TVS) is used as an initial investigation as it is simple, speedy, and cost-effective. However, it cannot differentiate intrauterine pathology with complete certainty.[6]Diagnostic hysteroscopy combined with histological examination of the biopsied

specimen is the gold standard for diagnosis of intrauterine abnormalities, due to its ability to directly visualize the uterine cavity; however, it has its own limitations. It is invasive, reasonably expensive, time-consuming, and involves use of anesthesia. Additionally, it is associated with complications such as uterine perforation and increased genitourinary infection.[7,8]TVSfollowed by hysteroscopy with histological examination of the obtained specimen is the most commonapproach for the management of AUB.[9]

Saline infusion sonography (SIS) is a relatively recent diagnostic procedure in which the uterine cavity is distended with saline to visualize the endometrial surface.It seems to be a less invasive and cheaper alternative to hysteroscopy. Additionally, it is an outpatient procedure, does not require anesthesia, and gives a clear visualization of the inner surface of both sides of the endometrium.[8]Furthermore, the nature of complications associated with SIS are mild, with an incidence rate of only 1-2% of infections reported, mostly as endometritis.[10,11]However, the diagnostic accuracy is not well established.

Hence, this study intended to evaluate and compare the diagnostic accuracy of saline infusion sonography (SIS) and hysteroscopy for diagnosing the causes of AUB.

Material and Methods

This cross-sectional, observational study was conducted in the Department of Obstetrics and Gynecology at a tertiary care hospital from December 2017 to June 2019 after institutional ethics committee's clearance.The minimum sample size was calculated by assuming a large effect size (w=0.5) at 95% significance level and 80% power.The sample size was approximately 32 for the Chi-square test of independence.

A total of 35 randomly selected pre- and peri-menopausal patients having AUB, abnormal uterine size of <12 weeks duration, and no other known significant medical illness or past history were included in the study after obtaining approval from the institutional review board (Annexure). Patients with acute pelvic inflammatory disease, those diagnosed with or suspected to have endometrial carcinoma (having carcinoma specific symptoms and pathology), and pregnant women were excluded from the study.

A written informed consent was obtained from each patient prior to the commencement of the study.A detailed history was obtained and relevant clinical examination was performed and recorded in a pre-designed proforma.In addition, care was taken to eliminate bias in the report by examination by same expert in the presence of same doctor.

Each patient underwent a baseline ultrasound assessment of the uterine cavity.TVS followedby SIS (with saline as the contrast medium) and then hysteroscopy was performed for uterine cavity assessment. TVS and SIS were performed with the help of a 7.5 MHz vaginal probe a day before surgery.

In TVS, the uterus was imaged in the sagittal plane, which includes the entire length of the cervical canal. As per the TVS, normal endometrium and uterine cavity were defined by a centrally placed echo-dense line within the uterus and a homogeneous endometrial lining with distinct margins from the myometrium. The thickness of the endometrium was measured from basalis to basalis in the longitudinal plane. Both walls of the endometrium, individually and combined, were used for measuring the endometrial thickness. SIS was performed immediately after TVS, without scheduling according tothe phase of the menstrual cycle.

For SIS, Foley's catheter No. 8 was introduced into the uterine cavity, the bulb inflated with 3 mL of normal saline, and mild traction given so as to place the bulb at the internal os. A 50-mL syringe containing normal saline was attached to the catheter. A vaginal probe was introduced and sterile saline was infused until the distension of uterine cavity was adequate to see any lesion or until pain was elicited, and the findings were noted. In most cases, 15 to 30 mL saline was adequate.After hysteroscopy, findings from macroscopic inspection of the hysteroscopy specimen and histological examination were compared with thoseof SIS and TVS. The examiners involved in the examination of these specimens were blinded to the findings of SIS and TVS.

Statistics analysis

Qualitative data was presented in the form of frequency and percentages. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated to checkthe diagnostic accuracy of SIS and hysteroscopy by adopting R software. A*P* value of<0.05 was considered statistically significant. Cohen's kappa was used to assess the diagnostic correlation between histopathology, SIS, and hysteroscopy.

Results

The maximum number of cases were in the age group 41 to 45 years (40%) followed by 36 to 40 yeas (37.1%). The most common presenting complaint was menorrhagia (57.14%). Table 1 illustrates the distribution of cases according to age and symptoms.

Of the 35 patients, 22 cases had had two pregnancies (62.9%), 8 cases had one (22.9%) and 4 cases (11.4%) had more than two pregnancies.Only one woman (2.86%) was neverpregnant earlier.Also, of the 35 cases, 19 had bornechildren twice(54.39%), 10 cases had one child (28.6%), and four cases (11.4%) had more than two children.Two women (5.71%) were nulliparous.Of the 35 cases, 8 cases (22.9%) had past history of abortion and the remaining 27 women (77.1%) had never had an abortion earlier.

Table 2 shows the comparison of findings of SIS and hysteroscopy with histopathology. Out of 35 cases, 19 (54.29%) cases were normal by SIS, 20 (57.14%) by hysteroscopy and 21 (60%) by histopathology. Intrauterine polyp was found in 8 (22.86%) cases in SIS and 7 (20%) cases by hysteroscopy. Histopathology was able to confirm 7 cases only.

Table 3 shows case to case comparison of hysteroscopy and SIS finding for uterine pathology with confirmatory histopathological findings. Out of total 35 cases, in 31 cases the findings of SIS and histopathological diagnosis were similar to each other. In 4 cases the findings differ between SIS and histopathology.

Out of total 35 cases, in 34 cases the findings of hysteroscopy and histopathological diagnosis were similar to each other. In 1 case the findings differ between hysteroscopy and histopathology.Table 4 illustrates the diagnostic value of SIS and hysteroscopy in comparison to the histopathological and confirmatory findings. The sensitivity and specificity of SIS were 92.86% and 85.71%, respectively. PPV was 81.25% and NPV was 94.74%. The accuracy of SIS was 88.57% compared to histopathological findings.The sensitivity of hysteroscopy was 100% and specificity was 95.24%. PPV was 93.33% and NPV was 100%. The accuracy was 97.14% compared to histopathological findings.

Cohen's kappa coefficient (K) was used to determine the degree of diagnostic agreement between histopathology and hysteroscopy and also between histopathology and SIS. The kappa value for the degree of diagnostic agreement between histopathology and hysteroscopy was 0.9412, indicating that there was almost a perfect agreement between histopathology and hysteroscopy. Values between 0.81 and 1.00 indicate perfect agreement.The kappa value for the degree of diagnostic agreement between histopathology and SIS was 0.7674, indicating a substantial agreement between histopathology and SIS. Values between 0.61 and 0.80 indicate substantial agreement.

Discussion

AUB is a very common complaint in women and is a major source of physical, financial, and psychological trauma in the affected patients. Thus, a rapid, non-invasive, and cost-effective diagnostic method would help alleviate this trauma.

In the present study,the highest number of cases were in the fifth decade of life (41 to 45 years) (40%) followed by 36 to 40 years (37.1%). This finding is in agreement with the studies conducted by Khan et al and Tangriet al.[6,12]Thus, AUB seems to be more common in the perimenopausal age group. It may be an expression of the hormonal milieu in this age group, or it could be the clinical presentation of benign or malignant lesions which show peak incidence in the fifth decade of life.[1,13]

In the present study, menorrhagia (57.14%) was the dominant symptom. This finding was in agreement with studies by Talukdar et al, Jetley et al, and Pillai et al.[1,14,15]This may be due to the predominance of endometrial polyps and fibroids in patients with AUB. Both these pathologies are an important cause of menorrhagia and together accounted for 37.14% of our total cases. The mechanism of their effect on menstrual blood loss is poorly understood but menorrhagia from fibroids may be due to abnormalities in the local venous drainage, enlargement of the uterine cavity,and abnormalities in prostaglandin production.[16]Similarly, menorrhagia from endometrial polyps may be due to abnormal microvasculature with thick-walled blood vessels and the incomplete shedding of the endometrial lining during menstruation.[13] This study showed that the maximum number of women with AUB had a history of two pregnancies (62.9%) and borne children twice (54.39%), whereas the incidence was lowest among women who were nulliparous (5.71%). These findings were mirrored by studies conducted by Khan R et al and Saheta et al.[17,18] However, literature suggests that parity per se has a limited role in the pathogenesis of AUB and it is important only in treatment planning.[17]

Although most of the cases in the present study presented with a normal uterus, the most common pathology associated with AUB was intrauterine polyp.According to literature, polyps account for 13%-50% of the etiology of AUB in premenopausal women and 30% of the etiology in peri- and post-menopausal women.[19]This coincided well with the findings of our study.

In the present study, hysteroscopy was more sensitive (100% vs. 92.86%), specific (95.24% vs. 85.71%), and accurate (97.14% vs. 88.57%) than SIS and also had higher predictive values (93.33% vs. 81.25% PPV; 100% vs. 94.74% NPV) than SIS.The kappa coefficient also showed better agreement between hysteroscopy and histopathology (0.9412) as compared with SIS and histopathology (0.7674). These findings were similar toa study byDraz et al.[8] However, these findings were contrary to those of Khan et al. whose study demonstrated higher sensitivity and NPV in SIS as compared to those of hysteroscopy and similar specificity and PPV in both these techniques.[6] One of the reasons for these contradictory findings may be the larger sample size in that study (n=101) as compared with our study (n=35).

Although hysteroscopy was proven to be a slightly more accurate diagnostic modality for pathologies in this study, literature reports that it is not only an expensive and invasive procedure but unnecessary in 50% of the women who have normal uterus.[6]This entails that a majority of women are subjected to an unnecessary invasive procedure under anesthesia. This is supported by our study whereina majority of patients had normal uterine pathology. Furthermore, Widrich et al have reported that distinguishing between large polyps and pedunculated myoma is difficult by either hysteroscopy or SIS technique. However, as both these pathologies can be treated with hysteroscopic resection, the treatment does not change even if lesions are confused with each other.[20] Thus, utilizing hysteroscopy as a first-line diagnostic procedure unnecessarily results in an invasive procedure for the patient along with the anxiety associated with a surgical procedure.

Thus, it can be concluded that SIS can be used as a first-line diagnostic technique for AUB. Hysteroscopy should be reserved for cases where an intrauterine lesion has already been diagnosed on SIS or when SIS is inconclusive. Limitations of this study include its small sample size and the use of isolated SIS without a guided biopsy. Future studies with a larger sample size and combination of SIS with guided endometrial biopsies would further increase the sensitivity and specificity of the procedure.

Conclusion

In summary, hysteroscopy has slightly better accuracy compared to SIS.However, SIS is rapid, safe, painless, and a less invasive method in comparison to hysteroscopy and can be used as afirst-line diagnostic modality in patients with AUB. In addition, the acceptable statistical agreement between the techniques will be highly useful in the healthcare centres with limited facilities.

Informed Patient Consent

We have obtained all appropriate written informed consent forms from the patient after obtaining approval from the institutional ethics board.

References

1. Talukdar B, Mahela S.Abnormal uterine bleeding in perimenopausal women: Correlation with sonographic findings and histopathological examination of hysterectomy specimens.J Midlife Health. 2016;7:73-77.
2. Moschos E, Ashfaq R, McIntire DD, Liriano B, Twickler DM. Saline infusion sonography endometrial sampling compared with endometrial biopsy in diagnosing endometrial pathology. Obstet Gynecol.2009;113:881-887.
3. de Kroon CD, Jansen FW. Saline infusion sonography in women with abnormal uterine bleeding: An update of recent findings. CurrOpinObstet Gynecol.2006;18:653-657.
4. Ryu JA, Kim B, Lee J, Kim S, Lee SH. Comparison of transvaginal ultrasonography with hysterosonography as a screening method in patients with abnormal uterine bleeding. Korean J Radiol.2004;5:39-46.
5. Lee SI. An imaging algorithm for evaluation of abnormal uterine bleeding: Does sonohysterogrphy play a role? Menopause.2007;14:823-825.
6. Khan F, Jamaat S, Al-Jaroudi D. Saline infusion sonohysterography versus hysteroscopy for uterine cavity evaluation. Ann Saudi Med.2011;31:387-392.
7. Daniilidis A, Pantelis A, Dinas K, Tantanasis T, Loufopoulos PD, Angioni S, et al. Indications of diagnostic hysteroscopy, a brief review of the literature. Gynecol Surg.2011;9:23-28.
8. Draz MH, El-Sabaa TM, El Shorbagy SH. Saline infusion sonography versus hysteroscopy in the evaluation of uterine cavity in women with unexplained infertility. Tanta Med J.2017;45:155-159.
9. Glanc P, Betel C, LevToaff A. Sonohysterography: Technique and clinical applications. Ultrasound Clin.2008;3:427-431.
10. Goyal AS, Chaudhari SJ, Shrivastava AR, Verma RN. Comparison of transvaginal sonography and saline infusion sonohysterography for the diagnosis of causes of abnormal uterine bleeding: a diagnostic accuracy study. Int J Reprod Contracept ObstetGyneco.l 2016;5:1566-1570.
11. Munro MG, Critchley HO, Broder MS, Fraser IS; FIGO Working Group on Menstrual Disorders. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. Int J Gynaecol Obstet.2011;113:3–13.
12. Tangri MK, Srivastava AK. Diagnostic accuracy of saline infusion sonography as compared to hysteroscopy in premenopausal women with abnormal uterine bleeding. Int J Reprod Contracept Obstet Gynecol. 2017;6:682–687.
13. Hapangama DK, Bulmer JN.Pathophysiology of Heavy Menstrual Bleeding. Womens Health (Lond).2016;12:3–13.
14. Jetley S, Rana S, Jairajpuri ZS. Morphological spectrum of endometrial pathology in middle-aged women with atypical uterine bleeding: A study of 219 cases. J Midlife Health.2013;4:216–220.
15. Pillai SS. Sonographic and histopathological correlation and evaluation of endometrium in perimenopausal women with abnormal uterine bleeding. Int J Reprod Contracept ObstetGynaecol. 2014;3:113–117.
16. West CP, Lumsden MA. Fibroids and Menorrhagia.Baillieres Clin ObstetGynaecol.1989;3:357-74.
17. Khan R, Sherwani RK, Rana S, Hakim S, Jairajpuri ZS. Clinco-Pathological Patterns in Women with Dysfunctional Uterine Bleeding.Iran J Pathol.2016;11:20–26.
18. Saheta A, Hariharan C, Sharma U.Abnormal uterine bleeding. IOSR Journal of Dental and Medical Sciences.2014;13:63–67.

19. Nijkang NP, Anderson L, Markham R, Manconi F. Endometrial polyps: Pathogenesis, sequelae and treatment. SAGE Open Med.2019;7:2050312119848247.
20. Widrich T, Bradley LD, Mitchinson AR, Collins RL. Comparison of saline infusion sonography with office hysteroscopy for the evaluation of the endometrium. Am J Obstet Gynecol. 1996;174:1327-1334.

Table 1: Distribution of patients according to age and symptoms

Parameters	**Frequency n (%)**
Age (years)	
21-25	1 (2.86)
26-30	1 (2.86)
31-35	4 (11.43)
36-40	13 (37.14)
41-45	14 (40)
46-50	2 (5.71)
Total	35
Symptoms	
Menorrhagia	20 (57.14)
Metrorrhagia	2 (5.71)
Menometrorrhagia	5 (14.29)
Polymenorrhea	5 (14.29)
Polymenorrhea	3 (8.57)
Total	35

Table 2: Comparison of findings of various types of lesions in SIS and hysteroscopy with histopathological findings

Findings	**Count (%)**		
	SIS	**Hysteroscopy**	**Histopathology**
Intrauterine Polyp	8 (22.86)	7 (20)	7 (20)
Polyp + Fibroid	1 (2.86)	1 (2.86)	1 (2.86)
Submucous Fibroid	5 (14.29)	6 (17.14)	5 (14.29)
Fibroid + Hyperplasia	1 (2.86)	0 (0)	0 (0)
Endometrial Hyperplasia	1 (2.86)	1 (2.86)	1 (2.86)
Normal Uterus	19 (54.29)	20 (57.14)	21 (60)
Total	35	35 (100)	35 (100)

Table 3: Comparison of findings from SIS and hysteroscopy with histopathology

	Histopathology findings				**Total**
	Cases with lesion (n=14)	**Percentage (%)**	**Normal uterus (n=21)**	**Percentage (%)**	
SIS					
Cases with lesion	13	86.7	3	15.0	16
Normal Uterus	1	6.7	18	90.0	19
Hysteroscopy	–	–	–	–	–
Cases with lesion	14	93.3	1	5.0	15

Normal Uterus	0	0.0	20	100.0	20

Table 4: Diagnostic test values of SIS and hysteroscopy in comparison with histopathology

Statistic	**Formula**	**SIS**		**Hysteroscopy**	
		Value (%)	**95% CI**	**Value (%)**	**95% CI**
Sensitivity	$\frac{a}{a+b}$	92.86	66.13% to 99.82%	100.00	76.84% to 100%
Specificity	$\frac{d}{c+d}$	85.71	63.66% to 96.95%	95.24	76.18% to 99.88%
Positive Predictive Value	$\frac{a}{a+c}$	81.25	60.08% to 92.58%	93.33	67.40% to 98.96%
Negative Predictive Value	$\frac{d}{b+d}$	94.74	72.98% to 99.17%	100	–
Accuracy	$\frac{a+d}{a+b+c+d}$	88.57	73.26% to 96.80%	97.14	85.08% to 99.93%