

The Comparative Study of Transvaginal Sonography and Endometrial Biopsy

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Abstract

Introduction: Dysfunctional uterine bleeding (DUB) is a common disorder of reproductive age group of females.

Aims: The aim of the study was to correlate transvaginal ultrasonography and histopathological findings of endometrial biopsy in patients of DUB in age group of ≥ 35 years.

Materials and Methods: It was a comparative study conducted from November 1, 2009, to March 31, 2011. A total of 150 new patients of DUB were included in this study. They underwent transvaginal ultrasonography in pre- and post-ovulatory phase and endometrial biopsy in premenstrual phase and their findings were correlated.

Results: Transvaginal sonography has 96% sensitivity and 96% specificity for endometrial thickness of < 12 mm for predicting normal endometrium on histopathology. Furthermore, the presence of findings such as trilaminar pattern, hypoechoic endometrium, absence of any linear abnormalities, and normal interface between endometrium and myometrium has a good correlation with secretory endometrium on histopathology.

Conclusion: Transvaginal ultrasonography can be used as first line non-invasive diagnostic modality for evaluating patients of DUB in ≥ 35 years of age group.

Key words: Dysfunctional uterine bleeding, Ultrasonography, Women

INTRODUCTION

Dysfunctional uterine bleeding (DUB) is the abnormal uterine bleeding without any clinically detectable organic, systemic, and iatrogenic cause. It commonly occurs in extremes of reproductive age group.^[1] It has been evaluated by both invasive and non-invasive diagnostic methods. Invasive methods include endometrial biopsy, dilation and curettage, and hysteroscopy in which endometrial biopsy (EB) is the gold standard painful procedure which has less patient acceptability. Non-invasive methods include transvaginal sonography (TVS) and saline infusion sonography which are painless diagnostic methods and provide good information regarding endometrium and endometrial cavity.

Endometrial biopsy has histopathological findings which can range from secretory endometrium to proliferative/disordered proliferative/simple hyperplasia/complex hyperplasia and atypical hyperplasia in patients of DUB.^[2] TVS has certain characteristic endometrial findings for normal and abnormal endometrium. The presence of trilaminar pattern, hypoechoic endometrium, absence of linear abnormalities, normal interface between endometrium and myometrium, absence of focal and diffuse thickening in proliferative phase predicts normal endometrium, and vice-versa. Endometrial thickness (ET) in premenstrual phase also get affected in patients with abnormal endometrium on histopathology.

Since EB is a painful invasive procedure, there is a need to establish a diagnostic modality which should be painless and non-invasive and thus can be used as a first line diagnostic method in patients of DUB. Hence, this study was conducted to correlate TVS and EB histopathological findings so that above need could be met.

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MATERIALS AND METHODS

This was a comparative study of TVS and histopathological findings of EB which was conducted in the Gynaecology Outpatient Department of Smt. Sucheta Kriplani Hospital, N. Delhi, from November 1, 2009 to March 31, 2011. A total of 150 new patients of DUB in age group of ≥ 35 years were recruited by randomization procedure.

All 150 patients with c/o heavy or prolonged bleeding with regular or irregular cycles which is not due to any organic, systemic, or iatrogenic cause were included in this study. Patients having intrauterine contraceptive device or having any organic, systemic, or iatrogenic cause were excluded from this study. A written and verbal informed consent was obtained from all the patients and approval was obtained from ethical committee.

These patients were clinically evaluated by detailed history, general physical, systemic, and pelvic examination. Thereafter, certain blood investigations were carried out such as complete Hemogram, serum estradiol (measured in first half of menstrual cycle), and serum progesterone levels (measured on day 21 of menstrual cycle). Levels were evaluated using enzyme-linked immunosorbent assay method.

These patients then underwent TVS in both preovulatory and postovulatory phase of cycle. TVS was done with a probe of 4–9 Hz. Scan was performed through the anterior vaginal wall, anterior vaginal fornix, posterior vaginal fornix, and lateral fornices. Following features such as trilaminar pattern of endometrium in preovulatory phase, type of echogenicity of endometrium, any linear abnormalities, regularity of interface between endometrium and myometrium, homogeneity of myometrium, any focal thickening of endometrium, cystic spaces in endometrium, and fluid in endometrial cavity in both the half of menstrual cycle were looked for.

Normal findings in proliferative phase were described as presence of trilaminar pattern and hypoechoic endometrium. Normal findings in secretory phase were described as endometrial thickness of 7–14 mm and hyperechoic endometrium. Furthermore, findings like no linear abnormalities, regular interface between endometrium and myometrium, normal homogenous myometrium, no focal or diffuse thickening, and absence of cystic spaces in endometrium in both the phases of menstrual cycle were considered as predictor of normal endometrium.

EB was then performed in premenstrual phase. Biopsy was taken by EB curette. It was fixed in 10% neutral buffered formalin and then specimen was embedded in wax to

make blocks. A microtome was used to slice off the block in form of ribbon. It was then transferred to warm water bath and placed in dry oven. Slides were then stained with hematoxylin and eosin stain and were then examined. Following histology were looked for – normal proliferative endometrium, normal secretory endometrium, disordered proliferative endometrium, simple hyperplasia, complex hyperplasia, atypical hyperplasia, endometrial atrophy, and endometrial carcinoma.

The results of TVS and EB findings were correlated and analyzed using Pearson's Chi-square test and sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and *P* value were calculated and interpreted.

RESULTS

A total of 150 patients of DUB in age group of ≥ 35 years excluding those with any organic/systemic/iatrogenic cause were recruited in this study. They were clinically evaluated and TVS and EB was performed after informed consent. The findings of TVS and EB were correlated then. Correlation was also done with respect to their hormonal levels, that is, serum estradiol and serum progesterone levels.

In this study, trilaminar pattern in TVS finding was present in 54% of patients. Hypoechoic endometrium in preovulatory phase was present in 56% of patients. endometrial thickness (ET) in premenstrual phase of ≥ 12 mm and ≥ 15 mm was present in 63% and 87%, respectively. Mean ET was 12.6 ± 1.46 mm.

In EB findings, secretory endometrium was present in 35%, proliferative endometrium in 47%, disordered proliferative endometrium in 17%, and simple hyperplasia in 1% was present. Hence, ovulatory DUB constituted 35% and anovulatory DUB constituted 65% of patients.

During correlation of TVS and EB findings, it was seen that trilaminar pattern was present in 75% of secretory endometrium, 34% of proliferative endometrium, and 68% of disordered proliferative endometrium and was absent in case of simple hyperplasia. Hence, the sensitivity, specificity, PPV, NPV, and *P* value of TVS using trilaminar pattern as criteria for detecting normal and abnormal endometrium were 58%, 75%, 81%, 49%, and <0.01 , respectively.

Regarding echogenicity, hypoechoic endometrium in preovulatory phase was present in 74% of secretory endometrium, 44% of proliferative endometrium, and 56% of disordered proliferative endometrium and was absent in simple hyperplasia. Sensitivity, specificity, PPV, NPV, and

P value of TVS using echogenicity as criteria for detecting normal and abnormal endometrial histopathology were 54%, 74%, 79%, 46%, and 0.002, respectively.

ET of <12 mm in premenstrual phase was present in 96% of secretory endometrium, 4% of proliferative endometrium, 4% of disordered proliferative endometrium, and absent in simple hyperplasia. ET of <15 mm was present in 100% of secretory endometrium, 79% of proliferative endometrium, and 84% of disordered proliferative endometrium.

Combined mean ET of anovulatory DUB (proliferative/disordered proliferative/simple hyperplasia) was 13.4 ± 1.06 mm and mean ET in ovulatory DUB (secretory endometrium) was 11.1 ± 0.80 mm. Sensitivity, specificity, PPV, NPV, and *P* value using ET as criteria for detecting normal and abnormal endometrial histopathology were – for 12 mm – 96%, 96%, 98%, 93%, and <0.01 and for 15 mm – these values were 21%, 100%, 100%, 41%, and <0.01, respectively.

It was also observed that serum estradiol was raised in 93% of anovulatory DUB and only 2% of ovulatory DUB. Serum progesterone was lower than normal in 94% of anovulatory DUB and only 2% of ovulatory DUB. The sensitivity, specificity, PPV, NPV, and *P* value for serum estradiol in detecting abnormal histopathology were 93%, 98%, 99%, 88%, and <0.01, respectively. Sensitivity, specificity, PPV, NPV, and *P* value of serum progesterone in detecting abnormal endometrial histopathology were 94%, 98%, 99%, 90%, and <0.01, respectively.

DISCUSSION

This was a comparative study of TVS findings with histopathological findings of EB in patients of DUB in age group of ≥ 35 years. For detection of endometrial histopathology, EB has been recommended as a gold standard by American college of Obstetricians and Gynecologists (ACOG) (2004) for patients of age group ≥ 35 years and for patients who are chronic anovulatory and have been bleeding which is refractory to medical management.^[3] Since it is an invasive and often painful procedure, studies on alternate non-invasive diagnostic modality like TVS were thought of which can reduce number of unnecessary EBs in patients of DUB.

Earlier studies have focused only on ET which is subjected to extensive changes during the reproductive period. These studies have shown that using ET as only criterion proved to have low sensitivity (64–88%) and low specificity (46–75%). Recently, few studies have been done on the use of TVS as an initial non-invasive diagnostic modality using other parameters for detection of endometrial pathology in different age groups.

In this study, parameters of TVS such as trilaminar pattern in late proliferative phase, echogenicity of endometrium, fluid in endometrial cavity, homogeneity of myometrium, and interface between endometrium and myometrium and central linear abnormalities were studied and their findings were collaborated with histopathological findings of EB.

In this study, 54% of patients had normal trilaminar pattern in late proliferative phase. It was further seen that in patients with ovulatory DUB, 75% of them had normal trilaminar pattern. This might be due to some of the women presenting very early in proliferative phase when endometrium has not converted into normal trilaminar pattern.

In women with anovulatory DUB with proliferative type of endometrium, 66% had absent trilaminar pattern. This can be because of wrong interpretation or wrong timings of EB and few of the patients may actually be of ovulatory type of DUB as seen by presence of normal serum estradiol and serum progesterone levels in them.

In a study conducted by Abe *et al.*^[4] on the use of non-triple layer ultrasonic finding in biopsy recommendation for premenopausal women, they found that the application of TVS using non-triple layer criteria is a highly accurate first step for the selection of premenopausal patients of DUB for EB which may reduce the number of unnecessary EBs by 25%.^[4] They found that “abnormal” TVS criteria could detect disease states in 90% of patients with sensitivity of 94.6% and specificity of 77.2% (*P* < 0.01).

In ovulatory DUB, normal hypoechoic endometrium was present in 74% of patients while in anovulatory DUB, 46% had normal hypoechoic endometrium. Normally endometrium is hypoechoic in proliferative phase and gets hyperechoic in secretory phase. A change in echogenicity of endometrium during proliferative phase is suspicious of endometrial pathology. These echogenic criteria were also used by Abe *et al.* in his study.

In present study, sensitivity, specificity, PPV, NPV, and *P* value of TVS using ET as criteria for detecting normal and abnormal endometrial histopathology were – for 12 mm as cut off, these values were 96%, 96%, 98%, 93%, and <0.01 and for 15 mm as cut off, these values were 21%, 100%, 100%, 41%, and <0.01, respectively. Hence, it was seen that a cut off of 12 mm has high sensitivity and specificity in differentiating normal from abnormal endometrium. Increasing the cut off to 15 mm decreases the sensitivity to 21% but specificity and PPV increases to 100%.

In a study conducted by Nazeeb *et al.*,^[5] on role of transvaginal sonography in assessment of abnormal uterine bleeding in premenopausal age group, cut off of

8 mm was taken for suspicious endometrial pathology and transvaginal sonography was able to detect most of the endometrial pathologies. They found sensitivity to be 74% and specificity to be 72%.

In another study conducted by Islam *et al.*,^[6] on transvaginal sonography regarding its sensitivity and specificity, cutoff of endometrial thickness was taken as 14 mm and below that no serious endometrial pathology was found. It was found that the sensitivity, specificity, negative predictive value and positive predictive value for proliferative endometrium were -79%, 100%, 78% and 100% respectively, for secretory endometrium – 100%, 96%, 100% and 79% respectively, for endometrial hyperplasia - 100%, 93%, 100% and 79% respectively and for endometrial carcinoma – 100%, 99%, 100% and 33% respectively.

In this study, 98% of ovulatory DUB had S. estradiol levels in normal range while in anovulatory DUB, 93% had high estradiol levels. The high estradiol levels in anovulatory DUB are the cause of anovulation leading to presence of proliferative, disordered proliferative endometrium, and simple hyperplasia. In one patient who had simple hyperplasia, serum estradiol level was very high (>525 pg/ml). There is a good correlation with high estradiol levels and presence of non-secretory endometrium in histopathology.

CONCLUSION

From this study, it can be concluded that in the absence of other significant findings such as loss of interface between endometrium and myometrium, heterogeneous myometrium, heterogeneous echotexture of endometrium in proliferative phase, and ET of <12 mm has a good correlation with secretory endometrium on histopathology. Hence, patients with these findings can be managed without any invasive diagnostic procedure.

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