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Perimenopausal women presenting with abnormal uterine bleeding: Endometrial thickness

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Abstract
Relaxin is released by granulocytes. This causes dissolution of stromal fibres. The stratum functionalis is broken down to be discharged as menstruating endometrium. The stratum basalis is not shed from which regeneration begins. The presence of spiral arterioles, are the characteristic features of the endometrium. The key event in the menstruation as postulated by Markee is the intense vasoconstriction of spiral arterioles about 24 hours prior to menstruation, results in ischaemic necrosis of the endometrial segment supplied by them. This necrotic endometrium gets separated with accumulation of blood underneath. Thus, the endometrial shedding begins at various places with the bleeding lasting over 2-7 days period. Written informed consent taken from all patients enrolled in the study. They were evaluated by history, clinical examination and relevant investigations. Transvaginal ultrasound and endometrial biopsy done for all subjects. The endometrial biopsy specimen report obtained and compared and correlated with endometrial thickness by TVS. In perimenopausal women, when endometrial thickness of 14mm on transvaginal ultrasound was taken as cut off, the modality had sensitivity of 97.71% and specificity of 84.21 %. P value with chi square test was found to be < 0.05.

Keywords: Perimenopausal women, abnormal uterine bleeding, endometrial thickness

Introduction
There are many theories proposed to explain the menstruation. The initiating event is a fall in the estrogen and progesterone levels. Corpus luteum regresses about 4 days prior to menstruation [1, 2]. The changes are:

1. Vascular change
The presence of spiral arterioles, are the characteristic features of the endometrium. The key event in the menstruation as postulated by Markee (1950) is the intense vasoconstriction of spiral arterioles about 24 hours prior to menstruation, results in ischaemic necrosis of the endometrial segment supplied by them. This necrotic endometrium gets separated with accumulation of blood underneath. Thus, the endometrial shedding begins at various places with the bleeding lasting over 2-7 days period.

2. Prostaglandin
The prostaglandins are synthesized in the endometrium and to some extent in myometrium from the arachidonic acid. The activation of the enzyme phospholipaseA2 is the rate limiting step in the prostaglandin synthesis. Progesterone promotes the formation of lysosomes in the endometrium. Progesterone has got stabilizing effect and estrogen has labilizing effect on lysosomes. Withdrawal of progesterone preceding the menstruation causes breakdown of lysosomes and release of phospholipaseA2, which acts on the phospholipids on the cell walls and produce large amount of arachidonic acid resulting in initiation of prostanoid cascade and the synthesis of various prostaglandins. In the proliferative phase of normal menstruation the synthesis of PGF2α and PGE2 are in 1:1 proportion. However in the secretory phase there is increase in PGF2α secretion and PGF2α & PGE2 ratio becomes 2:1 causing vasoconstriction, platelet aggregation and myometrial contraction as predominant actions. Thus, relative proportion of different prostaglandins in the endometrium is probably responsible for blood flow and dysmenrrhoea [3].

3. Changes in the ground substance
Acid mucopolysaccharides (AMP) is the most common ground substance, that is carbohydrate

which exist as easily split complex with protein. It is synthesized in the stromal cells and laid down by the effect of estrogen. AMPs are present during the proliferative phase and absent during major portion of secretory phase. This increases vascular permeability and allows a free flow of nutrients and metabolites. During the last week of secretory phase AMPs reaccumulate only in the compacta and around spiral arterioles. During menstruation hydrolytic enzymes depolymerize AMP and it loses gel like consistency and facilitates breakdown of the endometrium.

4. Role of Relaxin

Relaxin is released by granulocytes. This causes dissolution of stromal fibres. The stratum functionalis is broken down to be discharged as menstruating endometrium. The stratum basalis is not shed from which regeneration begins [4].

Regeneration

Regeneration of the endometrium begins within 48 hours after the onset of bleeding (Ferenczy 1976). Re-epithelialization commences from the basal layer of endometrium, which is not shed and this regeneration will be completed in 3-4 days [5].

Methodology

Written informed consent taken from all patients enrolled in the study. They were evaluated by history, clinical examination and relevant investigations. Transvaginal ultrasound and endometrial biopsy done for all subjects. The endometrial biopsy specimen report obtained and compared and correlated with endometrial thickness by TVS.

Study instrument: Transvaginal ultrasonography using SIEMENS ACUSON *****300 5 – 9 M Hz TVS probe. Ultrasound will be done by the transvaginal route. Ultrasound variables to be studied include endometrial thickness, endometrial echogenicity, endometrial-myometrial interface and myometrium.

1. Endometrial thickness measured in the sagittal plane of the uterus, at the thickest part of the endometrium. The thickness includes basal layers of both anterior and posterior uterine walls. Echogenicity of the endometrium noted. Endometrial-myometrial interface noted. Any abnormal pathology such as polyps, abnormal growth noted.
2. Uterus completely assessed longitudinally and transversely for myometrial pathology. Myometrium studied for asymmetric myometrial thickness, globular enlargement of uterus, myometrial cysts, and linear striations.
3. Colour Doppler ultrasound will be used where required – to distinguish adenomyosis and leiomyoma, endometrial hyperplasia and endometrial polyps.

Patient Preparation

Patient informed consent taken and asked to empty her bladder completely. This contributes greatly to patient comfort and acceptance of this technique. The best position is the dorsal position employed for vaginal examination. A transabdominal sonogram is done prior to vaginal study to exclude large masses and if uterus is more than 10 cms as in such conditions, the vaginal study will be suboptimal due to its limited field of view.

Transducer Preparation

Vaginal transducer is between 5-7.5 MHz in frequency and the size of the sector image is usually between 900 and 1150. The transducer should be covered by a condom filled with approximately 5ml of ultrasonic gel. Additional gel may be applied to the outside of the condom prior to its insertion, but this should be omitted in cases of infertility. Following completion of examination, the transducer assembly should be immersed in disinfectant for ten minutes.

Results

Table 1: Endometrial Thickness

Endometrial thickness (mm)	No. of patients (%)
5 – 9.9	52 (34.67)
10 – 14.9	81 (54)
15 – 19.9	11 (7.33)
≥ 20	6 (4)
Total	150

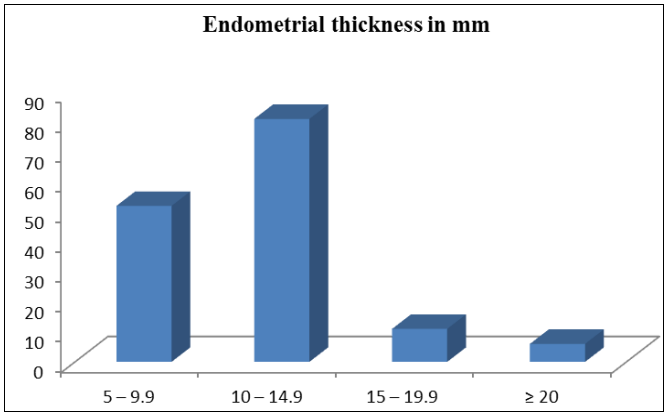

Fig 1: Endometrial Thickness

TVS examination revealed 52 out of the 150 patients to have endometrial thickness between 5 and 9.9 mm, thus accounting for 34.6% of patients. 54% patients had endometrial thickness between 10 and 14.9 mm.

In perimenopausal women, when endometrial thickness of 14mm on transvaginal ultrasound was taken as cut off, the modality had sensitivity of 97.71% and specificity of 84.21 %. P value with chi square test was found to be < 0.05

Therefore it can be seen that with a endometrial thickness less than 14mm the histopathology report was normal endometrium either secretory or non-secretory. An endometrial stripe thickness more than 14mm has been found to be associated with hyperplasia, adenomatous carcinoma and polyp.

Discussion

Suman Agarwal, Rehana Nazam, Chitra Sandeep Diwan studied the role of transvaginal sonographic assessment of endometrium; a prospective cohort study in 2014. Results of D and C and TVS compared and contrasted. Endometrial pathology was found in 38 patients. Endometrial hyperplasia was diagnosed in 13, polyps in 14, endometrial carcinoma in 5 cases. An abnormal sonography was found in 41 out of 70 cases.

Thus concluded that TVS is non-invasive, simple, reliable technique to carry out and detect lesions as a first line of diagnostic modality for the females complaining of uterine bleeding in majority of cases [6].

Ambreen Qureshi, Farhat Ali, Liaquat Malik, studied the accuracy of TVS in detecting endometrial abnormalities in women with peri and post-menopausal bleeding in 2015.

In this study, with endometrial thickness cut off point of 6 mm in perimenopausal women, sensitivity and specificity was 83.3% and 78.2% respectively, in post-menopausal women at cut off

point of 4mm sensitivity and specificity was 87.5% and 77.3%. This study concluded that abnormal endometrial pathology had a mean endometrial thickness that was significantly higher than patients with normal endometrium [7].

Col (Dr) P K Roy, r Pooja Singh, Dr Vijaykumar Singh studied the endometrial thickness as a test for endometrial cancer in women with abnormal postmenopausal and perimenopausal vaginal bleeding and its histopathological correlation in 2013.

Out of 75 cases, endometrial thickness >12mm was seen in 73.4% of perimenopausal and 25.3% of postmenopausal women. In perimenopausal women with abnormal bleeding, histopathology showed benign hyperplasia in 51%, proliferative endometrium in 26.5%, secretory endometrium in 4.08%, atropic endometrium in 2.05%, atypical hyperplasia in 10.2% and carcinoma in 6.12%. In majority, endometrial thickness by TVS may be helpful in planning investigation protocol for further management [8].

Suna Ozdemir, Cetin celik, Kazum Gzginc *et al.* evaluated the endometrial thickness with TVS and histopathology in premenopausal women with AUB in 2009. 144 premenopausal women with AUB were evaluated.

Out of 144 women, 78.4% had normal endometrium, 21.6% had abnormal endometrium and endometrial thickness of >8mm had a sensitivity of 83.6%, specificity of 56.4% and negative predictive value of 95.6% to detect the endometrial pathology. Endometrial thickness >8mm more likely than that of 8mm or less to be indicated with endometrial biopsy in a premenopausal uterine bleeding [9].

Oddvar Bakos, Gun Heimer studied the relation of TVS with the histopathological findings in pre and perimenopausal women. Ultrasonographically both normal and pathological endometrial changes could be detected.

82.5% of the women had a endometrium characterised as normal. The endometrial phase determination correlated with the histological findings in approximately 50% of the women. Endometrial hyperplasia was found in 12% and endometrial polyps in 4%.concluded TVS is as effective as D & C for depicting the endometrium in pre and perimenopausal women with irregular bleeding [10].

Shinde CD, Patil P G, Mane R studied the Endometrial thickness as a guideline for the treatment of Dysfunctional uterine bleeding in premenopausal women

Among 60 cases of abnormal uterine bleeding, 23 were more than 36 years of age. In them bleeding disorders had more severe symptoms. Endometrial thickness was more than 8mm. Endometrial thickness among younger age group was less than 8 mm. Perimenopausal women had endometrial thickness between 8- 11 mm in perimenopausal age group women, preferred line of treatment will be either dilatation and curettage or hysterectomy when endometrial thickness is more than 8mm [11, 12].

Conclusion

- Among normal endometrium secretory endometrium accounts for 45.5%
- Endometrial hyperplasia is noticed in 8% cases and endometrial carcinoma 3%
- The sensitivity, specificity for TVS is 97.7%, 84.2% respectively in detecting abnormal endometrium with an Endometrial thickness cut off of 14mm.

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