

Uterine Cavity Assessment and Endometrial Hormonal Receptors in Women with Peri and Post Menopausal Bleeding

Ahmed Mohamed Maged

Cairo University, Egypt

Objectives: To compare the accuracy of 2D-Transvaginal ultrasound (TVUS), saline infused sonohysterography (SIS) and hysteroscopy (DH) in assessment of the uterine cavity in women with peri- and postmenopausal bleeding and to study the expression of endometrial estrogen receptors (ER) and progesterone receptors (PR) in them. **Study design:** 100 women with abnormal uterine bleeding (peri and postmenopausal) were subjected to TVUS, SIS and DH and fractional curettage followed by histopathological examination and immunohistochemical analysis for ER and PR. **Results:** Measurement of endometrial thickness by TVUS showed a significant difference between normal and atrophic endometrium and between atrophic endometrium and endometrial polyp (P value 0.004 and 0.001 respectively) DH had the best sensitivity, specificity, PPV and NPV as a diagnostic procedure followed by SIS then TVUS (97.7, 100, 100, 99.4 % vs. 74, 91.2, 67.3, 93.5 and 52.9, 89.4, 56.3, 88.1 respectively) Both ER and PR scoring among glands and stroma showed a significant difference between normal and abnormal endometrium. ER expression in glands showed a significant difference between endometrial polyp and surrounding endometrium (P value 0.006) **Conclusions:** Sonohysterography is superior to ultrasound and very close to hysteroscopy, especially with intra-cavitary lesions. Hysteroscopy remains the gold standard for uterine cavity assessment, but cannot replace the histopathology. The expression of endometrial steroid receptors is important in the pathogenesis of endometrial polyps and endometrial hyperplasia.

Abnormal uterine bleeding (AUB) is the cause of many gynecological visits in pre and postmenopausal and can be due to the presence of either benign conditions or the presence of endometrial cancer [1]. Dilatation and curettage (D&C) is the currently accepted method for diagnosing diffused endometrial conditions as endometrial cancer and hyperplasia. However, when focal endometrial conditions (as endometrial polyps and leiomyomas) or myometrial conditions (such as

adenomyosis) are present, D&C is not capable of diagnosing them [2].

Transvaginal ultrasound (TVUS) is a method routinely used for differentiating between the causes of AUB. However, in TVUS images it is difficult to distinguish between a thickened endometrial lining and other diffuse or focal endometrial abnormalities [3]. An improved TVUS method is saline infused sonohysterography (SIS) which allows uterine abnormalities to be seen more clearly by pushing apart the walls of the uterine cavity with saline infused into the cavity [4]. Hysteroscopy (DH) with biopsy has become the gold standard for evaluation of the uterine cavity, as a reliable and safe method in routine outpatient settings [5].

Studying the immunohistochemical reactivity of the postmenopausal endometrium using monoclonal antibodies against ERs (estrogen receptors) and PRs (progesterone receptors) showed thicker endometrium in menopausal women for 1 to 10 years than in those who were menopausal for more than 10 years. Within the glands +ve ER was found in 26/33 and +ve PR was found in 18/33 of cases [6].

Endometrial polyps (EP) are a frequent cause of AUB, but their pathogenesis is poorly understood. EP may result from a decrease in ER and PR expression in stromal cells [7]. The aim of this study is to compare the accuracy of both 2D TVUS and SIS in relation to DH in assessment of uterine cavity and to detect ER and PR in endometrium and their association with endometrial polyps in women with peri and postmenopausal bleeding.

The present prospective study included 100 patients with AUB who attended the outpatient gynecology clinic at Kasr El-Aini Hospital in Cairo, Egypt, between June 1, 2011, and October 31, 2014. The study was approved by the local Ethics Committee and informed consents about the study and expected value and outcome were obtained from all participants.

The 100 women included in our study were older than 45 years with AUB for more than 3 months duration. Of these women 50 had postmenopausal bleeding, 10 had premenopausal menorrhagia, 4 had premenopausal metrorrhagia and 36 had premenopausal menometrorrhagia. Exclusion criteria included history of hormonal treatment or hormonal contraception within the last 6 months. Women who had used IUD or those had hysteroscopy or fractional curettage done within the last 6 months were also excluded.

All the patients were subjected to Full history, clinical examination including general, abdominal and pelvic examination and Laboratory investigations as complete blood count, coagulation profile, fasting and post-prandial blood sugar, liver and kidney functions and pregnancy test (for the premenopausal women).

Conventional TVUS was done to all participants to measure the uterine size and endometrial thickness and other pathology. TVUS was done with an empty bladder in the lithotomy position using the Sonoace-X6 (Medison Co. Ltd., Korea) ultrasound machine, with an endovaginal curved linear probe (EV 4-9/10 ED) with frequency 4-9 MHz. SIS was performed for all patients at the same setting of TVUS. With the patient in the lithotomy position, a speculum was inserted into the vaginal introitus. The cervical os was localized and cleaned with a povidone-iodine solution. A 6 or 8 French Foley's catheter was inserted through the external cervical os into the cervical canal. Its balloon tip was inflated with 2-3 mL of saline, depending on patient comfort, to help hold it in place. The speculum was then removed.

The vaginal probe was then reinserted and a 5-10 mL syringe filled with sterile saline was attached to the catheter. Fluid was instilled while the transducer was moved from side to side (cornua to cornua) in a long-axis projection then the transducer was rotated 90° into an axial plane. More fluid was instilled while fanning down toward the endocervical canal and up toward the uterine fundus to obtain a detailed survey of the endometrium. Every portion of the uterine cavity should be imaged, to exclude any focal abnormality as polyps, myomas, hyperplasia, and carcinoma. Any detected intrauterine pathology is described; including its shape, size and site.

The hysteroscope used in this study was Karl Storz (Germany). It is a rigid continuous flow panoramic hysteroscope, 25 cm in length, 4 mm in diameter with an outer sheath 5 mm diameter and 30° fiberoptic lens. The light source used in this study was a metal halide automatic light source from Circon ACMI G71A (Germany) with a 150 Watt lamp, connected to the hysteroscope through a fibro-optic cable.

The technique used to provide constant uterine distention was by attaching plastic bags of saline. Infusion pressure was elevated by pneumatic cuff under manometric control at a pressure of 100-120 mmHg. The procedure was monitored using a single chip video and the image is displayed on a monitor visible to the operator. The camera was Karl Storz (Germany) with a focal length varying from f 70 to f 140.

Detailed hysteroscopic examination was performed under general anesthesia with the patient in the lithotomy position, cleaning the area around the vulva, vagina and the cervix with a nonfoaming aseptic solution, Emptying the bladder by a metal catheter, Bimanual examination, Introduction of a vaginal retractor into the vagina to expose the cervix and a multiple toothed volsellum was applied to the anterior lip of the cervix, The endocervical canal was curetted before introduction of the telescope, Dilatation of the cervix was needed—in some cases—up to Hegar no. 6; but it was better to be avoided as the tight cervical os avoids loss of the distending medium, The telescope was introduced through the external cervical os under direct vision, Once the cavity was entered, a panoramic view of the uterine cavity then systematic; first the fundus, then anterior, posterior and lateral walls of the uterus consecutively, ending by visualization of the utero-tubal junctions, The thickness, colour, aspect and vasculature of the mucous membrane lining the uterine cavity was observed and recorded. If there was any intrauterine pathology detected; the shape, size and site were estimated. If an endometrial polyp was found it was removed using a ring forceps. At the end of the procedure, the hysteroscope was slowly withdrawn through the cervical canal to visualize it.

Endometrial curettage was done to all patients, and specimens were fixed in Formalin 10% solution for histopathological examination. Patients in whom endometrial polyps were found by hysteroscopy, had polypectomy performed before curettage. The first

sample was taken from the endocervical canal before hysteroscopy or cervical dilatation. Following diagnostic hysteroscopy, cervical dilatation up to Hegar no. 7 or 8 was done. A sharp curette was introduced into the uterine cavity, and curettage was done starting with the fundus then posterior, anterior, right and left lateral walls consecutively.

Histopathological examination, all curettage and polypectomy specimens were embedded in paraffin wax, then slides were prepared to be stained by the conventional Haematoxylin and Eosin (H & E) stain.

The main characteristics of the study group including age, parity and diagnosis of lesion were shown in Table 1. There was no relation between either age or parity to diagnosis. TVUS could detect all cases with submucous myoma (SMF), half of cases with endometrial polyps and endometrial atrophy, only 2/16 of women with normal endometrium and over diagnosis of endometrial hyperplasia. SIS could detect all cases with SMF, most cases with endometrial polyp and endometrial hyperplasia, 10/16 of cases with endometrial atrophy and normal endometrium.

Our study concluded that measurement of endometrial thickness using TVUS has limited value in differentiation

of causes of thickened endometrium and SIS is superior in assessment of the uterine cavity. It can be used as the primary method for the detection of the uterine cavity among women with AUB. SIS improves the efficiency of TVUS as a diagnostic tool, especially with intra-cavitary lesions as endometrial polyps and SMF. DH remains the gold standard for assessment of the uterine cavity, but cannot replace the histopathology.

Our study found that the expression of ER and PR plays an important role in the pathogenesis of endometrial polyps and endometrial hyperplasia..

Antunes and colleagues studied ER and PR expression in the glandular epithelium and stroma of benign and malignant endometrial polyps of 390 postmenopausal with endometrial polyps who underwent surgical hysteroscopy.

They concluded that polyps in postmenopausal patients have high ER expression in the stroma and glandular epithelium. However, this expression is lower in premalignant /malignant polyps compared with benign polyps. These results indicate that lower ER expression may be one more risk factor for the malignancy potential of polyps in postmenopausal females.