

Targeted and tailored diagnostic strategies in women with perimenopausal bleeding: advantages of the sonohysterographic approach

Carla Verrotti, Gianluca Benassi, Eleonora Caforio, Giovanni Battista Nardelli

Department of Gynecologic, Obstetric and Neonatal Sciences, Unit of Obstetrics and Gynecology, University Hospital of Parma, Parma, Italy

Abstract. *Background and aim of the work:* Diagnosis and treatment of endometrial pathology nowadays ranges from clinical examination to transvaginal ultrasound (TVS), saline infusion sonohysterography (SIS), hysterosalpingography (HSG) and hysteroscopy (HYS). However, many gynaecologists prescribe blind endometrial biopsies, such as Vacuum ABRASion (VABRA), as single strategy. The purpose of this work is to evaluate whether the procedure of VABRA should still be performed alone in perimenopausal women with abnormal uterine bleeding, compared to biopsies and samples obtained after a previous transvaginal sonohysterography. *Methods:* We retrospectively reviewed the records of 216 patients referred to our Ultrasonography and Day-Surgery Center between November 2005 and December 2006 with persistent premenopausal uterine bleeding, spotting or postmenopausal bleeding. One hundred and five out of 216 pts. (48.6%), defined as Group "A", underwent a sole endometrial sampling by VABRA; 111 out of 216 pts. (51.4%), Group "B", had a SIS first. *Results:* Vabra showed a poor sensitivity in the diagnosis of polyps (19%) and submucosal myoma, with a negative predictive value of 73.4%. Likelihood ratio for test negative was 0.81, with an overall diagnostic accuracy of 75%. *Conclusions:* This study confirms that blind endometrial biopsies should no longer be performed as the only diagnostic strategy in perimenopausal women with abnormal uterine bleeding. On the other hand, a sonohysteroscopy-guided approach allows an accurate detection of focal lesions; nevertheless, it should not be forgotten that SIS is an ultrasound based procedure, and may provide further information on endometrial thickness, myomas, ovaries and pelvis. (www.actabiomedica.it)

Key words: Sonohysterography, endometrial, vabra, biopsy, abnormal uterine bleeding

Introduction

Abnormal uterine bleeding (AUB) is overall the most common symptom for gynaecological visits in the peri- and postmenopausal age (1), involving about 15% of women.

Besides systemic, iatrogenic or hormonal age-related causes, an endometrial pathology (polyps, submucous myomas, endometrial hyperplasia, and endometrial carcinoma) should always be suspected, and evaluation appears to be mandatory.

Diagnosis and treatment of endometrial pathology can nowadays benefit from well-established techniques, ranging from clinical examination to transvaginal ultrasound (TVS), saline infusion sonohysterography (SIS), hysterosalpingography (HSG) and hysteroscopy (HYS) (2).

However, many gynaecologists still prescribe a simple blind endometrial sampling to detect hyperplasia or carcinoma.

The sensitivity of these biopsies for the detection of abnormalities has been reported to be as high as 96

percent in literature (3-5). However, this procedure may miss up to 18 percent of focal lesions (6), including polyps and fibroids, since only a small part of the endometrium may be sampled at a time.

Dilatation and curettage (D&C), the former gold standard, and VABRA are now recognized as other blind sampling techniques which often sample less than half of the endometrium and should no longer be performed, with limited exception (7, 8).

On the contrary, SIS is a well known procedure in which transvaginal ultrasonography diagnostic power is enhanced by the instillation of sterile saline solution in the uterine cavity, as contrast medium. It allows a better visualization of the endometrial cavity for the detection of polyps and fibroids (9).

The purpose of this work is to evaluate whether the procedure of VABRA should still be performed alone in perimenopausal women with abnormal uterine bleeding, compared to biopsies and samples obtained after a previous transvaginal sonohysterography (10).

Materials and methods

We retrospectively reviewed the records of patients referred to Ultrasonography and Day-Surgery Center of the Unit of Obstetrics and Gynecology, Department of Gynecologic, Obstetrics and Neonatal Sciences University Hospital of Parma, between November 2005 and December 2006 with persistent premenopausal uterine bleeding, spotting or postmenopausal bleeding.

All women were evaluated in the lithotomy position through clinical and specular examination in order to exclude bleeding from cervical dysplasia or cervical polyps. All of the patients had a negative Papanicolaou smear screening (Pap-test) that had been carried out in the last 24 months.

Eligible patients underwent either a sole blind endometrial sample by VABRA, using a 3 mm endometrial catheter (Endometrial system 3 mm, Byogin S.N.C., Italy) or a sonohysterography, using the same 3 mm device for endometrial filling with the above mentioned technique. Under sonographic vision, physiologic sterile saline solution (NaCl 0.9%) was injected

into the uterine cavity through the catheter. VABRA and SIS were performed without analgesia.

The ultrasound system was a real-time Astro Doppler scanner (Hitachi Ltd., Tokyo, Japan) equipped with high resolution endovaginal transducer 5-7.5 MHz.

In the case of polyp or submucous myoma the patient, after SIS, was redirected towards an appropriate operative hysteroscopic day-surgery, and in the case of a negative response an office VABRA biopsy was performed.

All collected specimens underwent a histological examination at our Pathology Department. Histological diagnoses were made according to the current World Health Organization classification (11). The term "fragment of polyp" was introduced when materials from VABRA biopsies highly resembled an endometrial polyp, yet without the classical macroscopic appearance.

Results

Two hundred and sixteen patients were included in the study, aged between 44 and 56 years (mean = 49.4): 147 were premenopausal (68%) and 69 were postmenopausal (32%). Age, gravidity, parity were similar in both groups.

One hundred and five pts. out of 216 (48.6%), defined as Group "A", underwent a sole endometrial sampling by VABRA; 111 out of 216 pts. (51.4%), Group "B", had a SIS first.

We could not insert the catheter in 6 out of 105 (5.7%) women of group A because of cervical stenosis or discomfort. In group "B", 11 out of 111 pts. (10%) did not successfully complete a sonohysterography for the same reasons and these patients all underwent a hysteroscopy with general anaesthesia for a definitive diagnosis.

Adequate samples were obtained from the remaining patients. Distension of the endometrial cavity was achieved with 2 to 25 mL of fluid; an overall mean of 8.4 ml saline solution was sufficient to define acceptable sonographic view of the endometrial cavity.

In group "A", a normal or atrophic endometrium was found in 83 (79.1%) subjects; 8 (7.6%) had a

“fragment of polyp” at histological evaluation, 5 (4.8%) showed endometrial hyperplasia, and 3 had (2.8%) endometrial cancer.

In group “B”, 34 polyps (30.5%) and 4 (3.6%) submucosal myomas were found at preliminary sonohysterography, and underwent operative hysteroscopy. Two cases of endometrial polyp were not confirmed by successive hysteroscopy, with a false positive rate of 5.8%. All of the 62 negative patterns underwent endometrial sampling with VABRA, 4 of which showed hyperplasia and 58 showed a normal or atrophic endometrium.

Thirty-two polyps were found benign at histological evaluation; one showed an adenocarcinoma, giving a malignancy prevalence among these focally growing lesions of 3%, as described in literature (12) (Table 1).

The sensitivity of Vabra in the detection of polyps were 19.0% with a negative predictive value of 73.4%, confirming SIS as the gold standard. Obviously, VABRA missed 100% of submucosal myoma.

Since VABRA can provide a histological assessment, specificity and positive predictive value were both 100%. Likelihood ratio for test negative was 0.81, with an overall diagnostic accuracy of 75%.

Conclusions

This study confirms that blind endometrial biopsies should no longer be performed as the sole diagnostic strategy in perimenopausal women with abnor-

mal uterine bleeding. We choose VABRA among a wide variety of devices because of its proved superiority (3).

Our results show how poor the VABRA diagnostic power is in the detection of endocavitarian focal lesions, with only a 19% sensitivity. Usually, the catheter misses the polyp and the mioma, and only in a few lucky cases the cutting openings combined with the vacuum effect broke and removed part of it (13). Gynaecologists should be aware of this and be discouraged in carrying on such a practice.

On the other hand, a sonohysterography-guided approach allows an accurate detection of focal lesions; the following hysteroscopic operative procedure should be performed in optimal conditions, and the polyp should be removed in its entirety.

Both Vabra and SIS resulted unsuccessful in the cases of cervical stenosis; nevertheless, it should not be forgotten that SIS is an ultrasound based procedure, and may provide further information on endometrial thickness, myomas, ovaries and pelvis (14). Hysteroscopy under general anaesthesia should be considered in these patients, as in those at high risk for endometrial cancer (15).

There is currently no evidence that any intrauterine diagnostic procedure using fluid may disseminate endometrial cancer cells into the peritoneum, thereby worsening the stage or lowering the vital prognosis of the patients.

Data confirm that saline infusion sonohysterography is a safe, cost effective, easy tool for endometrial investigation (16, 17), and may be included in any

Table 1. Outcomes and histological diagnosis

Pathological diagnosis	Group A VABRA (n = 105)	Group B SIS (n = 111)	Hystolological assessment after SIS
Failed	6 (5.7%)	11 (10%)	
No abnormality	83 (79.1%)	62 (56%) *	60
Endometrial polyp	8 (7.6%)	34 (30.4%) *	31
Submucous myoma	0 (0%)	4 (3.6%)	4
Endometrial hyperplasia	5 (4.8%)		4 (6%) over “no abnormality”
Adenocarcinoma	3 (2.8%)		1 (3%) over “polyp”

* p < 0.05

standard protocol flow-chart for the management of AUB (18, 19). Literature reports nearly equal results when compared to hysteroscopy (20), with less cost; it definitely allows a better visualization of myometrium in the assessment of myomas. We are currently dealing with a survey now comparing SIS, hysteroscopy, and 4D transvaginal ultrasound with high resolution probe for the diagnosis of endometrial pathology, with preliminary results expected to be available by the early 2009.

References

- Nicholson WK, Ellison SA, Grason H, Powe NR. Patterns of ambulatory care use for gynecologic conditions: a national study. *Am J Obstet Gynecol* 2001; 184: 523-30.
- Epstein E, Ramirez A, Skoog L, Valentin L. Transvaginal sonography, saline contrast sonohysterography and hysteroscopy for the investigation of women with postmenopausal bleeding and endometrium > 5 mm. *Ultrasound Obstet Gynecol* 2001; 18: 157-62.
- Rodriguez GC, Yaqub N, King ME. A comparison of the Pipelle device and the Vabra aspirator as measured by endometrial denudation in hysterectomy specimens. *Am J Obstet Gynecol* 1993; 168: 55-9.
- Fothergill DJ, Brown VA, Hill AS. Histological sampling of the endometrium. A comparison between formal curettage and the Pipelle sampler. *Br J Obstet Gynecol* 1992; 99: 779-80.
- Stock RJ, Kenbour L. A pre-hysterectomy curettage. *Obstet Gynecol* 1990; 76: 1000.
- Winkler B, Alvarez S, Richart RM, et al. Pitfalls in the diagnosis of endometrial neoplasia. *Obstet Gynecol* 1984; 64: 185-94.
- Epstein E, Ramirez A, Skoog L, Valentin L. Dilatation and curettage fails to detect most focal lesions in the uterine cavity in women with postmenopausal bleeding. *Acta Obstet Gynecol Scand* 2001; 80: 1131-6.
- Bettocchi S, Ceci O, Vicino M, Mareello F, Impedovo L, Selvaggi L. Diagnostic inadequacy of dilatation and curettage. *Fertil Steril* 2001; 75: 803-5.
- de Kroon CD, de Bock GH, Dieben SW, Jansen FW. Saline contrast hysterosonography in abnormal uterine bleeding: a systematic review and meta-analysis. *BJOG* 2003; 110: 938-47.
- Aviram R, Michaeli G, Lew S, et al. The value of sonohysterography combined with cytological analysis of the fluid retrieved from the endometrial cavity in predicting histological diagnosis. *Ultrasound Obstet Gynecol* 1999; 14: 58-63.
- Robboy SJ, Anderson MC, Russell P. *Pathology of the Female Reproductive Tract*. Churchill Livingstone: Edinburgh, 2002.
- Brand A, Duduc-Lissoir J, Ehlen TG, Plante M. Diagnosis of endometrial cancer in women with abnormal vaginal bleeding. SOGC Clinical Practice Guidelines. *J Soc Obstet Gynecol Can* 2000; 22 (1): 102-4.
- Guido RS, Kanbour-Shakir A, Rulin MC, Christopherson WA. Pipelle endometrial sampling. Sensitivity in the detection of endometrial cancer. *J Reprod Med* 1995; 40: 553-5.
- Leone FP, Lanzani C, Ferrazzi E. Use of strict sonohysterographic methods for preoperative assessment of submucous myomas. *Fertil Steril* 2003; 79: 998-1002.
- Farrell SA, Samson S, Ash S, Flowerdew G, Andreou P. Risk categories for abnormal endometrial biopsy in dysfunctional uterine bleeding. *J Soc Obstet Gynecol Can* 2000; 22 (4): 265-9.
- Dijkhuizen FP, Mol BW, Bongers MY, Brolmann HA, Heintz AP. Cost-effectiveness of transvaginal sonography and saline infused sonography in the evaluation of menorrhagia. *Int J Gynaecol Obstet* 2003; 83: 45-52.
- Mihm LM, Quick VA, Brumfield JA, Connors AF Jr, Finerty JJ. The accuracy of endometrial biopsy and saline sonohysterography in the determination of the cause of abnormal uterine bleeding. *Am J Obstet Gynecol* 2002; 186: 858-60.
- Jones K, Bourne T. The feasibility of a "one stop" ultrasound-based clinic for the diagnosis and management of abnormal uterine bleeding. *Ultrasound Obstet Gynecol* 2001; 17: 517-21.
- Leone FPG, Lanzani C, Ferrazzi E. Sonohysterographic endometrial sampling: the new gold standard in the management of abnormal uterine bleeding? 57th ASRM Annual Meeting - Orlando, Florida, October 20-25, 2001. *Fertil Steril* 2001; (Suppl): S189, P-229.
- Farquhar C, Ekeroma A, Furness S, Arroll B. A systematic review of transvaginal ultrasonography, sonohysterography and hysteroscopy for the investigation of abnormal uterine bleeding in premenopausal women. *Acta Obstet Gynecol Scand* 2003; 82: 493-504.

Accepted: 7th July 2008

Correspondence: Carla Verrotti

Department of Gynecologic, Obstetric and Neonatal Sciences

Unit of Obstetrics and Gynecology

University Hospital of Parma

Via Gramsci 14, 43100 Parma, Italy

E-mail: carla.verrottidianella@unipr.it; www.actabiomedica.it