Endometrial biopsy in the diagnosis of abnormal uterine bleeding with a new intra-sheath device during hysteroscopy: preliminary study.

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Synopsis

Endometrial biopsy can be performed with a new endosheath hysteroscopic device in almost absence of pelvic pain

Abstract:

OBJECTIVE: To evaluate the efficacy and histological adequacy of a new 3 millimetres endometrial sampler modified device, and to compare it with a traditional Vabra endometrial cannula. STUDY DESIGN: Thirty-six consecutive women with abnormal uterine bleeding (AUB) and/or intrauterine pathologies were considered eligible for the study and included in a prospective randomized trial. Patients were randomly assigned in two groups. Group A (n = 19) underwent endometrial biopsy with a conventional 3 millimetres Vabra endometrial sampling device. In group B (n = 17) endometrial biopsy was performed following an office hysteroscopy, introducing the new device throughout the diagnostic sheath of the hysteroscope, left inside the uterine cavity, after having withdrawn only the optic. Hysteroscopy was performed either with a 2.9 millimetres or 4 millimetres rigid hysteroscopes and fluid medium for uterine distension. Main outcome measures were: pain score referred by patients both during hysteroscopy and endometrial biopsy, adequacy of sampling, and side effects. Pain was evaluated by using a 10 point visual analogue scale (VAS). The Student's *t*-test, and the Fisher's exact test were used where appropriate. Significance was set at $p < .05$. RESULTS: Adequacy of endometrial sampling was similar for both devices and was realized in 10 out 19 for traditional Vabra and in 10 out 17 for endosheath device ($p = .485$). Pain score was significantly less when the endosheath was used ($p < 0.001$). Side effects were sometimes remarkable when traditional biopsy was performed. CONCLUSIONS: The endosheath Vabra modified device is a useful technique to perform endometrial biopsy in almost absence of pelvic pain. Nevertheless, the high failure of adequacy of histological specimens may represent a diagnostic limit, mainly for those patients at risk for endometrial carcinoma or atypical endometrial hyperplasia. Any failure to obtain adequate endometrial material would suggest to perform more accurates methods of histological assessment.

Keywords: endometrial biopsy, hysteroscopy, pelvic pain, Vabra sampler device.

Body of text

INTRODUCTION

Endometrial biopsies are currently carried out using many devices varying in thickness, material and shape.[1] All of these have a variable accuracy in terms of adequacy of endometrial sampling and can cause discomfort mainly in menopause. In fact, menopause can influence or modify the normal anatomy of the cervical canal making difficulty in performing hysteroscopy and endometrial biopsy in outpatient setting. In a previous study we stated that menopausal condition is an important factor influencing the feasibility of the hysteroscopic procedures.[2] Menopause is a critical period of woman life in which hormonal factors, can influence the endometrial thickness; in this case transvaginal ultrasound,[3] hysteroscopies,[4] and or endometrial biopsy[5] are mandatory.

At present, hysteroscopy is an useful diagnostic tool in distinguishing intrauterine pathologies[6] but in case of abnormal uterine bleeding it can't always differentiate between normal and abnormal endometrium. Previous reports showed that transvaginal ultrasound, hysteroscopy and endometrial biopsy may increase diagnostic accuracy for endometrial carcinoma.[7-8] Endometrial sampling is than recommended when hysteroscopy shows a thick endometrium or an uneven shaped mucosa, or when endometrial visualization is not achievable or is less than optimal.

A lot of devices in different shapes and materials are utilized in order to perform endometrial sampling such as Novak's curette,[9] Vabra,[10] Pipelle,[11] Masterson's curette,[12] Accurette,[13] Endorette,[14] Gynoscann,[15] Leicester endometrial needle,[16] Cornier Pipelle,[17-18] Explora,[19] Tao Brush method.[20] Most of these instruments showed about 80% in diagnostic accuracy for endometrial cancer. Vabra is one of the most accepted endometrial biopsy device;[21-22] in a previous study it has been shown a 25% of failure for endometrial tissue retrieval.[21] Moreover Vabra was significantly more painful as compared to other sampler devices.[22] Pipelle is another utilised devices for outpatient endometrial sampling.[23-27] In a previous study Pipelle showed a 80% in diagnostic accuracy for endometrial hyperplasia, but in about a 23% it failed to give a sufficient endometrial sampling for histologic diagnosis.[28]

Moreover, pain referred by patients during the procedure not always has been studied and analysed. To take control of pain during hysteroscopy and or endometrial biopsy many authors used performing topical anaesthesia.[29-30-31]

In order to decrease pain during endometrial biopsy Di Spiezio et. al. have modified a Pipelle endometrial sampler introduced into the uterine cavity through the same outer hysteroscope sheath into which had been before passed the hysteroscopic optic; this technique was described as "no touch".[32]

Following this correct and useful idea a new device has been by us modified and adapted to our needs. In order to facilitate endometrial sampling after hysteroscopy and to decrease pain associated with endometrial biopsy, we have modified a 3 millimetres wide Vabra device taking its original length of 30 centimetres to 36 centimetres, that can be introduced into the uterine cavity throughout the diagnostic sheath of the hysteroscope. The new device is a flexible

polyethylene suction device, opened and jagged distally so as to permit by a scraping and rotation movements to obtain an adequate sample for hystological diagnosis both from the uterine fundus and from the uterine walls. This device is also easy of being manoeuvred into the uterine cavity thus permitting to take in a painless way endometrial material. To evaluate the reliability, diagnostic accuracy and tolerability of this new device, we compared it with a traditional 3 millimetres Vabra cannula, analyzing the pain referred by patients during endometrial biopsy and the adequacy of endometrial samples for histologic diagnosis.

Material and methods

Thirty-sex patients with AUB and in which hysteroscopy had showed an uneven endometrium or intrauterine pathologies were allocated randomly in two groups. Randomization was done by pulling sealing number from a box. . Before hysteroscopy all patients were requested to perform transvaginal ultrasound. A 2.9 or a 4 millimetres fore-oblique rigid optics, fitted respectively with a 3.5 or a 5 mm outer diagnostic sheath, and normal saline solution as distension medium were used to perform hysteroscopy. In group A (n = 19) endometrial sampling was performed just after hysteroscopy in a traditional way without using any tenaculum. In group B (n = 17), as soon as panoramic hysteroscopy was performed the hysteroscope was unlocked and withdrawn outside, leaving the sheath inside the uterine cavity. Than, the new modified device was inserted through the sheath until a feeling touch of the fundus was perceived. At this point we performed endometrial sampling simply moving or rotating the tip of the sampler into the desired directions.

During hysteroscopy and biopsy both groups of patients was asked to rate the pain experienced on a 10-cm visual analogue scale (0 = no pain, 10 = worst imaginable pain). Pain score was recorded by the same nurse as external observer during hysteroscopy and during endometrial biopsy. Each different procedure was stopped when the reported pain score reached or exceeded 7, the value willingly defined by us as intolerable pain. Histological diagnostic accuracy was evaluated for both endometrial sampling devices. The withdrawn endometrial sampling was submitted for hystological analysis. All patients with inadequate biopsies, as referred by pathologist, or with atypical endometrium were subsequently submitted to dilatation and curettage (D&C) or transcervical resectoscopy in our hospital day surgery unit.

Parameters and results are globally reported in Table I.

All the hysteroscopies were performed with a minimally invasive technique using the smallest speculum in order to see the external uterine orifice. When speculum was well placed we introduced the hysteroscope laterally to the speculum; after hysteroscopy was performed we never used tenaculum, to make traction on uterine cervix, or any cervical dilators. The Student's *t*-test and Fisher's exact test was performed where necessary for statistical analysis.

Significance was set at $p < 0.5$. For the statistical evaluation the SPSS statistical software (version 11 for Windows; Chicago, Ill) was utilized.

Results

The age was 54.8 ± 8.4 for group A (n = 19) and 53.3 ± 7.1 for group B (n = 17) and the Body Mass Index (BMI) was 26.6 ± 5.2 and 25.9 ± 5 respectively. Demographic features are reported on Table II.

All endometrial biopsies were completed within 30-90 seconds. The adequacy of endometrial sampling was similar for both devices, in fact, histological diagnosis was made in 10 out 19 in group A and in 10 out 17 in group B; this difference was not significant. The new endometrial sampling device was less painful compared to the traditional Vabra which was inserted in a blind way. Levels of pain referred were significantly stronger when endometrial biopsy was performed by a classical Vabra sampling device $p < 0.001$. In group A, there were four patients reporting important side effects like pelvic pain, nausea, vomit, low blood pressure and bradycardia most of them probably a consequence of a vagal syndrome. No untoward effects were seen after endosheath endometrial biopsy.

Adequacy of samples and pain were not influenced by the diameter of optic previously used to perform hysteroscopy. In 5 out 9 and in 4 out 9 patients in group A whom we couldn't perform adequate sample the 4 and 2.9 millimetres optic were utilized respectively. In group A, as regard intolerable pain during biopsy, in 5 out 7 and in 2 out 7 patients a 2.9 and a 4 millimetres optic were respectively utilized before in order to perform hysteroscopy.

In group B inadequate sample was taken in 3 out 7 after having utilized 4 millimetres hysteroscope while nobody reported intolerable pain during biopsy.

Endometrial biopsy performed after having used 2.9 millimetres hysteroscope with a 3.5 millimetres outer sheath was more painful with conventional Vabra sampler and was less painful if performed after having used a 4 millimetres hysteroscope with a 5 millimetres outer sheath (Figure 1). This could be explained by the mean that if we can enter through the cervical canal with a wider optic also we have less difficulty in introducing a 3 millimetres endometrial sampler device.

Conclusions

Outpatients hysteroscopy with endometrial biopsy is a valuable first-line investigation for abnormal uterine bleeding and for endometrial thickening,[33] but the gold standard for a diagnosis remains histology.[34]

Our preliminary results showed a good effectiveness of the endometrial sampling procedure making also a facilitation of the handle procedures and with a good tolerance of the uterine pain referred by patients. The biopsy was obtained through the use of an endometrial suction catheter that is inserted through an endoscopic outer sheath into the uterine cavity. Twirling the catheter while moving it in and out of the uterine cavity enhances uptake of uterine tissue, which is aspirated into the catheter and removed. The procedure was performed in all patients submitted to a previous

hysteroscopy and this is another important point to be considered as we know how painful is sometimes endometrial biopsy performed in an outpatient setting, particularly in menopause women. Endometrial sampling with a modified Vabra device was well tolerated causing occasionally only slight discomfort. Intra-operative and post-operative cramping were the only untoward side effects.

Moreover, the 36 centimetres long device makes the possibility to perform a brief sliding of the hysteroscopic sheath along to the outside of the vagina in order to facilitate the bioptic movements into the uterus. A mechanism of suction inherent in the Vabra system permits also to obtain and to pick up, may be, almost all the undermined endometrium.

Our data suggest that the a modified Vabra is an effective alternative to a classic endometrial Vabra sampler, causing less pain also as we don't need to pull the uterine cervix or to dilate the cervical canal. Nevertheless, endometrial tissue sampling we can take is sometimes not enough for histological diagnosis. In these cases, failure to obtain an adequate endometrial material in high risk patients for endometrial cancer would suggest performing other sampling techniques such as endometrial curettage.

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Figure legends and table

Table I: Patients' global characteristics and results

age	BMI	parity	mp	device	PB	PH	optic	hysteroscopic results	adequacy	post-biopsy hystology	side effects	final histologic result
50	22,7	yes	no	TV	8	0	2,9	atrophic endometrium	yes	atrophic endometrium	pelvic pain, vagal syndrome	/
35	22,7	no	no	TV	10	2	2,9	endometrial polyp	yes	polypoid endometrium	pelvic pain, vagal syndrome	polypoid endometrium
55	25,3	yes	yes	TV	6	2	4	atypical endometrium	no	/	no	decidual-like endometrium
58	24,9	yes (cs)	yes	TV	2	0	4	disfunctional endometrium	no	mucus	no	secretive endometrium
57	20,4	yes	yes	TV	3	2	4	endometrial polyp and atrophic em	no	not diagnostic	no	endometrial polyp
55	31,8	yes	no	TV	8	7	4	IUO stenosys	no	not diagnostic	no	proliferative endometrium
47	27,1	yes	no	TV	8	3	2,9	SGH	no	/	strong pelvic cramps	CGH
61	37,1	yes	yes	TV	8	7	4	not evaluated	no	/	no	atrophic endometrium
58	33,9	yes	yes	TV	10	4	2,9	endometrial polyp	no	/	strong pelvic cramps	endometrial polyp
68	24,6	yes	yes	TV	3	3	4	SGH	yes	proliferative endometrium	no	/
48	22,7	yes	no	TV	2	4	4	endometrial polyp	yes	proliferative endometrium	no	endometrial polyp
56	22,7	yes	yes	TV	4	3	4	endometrial polyp	yes	SGH	no	polyp with SGH
65	23,6	yes	yes	TV	2	2	4	AGH	yes	AGH	no	endometrial adenocarcinoma
49	26,0	yes	no	TV	2	2	2,9	SGH	yes	secretive endometrium	no	/
58	24,6	yes	yes	TV	4	1	2.9	endometrial adenocarcinoma	no	/	no	endometrial adenocarcinoma
71	39,5	yes	yes	TV	9	9	2.9	not evaluated	no	/	no	atrophic em
53	27,5	yes	no	TV	5	2	2.9	endometrial polyp	yes	atypical hyperplasia	no	AGH
54	24,6	yes	yes	TV	6	4	2.9	SGH	yes	proliferative	no	/

										endometrium		
44	23,7	yes	no	TV	3	3	4	dysfunctional endometrium	yes	proliferative endometrium	no	/
42	21,6	no	no	ES	4	5	2,9	secretive endometrium	yes	secretive endometrium	no	/
54	21,3	yes	yes	ES	5	6	2,9	polyp with secretive endometrium	yes	secretive endometrium	no	endometrial polyp
56	21,1	yes	yes	ES	2	3	4	secretive endometrium	yes	secretive endometrium	no	/
52	31,8	yes	no	ES	3	2	2,9	secretive endometrium	yes	secretive endometrium	no	/
59	19,2	yes (cs)	yes	ES	3	0	2,9	SGH	no	/	no	secretive endometrium
55	28,2	yes	no	ES	1	7	4	proliferative endometrium with a submucous myoma	no	/	no	submucous myoma and proliferative endometrium
61	28,6	yes	yes	ES	2	7	4	atrophic endometrium	no	/	no	atrophic endometrium
52	24,2	yes	no	ES	2	0	2,9	dysfunctional endometrium	no	/	no	SGH
51	35,9	yes	no	ES	2	2	4	dysfunctional endometrium	yes	secretive endometrium	no	/
47	24,9	yes	no	ES	0	0	4	proliferative endometrium	yes	proliferative endometrium	no	/
56	32,0	yes	yes	ES	2	2	2,9	dysfunctional endometrium	yes	proliferative endometrium	no	/
54	22,2	yes	no	ES	2	4	4	dysfunctional endometrium	yes	proliferative endometrium	no	/
52	34,0	yes (cs)	yes	ES	2	5	2.9	atrophic endometrium	no	/	no	atrophic em
69	26,0	yes	yes	ES	2	2	4	CGH	no	/	no	SGH
44	21,0	yes	no	ES	0	0	2.9	endometrial polyp	no	/	no	endometrial polyp
42	24,3	no	no	ES	4	0	4	dysfunctional endometrium	yes	polypoid GH	no	polypoid GH
61	23,4	yes	yes	ES	0	4	2.9	endometrial polyp	yes	AGH	no	AGH

cs = cesarean section; mp = menopause; BMI = body mass index; TV = traditional Vabra; ES = endosheath device;

PB = pain after biopsy; PH = pain after hysteroscopy; GH = glandular hyperplasia; SGH = simple glandular hyperplasia; CGH = cystic glandular hyperplasia; AGH = atypical glandular hyperplasia

Table II. Demographic features of the patients

	Total (n = 36)	**TV (n = 19)**	**ES (n = 17)**	***P* value**
Age (yr)	54.1 ± 7.7	54.8 ± 8.4	53.3 ± 7.1	NS
Body mass index (kg/m^2)	26.3 ± 5	26.6 ± 5.2	25.9 ± 5	NS
Parity	33 (91,7%)	18 (50%)	15 (41.7%)	NS
Menopause	19 (52.8%)	11 (30.6%)	8 (22.2%)	NS

Mean ± SD. *NS*, Not significant ($P > .05$).

Figure 1: Relation between pain, kind of biopsies and diameter of hysteroscopes