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Comparison of Tissue Adequacy from Office-based Endometrial Sampling between Manual Vacuum Aspiration and the Wallach Endocell in Premenopausal and Perimenopausal Women with Abnormal Uterine Bleeding: A randomized controlled trial

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ABSTRACT

Objectives: To investigate the tissue adequacy rate of endometrial biopsy devices (Wallach Endocell® and manual vacuum aspiration [MVA]), focusing on premenopausal and perimenopausal women, in an outpatient setting.

Materials and Methods: In this randomized controlled trial, 290 premenopausal or perimenopausal women with abnormal uterine bleeding who planned to undergo an endometrial biopsy were randomized to Ipas MVA Plus® (n = 146) and Wallach Endocell® (n = 144). The primary outcome was tissue adequacy for pathological examination, which was evaluated by two pathologists. Secondary outcomes were the amount of endometrial tissue, postoperative pain scores, immediate complications of the procedure, patient satisfaction, and operator satisfaction.

Results: The mean and standard deviation of participants' age were 42.8 ± 5.9 and 43.6 ± 5.8 years in the MVA and Endocell groups, respectively. Tissue adequacy for pathological examination in the MVA and Endocell groups was 95.2% and 95.8%, respectively. Both methods did not show differences in tissue adequacy (p = 1.00). The median amount of endometrial tissue was slightly higher in the MVA group than in the Endocell group (2.1 g vs 1.8 g, p = 0.02). The pain score during the procedure was slightly higher in the MVA group than in the Endocell group (p < 0.01). Patient satisfaction and operator satisfaction did not differ between groups. The complications that we found were pelvic pain and pelvic infection,

which did not differ between groups (1.4% vs 2.8%, p = 0.4).

Conclusion: There was no evidence that the efficacy of endometrial tissue biopsy by MVA or Endocell was different in terms of tissue adequacy for pathological diagnosis. Both devices showed a very high percentage of tissue adequacy and very low adverse effects.

Keywords: abnormal uterine bleeding, endocell, endometrial biopsy, manual vacuum aspiration.

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การศึกษาแบบสุ่มเปรียบเทียบความเพียงพอของชิ้นเนื้อจากการดูดตัวอย่างเยื่อบุโพรงมดลูกด้วยเครื่องมือดูดสุญญากาศมือถือเทียบกับ Wallach Endocell ในสตรีวัยเจริญพันธุ์และวัยใกล้หมดประจำเดือนที่มีภาวะเลือดออกผิดปกติจากโพรงมดลูก

ชญานิศ อภิรักษ์วิริยะ, สมสุข สันติเบ็ญจกุล, พฐู ตันฑ์ไพโรจน์, นพดล ไชยสิทธิ์, ชินา โอฬารรัตนพันธ์, นิพนธ์ เขมะเพชร, สุรสิทธิ์ ชัยทองวัฒนา, อรรณพ ใจสำราญ

บทคัดย่อ

วัตถุประสงค์*: เพื่อศึกษาอัตราความเพียงพอของชิ้นเนื้อจากการดูดตัวอย่างเยื่อบุโพรงมดลูกด้วยเครื่องมือดูดสุญญากาศมือถือเทียบกับ Wallach Endocell ในสตรีวัยเจริญพันธุ์และวัยใกล้หมดประจำเดือนที่มีภาวะเลือดออกผิดปกติจากโพรงมดลูก ในการตรวจแบบผู้ป่วยนอก*

วัสดุและวิธีการ*: การศึกษานี้เป็นการศึกษาทดลองแบบสุ่มในสตรีวัยเจริญพันธุ์และวัยใกล้หมดประจำเดือนที่มีภาวะเลือดออกผิดปกติจากโพรงมดลูกจำนวน 290 คนที่จำเป็นต้องได้รับการตรวจวินิจฉัยด้วยการดูดชิ้นเนื้อจากเยื่อบุโพรงมดลูก แบ่งกลุ่มโดยการสุ่มตัวอย่าง สตรี 146 คนได้รับการตรวจด้วยเครื่องมือดูดสุญญากาศมือถือและสตรี 144 คน ได้รับการตรวจด้วย Endocell วัตถุประสงค์หลักเพื่อประเมินอัตราความเพียงพอของชิ้นเนื้อในการตรวจทางพยาธิวิทยา ซึ่งประเมินโดยพยาธิแพทย์สองคน วัตถุประสงค์รองคือ ปริมาณชิ้นเนื้อที่ได้ อาการปวด ภาวะแทรกซ้อน รวมทั้งความพึงพอใจของผู้ป่วยและแพทย์ผู้ทำหัตถการ

ผลการศึกษา*: อายุเฉลี่ยของสตรีที่ได้รับการตรวจด้วยเครื่องมือดูดสุญญากาศมือถือและ Endocell เท่ากับ 42.8 และ 43.6 ปีตามลำดับ อัตราความเพียงพอของชิ้นเนื้อในการตรวจทางพยาธิวิทยาเท่ากับร้อยละ 95.2 และ 95.8 ตามลำดับ สำหรับค่ากลางของปริมาณชิ้นเนื้อที่ได้คือ 2.1 กรัมในกลุ่มที่ตรวจด้วยเครื่องมือดูดสุญญากาศมือถือและ 1.8 กรัมในกลุ่ม Endocell (p = 0.02) อาการปวดที่เกิดจากการตรวจพบมากกว่าในกลุ่มที่ได้รับการตรวจด้วยเครื่องมือดูดสุญญากาศมือถือ*

(p < 0.01) สำหรับความพึงพอในของผู้ป่วยและแพทย์ผู้ทำหัตถการไม่แตกต่างกัน ภาวะแทรกซ้อนที่พบ ได้แก่ การติดเชื้อ อาการปวดท้อง พบว่าอัตราการเกิดไม่แตกต่างกันในทั้งสองกลุ่ม (1.4% เทียบกับ 2.8%, p = 0.40)

***สรุป**: ยังไม่พบความแตกต่างในแง่ประสิทธิภาพของวิธีการดูดชิ้นเนื้อจากโพรงมดลูกด้วยเครื่องมือดูดสุญญากาศมือถือ และ Endocell ในแง่ความเพียงพอของชิ้นเนื้อในการตรวจทางพยาธิวิทยา เครื่องมือทั้งสองชนิดมีประสิทธิภาพสูงในการเก็บชิ้นเนื้อและมีภาวะแทรกซ้อนต่ำมาก*

***คำสำคัญ**: เลือดออกผิดปกติจากโพรงมดลูก, endocell, การดูดตัวอย่างชิ้นเนื้อเยื่อบุโพรงมดลูก, เครื่องมือดูดสุญญากาศ*

Introduction

Abnormal uterine bleeding (AUB) is a common problem in clinical practice that leads women to visit gynecologists. The prevalence of approximately 3-30% among reproductive-aged women[1]. Approximately one-third of women are affected at some point in their life[2, 3]. The pattern of bleeding and age of the patient can help assess bleeding etiology. The initial uterine evaluation in women with abnormal uterine bleeding after detailed history taking and physical examination are transvaginal ultrasound (TVUS) in women with enhanced risk for structural abnormality or endometrial sampling in women with enhanced risk of endometrial hyperplasia[1]. Selection for endometrial sampling is based on a combination of risk factors for the presence of premalignant or malignant changes, comprising a combination of age, personal and genetic risk factors, and transvaginal ultrasound (TVUS) screening for endometrial echocomplex thickness. In cases that endometrial sampling cannot retrieve adequate endometrial tissue or suspected the focal uterine cavity lesion, the standard method for evaluating endometrial pathology is hysteroscopy[1]. Hysteroscopy can be performed in an office setting or in an operating theater setting, with or without general anesthesia. However, hysteroscopic procedures require complex instruments, trained personnel, and specialized gynecologists. Office-based endometrial sampling using vacuum aspirator devices is increasingly used because of several advantages. For example, the setting is in an outpatient clinic; the procedure does not require anesthetic; they require a shorter operative time and less cost and equipment. The adequacy of the samples is essential because the use of aspiration techniques implies that the pathology is global rather than focal. However, a previous study revealed that tissue adequacy was 85.6% when using the Wallach Endocell® device (CooperSurgical, Inc., Trumbull, Connecticut, USA)[4], and the detection rates for endometrial carcinoma in postmenopausal and premenopausal women were 99.6% and 91.0%, respectively[5]. Therefore, office-based endometrial aspiration sampling techniques can be used as initial steps to diagnose endometrial pathology.

Office-based endometrial sampling techniques are divided into two categories based on the equipment used: 1) low-pressure devices, such as Pipell® (CooperSurgical, Inc., Trumbull, Connecticut, USA) and Wallach Endocell®, 2) high-pressure devices, such as Vabra aspirator® (Sterylab, Rho, Milan, Italy) and manual vacuum aspiration (MVA). High-pressure devices are superior in terms of endometrial cell volume collection, and the use of such devices should result in a better pathological diagnosis. The Wallach Endocell® is disposable while MVA is a reusable device. MVA has not been widely used for endometrial biopsy, but it is often used in abortions. Therefore, Thai gynecologists are not familiar with the use of MVA to detect endometrial

pathologies.

Endometrial sampling with Endocell®[4,5] revealed that tissue adequacy and detection rate of endometrial carcinoma and atypical hyperplasia are within an acceptable range and that the direct medical cost of endometrial sampling from the patient's perspective is much less than that of hysteroscopy. However, there is limited information on the tissue adequacy, detection rate, and cost-effectiveness of MVA in evaluating endometrial pathology. The characteristics of MVA, which can create a higher negative pressure than Wallach Endocell®, may provide a greater amount of endometrial tissue in which it enhances the better pathological evaluation. This study aimed to investigate the tissue adequacy between Wallach Endocell® and MVA, focusing on premenopausal and perimenopausal women in an outpatient setting.

Materials and Methods

This was a randomized controlled trial, a parallel study, retrospectively registered in the Thai Clinical Trials Registry (study ID TCTR20160225001) and approved by the Chula IRB 35-55. Eligible participants were premenopausal and perimenopausal women with AUB who planned to undergo an endometrial biopsy at King Chulalongkorn Memorial Hospital between November 2012 and October 2013. Inclusion criteria were age over 30 years, premenopausal or perimenopausal status, having an indication for endometrial sampling, and providing written informed consent. We excluded women with active pelvic inflammatory disease, unstable hemodynamic status, or pregnancy. Baseline characteristics, such as parity, number of vaginal deliveries, body mass index, underlying disease, and pattern of AUB were collected. The study participants were randomized into two groups using a block of four randomization techniques. A biostatistician, who was not involved in data analysis, conducted a computer-generated randomization sequence. To ensure concealment, the allocation was placed inside of opaque envelopes and sealed. A 1:1 allocation ratio was used for the MVA and Endocell group. The allocation sequence was concealed until the endometrial biopsy procedure. Participants underwent endometrial sampling according to the assigned protocol. Participants and pathologists were blinded to the sampling method. The sample size was calculated based on the results of a previous study[5] (85.6% of tissue adequacy rate using Endocell endometrial biopsy) and the expected tissue adequacy using MVA was 95.6%. A total of 290 participants were included, and the calculation was based on a statistical significance level of 0.05% to yield a power of 90%.

The endometrial biopsy was performed in the outpatient clinic on the same day as the participants enrolled in the study. Endometrial biopsy was performed in the following steps. First, a bimanual pelvic examination was performed to identify the size, shape, and orientation of the uterus. Then, a bivalve speculum or vaginal retractor was inserted, and the vagina and cervix were cleaned with 10% povidone-iodine solution. According to the protocol, group A was assigned to Ipas MVA Plus® (Ipas, Chapel Hill, NC, USA) with an Ipas 3-mm cannula, while group B was assigned to the Wallach Endocell® as the endometrial biopsy device. An Ipas 3 mm cannula and Ipas MVA Plus® were reusable devices. The Ipas 3-mm cannula was 23 cm in length and 3-mm in outer diameter. After insertion of the Ipas 3-mm cannula, the cannula was attached to a 60-ml double-valve syringe, which was locked to create negative pressure. Endometrial tissue was aspirated into the syringe when the valve was turned on. The Wallach Endocell® was a disposable flexible plastic cannula diameter (24.3-cm in length and 3.1-mm in outer diameter). After insertion of the cannula, the plunger was smoothly drawn back to the stop, creating a negative pressure within the sheath. In cases where the cannula could not be inserted, a tenaculum was used to straighten the cervico-uterine angle in patients by grasping the anterior lip and gently drawing outward in direction. If the uterine cavity could not be accessed, misoprostol (400 mcg) was inserted into

the vagina for 3 hours, and the procedure was repeated. Endometrial tissue was collected with at least four complete back-and-forth passes with the device from the fundus to the internal os. Each specimen was expelled into a formalin container. Before removing the device, the depth of the uterus was checked and recorded. The amount of endometrial tissue, postoperative pain scores, operative time, and immediate complications of the procedure were recorded. Tissue adequacy of the procedure was defined as the presence of both adequate endometrial glands and stroma to identify endometrial histology, as reported by two pathologists who were blinded to the endometrial sampling procedure. In case of a discrepancy in pathological results, the final pathological diagnosis was made based on the consensus of both pathologists after reviewing the specimens together. Patient and doctor satisfaction were collected on the same day using a visual analog scale. Data were analyzed using STATA version 17 (StataCorp LLC, College Station, TX, USA). Continuous variables were represented as mean (standard deviation [SD]) or median (interquartile range), while categorical variables were represented as numbers and percentages. The unpaired t-test was used to compare normally distributed continuous variables, and the Wilcoxon rank-sum test was used for a skewed distribution. Categorical variables were compared using Fisher's exact test.

Results

This study enrolled 290 women with AUB required endometrial biopsy. A total of 146 women were assigned to receive endometrial biopsy using Ipas MVA Plus®, and 144 women were assigned to using Wallach Endocell®. Each participant underwent an endometrial biopsy with an instrument as assigned. The study flow is shown in Fig. 1. The mean age ± SD was 42.8 ± 5.9 and 43.6 ± 5.8 years in the MVA and Endocell groups, respectively. The baseline characteristics are shown in Table 1. The majority of the participants in both groups were parous and had at least one vaginal delivery. The characteristics of abnormal bleeding did not differ between the two groups.

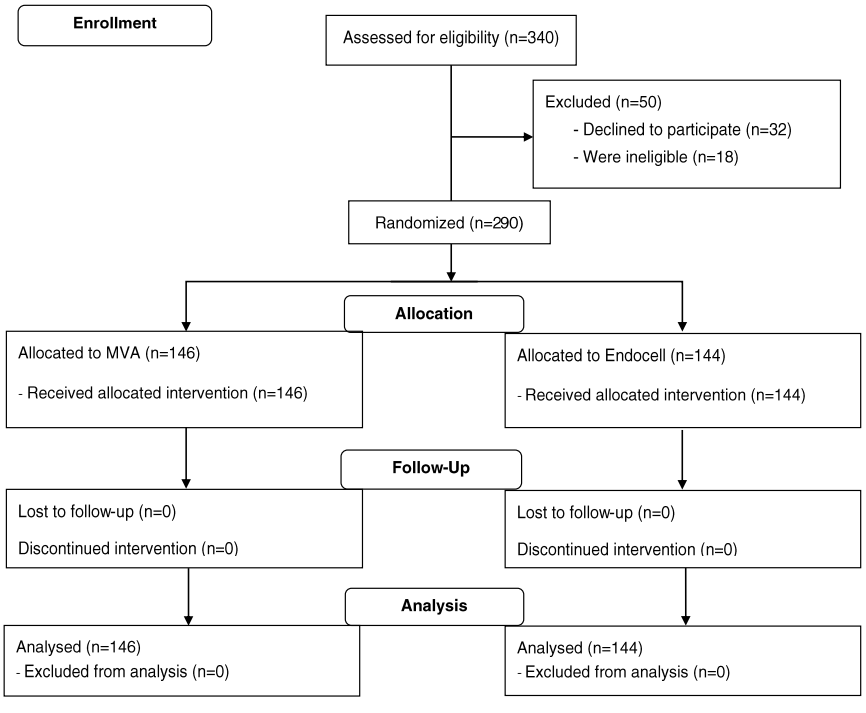

Fig. 1. CONSORT flow diagram

Table 1. Baseline characteristics of the groups

Characteristics	MVA (n = 146)	Endocell (n = 144)
Age (years), n (%)		
< 35	15 (10.3)	10 (6.9)
35 - 49	114 (78.1)	111 (77.1)
> 50	17 (11.6)	23 (16.0)
Parity, n (%)		
0	32 (21.9)	45 (31.3)
1	42 (28.8)	40 (27.8)
2	51 (34.9)	44 (30.6)
> 3	21 (14.4)	15 (2.4)
Vaginal birth, n (%)		
0	74 (50.7)	76 (52.8)
1	27 (18.5)	31 (21.5)
2	25 (17.1)	28 (19.4)
> 3	20 (13.7)	9 (6.3)
Duration of a recent episode of AUB (days), median (IQR)	16 (7-40)	14 (7-21)
Years since the last child, median (IQR)	11 (4-17)	11 (0-19)
Menarche (years), n (%)		
≤ 11	15 (10.3)	15 (10.4)
12-15	114 (78.1)	103 (71.5)
≥ 16	17 (11.6)	26 (18.1)
BMI (kg/m^2), n (%)		
< 18.5	8 (5.5)	4 (2.8)
18.5-22.9	45 (30.8)	54 (37.5)
23-24.9	20 (13.7)	22 (15.3)
25-29.9	55 (37.7)	42 (29.2)
≥ 30	18 (12.3)	22 (15.3)
AUB type, n (%)		
Intermenstrual bleeding	47 (32.2)	40 (27.8)
Heavy menstrual bleeding	47 (32.2)	51 (35.4)
Heavy menstrual bleeding and intermenstrual bleeding	36 (24.7)	39 (27.1)
Others[a]	16 (11.0)	14 (9.7)
DM, n (%)		
No	138 (94.5)	135 (93.8)
Yes	8 (5.5)	9 (6.3)
HT, n (%)		
No	136 (93.2)	129 (89.6)
Yes	10 (6.9)	15 (10.4)
Dyslipidemia, n (%)		
No	139 (95.2)	138 (95.8)
Yes	7 (4.8)	6 (4.2)
Anemic symptoms, n (%)		
No	85 (58.2)	85 (59.3)
Yes	60 (41.1)	59 (41.0)

MVA: manual vacuum aspiration, AUB: abnormal uterine bleeding, BMI: body mass index, DM: diabetes mellitus, HT: hypertension, IQR: interquartile range
[a] Others, e.g., oligomenorrhea.

An endometrial biopsy could be performed in all participants in whom no other sedation was required; the biopsy procedure was mostly performed by the attending physicians in both groups (76.3% vs 70.8%, p = 0.35). In the MVA group, the tenaculum was needed to facilitate the cannula insertion more than in the Endocell group, but the requirement for misoprostol to ripen the cervix before cannula insertion was not different. The only complication of misoprostol was pelvic pain, with an incidence of 22.2%. The pain score during the procedure was slightly higher in the MVA group than in the Endocell group, which was statistically significant. The mean difference in pain score during the procedure was 1.13 (0.53-1.74), as shown in Table 2. Participants in the MVA group needed more pain medication immediately after the procedure compared to the Endocell group (32.9% vs 17.4%, p < 0.01). Patient satisfaction and operator satisfaction did not differ between the two groups. Complications that we observed after the procedure were pelvic pain and pelvic infection, which did not differ between the two groups.

Table 2. Details of endometrial sampling procedure

	MVA (n = 146)	Endocell (n = 144)		p value
Type of operator, n (%)				
Resident	35 (24.0)	42 (29.2)		0.35[a]
Attending	111 (76.0)	102 (70.8)		
Uterine depth, median (IQR)	7.5 (7-8)	7 (7-8)		0.38[b]
Tenaculum used, n (%)				
No	50 (34.5)	71 (49.3)		0.01[a]
Yes	96 (67.5)	73 (50.7)		
Misoprostol used, n (%)				
No	140 (95.9)	141 (97.9)		0.50[a]
Yes	6 (4.1)	3 (2.1)		
Pain score (VAS), mean (SD)	5.6 (2.7)	4.5 (2.6)	MD 1.13 95%CI (0.53-1.74)	
Use of a pain killer immediately after the procedure				
No	98 (67.1)	119 (82.6)		< 0.01[a]
Yes	48 (32.9)	25 (17.4)		
Patient satisfaction, mean (SD)	4.4 (0.6)	4.4 (0.6)	MD 0.02 95%CI (-0.12–0.15)	0.83[c]
Operator satisfaction, mean (SD)	4.2 (0.7)	4.3 (0.6)	MD -0.04 95%CI (-0.20–0.12)	0.63[c]
Complications within 2 weeks				
No	144 (98.6)	140 (97.2)		0.40[a]
Yes, e.g., pelvic pain, pelvic infection	2 (1.4)	4 (2.8)		

MVA: manual vacuum aspiration, IQR: interquartile range, MD: mean difference, VAS: visual analog scale, SD: standard deviation
[a] Fisher's exact rest, [b] Wilcoxson rank-sum test, [c] unpaired t-test.

Tissue adequacy for pathological examination in the MVA and Endocell groups was 95.2% and 95.8%, respectively. Both methods did not show differences in tissue adequacy. The median amount of endometrial tissue was slightly higher in the MVA group than in the Endocell group (2.1 g vs 1.8 g, p = 0.02), but this difference did not affect the adequacy of the pathological diagnosis. The mean difference in endometrial tissue was 0.59 g (0.01-1.08, p = 0.02). Age, parity, and vaginal birth did not affect the adequacy of endometrial tissue between biopsy procedures. However, the tissue adequacy rate tended to be higher in younger women, as shown in Table 3. Among the 13 women who had inadequate tissue, five women underwent uterine curettage, and one woman underwent a hysterectomy, while five women did not

undergo further investigation. The clinical signs of AUB improved after 6-month follow-up, and two women were lost to follow-up. The histopathological findings of women with adequate tissue are shown in Table 4.

Table 3. Tissue adequacy of the groups in all participants and stratified by age, parity, and number of vaginal births

	MVA (n = 146)	Endocell (n = 144)	p value[a]
Participant, n (%)	139 (95.2)	138 (95.8)	1.00
Age group (years), n(%)			
< 35	15 (100)	10 (100)	1.00
35 - 49	109 (95.6)	107 (96.4)	1.00
≥ 50	15 (88.2)	21 (91.3)	1.00
Parity, n (%)			
0	29 (90.6)	44 (97.8)	0.30
1	41 (97.6)	39 (97.5)	1.00
≥ 2	69 (95.8)	55 (93.2)	1.00
Vaginal birth, n (%)			
0	69 (93.2)	72 (94.7)	0.74
1	27 (100)	29 (93.6)	0.49
≥ 2	43 (95.6)	37 (100)	0.49

MVA: manual vacuum aspiration, [a] Fisher's exact test.

Table 4. Pathological diagnosis of the groups

	MVA	Endocell	p value
Amount of endometrial tissue (gram), median (IQR)	2.1 (1.2 - 3.6)	1.8 (1.1 - 2.9)	0.02[a]
Physiological results (n = 173), n (%)			
Proliferative endometrium	57 (67.1)	63 (71.6)	0.14[b]
Secretory endometrium	17 (20.0)	21 (23.9)	
Menstruation	1 (1.2)	2 (2.3)	
Inactive endometrium	8 (9.4)	2 (2.3)	
Atrophic endometrium	2 (2.4)	0	
Pathological results (n = 77), n (%)			
Endometrial polyp	33 (76.7)	22 (62.9)	0.59[b]
Persistent proliferative phase	8 (18.6)	10 (28.6)	
Submucous myoma	1 (2.3)	1 (2.9)	
Endometritis	1 (2.3)	2 (5.7)	
Endometrial hyperplasia (n = 26), n (%)			
Simple hyperplasia without atypia	8 (72.7)	12 (80.0)	0.40[b]
Complex hyperplasia without atypia	1 (9.1)	0	
Simple hyperplasia with atypia	1 (9.1)	3 (20.0)	
Complex hyperplasia with atypia	1 (9.1)	0	
CA endometrium (n = 1), n (%)	0	1 (100)	

MVA: manual vacuum aspiration, IQR: interquartile range
[a] Wilcoxson rank-sum test; [b] Fisher's exact test.

Discussion

This study showed very high percentages of tissue adequacy from both endometrial tissue biopsy devices, MVA and Endocell. The tissue adequacy

using MVA device was 95.2% and using Endocell device was 95.8%. The degree of negative suction pressure from the MVA affects the amount of collected endometrial tissue; as shown in our study, the amount of endometrial tissue from the MVA device was significantly higher than that from the Endocell device. However, the mean difference in the collected tissue was small, only 0.59 g and did not affect the pathological diagnosis. The tissue adequacy rate in our study was higher than Wanijasombutti's study[4], which showed an 83.3% tissue adequacy rate using the MVA device and an 81.1% tissue adequacy rate using the Endocell device. However, the tissue adequacy rate was comparable between the two devices, similar to our study. Another study[6] showed that the tissue adequacy rate using MVA endometrial sampling was 87.8%. For Endocell endometrial biopsy devices, previous studies[4,7] reported a tissue adequacy rate of 72.7-85.6%. Previous studies[8,9] on Karman endometrial aspiration showed a tissue adequacy rate of 76.4-86.7%. Our study showed a higher tissue adequacy rate compared to previous studies[4, 6, 7]. The factor that may have affected this outcome was the menopausal status of the participants. Our study included only premenopausal and perimenopausal women, but previous studies[4, 6, 7] included both premenopausal and postmenopausal women. The effect of estrogen level, which impacts endometrial growth, also plays an important role in endometrial thickness and tissue adequacy for pathological examination. As in our study, a higher tissue adequacy rate was found in the younger age group. Even in the premenopausal and perimenopausal age group, our study showed that MVA and Endocell devices still provided a comparable tissue adequacy for pathological examination.

Our study found that the endometrial pathology in patients with AUB of both endometrial biopsy devices was not different. Pathological examination revealed 62.5% physiologic endometrium, 27.8% pathological endometrium, 9.4% endometrial hyperplasia, and 0.4% endometrial carcinoma. The most common benign pathologic endometrium was endometrial polyp (71.4%), followed by persistent proliferative endometrium (23.4%), endometritis (3.9%), and submucous myoma (2.6%). The sequence of endometrial pathological findings was similar to that of a previous study[10].

The pain score was slightly higher in the MVA group than in the Endocell group, which was statistically significant. This result is mainly related to the degree of negative suction pressure of the 60 ml MVA syringe. Furthermore, the MVA group also needed a tenaculum to facilitate cannula insertion more than the Endocell group, which also affected the pain. However, the patient satisfaction score did not differ between the groups. Our study found cervical stenosis in 3.1% of the participants which was not different between groups. After insertion of 400 µg misoprostol transvaginally for 3 h, we were able to access the uterine cavity in all participants without the need for analgesia. Cervical priming may be an optional way to overcome cervical stenosis without requiring cervical dilatation or analgesia, which is less practical in an outpatient setting. Previous studies[11,12] also showed the effectiveness of misoprostol in facilitating cervical dilatation, decreasing the duration of the endometrial biopsy procedure, and lowering the pain score compared to placebo. The only side effect we found from misoprostol insertion was pelvic pain. Other side effects are rare and fully reversible. The following symptoms may occur: diarrhea, shivering, nausea, vomiting, increased body temperature, and skin rash[13]. Endometrial sampling with both devices showed a small risk of complications. The rate of complications was not different between the two groups. Severe pelvic pain is the most common complication, but can be resolved with non-steroidal anti-inflammatory drugs, and hospital admission or opioid analgesia are not necessary. Pelvic infection was found in 0.7% in our study. Routine administration of antibiotic prophylaxis in endometrial biopsies is not recommended[14,15]. A careful history and pelvic examination for recent cervicitis or pelvic infection should be performed in every woman before performing an endometrial biopsy; if there are any

signs of cervical or pelvic infection, the procedure should be postponed.

Our data showed that tissue adequacy for pathological diagnosis from both endometrial biopsy devices were not different. The side effects from both procedures were very low and there was no difference. However, the pain associated with procedure was less in the endocell group than the MVA group. Therefore, in terms of the discomfort associated with the procedure, Endocell may be a good option.

This was a prospective, randomized, parallel study. Both participants and certified gynecologic pathologists were blinded to the procedure. In our clinical practice, the initial uterine evaluation in women with abnormal uterine bleeding after detailed history taking and physical examination are transvaginal ultrasound (TVUS) in women with enhanced risk for structural abnormality or endometrial sampling in women with enhanced risk of endometrial hyperplasia[1]. Therefore, not all participants were evaluated by TVUS before endometrial biopsy. Another limitation of our study is that participants with inadequate tissue for pathological diagnosis did not undergo a hysteroscopic procedure to obtain a definite diagnosis of the cause of AUB. However, we followed-up with all of these participants, and no further endometrial pathologies or cancers were detected. MVA is a reusable device that can reduce the cost for the patient who receives an endometrial biopsy. The personnel who process the instruments need to be well-trained in cleaning and disinfecting the instrument. Otherwise, the instrument will be damaged.

Conclusion

There was no evidence that the efficacy of endometrial tissue biopsy by MVA or Endocell was different in terms of tissue adequacy for pathological diagnosis. Both devices showed a very high percentage of tissue adequacy and very low adverse effects.

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Potential conflicts of interest

The authors declare no conflicts of interest.

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