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Original Article

Hysteroscopic evaluation of endometrial changes and fallopian tubal functions in women using progestin-only contraceptives

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Abstract The purpose of this prospective study was to investigate whether office hysteroscopy (OH) can be used to assess the mechanisms of action of progestogen-only contraceptives (POCs), diagnose possible local causes of abnormal uterine bleeding (AUB), and support the treatment plan of symptomatic patients using POCs compared with those who do not use hormones. The study included 140 women who were divided into two groups. Group A consisted of 70 women who used POCs, whereas group B consisted of 70 women who did not use hormones. They were successively examined using transvaginal ultrasonography (TVS), OH, and endometrial sampling. The TVS results were consistent with those of OH and histopathology. The changes in endometrial thickness and vasculature, as well as fallopian tube (FT) functions, were significantly more pronounced in POC users than in non-POC users. There was a significant reduction in the peristalsis of the proximal part of the FT, as well as a reduction in the bubble flow test in group A compared with group B. In addition, the combination of peristalsis and the bubble flow test (Darwishscope test) was significantly lower in group A. It was concluded that using OH as a simple diagnostic tool in women with POCs would contribute to a better understanding of the mechanisms of endometrial and FT effects and explain some local endometrial causes of AUB. This ensures that the combination of TVS and OH would limit routine endometrial sampling in POCs users.

Key words: Endometrium, Fallopian tubes, Hysteroscopy, Contraception, Progestins, Ultrasonography

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INTRODUCTION

An increasing number of progestogen-only contraceptives (POCs) are being used worldwide because they have no estrogen-related side effects or complications, do not interfere with breastfeeding, and interest in long-acting reversible contraceptive methods (LARC) is increasing. The possible mechanisms of the contraceptive action of POCs include inhibition of ovulation at varying percentages, alteration of the biophysical properties of cervical mucus, reduction of fallopian tube (FT) ciliary motility and tubal contractile muscle strength, and/or alteration of endometrial receptivity.[1] However, the incidence of unwanted and distressing forms of abnormal uterine bleeding (AUB) was sign-

ificantly higher with POCs than with other methods.[2-7] There is a need for a better understanding of the mechanisms of AUB in women using POCs,[8] and thus for individualized treatment rather than the current empirical lines of therapy.[9]

Office hysteroscopy (OH) has long been used to examine the uterine cavity in many gynecological conditions such as AUB,[10] unexplained infertility, and recurrent pregnancy loss.[11,12] In recent years, we have extensively studied the proximal part of the FT using a bubble flow test and physiological peristalsis via OH.[12] In addition, the combination of the bubble flow test and peristalsis (Darwishscope test) proved to be better than either test alone for assessing the function of the proximal part of the FT.[13] This study aimed to assess whether OH can be used to evaluate the mechanisms of action of POCs, diagnose possible local causes of AUB, and support in developing a treatment plan for patients experiencing symptoms who use POCs compared to those who do not use hormones.

METHODS

This prospective cross-sectional study was conducted between August 2021 and July 2023 at the OH unit of the Women's Health University Hospital of Assiut University, in women of childbearing age who had undergone OH for various indications. This study was approved by the ethics committee of the Faculty of Medicine (No. 17101330) and registered on ClinicalTrials.gov (NCT04368104). The sample size was calculated using G*Power 3.1.3 software (Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany) and amounted to 140 cases, which were divided into two groups according to the use of POCs. Group A included 70 patients who used any method of POCs and complained of AUB with or without abnormal transvaginal ultrasonography (TVS). Group B comprised women with infertility who underwent OH during the same period but did not use hormones or contraceptives. After preoperative counseling, all patients agreed to provide written consent. A complete medical history was obtained from all patients, including a history of contraceptive use (method, duration, regularity of use, side effects, complications, and any interruptions), a therapeutic history, and a thorough physical examination. Clinically, biochemically, or sonographically diagnosed pregnancies, recent stroke or ischemic heart disease, heavy vaginal bleeding, active pelvic inflammatory disease, coagulopathies, and severe comorbidities, such as severe hypertension and severe cardiac, neurological, or breast disease, were excluded from this study. Women using any form of contraception or hormones were excluded from group B. The vulva, vagina, and thighs were disinfected with a 10% povidone-iodine solution. Subsequently, sterile drapes were applied. OH was performed with a rigid 2.6 mm 30° scope with a 3.2 mm outer sheath (Karl Storz, Tuttlingen, Germany). Initially, a vaginoscopic approach was attempted in all cases; however, if difficulties were encountered, the anterior lip of the cervix was grasped using a multitoothed volsellum. The uterus was then distended with normal saline at a pressure of 60-80 mmHg, which was generated by a pneumatic sphygmomanometer cuff wrapped around a 500 mL 0.9% saline infusion bottle. The endoscope, connected to a 250 W Xenon light source, was carefully inserted through the cervical canal and internal os. To perform a perfect hysteroscopic assessment of the endometrial cavity, the following steps were followed: a clear panoramic view of the uterine cavity was achieved by placing the hysteroscope into the cervical canal and waiting for a while to achieve homogeneous dilation and drainage of blood clots from the cervix. The uterine cavity should be examined systematically, starting with the anterior and posterior fundus and lateral walls. The examination is considered complete when both tubal ostia have been reached, and any gross pathology, such as septum, adhesions, polyp(s), myoma, or any proliferation, has been described. Hysteroscopic assessment of the endometrial thickness began with a revision of the TVS report. During TVS, an endometrium (EM) of 8-11 mm was considered normal. For OH, the EM was considered normal if it appeared to be of normal thickness, with moderately developed glandular orifices, and evenly distributed blood vessels in a healthy endometrium. For TVS, a thin EM was assumed if it was ≤7 mm. In OH, a thin EM was assumed

when narrow glandular openings and thin, poorly distributed blood vessels were observed in the fragile endometrium.[14] In the TVS, a thick EM was assumed when it measured 12-16 mm (excluding the secretory phase). A thick EM was identified in the OH as diffusely increased thickness with prominent glandular orifices. In TVS, endometrial hyperplasia is assumed when the EM appears as an echogenic diffuse smooth thickening >10 mm. Hysteroscopically, it is recognized as local or diffuse endometrial thickening with a papillary or polypoid appearance, abnormal vascular patterns, glandular cysts, and glandular outlets with abnormal architectural features.[15]

In addition to the subjective assessment of endometrial thickness, a simple hysteroscopic endometrial thickness test was performed. The telescope was advanced until the fundus was reached and then extracted along the posterior wall up to the cervix with gentle pressure. If a significant furrow (half the circumference of the hysteroscopic sheath) formed along the pathway, the EM was considered thick. If there was no furrows were observed, the EM was mostly thin. If a shallow furrow (one-quarter of the circumference of the hysteroscopic sheath) is formed, it is mostly a normal EM. The endometrial vasculature appeared normal, congested, with petechiae, ecchymosis, and abnormal or suspicious vascular patterns. The endometrial color was pale, pink, reddish, or dark red, as previously described.[10] All cases reported bleeding upon touching.

The next step in all cases was to assess FT function. Prerequisites for successful access to the FT via hysteroscopy include the utilization of a 300 mm telescope and skillful use of its rotation to reach both cornua (tilting it to the right to see the left side and vice versa). The fundamental anatomic triad (Darwish hysteroscopic triad) was observed (Darwish triad, DT).[16] This is the conical part of the FT (Fig. 1A). Its base is a fine cornual circle (ostium) representing the end of the endometrial cavity. The ostium is followed by a shallow conical groove, which is the converging wall of the first millimeter of the intramural part of the FT. Finally,

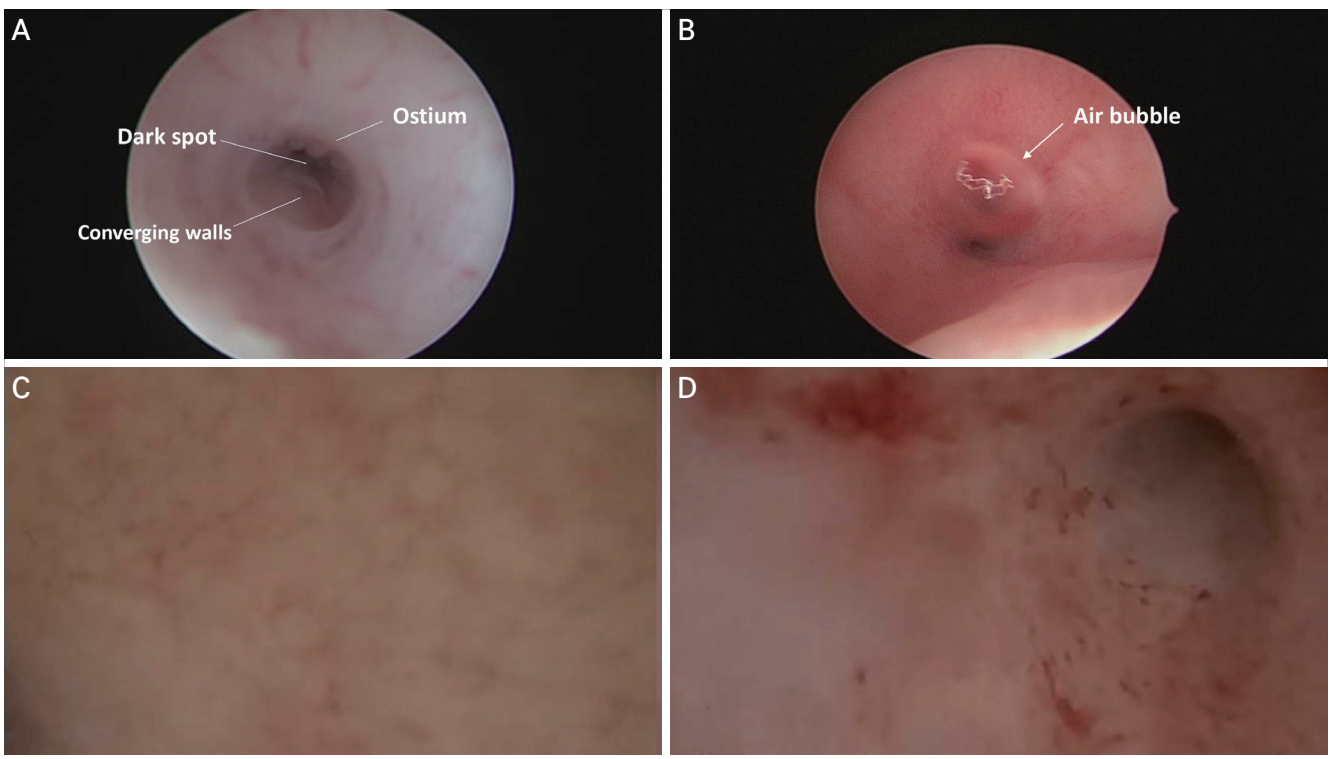

Figure 1. (A) Darwish hysteroscopic triad. (B) Bubble flow test (a bubble is seen at the ostium). (C) Congested thin endometrium with evident capillaries. (D) Congested thin endometrium in the form of dilated, tortuous, and worm-like capillaries.

a distal pinhole dark spot (the narrowest part of the FT) represents the summit of the cone. Considering DT is essential in evaluating tubal patency and physiology during hysteroscopy. If the DT was clearly accessible, a comment was provided regarding its shape. If there were osteal lesions, such as tiny polyps or fine adhesions, which may hinder the proper evaluation of tubal anatomy and physiology, the hysteroscopist would report them. The passage of air bubbles in the irrigating fluid towards the DT has been reported. If there was no air bubbles were observed, the hysteroscopist injected 2 mL of air into the rubber end of the sterile infusion set. The results of the hysteroscopic bubble suction test were considered positive if air bubbles passed through the DT within 1 minute (Fig. 1B). During this period, neither air injection nor increased pressure was applied. If no passage of gas bubbles occurred, the examiner waited for 1 minute to exclude tubal spasms. If there were no passage of bubbles through the DT and their accumulation at the cornual end, the test was considered negative. Simultaneously, careful visualization of any changes in the shape of the ostium and the intramural part of the FT, particularly during the passage of air bubbles, was recorded in all cases. Tubal peristalsis is defined as the rhythmic opening and closing of the ostium and intramural fallopian tube under constant intrauterine pressure, that is, periodic changes in the DT in the form of widening followed by collapse on meticulous observation. If the ostium and intramural part of the tube were opened, followed by the collapse and non-visualization of the dark pinhole spot of the DT for a while, positive peristalsis was reported. The same procedure was repeated on the contralateral side. At the end of OH, Novak's curette biopsies of the most suspicious areas of EM were obtained under hysteroscopic guidance and sent for histopathological examination.

The SPSS version 24 (IBM, Armonk, NY, USA) was used to analyze the data. Quantitative data were expressed as mean±standard deviation. Qualitative data were expressed as frequencies and percentages. The independent-sample

Table 1. Sociodemographic data of studied patients

Characteristic	Study group (n=70)	Control group (n=70)	Test	*P*-value
Age (years)	29.81±4.96	31.29±5.53	1.67†	0.10
Parity	3 (1-5)	2 (0-3)	845‡	0.001*
Residence				
Rural	39 (55.7)	42 (60.0)		
Urban	31 (44.3)	28 (40.0)	0.264§	0.608
Education				
Illiterate	39 (55.7)	35 (50.0)		
Primary school	18 (25.7)	20 (28.6)		
Secondary school	10 (14.3)	13 (18.6)		
High level	3 (4.3)	2 (2.9)	0.913§	0.822
Occupation				
Housewife	62 (88.6)	65 (92.9)	0.763§	0.382
Employee	8 (11.4)	5 (7.1)		
Infertility				
Yes	0 (0.0)	62 (88.0)	107.72§	<0.001*
No	70 (100.0)	8 (12.0)		

Values are presented as frequency (%), mean±standard mediation, or median (range).

**P*-value was significant if <0.05.

†Independent *t*-test.

‡Mann Whitney *U* test.

§Chi square test.

t-test and Mann-Whitney *U* test were used to compare the means of normally and abnormally distributed data, respectively. The chi-squared test was used to compare nonparametric data. Probability (*P*-value) <0.05 was considered significant, <0.001 was considered highly significant, and >0.05 was considered non-significant.

RESULTS

This prospective study included 140 patients who underwent OH and were divided into two groups. Group A used POCs, whereas group B included infertile women who did not use any hormones. There were no statistically significant differences between the groups regarding sociodemographics, apart from parity and infertility, as shown in Table 1. Group A was using POCs in the form of traditional progesterone-only pills (POP) containing levonorgestrel (LNG) 0.03 mg (Microlut; Bayer, Leverkusen, Germany) in 21 cases, desogestrel-containing POP 75 g (Cerazette; MSD, Rahway, NJ, USA) in 11 cases, etonogestrel implants 68 mg (Implanon; MSD) in 16 cases, medroxyprogesterone acetate (MPA) 150 mg (Depo-Provera; Pfizer, New York, NY, USA) in 20 cases, and LNG intrauterine system (IUS) 52 mg (Mirena; Schering AG, Berlin, Germany) in two cases. The mean duration of exposure to POCs was 6.56±3.05 months, with a range of 3 to 18 months. Table 2 shows the

Table 2. Indications of office hysteroscopy among studied patients

Indication of office hysteroscopy	Study group (POCs) (n=70)	Control group (infertility) (n=70)	Chi-square test	*P*-value*
Breakthrough bleeding	34 (48.6)	0 (0.0)	118	<0.001
Menorrhagia	18 (25.7)	8 (11.4)		
Metrorrhagia	11 (15.7)	0 (0.0)		
Suspected IU lesion by TVS	7 (10.0)	0 (0.0)		
Unexplained infertility	0 (0.0)	31 (44.3)		
Pre-ICSI	0 (0.0)	31 (44.3)		

Values are presented as frequency (%).

POC: progestogen-only contraceptive, IU: intrauterine, TVS: transvaginal ultrasonography, ICSI: intracytoplasmic sperm injection.

**P*-value was significant if <0.05.

Table 3. Indications of office hysteroscopy among studied patients

Characteristic	Study group A						Control group B (n=75)	Chi-square	*P*-value*
	Total (n=70)	MPA (n=20)	Microlut (n=21)	Implanon (n=16)	Cerazette (n=11)	Mirena (n=2)			
Endometrial thickness									
Normal	36 (51.4)	5 (25.0)	14 (66.7)	6 (37.5)	9 (81.8)	2 (100.0)	60 (85.7)	19	<0.001
Thin	27 (38.3)	12 (60.0)	7 (33.3)	7 (33.3)	1 (9.1)	0 (0.0)	1 (1.4)	30	<0.001
Polyp	3 (4.3)	2 (10.0)	0 (0.0)	0 (0.0)	1 (9.1)	0 (0.0)	7 (10.0)	1.72	NS
Subseptate uterus	3 (4.3)	0 (0.0)	0 (0.0)	3 (18.7)	0 (0.0)	0 (0.0)	1 (1.4)	1.03	NS
Endometrial hyperplasia	1 (1.4)	1 (5.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.4)	-	NS
Endometrial vasculature									
Normal	45 (64.3)	4 (20.0)	17 (81.0)	12 (75.0)	10 (90.9)	2 (100.0)	61 (87.1)	9.95	0.002
Pale	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (7.1)	22.62	<0.001
Congested	25 (34.7)	16 (80.0)	4 (19.0)	4 (25.0)	1 (9.1)	0 (0.0)	4 (5.7)	19	<0.001

Values are presented as frequency (%).

MPA: medroxyprogesterone acetate, NS: no significance.

**P*-value was significant if <0.05.

Table 4. Hysteroscopic evaluation of the Fallopian tubes in both groups

Characteristic	Study group (n=70)	Control group (n=70)	Chi-square	*P*-value*
Darwish hysteroscopic triad (FT) access				
Right tube	65 (92.8)	64 (91.4)	1.14	NS
Left tube	65 (92.8)	66 (94.2)	1.90	NS
Positive bubble flow test within 1 minute				
Right tube	28 (40.0)	45 (64.3)	8.27	0.004
Left tube	30 (42.9)	47 (67.1)	8.34	0.004
Positive bubble flow test within 2 minutes				
Right tube	29 (41.4)	48 (68.6)	10.40	0.001
Left tube	31 (44.3)	49 (70.0)	9.45	0.002
Total positive test				
Right tube	29 (41.4)	48 (68.6)	10.40	0.001
Left tube	31 (44.3)	49 (70.0)	9.45	0.002
Positive tubal peristalsis				
Right tube	16 (22.8)	35 (50.0)	11.10	<0.001
Left tube	21 (30.0)	33 (47.1)	3.65	0.056
Darwishscope test (combined bubble and peristalsis)				
Right tube	15 (21.4)	33 (47.1)	10.30	0.001
Left tube	17 (21.2)	29 (41.4)	3.92	0.048

Values are presented as frequency (%).

FT: fallopian tube, NS: no significance.

**P*-value was significant if <0.05.

indications for OH in both groups. The only significant difference between the two groups was the documentation of viscid cervical mucus in 26 cases (37.1%) in group A out of 32 cases using POP compared to zero cases in group B (*P*<0.001). Regarding the endometrial cavity, most cases in both groups showed normal appearance, thickness, color, and vasculature. However, in group A, thin EM and abnormal vasculature were significantly higher than those in group B (27 [38.3%] vs. 1 [1.4%] and 25 [34.7%] vs. 4 [5.7%], respectively), as shown in Table 3. Preoperative TVS was consistent with OH comments on endometrial thickness in most cases in both groups. Fig. 1C shows a congested EM with obvious capillaries, while Fig. 1D shows dilated, tortuous, and worm-like capillaries prone to easy bleeding upon touch in the cases of AUB in group A. Access to DT to assess FT was successful in most cases in both groups. However, due to excessive bleeding, it was unsuccessful in a few patients (Table 4). FT function assessment revealed a significant reduction in peristalsis in the proximal part of the FT, in addition to a decreased bubble flow test in group A than in group B. Moreover, the combination of peristalsis and bubble flow tests (Darwishscope test) was significantly lower in the POCs group, especially for the right FT. Only 21 (30%) and 20 patients (29%) in both groups were satisfied with OH, respectively, but the rest were dissatisfied because of painful endometrial sampling using a Likert scale. The histopathological diagnosis was consistent with the hysteroscopic diagnosis in both groups.

DISCUSSION

Hormonal contraceptive use, including POCs, has increased worldwide, accounting for almost 50% of contraceptive methods.[17] It is well-documented that POCs may induce a progressive reduction of endometrial thickness over the course of treatment,[18,19] as supported by the findings of this study of OH subjective assessment. A simple and easy practical technique was used to assess endometrial

thickness by applying gentle pressure along the entire posterior wall. These findings were consistent with the preoperative TVS and histopathological results in all cases. Additional advantages of OH over TVS include being the gold standard diagnostic tool for observing tiny lesions or abnormal vasculature and assessing FT function. OH provides a visual assessment of the EM vasculature. It was able to diagnose a normal endometrial vasculature pattern in 45 patients (64.3%) and a congested pattern in 25 POCs users (34.7%). Endometrial findings have been previously reported in greater detail, particularly in users of norplant implants,[20] but were solely based on endometrial sampling. A hysteroscopic diagnosis of a free endometrial cavity or any intrauterine lesion (supported by normal TVS) minimizes the burden on the pathologist by eliminating unnecessary samplings.[21] Moreover, it also alleviated invasive endometrial sampling pain, which was experienced by 49 (70%) and 50 patients (71%) in groups A and B, respectively. Furthermore, this also alleviated the anxiety and stress of waiting several days for biopsy results. In addition to the fact that these women are usually young and receiving progestins, OH plus TVS would eliminate unnecessary routine endometrial sampling. The collective advantages of OH include *in vivo* observation of the entire endometrial cavity, vessel morphology and distribution, and accurate information about non-vascular structures that may not be accessible by blind biopsies.[22]

Practical methods to examine the different mechanisms of action of POCs include simple speculum examination to detect viscid cervical mucus, TVS, hormonal assays to diagnose inhibited ovulation and endometrial thickness, and invasive endometrial tissue sampling for histopathological examination. In modern practice, women require a simpler and less invasive method than painful endometrial curettage. In this study, the hysteroscopic assessment of endometrial thickness was consistent with preoperative TVS and histopathology in all cases. Since both TVS and OH findings were consistent, we believe that they would be complementary in the quick assessment of endometrial abnormalities. Specific clinical characteristics of the patients should be considered, as previously recommended.[21] However, the advantages of OH over TVS include being the gold standard diagnostic tool for observing tiny lesions or abnormal vasculature and assessing FT function.

Normal and thin EM were diagnosed in 36 (51.4%) and 27 cases (38.3%) using POCs, respectively. Moreover, endometrial polyps were easily diagnosed and treated in three cases (4.3%). In this study, a simple and practical method was used to assess endometrial thickness by applying gentle pressure along the entire posterior wall with the tip of the telescope to check for endometrial furrow formation. Similarly, OH offers a visual assessment of the EM vasculature. It was able to diagnose a normal endometrial vasculature pattern in 45 patients (64.3%) and a congested pattern in 25 POCs users (34.7%). A hysteroscopic diagnosis of a free endometrial cavity or any intrauterine lesion (supported by normal TVS) minimizes the burden on the pathologist by eliminating unnecessary samplings.[22] Moreover, it also alleviated invasive endometrial sampling pain, which was experienced by 49 (70%) and 50 patients (71%) in groups A and B, respectively. Furthermore, it alleviated the anxiety and stress of waiting several days for biopsy results. In addition to the fact that these women are usually young and receiving progestins, OH plus TVS would eliminate unnecessary routine endometrial sampling. The collective advantages of OH include *in vivo* observation of the entire endometrial cavity, vessel morphology and distribution, and accurate information about nonvascular structures that may not be accessible by blind biopsies.[23]

Regarding the effect of POCs on the FT, it is postulated that they may lead to a 40-50% reduction in the epithelial ciliary beat frequency and decreased contractions of the longitudinal muscular layer of the human FT compared with the baseline value. The former has been proven in an animal study[24] while the latter has been proven in an *in vitro* study.[25] In a pilot study, repeated hysterosalpingography (HSG) was used to confirm functional proximal FT occlusion in women using depot MPA.[26] Repeated HSG pain, irradiation, and invasiveness, in addition to ethical controversies, are the significant disadvantages of this study. For

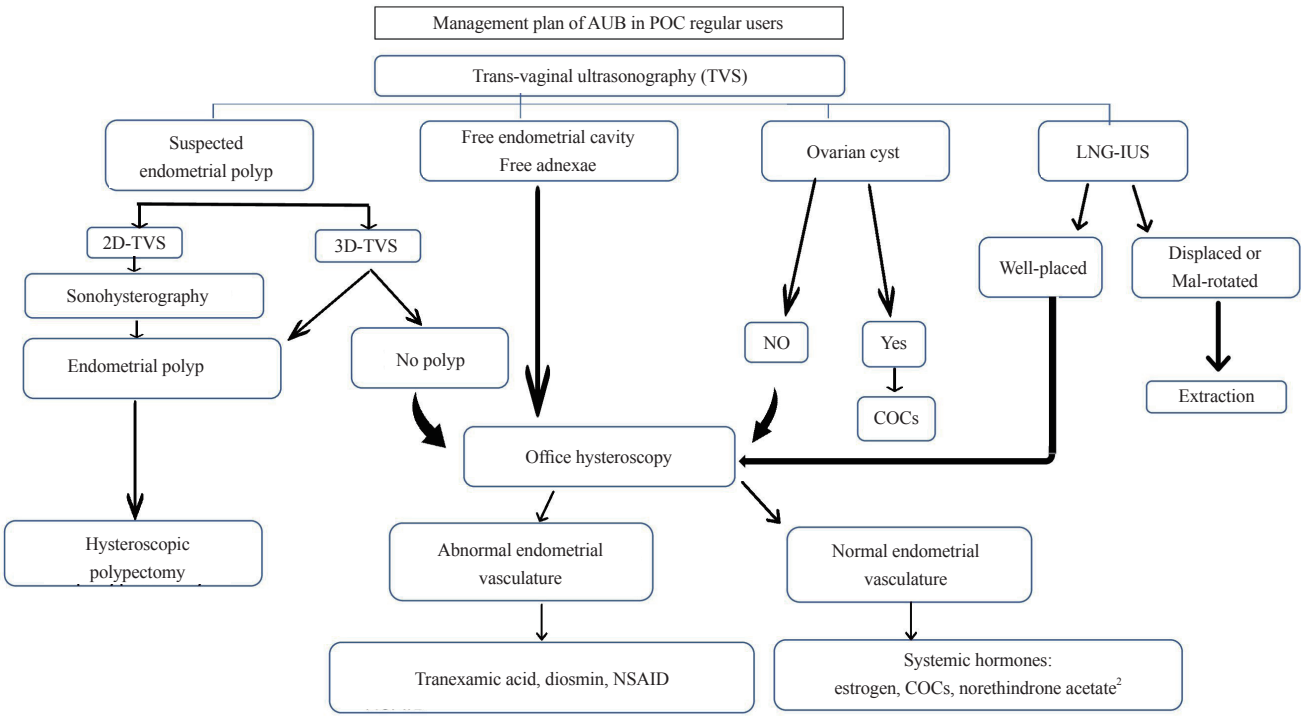

Figure 2. Management plan of abnormal uterine bleeding in POC regular users. AUB: abnormal uterine bleeding, POC: progestogen-only contraceptive, LNG: levonorgestrel, IUS: intrauterine system, COC: combined oral contraceptive, NSAID: nonsteroidal anti-inflammatory drug.

the past decade, our institution has been interested in study of the FT function utilizing hysteroscopy.[11-13,16] The unique advantage of using OH to assess FT in POCs users was addressed in this study. This confirmed the postulated effect of POCs on the FT by statistically significant negative peristalsis and negative bubble flow tests in the proximal part of the FT, which are mostly attributed to the direct effect of progestins on the FT. In this study, negative bubble flow test results in POCs users indicated that the passage of bubbles to the FT is not a passive phenomenon but is controlled by the peristalsis of the proximal part of the FT. This observation is supported by using the lowest intrauterine pressure sufficient for proper visualization and observing bubbles waiting for some time at the ostia, which contributed to reporting at 1 and 2 minutes (Table 4). Lastly, OH was diagnosed as viscid cervical mucus in 26 of the 32 cases using POP. To the best of our knowledge, this is the first study to document the mechanisms of action of POCs utilizing OH, including the *in vivo* observation of the entire endometrial cavity, endometrial thickness, vessel morphology and distribution, accurate assessment of FT function, and easy detection of viscid cervical mucus. An important issue was selecting a control group without hormonal treatment to avoid bias in interpreting the endometrial and FT changes with the use of POCs.

Different forms of AUB with POCs contribute to the high incidence of discontinuation and subsequent undesired pregnancy. In addition to systemic hormonal imbalances, local endometrial causes have been suggested. Despite well-documented endometrial thinning in most cases at the EM level, there is a paradoxical increase in vascular defects that commonly cause occasional spotting. Bleeding with POCs may be attributed to fragile vessels due to a lack of stromal support, secondary to progestogen-induced endometrial dysfunction, which inhibits uterine vascular smooth muscle cell survival.[27] A human and animal study confirmed that endometrial thin-walled, hyperdilated, fragile microvessels were due to reduced proliferation of human and guinea pig endometrial vascular smooth muscle cells (VSMCs) in cases using long-acting POCs, as confirmed by altered transcrip-

tion of some genes in the cultured endometrium.[28] Others have suggested using transvaginal color and pulsed Doppler ultrasonography as tools to detect increased blood perfusion in the uterine and spiral arteries, a significant decrease in RI and PI, and increased blood flow in the subendometrial vessels.[29] Despite interesting Doppler studies, clinical decision-making cannot be based on these findings. More research is needed to gain a deeper understanding of the mechanisms and establish long-term interventions to manage bleeding irregularities in POCs.[18] The use of OH in this study shortens this narrative. It properly assesses the endometrial thickness and vasculature and excludes any intrauterine organic causes within a few minutes. Interestingly, it can diagnose a congested endometrium with easy bleeding, confirming a local vascular cause that may respond to vascular supportive therapy. In this study, normal endometrial thickness and vasculature diagnosed by OH were valuable negative findings, as they directed the gynecologist towards systemic causes such as improper or irregular use. In this study, hysteroscopic access to the cornual parts of the endometrial cavity was successful in more than 90% of the cases, despite AUB in many of them. This can be attributed to the use of a simple pump to wash blood clots from the endometrial cavity, as described in a previous study.[10]

Despite the findings of this study being descriptive and based on OH, incorporating TVS and endometrial sampling would provide additional insights into the mechanism. However, the heterogeneity of types, doses, duration, and routes of administration of POCs, the small sample size, including only symptomatic POCs users, the infrequent patient attendance for follow-up, and the lack of laparoscopic control of the impact of POCs on FT function due to ethical considerations were the main limitations. Moreover, this study lacks an assessment of the potential confounders of AUB. More studies on the endometrial pattern of individual types of POP are required, particularly after the introduction of the new generation of high-dose 4 mg drospirenone-only pills (DOP), which are administered for 24 days with 4 days off.[30] Additionally, hysteroscopic assessment of the endometrium is subjective, with possible intra-observer variations. Finally, the heterogeneity of group B is an additional limitation. This study calls for a universally agreed-upon classification of normal and abnormal endometrial vasculature in POCs users and non-users to facilitate appropriate interventions. We invited interested hysteroscopists to share their research on normal and abnormal endometrial vasculature in different types of POCs, as observed by OH, such as dilated, tortuous, and worm-like capillaries (endometrial vascular dystrophy), believed to be caused by thrombosed capillaries.[31] The widespread use of OH in clinics, attending concise training courses, and increasing the orientation of gynecologists on technical skills would enhance their use in the field of contraception for the proper study of endometrial changes and help explain some related side effects. In conclusion, using OH as a simple diagnostic tool in cases of POCs would contribute to a better understanding of the mechanisms of endometrial and FT effects and help explain some local endometrial causes of AUB. Furthermore, this assures that the combined TVS and OH restrict the need for routine invasive endometrial sampling for POCs users. In the era of precision medicine, the incorporation of OH into the diagnostic work-up algorithm for the management of AUB in regular POC users would help construct an individualized management plan, as shown in Fig. 2.

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