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Functional ovarian cysts in users of combined oral contraceptives versus medroxyprogesteroneacetate (M.P.A)

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Abstract

Introduction: Hormonal contraceptives are prescribed at two main regimens; the combined formula of estrogen and progestin and the progestogen-only formula of either progesterone only or one of its synthetic analogs (progestins). Despite their use, the combined oral contraceptives (OCS) don't suppress the ovarian follicular development, completely. The level of follicular activity during OC use depends on factors such as the type and dose of steroids administered, the administration schedule, the user's adherence to the regimen, and the individual's response to the hormones.

Aim of the study: To evaluate the relationship between functional ovarian cysts and users of combined oral contraceptive pills and Medroxyprogesterone acetate (MPA).

Subjects and Methods: A Prospective observation study conducted in the Department of Obstetrics and Gynecology, Faculty of Medicine, Fayoum University, involving 200 women divided into two groups:

Results: Our results showed that 9% of patients in group A have follicles 10–30 mm and 4% have cysts \geq 30 mm, while in group B, 17% have follicles 10–30 mm and 12% have cysts \geq 30 mm, with a significant difference between both groups ($P < 0.001$). Also, the mean cyst diameter in groups A and B were 47.6 mm and 59.3 mm, respectively, without any significant difference.

Conclusions: Combined Oral Contraceptive pills have a low risk of follicular cyst formation than medroxyprogesterone acetate injection.

Key words: Functional Ovarian Cysts; Combined Oral Contraceptives; medroxyprogesteroneacetate.

1. Introduction

Combination methods, which contain both estrogen and progestin, and progestogen-only methods, which contain only progesterone or its synthetic analogs (progestins), are the two primary forms of hormonal contraceptive formulations [1].

Although combination oral contraceptives (OCs) can slow ovarian

follicular growth, they do not entirely prevent it. The type and number of steroids used, the administration protocol, user compliance, and the individual reaction of the woman taking the hormones all influence the degree of follicular activity during OC use [2]. Follicle cysts, including functional ovarian cysts, luteinized unruptured follicles (LUFs),

and larger follicles, have been found in women who use OCs. The definition of follicle cysts varies between reports, with functional ovarian cysts defined as nonpathological follicular cysts (i.e., anovulatory), corpus luteum cysts, or other unspecified ovarian cysts measuring more than 20 mm in diameter and detected by ultrasonography or surgical examination [3].

Furthermore, data suggests that women who take multiphasic or low-dose monophasic combination OCs are more likely to develop follicular cysts than women who take moderate-dose monophasic OCs [4].

Hormonal contraceptives have been linked to a higher risk of venous thromboembolism (VTE), especially in women who smoke or have a history of VTE [5]. The risk of VTE, on the other hand, is generally minimal

and varies depending on the type of hormonal contraception used [6].

Hormonal contraceptives have been demonstrated to provide various non-contraceptive benefits, including lowering the incidence of ovarian and endometrial cancer [7].

Women who are unable to utilize combination hormonal contraceptives owing to medical contraindications or personal preferences may benefit from the use of progestogen-only techniques, such as the levonorgestrel intrauterine device (IUD) and the progestogen-only tablet [8].

The effectiveness of hormonal contraceptives depends on proper and consistent use. Counseling and education on the correct use of hormonal contraceptives can improve compliance and reduce unintended pregnancies [9].

So, the current study aimed to evaluate the relationship between functional ovarian cysts and users of combined oral contraceptive pills and Medroxyprogesterone acetate (MPA).

2. Subjects and methods

2.1. Subjects

The current prospective observational study sought to determine the prevalence of functional ovarian cysts in women who used combined oral contraceptive pills rather than Depo-Provera injections. From March 2019 to May 2021, the research was carried out at Fayoum University's Faculty of Medicine's Obstetrics and Gynecology Department. The study involved 200 women divided into two groups: Group A (100 women who used Microcept (combination oral contraceptive pills) and Group B (100 women who used Depo-Provera injections).

Inclusion criteria

The inclusion criteria were all women of reproductive age (18-35 years).

Exclusion criteria

The following criteria were used to exclude participants from the study: Known ovarian pathology, endometriosis, ovarian Cancer, polycystic ovary, uterine and broad ligament fibroid, P.I.D, tubo-ovarian abscess and hydrosalpinx.

Ethical considerations

The study's ethical considerations included obtaining written informed consent from all participants and informing them

about the objectives of the study, the examination, and the investigations that had been conducted, as well as the confidentiality of their information and their right not to participate in the study.

2.2. Study design

A complete history, clinical examination, and transvaginal ultrasound were performed on the individuals. The ultrasound was performed with a Chinese Chison ECO 2 and a 6 MHz vaginal probe. To prevent cross-contamination, a disposable cover was placed

2.3. Statistical Methods

The statistical analysis of the study will be conducted using SPSS software version

3. Results and Discussion

The menstrual features of two groups of women were compared in the current study. The incidence of irregular menstrual cycles was lower in Group A (14% vs. 18%),

over the probe, and coupling gel was employed for insertion. The pelvic organs were thoroughly scanned utilizing three basic procedures, and any abnormalities in appearance were noted. Any fluid-filled mass larger than 30 mm in diameter that survived for more than two cycles was recognized as a functional ovarian cyst. All observed enlarged follicles and cysts were measured in three dimensions, and their size, type, and duration were noted. The examinations were conducted in the same order for all women.

21.0 (IBM Corporation, Armonk, NY, USA) and the chi-square test for qualitative data, with a P-value less than 0.05 considered statistically significant.

with a statistically significant difference ($P < 0.001$). Furthermore, there was a significant difference in spotting between the two groups ($P = 0.013$) (Table 1 and Figure 1A, B).

Table 1: Baseline characteristics with details of studied patients.

Parameter	Group A (n=100)	Group B (n=100)	P-value#
Age (years) Mean \pm SD	31.2 \pm 4.0	28.8 \pm 3.4	0.517
BMI (kg/m ²) Mean \pm SD	23.6 \pm 2.9	25.2 \pm 4.1	0.325
Parity N (%)	1	22 (22%)	0.262
	2	38 (38%)	
	≥ 3	40 (40%)	
Abortion N (%)	1	11 (11%)	0.715
	2	15 (15%)	
	≥ 3	4 (4%)	
Duration of hormonal use (months) Mean +SD	34.7 \pm 5.9	29.3 \pm 3.5	0.147
Menses N (%)	Regular	84 (84%)	< 0.001*
	Irregular	16 (16%)	
	Menorrhagia	7 (7%)	
	Spotting	3 (3%)	
		9 (9%)	0.013*

Chi-Square test; * Statistically significant difference ($P < 0.05$).

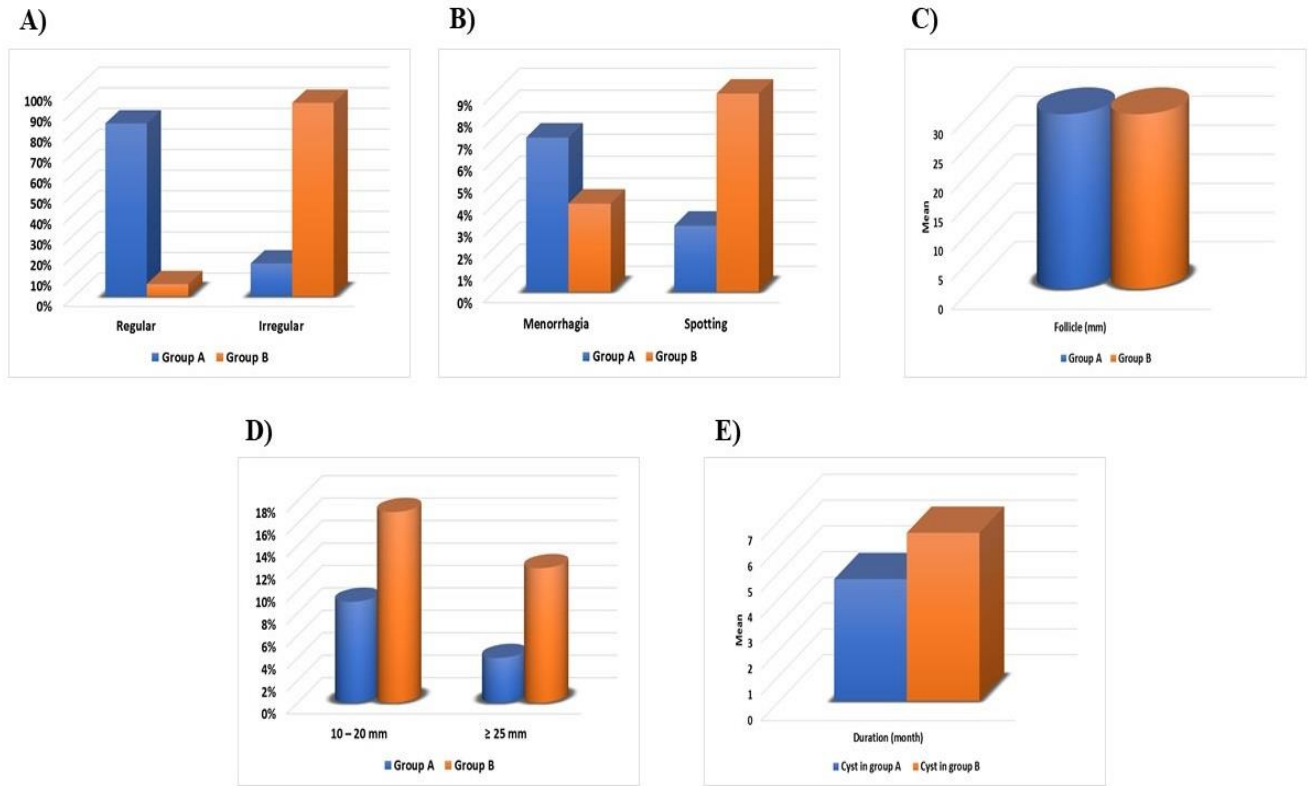


Figure 1: Comparison between both groups in regards of different ovarian features. A) Menses regularity, B) menorrhagia and spotting, C) number of follicles seen by ultrasound, D) size of follicles seen by ultrasound, E) the time of cyst appearance from the start of contraception.

However, Matteson *et al.* (2013) discovered that combined oral contraceptive pills reduced heavy menstrual bleeding (HMB) by 35% to 69% [10]. Although the review favored the LNG IUS above the COCP, there was insufficient data to measure quality of life, contentment, or adverse events. Differences in inclusion criteria may explain the disparity between their study and ours.

Uhm and Perriera (2014) conducted a systematic review that assessed the efficacy of all contraceptives (LNG IUS, progestogens (oral, subcutaneous, depot, and implantable), and combined hormonal

contraceptives (oral, patch, and ring) for treating HMB [11]. While all contraceptives were successful, they discovered that the LNG IUS was superior and should be the first-line treatment for women with HMB who require contraception.

Our study found that 9% of patients in group A had follicles 10-30 mm and 4% had cysts 30 mm, compared to 17% of patients in group B who had follicles 10-30 mm and 12% had cysts 30 mm ($P < 0.001$).

The mean cyst diameter, on the other hand, did not differ substantially between the two groups (47.6 mm in group A and 59.3 mm in group B) (Table 2, Figure 1C, D).

Table 2: Characteristics of the follicles and cysts seen by ultrasound.

Parameter		Group A (n=100)	Group B (n=100)	P-value#
Number of follicles N (%)	10 – 20 mm	9 (9%)	17 (17%)	< 0.001*
	≥ 25 mm	4 (4%)	12 (12%)	< 0.001*
Cyst diameter (mm) Mean ±SD		47.6 ± 10.2	59.3 ± 12.7	0.163

Chi-Square test; * Statistically significant difference ($P < 0.05$).

Notably, randomized controlled trials found that using combined oral contraceptives did not hasten the clearance of functional ovarian cysts [12]. Lanes *et al.* (1992) found that women taking multiphasic pills, low-dose monophasic pills containing less than or equal to 35 μ of estrogen, and high-dose monophasic pills containing more than 35 micrograms of estrogen had lower rates of functional ovarian cysts [4].

Grimes *et al.* (2009) discovered that therapy with combination oral contraceptives did not speed up the clearance of functional ovarian cysts in any trial, which included 8 randomized controlled trials from four countries and a total of 686 women [12].

Despite being widely used for this reason, combination oral contraceptives do

not appear to be beneficial. Instead, a wait-and-see approach is good for two or three menstrual cycles, and surgical management may be needed if the cysts persist. Deb *et al.* (2012) compared 34 women who had been using a combined oral contraceptive containing 30 g of ethinyl estradiol and 150 g of levonorgestrel for over a year to 36 control subjects who had not used a combined oral contraceptive in the previous year in another study [13].

When compared to the control group, the combined oral contraceptive group had considerably fewer antral follicles measuring 6 mm and lower ovarian volume and vascular indices, while the number of small antral follicles measuring 2-6 mm was similar in both groups (Table 3, Figure 1E).

Table 3: Comparison between both groups regarding the time of cyst appearance from the start of contraception.

Parameter	Group A (n=4)	Group B (n=12)	P-value#
Cyst appearance from the start of contraception Mean ±SD	4.72 ±2.24	6.52 ±3.62	0.183

t student test

Spona *et al.* (2010) also evaluated 40 women who followed a 24/4-day regimen of a combination oral contraceptive containing 20 g of ethinyl estradiol and 2 g of chlormadinone acetate for three menstrual

cycles [14]. They looked at follicle-like structure size, hormone levels (estradiol and progesterone), cervical response, and endometrial thickness. The Hoogland and

Skouby score was used to determine the level of ovarian activity.

Bartlewski *et al.* (2004) investigated the effect of MPA treatment followed by GnRH-induced ovulation on anestrus ewes in a research. Experiment 1 results revealed no significant effect on ovulation rate or fraction of ovulating ewes [15]. According to the findings, MPA has a substantial inhibitory effect on gonadotrope function. Interestingly, when GnRH treatment began 24 hours following sponge removal in

Conclusion

Combined Oral Contraceptive pills have a lower risk of follicular cyst formation than medroxyprogesterone acetate injections.

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Ethical approval and consent to participate: The study's ethical considerations included obtaining written informed consent from all participants and informing them about the objectives of the

Experiment 2, all MAP-treated ewes ovulated and had full-length luteal phases, with no significant difference in LH surge amplitude compared to control sheep.

Upton *et al.* (2020) studied FSH, progesterone, estradiol, and calcium levels in the blood of DMPA acceptors and non-acceptors [16]. Their results revealed a significant difference ($P < 0.05$) between the two groups, demonstrating that DMPA contraception influences these hormone levels.

study, the examination, and the investigations that had been conducted, as well as the confidentiality of their information and their right not to participate in the study.

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