

Original Article

Comparison Between Combined Oral Contraceptive Pills and Progesterone-Only Pills in The Management of Functional Ovarian Cysts

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Abstract - *Background: There are different approaches that have been used for the management of functional ovarian cysts with various outcomes, and the optimal method is still controversial. Objective: This study aimed to compare the effectiveness of oral progesterone versus combined oral contraceptives in women with functional ovarian cysts. Patients and Methods: An observational prospective study was conducted at Tishreen University Hospital in Lattakia-Syria for the period of one year (2022-2023). The study included women with physiological ovarian cysts, who were divided into two groups: group 1 included 50 women who received treatment with oral dydrogesterone (10 mg twice a day), and group 2 included 50 women who received treatment with ethinylestradiol –drospirenone. The final outcome and side effects of treatment were compared between the two groups. Results: The ages of the study population ranged from 18 to 40 years, with a mean age of 32.41 ± 7.3 . There were no significant differences between the two groups regarding demographic characteristics, clinical manifestations, and ultrasound findings before treatment ($p > 0.05$). Compared with baseline, a significant decrease in the volume of cysts was observed after two months of therapy in group 1 (1.55 ± 0.1 versus 5.14 ± 1.3 , $p: 0.0001$) and group 2 (1.29 ± 0.1 versus 4.98 ± 1.9 , $p: 0.0001$). In addition, there was significant relieving of menstrual disruption, dysmenorrhea, and amenorrhea ($p: 0.0001$) in the two treatment groups. Complete resolution of cysts was observed after one cycle in 92% of the women in group 1 versus 90% in group 2, and side effects were less frequent in women who received oral progesterone without the presence of significant differences between the two groups ($p > 0.05$). Conclusion: Oral dydrogesterone is as effective as combined oral contraceptives for the resolution of physiological ovarian cysts with lower risks of side effects.*

Keywords - Combined oral contraceptive, Functional cysts, Outcome, Ovarian, Progesterone.

1. Introduction

Functional ovarian cysts are defined as ovarian follicles that fail to regress, continue to fill with fluid and disappear spontaneously within 4-6 weeks, which respond to cyclic hormonal changes [1,2,3]. Functional cysts represent the most common adnexal mass in the reproductive age group which include follicular, corpus luteum, and theca lutein cysts [4,5]. Most women with cysts are asymptomatic and diagnosed incidentally on pelvic examination, but may cause pelvic pain, usually in the second half of the menstrual cycle, delayed menses, or amenorrhea [6,7,8,9]. Ultrasound is considered the primary diagnostic method for the diagnosis of cysts, in which the size and appearance of cysts will guide diagnosis. Functional cysts often have a thin, rounded wall and unilocular appearance on a sonogram [10,11,12,13].

There are different approaches have been used for the management of functional cysts, varying according to the age of women. Cysts are usually monitored for 4-6 weeks in

premenopausal women, whereas surgical removal is recommended in postmenopausal women due to high frequency of cancer [14,15]. Oral contraceptives have long been used to speed the resolution of ovarian cysts, reducing ovarian activity and the probability of recurrence. Combined oral contraceptives inhibit the hypothalamic-pituitary-gonadal axis and ovulation process, as well as they may interfere with the formation of cysts and may even lead to the resolution of existing cysts [16,17]. Progesterone has similar effects to combined contraceptives, which inhibit ovulation and prevent the continuous development of functional cysts when applied in high doses [18,19]. The efficacy of oral contraceptives over expectant management for functional ovarian cysts has not been well established due to the high frequency of ovarian cysts in reproductive age, which is associated with significant morbidity, and the absence of local studies prompted to conduct of this study. Therefore, the objectives of this study were to 1- determine the differences between combined oral contraceptives and progesterone in the management of



functional ovarian cysts. 2- investigate the side effects of the two methods of treatment.

2. Patients and Methods

2.1. Study population

An observational prospective study of a group of women attending the Department of Obstetrics and Gynecology at Tishreen University Hospital in Lattakia-Syria during the one-year period (May 2022- May 2023). The inclusion criteria were all women with functional ovarian cysts that measure 4 to 7 cm. The exclusion criteria were the presence of one of the following: cysts greater than 8 cm, corpus luteum cysts, endometrial cysts, cystic ovarian teratoma, women older than 40 years and the presence of cardiovascular diseases. The following data were collected: history and physical examination were performed, as well as pelvic ultrasound for all patients to determine the presence of cysts and their characteristics. Patients were randomized into two groups: group 1 (50 women), who received oral dydrogesterone for 10 days on a dose of 10 mg twice a day (from day 16 to 25 of the cycle) and group 2 (50 women), who received Ethinylestradiol –Drospirenone on the 5th day of menstrual period. A post-treatment follow-up was done every one month for six months regarding alterations in cyst volume, clinical manifestations, and side effects in two groups.

2.2. Ethical Consideration

This study was performed following the Declaration of Helsinki, in which all patients were provided complete informed consent after discussion about the study.

2.3 Statistical Analysis

Statistical analysis was performed by using the IBM SPSS version 20. Basic Descriptive statistics included means, standard deviations (SD), median, Frequency and percentages. Chi-square test was used to examine the relationships between the two groups. Independent student t-tests were used to compare 2 independent groups. Friedman test was used for differences between groups when the dependent variable being measured is ordinal. All the tests were considered significant at a 5% type I error rate ($p < 0.05$), $\beta: 20\%$.

3. Results

A total of 100 women with functional ovarian cysts who were admitted to the Department of Obstetrics and Gynecology were included in the study. Ages ranged from 18 to 40 years (mean 32.41 ± 7.3 years). Age group 35-40 years they have represented the most frequent age group (44%), followed by 30-35 (29%), 25-30 (15%), and 18-25 (12%). Marital status was stratified as married (n: 92 cases) versus single (n: 8 cases). Majority of the women presented with irregularity of menstrual cycle (74%), followed by dysmenorrhea (50%) and amenorrhea (36%). Left-sided cysts (68 cases: 68%) were more frequently found than right-sided

cysts (32 cases: 32%), and cysts were unilateral in 97 cases (97%). Cysts varied in size from 4-5 cm in 78% of the patients to greater than 5 cm in 22%.

Table 1. Demographic and echographic characteristics of the study population

Variables	Result
Age (years)	32.4±7.3
Age group (n,%)	
18-25	12(12%)
25-30	15(15%)
30-35	29(29%)
35-40	44(44%)
Marital status	
Married	92(92%)
Single	8(8%)
Clinical manifestations	
Irregularity of the menstrual cycle	74(74%)
Dysmenorrhea	50(50%)
Amenorrhea	36(36%)
Location of cyst	
Unilateral	97(97%)
Bilateral	3(3%)
Side of cyst	
Right	32(32%)
Left	68(68%)
Cyst volume (cm)	
4-5	78(78%)
>5	22(22%)

Women were divided according to type of therapy into two groups: group 1 included women who received oral progesterone (50 women), and group 2 included women who received combined oral contraceptives (50 women).

The baseline characteristics of the participants were compared between groups (Table 2). There were no significant differences between the two groups regarding age, marital status, and characteristics of cysts (location, volume, side of cysts), $p > 0.05$.

In group 1, the mean age of women was 31.9 ± 6.8 years, and the age group 35-40 years represented the most frequent group (46%), followed by 30-35 (28%), 25-30 (16%) and 18-25 (10%). 90% of the women were married, and cysts were unilateral in 98%, located on the left side in 70%, with a volume of cysts in the range of 4-5 cm in 80% of the patients. In group 2, the mean age of women was 32.1 ± 5.9 years, and the age group 35-40 years represented the most frequent group (42%), followed by 30-35 (30%), 25-30 (14%) and 18-25 (14%). 94% of the women were married, and cysts were unilateral in 96%, located on the left side in 66%, with volume in the range of 4-5 cm in 76% of the patients.

Table 2. Demographic and echographic characteristics of the study population by comparison of the two group

Variables	Group 1	Group 2	p-value
Age (years)	31.9±6.8	32.1±5.9	0.8
Age group(n,%)			
18-25	5(10%)	7(14%)	0.3
25-30	8(16%)	7(14%)	
30-35	14(28%)	15(30%)	
35-40	23(46%)	21(42%)	
Marital status			
Married	45(90%)	47(94%)	0.09
Single	5(10%)	3(6%)	
Location of cyst			
Unilateral	49(98%)	48(96%)	0.9
Bilateral	1(2%)	2(4%)	
Side of cyst			
Right	15(30%)	17(34%)	0.1
Left	35(70%)	33(66%)	
Cyst volume (cm)			
4-5	40(80%)	38(76%)	0.5
>5	10(20%)	12(24%)	

The mean volume of cysts was 5.14±1.3 in group 1 versus 4.98±1.9 in group 2,p:0.2, which decreased significantly in group 1 to 1.8±0.2 after 1 month of treatment and to 1.55±0.1 after 2 months,p:0.0001 versus 1.37 ±0.4 and 1.29±0.1,p:0.0001 respectively in group2.

Table 3. Effects of treatment on cyst volume by comparison of the two group

Variables	Group 1	Group 2	p-value
Cyst volume (cm)			
Before treatment	5.14±1.3	4.98±1.9	0.2
After treatment			
1 month	1.8±0.2	1.37±0.4	0.07
2 months	1.55±0.1	1.29±0.1	0.9
p-value	0.0001	0.0001	

Alterations in cyst volume are represented in Figure 1.

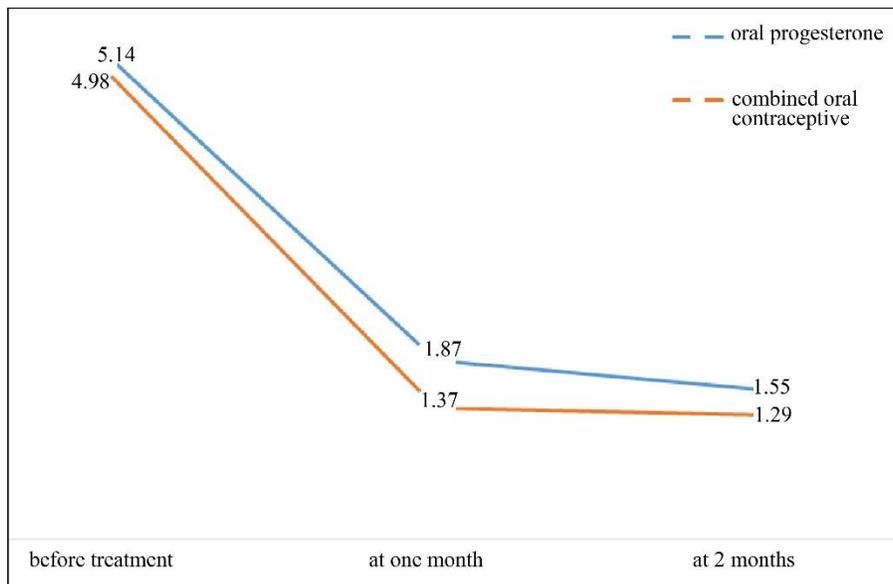


Fig. 1 Effects of treatment on cyst volume by comparison of the two group

Table 4. Effects of treatment on clinical manifestations by comparison of the two groups

Variables	Group 1	Group 2
Clinical manifestations		
Dysmenorrhea		
Before	24(46%)	26(52%)
After	5(10%)	3(6%)
p-value	0.0001	0.0001
Amenorrhea		
Before	19(38%)	17(34%)
After	4(8%)	3(6%)
p-value	0.0001	0.0001
Irregularity of the menstrual cycle	35(70%)	39(78%)
Before	4(8%)	2(4%)
After	0.0001	0.0001
p-value		

Previous findings were represented the Figure (2).

Irregularity of menstrual cycle, dysmenorrhea, and amenorrhea was detected in 70%, 46%, and 38%, respectively, in group 1, which decreased significantly to 8%, 10%, and 8%, respectively after treatment, $p:0.0001$. In group 2, irregularity of the menstrual cycle represented the most frequent clinical manifestation (78%), followed by dysmenorrhea (52%) and amenorrhea (34%), which decreased to 4%, 6% and 6%, respectively, after treatment, $p:0.0001$.

No difference in the resolution of cysts was observed between pre- and post-treatment in the two groups ($p>0.05$). 92% of the women in group 1 experienced resolution of cysts after one cycle, 4% after two cycles and 4% experienced persistence after treatment, whereas the resolution rate was 90% after one month, 6% after two months with persistence of cysts in 4% in group 2.

Table 5. Effects of treatment on resolution of cysts by comparison of the two group

Variables	Group 1	Group 2	p-value
Resolution of ovarian cysts			
After one cycle	46(92%)	45(90%)	0.8
After two cycles	2(4%)	3(6%)	0.1
Persistence of cysts	2(4%)	2(4%)	0.7

Previous findings were represented in the figure(3).

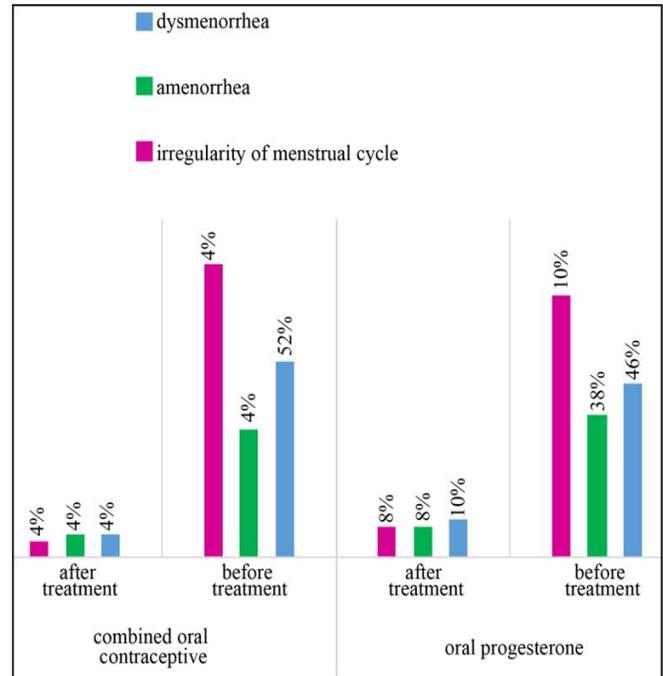


Fig. 2 Effects of treatment on clinical manifestations by comparison of the two group

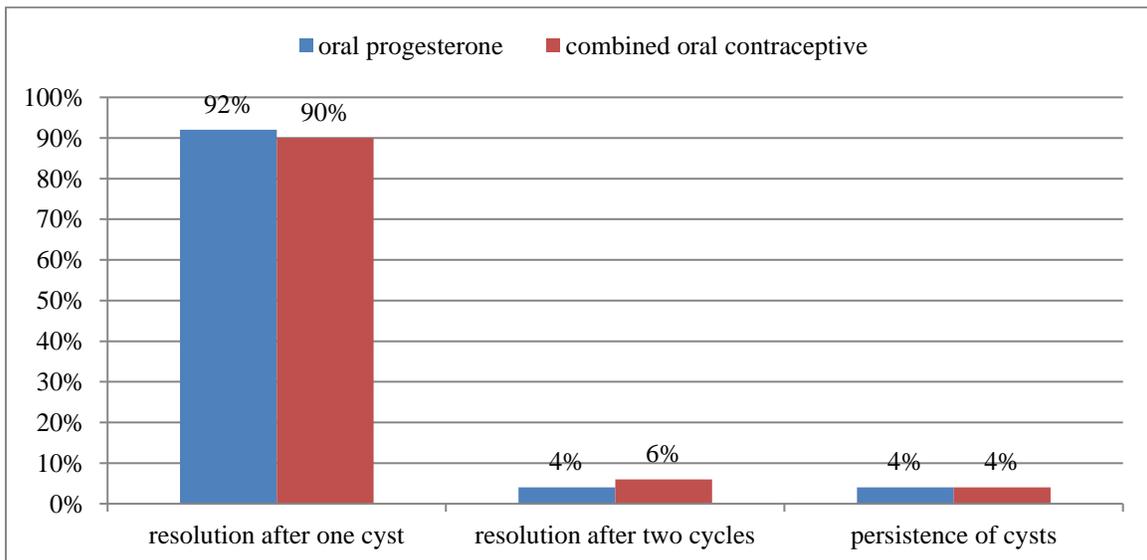


Fig. 3 Effects of treatment on the resolution of cysts by comparison of the two group

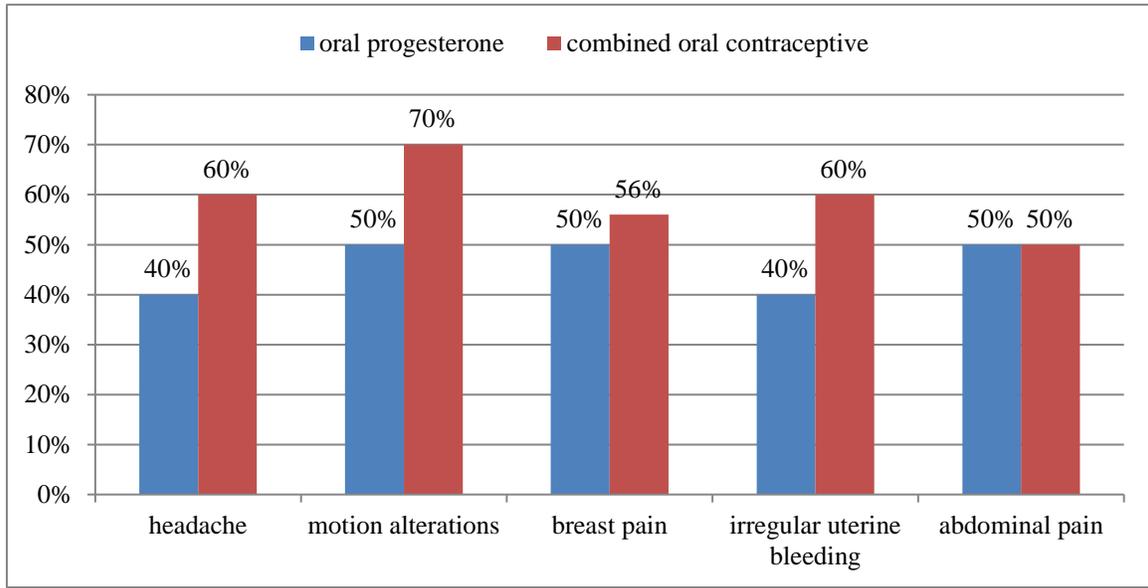


Fig. 4 Side effects of treatment by comparison of the two group

There were no significant differences between two groups regarding side effects(group 1 vs. group 2) as follows; headache(40% vs. 60%,p:0.06), alterations in mood(50% vs. 70%,p:0.05), breast pain(50% vs. 56%,p:0.2), irregular uterine bleeding(40% vs. 60%,p:0.06) , and abdominal pain(50% vs. 50%,p:1).

Table 4. Side effects of treatment by comparison of the two group

Complications	Group 1	Group 2	p-value
Headache	20(40%)	30(60%)	0.06
Motion alterations	25(50%)	35(70%)	0.05
Breast pain	25(50%)	28(56%)	0.2
Irregular uterine bleeding	20(40%)	30(60%)	0.06
Abdominal pain	25(50%)	25(50%)	1

4. Discussion

This observational prospective study in women with proven diagnosis of functional ovarian cysts attending the Department of Obstetrics and Gynecology for one year assessed for efficiency of oral progesterone in the management of cysts versus combined oral contraceptives as well as side effects of treatment in all patients. Our study results demonstrated the following findings: First, age groups (30-35) and (35-40) years represented the most frequent groups, and the majority of the women were married, which cysts can occur at any age but are much more common in women in reproductive age.

Second, the majority of cysts were unilateral and located on the left side in approximately two-thirds of patients. Third, irregularity of the menstrual cycle represented the most

frequent clinical symptom, and there were no statistically significant differences between the two groups regarding demographic characteristics and echographic findings (p<0.05). There was a significant decrease in the size of cysts after one month of the therapy in two groups without the presence of significant differences between them, which might be explained by the important effects of oral hormonal contraceptives in blocking ovulation and preventing new cysts from forming. In addition, there was a significant regression of clinical symptoms in all patients without significant differences between the two groups (p<0.05). Disappearance of cysts was reordered in the majority of patients in two groups after one treatment cycle. Finally, there were no significant differences between the two groups regarding side effects, but headache, alterations in mood, breast pain, and irregular uterine bleeding were occurred more frequently in women who received combined oral contraceptives.

These findings are comparable with a study conducted in Thailand by Sanersak et al. (2006) in 75 women with physiological ovarian cysts who managed either by combined oral contraceptive (33 women) or by expectant management(34 women) that remission rates of cysts were 63.6% in first group and 52.9%in second group after one month and increased to 72.7% and 67.7% respectively after the second month of therapy without significant differences between two groups[20]. Unlike the current study, oral contraceptive compounds did not have significant effects on the resolution rates of cysts in the Sanersak study.

Grimes et al. (2014) demonstrated in an analytical study that included 686 women with ovarian cysts that there were no benefits of oral contraceptives in the disappearance of cysts,

in which the majority of cysts disappeared spontaneously[21]. Unlike the current study, oral contraceptives did not have significant effects on cysts resolution in Grimes study.

Ismael et al. (2019) found in a study that included 96 women with functional ovarian cysts that treatment with combined oral contraceptives led to a significant decrease in cyst size (p:0.0001), menstrual disorders (p:0.0001) with complete disappearance in 94.8% of the patients[22]. There was an agreement between two studies regarding the beneficial effects of oral contraceptive compounds in the management of functional ovarian cysts.

El-Beree et al. (2021) demonstrated in a study conducted on 118 women with ovarian cysts who were managed either by combined oral contraceptive (59 women) or by expectant management(59 women) that there were no significant differences regarding remission rates of cysts between two groups(84.7% versus 78%) [23]. There were no significant advantages for oral contraceptives over expectant management in the management of cysts in the El-Beree study.

Najm et al. (2021) found in a study conducted on 870 women with functional ovarian cysts who were managed either by combined oral contraceptives (435 women) or by expectant management(435 women) that the disappearance

rate of cysts was 79.5% in patients who received contraceptive pills versus 59.5% in another group,p:0.0001[24]. There was an agreement with the current study regarding the beneficial effects of oral contraceptive compounds in the management of functional cysts.

Aly et al. (2022) demonstrated in a study conducted on 90 women with functional ovarian cysts who were managed either by progesterone (45 women) or by placebo (45 women) that the rate of complete resolution of cysts was 57.9% in the progesterone group versus 37.8% in the placebo group,p:0.05[25]. Unlike the current study, oral progesterone did not have significant effects on the resolution of cysts in Aly's study.

5. Conclusion

We can use either oral progesterone or combined oral contraceptive compounds for the management of functional ovarian cysts due to similar efficiency in the resolution of cysts but with favoring oral progesterone because of the low frequency of side effects.

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