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RESEARCH

Difference of Antral Follicle Count Between Users and Non-Users of Hormonal Contraception at M. Djamil Hospital Padang

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Abstract

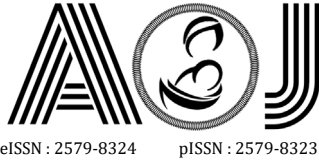
It remains controversial whether antral follicle count is influenced by hormonal contraception.. This study quantified the effect of hormonal contraception on sonographic ovarian reserve markers in 32 users and 32 non-users of hormonal contraception. This was a prospective clinical trial study and has been performed in gynecology Department of M. Djamil Hospital Padang, primary health care March to July 2014. Samples then divided into two groups, group A was users of non hormonal contraception and group B was users of hormonal contraception. On day 2–4 of the menstrual cycle transvaginal sonography was performed and measured repeatedly in the same individual before and after the use of one cycle oral contraceptives (for group B), and on first month and second month (for group A). Statistical analysis to assess significance using the unpaired t test and chi square on SPSS 18.0 for windows. There was no significant association of the antral follicle count between users than non-users of hormonal contraception ($p > 0,05$). There were no significant difference of antral follicle count between users and non- users of hormonal contraception. There were no significant difference of gain score of antral follicle count between users and non-users of hormonal contraception.

Keywords: Antral Follicle Count, Users Of Hormonal Contraception, Non-Users Of Hormonal Contraception

INTRODUCTION

Ovarian reserve is the number and quality of oocytes remaining in the ovary at any one time. Female oocytes reside in follicles, stored in the primordial phase, as ovarian reserves. Total ovarian reserve measurement can only be done histologically.¹

Currently in daily practice various kinds of ovarian reserve tests have been developed to quantitatively assess ovarian reserve, which can generally be divided into 3 groups, namely biochemical examination, provocation test and biophysical test. The first group of biochemical examinations using hormone levels, which is mostly done in the early follicular phase, such as serum FSH, Estradiol (E2), and inhibin B and anti-Müllerian hormone (AMH). The second group of provocative ovarian reserve tests can assess the endocrine response of the ovaries to exogenous stimuli. Examples of dynamic tests are the clomiphene citrate challenge test (CCCT), the exogenous FSH ovarian reserve test and the GnRH agonist



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stimulation test. The third group was biophysical examination with sonographic parameters, such as the antral follicle count (AFC) and ovarian volume measurement.

AMH and AFC are the best parameters for assessing ovarian reserve, but AMH is an invasive (blood serum) test and requires a relatively higher cost, whereas AFC is a non-invasive test and uses a lower cost.^{2,3}

AFC is the number of follicles measuring 2-10 mm which can be calculated using transvaginal ultrasound at the start of the menstrual cycle, i.e. on the first to the fourth day of the menstrual cycle (before the follicles begin to depend on FSH). The number of follicles that can be recruited during folliculogenesis varies widely, decreasing as women age. The rapid decline especially occurs after the age of 35. The number of antral follicles can be affected by age, use of hormonal contraceptives, obesity, use of drugs that are gonadotoxin (smoking, chemotherapy or radiation therapy), ovarian pathology (endometriosis or ovarian cysts), family history with premature ovarian damage. The examination is limited to obese patients, patients with a history of ovarian surgery, pelvic surgery and the presence of fibroids in the uterus (leiomyoma uteri).^{4,5}

The follicles present in the ovaries during a woman's life are not in a fixed number due to the process of follicle growth and apoptosis (programmed cell death). Folliculogenesis from preantral to ovulation takes \pm 85 days, where most of the time it grows without the influence of gonadotropins, then finally reaches the stage of depending on Follicle Stimulating Hormone (FSH) for its development for 14 days, the group of follicles has a different fate, only one follicle (in some cases more than one) may be selected to be the dominant follicle while another, which is unable to respond to FSH, develops atresia under the influence of tumor necrosis factor (TNF).^{4,5,6}

Women of reproductive age need to use contraception for various reasons, including economic reasons, mental readiness, age and health problems. Various contraceptive methods are available depending on the needs and purposes of use. One method of contraception that is easy to use and noninvasive is the Combination Oral Pill (POK).

POK generally contains 28 tablets consisting of 21 tablets of active substances (estrogen and progesterone) and 7 tablets free of active substances (placebo). During the use of POK active substance tablets, gonadotropin (FSH) suppression occurs, so that androgens become dominant and cause degenerative changes. Then during the use of active substance-free tablets it stimulates FSH release due to a decrease in the hormone estrogen. The increased FSH will stimulate the growth and development of follicles, but it cannot take place like normal folliculogenesis because FSH is again suppressed due to the use of new active substance tablets. This process occurs in a reversible manner, where with or without the role of FSH a set of preantral follicles will remain available and develop to a certain stage, and wait to be rescued by FSH before finally experiencing atresia.^{4,5,6}



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The Cochrane review found that with POK administration prior to the start of ovulation induction there was a decrease in AFC and a slight pregnancy rate. This is because these women need higher and longer doses of ovulation induction drugs to achieve pregnancy. 7,8

Based on this problem, there is a gap between theory and reality, so the researchers are interested in further investigating whether there is a difference in the number of antral follicle counts in users of hormonal and non-hormonal contraceptives, given the importance of reproductive function being able to return immediately after the use of hormonal contraceptive pills.

METHOD

This study was conducted using a clinical trial method and a prospective cohort design at the Gynecology Polyclinic Dr. M. Djamil Padang from March to July 2014. The subjects were included in the inclusion criteria and dropped out through the exclusion criteria divided into two groups, group A (non-hormonal contraceptive users), while group B (controls, namely users of hormonal contraceptives).

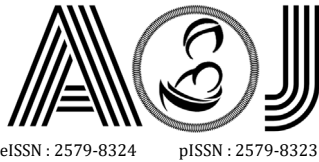
In both groups, the antral follicle count was examined using 2D ultrasonography (Aloka prosound α brand with transvaginal probe) during the early follicular phase (on the second, third or fourth day of the menstrual cycle) of follicles in the left and right ovaries were added up, the results were then recorded. . Group B was given a combined hormonal contraceptive pill containing 30 μ g ethinylestradiol and 150 μ g levonorgestrel produced by Fahrenheit® (21 active tablets and 7 placebo tablets) explained how to use it and asked to bring an empty package to monitor the evaluation of pill use. Subjects in both groups were asked to come back on the second, third and fourth day of the next menstrual cycle for a second antral follicle count examination. Statistical analysis to assess significance used paired t test and chi square on SPSS 18.0 for windows.

RESULTS

After selecting through inclusion criteria and dropping out through exclusion criteria, a sample of 64 people was obtained. Thus the sample size for each group was 32 subjects who were users of hormonal contraceptives and 32 subjects were the control group, namely users of non-hormonal contraceptives.

Differences in the number of antral follicle counts in users of hormonal and non-hormonal contraceptives.**a. Antral follicle counts in hormonal contraceptive users.****Table 1.** Number of antral follicle counts in users of hormonal contraception

	First month antral follicle count	Second month antral follicle count
<i>Mean</i>	$8,96 \pm 1,28$	$8,56 \pm 1,79$



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Based on Table 1., the mean value of antral follicle counts in users of hormonal contraception in the first month is 8.96 ± 1.28 and in the second month is 8.56 ± 1.79 . To test the difference between users of hormonal and non-hormonal contraceptives, it is necessary to look at the distribution and distribution of data whether it is normal or not, if it is normal then it will be tested with a paired t test. The test results for the distribution of users of hormonal and non-hormonal contraceptives showed that the distribution was normally distributed at $P > 0.05$. From the statistical test, it can be concluded that there is no significant relationship between the number of antral follicle counts in the first and second months of hormonal contraceptive users, because it has a P value > 0.05 ($P = 0.263$).

b. Antral follicle counts in non-hormonal contraceptive users.**Table 2.** Number of antral follicle counts in non-hormonal contraceptive users.

	First month antral follicle count	Second month antral follicle count
Mean	$9,37 \pm 2,66$	$9,25 \pm 2,83$

Based on Table 2, the average number of antral follicle counts in users of non-hormonal contraception in the first month was 9.37 ± 2.66 and in the second month it was 9.25 ± 2.83 . To test the differences between users of hormonal and non-hormonal contraceptives, it is necessary to look at the distribution and distribution of data whether it is normal or not, if it is normal then it will be tested by using the paired t t test. The test results of the distribution of users of hormonal and non-hormonal contraceptives showed that the distribution was normally distributed at $P > 0.05$. From the statistical test, it can be concluded that there is no significant relationship between the number of antral follicle counts in the first and second months of non-hormonal contraceptive users, because it has a P value > 0.05 ($P = 0.817$).

c. Differences in the number of antral follicle counts in users of hormonal and non-hormonal contraceptives.

Based on statistical tests in the two groups between users of hormonal and non-hormonal contraceptives, it can be concluded that there is no significant relationship between the number of antral follicle counts in the first month and the two groups, because it has a value of $P > 0.05$ ($P = 0.263$ and $P = 0.817$).

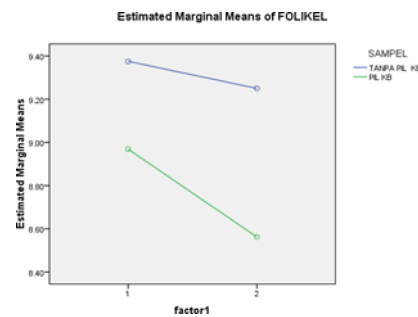


Figure 1. Diagram of the difference in the number of antral follicle counts in users of hormonal and non-hormonal contraceptives.

From Figure 1, it can be seen that the two diagrams between users of hormonal and non-hormonal contraceptives have decreased, but the statistical test results found it was not significant ($P > 0.05$).

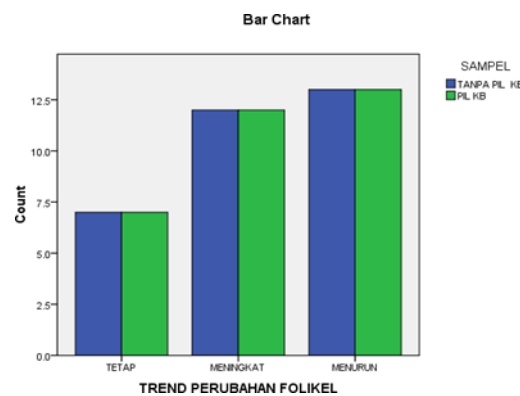


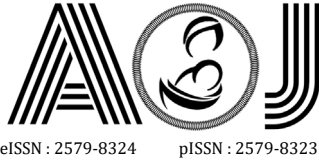
Figure 2. Trend of changes in antral follicle counts in users of hormonal and non-hormonal contraceptives

Figure 2 shows a trend of changes in users of hormonal and non-hormonal contraceptives, as many as 12 respondents using hormonal contraceptives and 12 respondents using non-hormonal contraceptives experienced an increase in the number of antral follicle counts in the first month and second month, and as many as 13 respondents who used hormonal contraception and 13 Respondents who used non-hormonal contraceptives experienced a decrease in the number of antral follicle counts, while 7 respondents who used hormonal contraception and 7 respondents who used non-hormonal contraceptives had a fixed antral follicle count.

d. Difference in gain score The number of antral follicle counts in users of hormonal and non-hormonal contraceptives

Table 3. Gain score for the number of antral follicle counts in users of hormonal and non-hormonal contraceptives.

Observation	Hormonal= (32) (Case)	Non hormonal= (32) (Control)	Significance
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To test the difference between users of hormonal and non-hormonal contraceptives, it is necessary to look at the distribution and distribution of data whether it is normal or not, if it is normal then it will be tested with a paired t test. The test results of the distribution of users of hormonal and non-hormonal contraceptives showed that the distribution was normally distributed at $P > 0.05$. Based on Table 3, it can be concluded that there is no significant relationship in the gain score of the number of antral follicle counts in the second month and the first month, both for hormonal and non-hormonal contraceptive users, because it has a P value > 0.05 ($P = 0.664$).

DISCUSSION**Antral follicle counts in hormonal contraceptive users.**

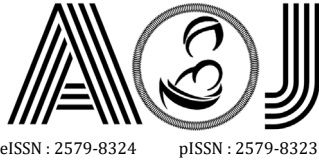
The number of antral follicle counts in hormonal contraceptive users in the first month was 8.96 ± 1.28 and at the second month was 8.56 ± 1.79 . This indicated a decrease in the mean number of antral follicle counts, but this result was not statistically significant with a value of $P > 0.05$ ($P = 0.263$). The decrease that occurred was not significant because in Figure 16 it can be seen that the trend of changes in follicles in users of hormonal contraceptives was varied, some decreased, increased and even persisted.

From several studies, it was stated that there was a decrease in ovarian volume and / or antral follicle count during the use of hormonal contraceptives.⁵

Based on the classic hypothesis by Gougeon (1996), that normal folliculogenesis lasts for 3 months, during which during the initial phase of follicular development is not influenced by gonadotropins and then becomes dependent on gonadotropins at the antral stage.⁵

For hormonal contraceptive users, the influence of estrogen in POK given on the fifth day of the menstrual cycle will suppress gonadotropins (FSH), so that androgens become dominant and cause degenerative changes. Then, during the use of free tablets, active substances stimulate the release of FSH due to a decrease in the hormone estrogen. The increased FSH will stimulate the growth and development of follicles, but it cannot take place like normal folliculogenesis because FSH is again suppressed due to the use of new active substance tablets. This process occurs in a reversible manner, where with or without the role of FSH a set of preantral follicles will remain available and develop to a certain stage, and wait to be rescued by FSH before finally experiencing atresia.^{4,5}

Gonadotropin suppression by POK is similar to childhood in that it is characterized by low gonadotropin levels in the pituitary gland and in the blood, minimal response of the pituitary gland to GnRH and maximal hypothalamic suppression. follicles continue to develop over time and often reach the antral stage, on ultrasound examination can find follicles measuring 2-15 mm.^{4,5}



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Antral follicle counts in non-hormonal contraceptive users.

The number of antral follicle counts in non-hormonal contraceptive users in the first month was 9.37 ± 2.66 and in the second month it was 9.25 ± 2.83 , this indicates a decrease in the mean number of antral follicle counts, but this result was not statistically significant. $P \text{ value} > 0.05$ ($P = 0.263$). The decrease that occurred was not significant because in Figure 2 it can be seen that the trend of changes in follicles in non-hormonal contraceptive users is varied, some are decreasing, increasing and even persisting.

Differences in the number of antral follicle counts in users of hormonal and non-hormonal contraceptives.

From Figure 1, the two diagrams (both hormonal and non-hormonal) show a decrease, but statistical tests found it was insignificant because the $P \text{ value} > 0.05$ (in both groups).

This is in accordance with the classic hypothesis by Gougeon (1996), that normal folliculogenesis lasts for 3 months, during which during the initial phase of follicular development is not influenced by gonadotropins and then becomes dependent on gonadotropins at the antral stage. Meanwhile, the influence of gonadotropins on the development of antral follicles to preovulatory.^{4,5}

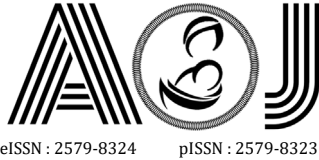
The difference in gain score was the number of antral follicle counts in the first month and the second month in users of hormonal and non-hormonal contraceptives.

From the statistical test, it can be concluded that there is no significant relationship in the difference between the number of antral follicle counts in the second month and the first month for both hormonal and non-hormonal contraceptives users, because it has a $P \text{ value} > 0.05$ ($P = 0.664$).

The mechanisms for determining which follicles and how many follicles will grow on any given day are unknown. So that the number of antral follicles that develop in each cycle is not fixed. Although several studies have shown a decrease in the number of antral follicle counts from 0.35 to 0.95 per year. 4,5,6

CONCLUSION

In this study, the mean value of the antral follicle count in users of hormonal contraception in the first month was 8.96 ± 1.28 and in the second month was 8.56 ± 1.79 , while the mean value of the number of antral follicle counts in users of non-hormonal contraception at month the first was 9.37 ± 2.66 and in the second month it was 9.25 ± 2.83 . There was no difference in the number of calculations and gain scores in users of hormonal and non-hormonal contraceptives.



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