Comparing the Effect of Using Combined Oral Contraceptive, Intrauterine Contraceptive Device and Subdermal Contraceptive Implant on Basal Ovarian Volume: A Longitudinal Prospective Study

KOMBİNE ORAL KONTRASEPTİF, RAHİM İÇİ KONTRASEPTİF ARAÇ VE CİLT ALTI KONTRASEPTİF İMPLANT KULLANIMININ BAZAL OVER VOLÜMÜNE ETKİSİNİN KARŞILAŞTIRILMASI: İLERİYE YÖNELİK İZLEM ÇALIŞMASI

Ali BALOĞLU, MD,[a] Levent KARCI, MD,[a] Burcu ÇETİNKAYA, MD,[a] İncim BEZİRCİOĞLU, MD[a]

Clinic of 1. Obstetrics and Gynecology, İzmir Atatürk Training and Research Hospital, İZMİR

Abstract

Objective: The aim of this study was to compare the effect of using combined oral contraceptive, intrauterine contraceptive device and subdermal contraceptive implant on basal ovarian volume.

Material and Methods: We included to study that 20 oral contraceptive users, 20 intrauterine contraceptive device users and 20 subdermal contraceptive implant users who applied to the Department of Family Planning Izmir Ataturk Educational Hospital. The ovarian volumes were measured before and 6 months after the treatment by ultrasonography. The study groups were investigated for parity, body mass index, and menarchial age in terms of the effects to ovarian volume.

Results: There was a statistically significant correlation between the ovarian volume with age and parity. Ovarian volume was significantly smaller in subdermal contraceptive implant and oral contraceptive groups. There was no statistical difference of ovarian volume in the intrauterine contraceptive device group.

Conclusion: This study showed us that ovarian volume decreases in oral contraceptive and subdermal contraceptive implant users.

Key Words: Contraceptives, oral, combined; intrauterine devices

Özet

Amaç: Bu çalışmada kombine oral kontraseptif, rahim içi kontraseptif araç ve cilt altı kontraseptif implant kullanımının bazal over hacmi üzerine etkisini karşılaştırmak amaçlanmıştır.

Gereç ve Yöntemler: İzmir Atatürk Eğitim ve Araştırma Hastanesi Aile Planlaması ünitesine başvuran 20 kombine oral kontraseptif, 20 rahim içi kontraseptif araç ve 20 cilt altı kontraseptif implant kullanıcısı araştırmaya dahil edildi. Over hacimleri yöntem kullanımına başlamadan önce ve 6 ay sonra ultrasonografiyle ölçüldü. Parite, menarj yaşı, vücut kitle indeksi gibi over hacmini etkileyen parametreler açısından çalışma grupları değerlendirildi.

Bulgular: Over hacmi ile yaş ve parite arasında istatistiksel olarak anlamlı korelasyon saptandı. Kombine oral kontraseptif ve cilt altı kontraseptif implant kullanıcılarında over hacmi anlamlı olarak daha küçük bulundu. Rahim içi kontraseptif araç kullanımıyla over hacimlerinde anlamlı değişiklik saptanmadı.

Sonuç: Bu çalışmada kombine oral kontraseptif ve cilt altı kontraseptif implant kullanıcılarında over hacminin azaldığı gösterildi.

Anahtar Kelimeler: Kombine oral kontraseptif, rahim içi araç

Turkiye Klinikleri J Gynecol Obst 2007, 17:350-355

Geliş Tarihi/*Received:* 27.02.2007 **Kabul Tarihi/*Accepted:*** 19.07.2007

It was presented as a poster at "9th Congress of the EuropenSociety of Contraception."

Yazışma Adresi/*Correspondence:* İncim BEZİRCİOĞLU, MD
İzmir Atatürk Training and Research Hospital
Clinic of 1. Obstetric and Gynecology, İZMİR
drincimbezircioglu@yahoo.com

The measurement of normal ovarian volume variables is important to determine parameters of abnormality. Transvaginal ultrasound is used for detection the changes in ovarian morphology and volume. Ovarian volume and antral follicle count measured by ultrasound was suggested to use very often in recent publications.[1,2]

Several studies have been carried out to establish the relationship between normal ovarian volume and age, menopausal status, and contraceptive methods.[1,3,4] Ovarian volumes were showed unchanged until the age of 39 in reproductive period and decreased progressively in postmenopausal period.[5-7] It may be a relation between ovarian volume and reproductive capacity.

The effects of oral contraceptives and intrauterine contraceptive devices on normal ovarian volume were investigated in various studies.[1,8] In the literature we haven't encountered any study that reflects the effect of subdermal contraceptive implant use on ovarian volume. Our paper is the only study that outlines the effect of subdermal contraceptive implant. The relation between contraceptive methods and ovarian volume may give an estimation later reproductive capacity.

The aim of this study was to compare the effect of using combined oral contraceptive, intrauterine contraceptive device and subdermal contraceptive implant on basal ovarian volume.

Material and Methods

This research was carried out in the Family Planning Department of Izmir Ataturk Educational Hospital from July 2005 to January 2006. The women presenting to our clinic for contraception counseling and use were included in this prospective, cross-sectional study. The participants were randomly selected from the women between 18-30 years of age who wanted to use intrauterine contraceptive device (Multiload 375®, Organon, The Netherlands) or oral contraceptive (Miranova®, Schering Ag-Germany) and subdermal contraceptive implant (Implanon®, NV Organon, oss, The Netherlands). Informed consent was obtained from every participant.

We matched the cases into three groups. In the first group there were 20 cases of oral contraceptive, in the second group 20 cases of subdermal contraceptive implant and in the third group 20 cases of intrauterine contraceptive device users.

The study groups were compared for their age, parity, body mass index (BMI), menarche in terms of the effect to ovarian volume. All women underwent transvaginal ultrasonography performed by using (Schimatzu SDU-450) 4-8 MHz transvaginal probe. The volumes of both ovaries were measured in the early follicular phase (3-5 days of cycle) of the menstrual cycle before treatment and sixth month after treatment. The maximal transverse (D1), anteroposterior (D2), and longitudinal (D3) diameters of the ovary were measured with electronic calipers. Ovarian volume was calculated using the following formula. Volume=D1x D2 xD3 x 0,523. Mean ovarian volumes (MOV) was calculated for both ovaries in the same women MOV: (Right ovarian volume+left ovarian volume)/2

All women had normal menstrual cycles with a mean length of between 24-35 days variably. They all have no contraindications to use contraceptive steroids. Women who had pregnancy in the last 3 months, who received any hormonal contraceptives or who had a history of ovarian surgery or inflammatory pelvic disease were excluded from this study. Women with having an ovarian cyst (larger than 25 mm) or ovarian mass detected by ultrasound or presenting sonographic signs of polycystic ovaries, and also the cases of ovaries that could not be visualized clearly by transvaginal ultrasound were excluded from our study.

We used Miranova® as an oral contraceptive drug, Multiload 375® as an intrauterine contraceptive device, Implanon® as a subdermal contraceptive implant in our study.

Implanon® is a new single rod subdermal contraceptive implant releasing etonorgestrel, the biologically active metabolite of desogestrel. Structurally it is made of 19 nortestesteron and has a high affinity for progesterone receptors in the target tissues. Implanon is primarily an ovulation inhibitor; therefore no ovulation is seen during the first two years of usage. It only suppresses the ovulation but does not effect the ovarian hormonal function.

Miranova® is a combined oral contraceptive drug that contains 0.1 mg levonergestrel+0.02 mg etinilestradiol and has its contraceptive effect by ovulation suppression with cervical changes.

Multiload 375® is an intrauterine contraceptive device that is made of polyetilen and copper wire (surface area 375 mm^2) and has a contraceptive effect by cooper as foreign substance reaction on endometrium.

Statistical analysis was performed using SPSS (The Statistical Package for the Social Sciences-Chicago, IL, USA) version 11.0 for Windows. Wilcoxon test was used to evaluate ovarian volume in each group before treatment and sixth month after treatment.

The relationship of age, menarche, BMI and ovarian volume were assessed by Pearson's correlation analysis. The relationship of parity and ovarian volume were assessed by Spearman's correlation analysis. Kruskal Wallis test was used to compare age, parity, BMI, menarche and ovarian volume. $p< 0.05$ was considered significant.

Results

Table 1 shows the general characteristics (age, menarche, BMI, parity) of the groups. There were no differences between the three groups in terms of age, menarche, BMI, parity and initial ovarian volume (MOV 1). We observed that the mean ovarian volume was 9.09 ± 1.07 cm^3 for the women between 18 and 30 years of age.

Correlation analysis revealed that the initial mean ovarian volume showed the highest negative correlation with age (r:-0.675, p:0.000). Parity was moderately correlated with the initial mean ovarian volume (r:-0.386, p:0.002).

Table 2 shows that the volume of the ovaries was measured before treatment (MOV 1) and 6 months after starting the treatment (MOV 2). MOV 1 was 9.35 ± 1.02 cm^3 in combined oral contraceptive group, 9.07 ± 1.18 cm^3 in subdermal contraceptive implant group and 8.85 ± 1.01 cm^3 in intrauterine contraceptive device group. MOV 2 was 7.27 ± 1.01 cm^3 in combined oral contraceptive group, 7.84 ± 0.73 cm^3 in subdermal contraceptive implant group and 8.88 ± 0.89 cm^3 in intrauterine contraceptive device group.

There was no statistically significant difference between MOV1 and MOV2 in intrauterine contraceptive device group (p: 0.823). As shown in table 2, MOV2 was significantly lower in combined oral contraceptive group and subdermal contraceptive implant group (p:0.0001, p:0.0001)

Table 1. General characteristics (age, menarche, BMI, parity) of the groups.

Variables (means ± SD)	All groups (n: 60)	Combined oral contraceptive (n: 20)	Subdermal contraceptive implant (n: 20)	Intrauterine contraceptive device (n: 20)	P value
Age (year)	23.68 ± 3.06	23.00 ± 3.02	23.90 ± 3.07	24.5 ± 3.11	0.536
Menarche (year)	12.71. ± 0.90	12.65 ± 0.74	12.50 ± 1.00	13.0 ± 0.91	0.254
BMI (kg/m^2)	20.41 ± 3.04.	20.30 ± 3.06	19.90 ± 3.11	21.05 ± 3.01	0.559
Parity	0.85± 0.70	0.75 ± 0.71	1.10 ± 0.64	0.70 ± 0.73	0.135
MOV1 (cm^3)	9.09 ± 1.07	9.35 ± 1.02	9.07 ± 1.18	8.85 ± 1.01	0.364

BMI: Body mass index MOV1: Initial ovarian volume Means ± SD: Means ± Standard deviation

Table 2. The volume of the ovaries before (MOV1) and sixth months after treatment (MOV2).

Ovarian volumes	Combined oral contraceptive (n: 20)	Subdermal contraceptive implant (n: 20)	Intrauterine contraceptive device (n: 20)
MOV1 (cm^3)	9.35 ± 1.02	9.07 ± 1.18	8.85 ± 1.01
MOV2 (cm^3)	7.27 ± 1.01	7.84 ± 0.73	8.88 ± 0.89
P values	**0.0001**	**0.0001**	0.823

Discussion

In this study we investigated the effects of oral contraceptive, subdermal contraceptive implant and intrauterine contraceptive device usage on ovarian volume.

Right and left ovarian volumes were measured by transvaginal ultrasound. Right and left ovarian volumes were averaged to generate only a single ovarian volume. Because there was no statistically significant difference between the ovaries in terms of volumes as also reported by other studies.[3,9] Similarly Andolff et al. and Merce et al. did not observe a statistically significant difference in right and left ovarian volume.[9,10]

We observed that the mean ovarian volume was 9.09 ± 1.07 cm^3 for the women between 18 and 30 years of age. van Nagell et al. found that average ovarian volume is 6.83 cm^3 after age 40, Granberg and Wikland found that average ovarian volume is 5.1 ± 3.1 cm^3 after age 29.[11,12] In these studies mentioned above; most of the patients were over 30 years of age. Tufan et al. found that average ovarian volume is 9.00 ± 3.3 cm^3 before age 26.[13] Our results were consistent with Tufan et al's study.

In our study, we also observed that the ovarian volumes decrease significantly with increasing age and parity**.** Opperman et al found that there is a negative correlation between FSH, age and ovarian volume.[6] Merz et al. found no correlation between parity, age and ovarian volume in 155 premenopausal women aged 16-52.[4] Faddy and Gasden Tepper et al. found correlation between ovarian age and small ovarian volume, follicle count.[5,14]

We haven't found any correlation between MOV 1 and BMI. The studies in the literature showed that ovarian volume wasn't correlated with BMI.[6-8]

In our study group who were using combine oral contraceptive, we observed a significant decrease in the ovarian volume six months after the beginning of the treatment. Our results were similarly to Christensen JT and Metha EA studies.[8,15]

In our study group patients who were using subdermal contraceptive implant, we observed a significant decrease in the ovarian volume 6 months after treatment. In the literatures we haven't encountered any study that inspects the effect of subdermal contraceptive implant over the ovarian volume. Our study is the first one that searches the effect of subdermal contraceptive implant over the ovarian volume.

In the previous studies, with the use of etonorgestrel FSH was found to be increasing in the first weeks of menstruel cycles. Estradiol, LH and progesterone were found to be decreasing for the whole cycles. These results all showed the ovulation suppression.[16,17] Combine oral contraceptive and subdermal contraceptive implant might be decreasing the ovarian volumes by making ovulation suppression.

Combined oral contraceptive and subdermal contraceptive implants inhibits the hypotalamo-hypophiser system. Because of the FSH and LH decrease, indirectly follicles become smaller and low in maturation. These are the causes of small ovarian volume. Fleisher and Kepple et al found that ovaries that consist of mature follicles are 2 times bigger than these that haven't got any mature follicles. They also showed that the ovaries become smaller in the postmenopausal period.[18]

Christensen et al. found a positive correlation between the use of intrauterine contraceptive device and the ovarian volumes. They suggest that ovarian volume increase may be due to the pelvic infections that were took place before.[8] Goldstuck suggested that the increasing ovarian volume in patients who were using intrauterine contraceptive device is due to the direct or local stimulation of ovaries by the pineal gland.[19]

An intrauterine contraceptive device causes biological foam that consists of fibrin bundle, phagocyte cells and proteolitical enzymes. Intrauterine contraceptive devices made of copper, which releases small amount of metal continuously causes more inflammatory response. All type of intrauterine contraceptive devices induces smooth cell muscle contractions and increased prostaglandin secretion that stimulates inflammatory process in the endometrial surface.[20] In our study;

we found an increased ovarian volume among the intrauterine contraceptive device users, but this was not a significant increase. The patients with previous history of pelvic infection were excluded.

Both combined oral contraceptive and subdermal contraceptive implant have an effect over cervical mucus because of progesterone component. Increase in the density and change the structure of cervical mucus causes difficult sperm penetration and decrease the possibility of ascendance infections and irritations. Decrease of irritant factors that reaches ovaries can be the cause of decreasing ovarian volume indirectly. This situation can be the cause of the difference of ovarian volume between the intrauterine contraceptive device group with combined oral contraceptive group and subdermal contraceptive implant group.

In conclusion, this study showed us that ovarian volume decreases in combined oral contraceptive and subdermal contraceptive implant users. There were no correlation between the intrauterine contraceptive device and ovarian volume. Ovarian volume decreased with age and parity but no association was observed between ovarian volume and body mass index and menarche.

Assessment of the ovarian volumes by the use of ultrasound may be a way to estimate the reproductive status of woman. Age related decline in antral follicle count can be considered to reflect the loss of reproductive potential.[21] Transvaginal ultrasound assessment of ovarian volume is a practical and cost effective technique for ovarian reserve testing.[22]

Ovarian volume measurement was reported to be an effective method to detect the potential of fertility and reproductive age.[23-25] Information about the effects of contraceptive methods on ovarian volume will let fertility potential be better estimated. According to current knowledge, it is not necessary to measure ovarian volumes before and during the use of contraceptive methods.

However, for women with very small basal ovarian volume and wish to have a baby in the future, it may be warning for fertility capacity to learn the ovarian volume before the usage of contraceptive methods. Also, to know the effects of contraceptive methods on ovarian volumes will help to evaluate the cases with small ovarian volumes for various causes.

REFERENCES

1. Nevin S, Merih B, Mansur K, Senol B, Sevda Y. Contraceptive methods and ovarian volume in healthy women. T Clin J Gynecol Obst 2000;10:174-7.
2. Granberg S, Wikland M. Comparison between endovaginal and transabdominal transducers for measuring ovarian volume. J Ultrasound Med 1987;6:649-53.
3. Higgins RV, Van Nagell JR, Woods CH, Thompson EA, Kryscio RJ. Interobserver variation in ovarian measurements using transvaginal sonography. Gynecol Oncol 1990;39:69-71.
4. Merz E, Miri-Tesanic D, Bahlmann F, Weber G, Wellek S. Sonographic size of uterus and ovaries in pre and postmenopausal women ultrasound. Obstet Gynecol 1996;7:38-42.
5. Tepper R, Zalel Y, Markov S, Cohen I, Beyth Y. Ovarian volume in postmenopausal age. Acta Obstet Gynecol Scand 1995;74:208-11.
6. Opperman K, Fuchs SC, Spritzer PM. Ovarian volume in pre-and perimenopausal women: a population-based study. Menopause 2003;10:209-13.
7. Cohen HL, Tice HM, Mandel FS. Ovarian volume measured by US: Bigger than we think. Radiology 1990;177: 189-92.
8. Christensen JT, Boldsen J, Westegaard JG. Ovarian volume in gynaecological healthy women using no contraception or using IUD or oral contraception. Acta Obstet Gynecol Scand 1997;76:784-9.
9. Andolf E, Jorgensen C, Svalenius E, Sundan B. Ultrasound measurement of the ovarian volume. Acta Obstet Gynecol Scand 1987;66:387-9.
10. Merce LT, Andrino R, Barco MJ, Dela Fuente F. Cyclic changes of the functional ovarian compartments; Echo graphic assessment. Acta Obstet Gynecol Scand 1990;69: 327-32.
11. van Nagell JA Jr, Higgins RV, Donaldson ES, Gallion HH, Powell DE. Transvaginal sonography as a screening method for ovarian cancer. A report of the first 1000 cases screened. Cancer 1990;65:573.
12. Granberg S. Wikland M. Comparison between endovaginal and transabdominal transducersfor measuring ovarian volume. J Ultrasound Med 1987;6:649-53.
13. Tufan E, Etler K, Durmusoglu F. Assessment of reproductive ageing patterns by hormonal and ultrasonographic ovarian reserve tests. Hum Reprod 2004;19:2484-9.
14. Faddy MJ, Gosden RG. A model confirming the decline in follicle numbers to the age of the menopause in women. Hum Reprod 1996;11:1484-6.
15. Metha EA, Matwijiw I, Lyons EA, Faimann C. Noninvasive diagnosis of resistant ovary syndrome by ultrasonography. Fertil Steril 1992;57:56-61.
16. Mulders TM, Dieben TO, Bennink HJTC. Ovarian function with a novel combined contraceptive ring. Hum Reprod 2002;17:2594-9.

17. Davies GC, Feng LX, Newton JR, Van Beek A, Coelingh-Bennink HJ. Release characteristics, ovarian activity and menstrual bleeding pattern with a single contraceptive implant releasing 3-ketodesogestrel. Contraception 1993;47:251-61.
18. Fleisher AC, Kepple DM. Normal pelvic anatomy and scanning techniques in: Transvaginal sonography. 2nd ed. Philedelphia: JB Lippincott Company; 1995. p.21-35.
19. Goldstuck ND. Do plain plastic and copper bearing intrauterine contraceptive devices have a control mechanism of action? Med Hypotheses 1987;23:125-30.
20. El Badrawi HH, Hafez ES, Barnhard MI, Fayad M, Shafeek A. Ultrastructural changes in human endometrium with copper and nonmedicated IUD's in utero. Fertil Steril 1981;36:41-9.
21. Bastos CA, Opperman K, Fuchs SC, Donato GB, Spritzer PM. Determinants of ovarian volume in pre-menopausal transition, and post-menopausal women: A population-based study. Maturitas 2006;53:405-12.
22. Erdem M, Erdem A, Biberoğlu K, Arslan M. Age-related changes in ovarian volume, antral follicle counts and basal follicle stimulating hormone levels: Comparison between fertile and infertile women. Gynecol Endocrinol 2003;17: 199-205.
23. Scheffer GJ, Broekmans FJM, Looman CWN, Blankenstein M, Fauser BCJM, deJong FH, teVelde ER. The number of antral follicles in normal women with proven fertility is the best reflection of reproductive age. Hum Reprod 2003;18:700-6.
24. Wallace WH, Kelsey TW. Ovarian reserve and reproductive age may be determined from measurement of ovarian volume by transvaginal sonograpy. Hum Reprod 2004;19: 1612-7.
25. Scheffer GJ, Broekmans FJM, Dorland M, Habbema JDF, Looman CWN, teVelde ER. Antral follicle counts by transvaginal sonograpy are related to age in women with proven natural fertility. Fertil Steril 1999;72:845-51.