

HJOG 2018, 17 (1), 1-8

Effects of oral contraceptives to bone mineral density of young women

Ververidou Niki¹, Servitzoglou Nafsika-Georgia², Siountas Anastasios²,
Vavilis Dimitrios³, Rouso David⁴, Karagiannis Vasileios⁴

¹Department of Obstetrics and Gynecology, School of Medicine, Faculty of Health Sciences, Aristotle University of Thessaloniki, Thessaloniki, Greece

²Medical Physics Laboratory, School of Medicine, Faculty of Health Sciences, Aristotle University of Thessaloniki, Thessaloniki, Greece

³1st Department of Obstetrics and Gynecology, School of Medicine, Faculty of Health Sciences, Aristotle University of Thessaloniki, Thessaloniki, Greece

⁴3rd Department of Obstetrics and Gynecology, School of Medicine, Faculty of Health Sciences, Aristotle University of Thessaloniki, Thessaloniki, Greece

Correspondence

Ververidou Niki, 106 Egnatias str, 54622, Thessaloniki Greece, 0030 6974934524, e-mail: nikiververidou@gmail.com

Abstract

The influence of consumption of contraceptives to female body's hormones could affect bone formation. The purpose of this study was to assess any possible change in bone density of young women who were taking oral contraceptives, compared with those who were not. Women who participated in this study were 18-25 years old and were divided into two groups, experimental and control. Contraceptive tablets containing 20 µgrs ethinyl estradiol and 3 mgr drospironone were given to women of the experimental group for 21 days. Data necessary for every woman was recorded (weight, height, gynecological age, chronological age). Bone density was measured at the lumbar spine [O2-O4] and femoral neck with the DEXA method [DMS Challenger]. Measurements were taken at the beginning of the study and after the period of 12 and 24 months. Our study concluded that oral contraceptive use did not cause any significant change to bone density group of young women.

Key words: Hormonal oral contraceptive, ethinyl-estradiol, drospironone, bone mineral density, Dual Energy X-ray Absorptiometry

Introduction

To study the correlation between the use of oral contraceptives and the change in bone mineral density, female population is usually divided into three

age groups, in that of minors between 12-19 years old, young adults between 21-35 years, and women who are in menopause. This division facilitates the analysis

Table 1. Date of birth and BMD values (gr/cm²) in the area of the lumbar spine during the two years of study, for the experimental group.

Date of birth	BMD (gr/cm ²)		
	0	12 months	24 months
13/7/1989	1,056	1,092	1,085
13/5/1987	1,089	1,083	1,099
12/6/1987	1,155	1,182	1,221
12/12/1987	1,177	1,190	1,212
15/12/1986	1,183	1,206	1,111
12/3/1988	1,069	1,082	1,101
2/1/1987	0,962	0,970	1,003
26/7/1986	0,978	1,010	1,018
30/6/1987	1,063	1,255	1,269
31/3/1988	1,237	1,080	1,106
5/8/1987	1,122	0,965	1,152
31/8/1987	1,120	1,040	1,060
21/8/1987	1,021	1,039	1,059
4/9/1987	1,022	1,038	1,062
8/9/1988	1,023	1,037	1,065
2/10/1989	1,016	1,040	1,060
8/8/1989	1,019	1,025	1,049
23/12/1986	1,033	1,056	1,074
6/9/1988	1,031	1,055	1,070
31/7/1988	1,029	1,056	1,072
5/5/1987	1,033	1,055	1,077
23/8/1989	1,029	1,001	1,077
12/1/1988	1,029	1,049	1,075
22/7/1987	1,100	1,123	1,146
23/8/1989	1,101	1,121	1,156
20/1/1988	1,115	1,126	1,139
5/4/1988	1,020	1,054	1,077
12/3/1988	1,069	1,095	1,101
13/5/1987	1,089	1,083	1,109
5/6/1988	1,114	1,133	1,158

because the results differ depending on each group¹.

Regarding juvenile females, in their majority, there is a correlation between the use of contraceptive pills and the reduction of bone density. According to the literature, the most sensitive and prone period of woman age with respect to changes in bone density, is the first three years after the start of menstruation. However, it has not been fully clarified, whether and how the influence of oral contraceptives, on the decrease in bone mineral density

of young women, is associated with the duration of the treatment and the type of contraceptive treatment received².

On the contrary, for the second group of healthy young women 21-35 years old, all surveys agree on the result that no correlation was found. It is interesting that the same conclusion was independent of the type and duration of the contraceptive regimen^{3,4,5,6,7}.

For women in menopause, oral contraceptives

Table 2. Date of birth and BMD values (gr/cm²) in the area of the femoral neck during the two years of study, for the experimental group.

Date of birth	BMD (gr/cm ²)		
	0	12 months	24 months
13/7/1989	1,177	1,188	1,204
13/5/1987	1,135	1,185	1,273
12/6/1987	0,940	0,949	0,973
12/12/1987	0,943	0,954	0,976
15/12/1986	0,948	0,958	1,237
12/3/1988	1,203	1,215	1,235
2/1/1987	0,805	0,805	0,836
26/7/1986	0,833	0,840	0,858
30/6/1987	0,945	1,017	1,039
31/3/1988	1,009	0,955	0,972
5/8/1987	1,029	1,101	1,685
31/8/1987	0,990	1,000	1,019
21/8/1987	0,982	0,99	1,020
4/9/1987	0,977	0,99	1,022
8/9/1988	0,993	1,001	1,025
2/10/1989	0,952	1,003	1,024
8/8/1989	1,002	1,009	1,021
23/12/1986	0,971	0,983	1,001
6/9/1988	0,969	0,982	1,002
31/7/1988	0,980	0,980	1,005
5/5/1987	0,978	0,981	0,998
23/8/1989	0,992	0,986	1,019
12/1/1988	0,983	1,002	1,022
22/7/1987	0,984	0,99	1,009
23/8/1989	0,971	1,002	1,008
20/1/1988	1,001	1,009	1,031
5/4/1988	0,988	0,985	1,005
12/3/1988	1,203	1,100	1,237
13/5/1987	1,193	1,185	1,229
5/6/1988	0,987	1,005	1,025

appear to have effects on bone density. Specifically, it has arisen from investigators, that taking contraceptives affected the bone metabolism and prevented the decrease of bone density.

This study investigates whether the administration of hormonal contraception in women 21-25 years old affects the bone density of the skeleton. This age was chosen because at that period bone density reaches maximum peak values.

Material and methods

Selection and sample collection

The study started in December 2009, at Hippocratio General Hospital of Thessaloniki when the first volunteers began to participate.

The choice of surveyed women was random. All participants were divided, by the method of lottery, into the experimental and the control group. Contraceptive pills containing 20 micrograms ethinyl estradiol and 3 mg drospirone were given to the

Table 3. Date of birth BMD values (gr/cm²) in the area of the lumbar spine during the two years of study for the control group.

Date of birth	BMD (gr/cm ²)		
	0	12 months	24 months
12/3/1988	1,069	1,100	1,101
13/5/1989	1,029	1,069	1,091
12/5/1986	1,068	1,089	1,093
12/5/1986	1,068	1,082	1,093
13/4/1988	1,069	1,099	1,109
2/9/1987	0,999	1,035	0,999
2/2/1989	0,980	1,02	1,044
22/11/1988	1,100	1,131	1,140
13/5/1987	1,021	1,029	1,055
14/6/1986	1,100	1,122	1,142
15/8/1987	1,050	1,075	1,094
14/2/1986	1,171	1,200	1,206
9/9/1990	1,101	1,125	1,114
4/5/1988	1,031	1,046	1,071
7/11/1986	1,033	1,044	1,077
18/11/1988	1,099	1,131	1,142
23/1/1987	1,032	1,041	1,075
1/8/1985	1,111	1,131	1,155
22/10/1989	1,112	1,132	1,156
11/11/1988	1,112	1,132	1,156
3/2/1988	1,177	1,194	1,200
9/8/1988	1,011	1,039	1,077
17/6/1986	1,008	1,019	1,043
1/8/1986	1,069	1,097	1,105
25/4/1989	1,097	1,130	1,144
29/3/1988	1,050	1,121	1,143
31/3/1989	1,098	1,132	1,147
14/12/1988	1,066	1,095	1,101
19/4/1988	1,097	1,132	1,141
22/4/1988	1,048	1,074	1,094
8/5/1988	1,100	1,123	1,111
18/4/1990	0,981	1,129	1,133
19/12/1986	1,029	1,070	1,090
25/7/1988	1,113	1,131	1,154
29/3/1988	1,050	1,121	1,143
8/9/1988	1,032	1,055	1,079
16/7/1989	1,115	1,139	1,159

experimental group for 21 days.

The initial number of women participated in the study was 130 (experimental group, n = 65 and control group, n = 65). The final number of women who

completed the study and provided reliable results was much smaller, reaching the number of 67. This reduce was mainly due to the fact that many women were not consistent in study's programme, and thus

Table 4. Date of birth and BMD values (gr/cm²) in the area of the femoral neck during the two years of study for the control group.

Date of birth	BMD (gr/cm ²)		
	0	12 months	24 months
12/3/1988	1,203	1,211	1,237
13/5/1989	1,085	1,190	1,204
12/5/1986	1,183	1,192	1,090
12/5/1986	1,183	1,192	1,218
13/4/1988	1,102	1,173	1,229
2/9/1987	0,838	0,868	0,893
2/2/1989	0,920	0,944	0,988
22/11/1988	0,970	0,987	0,999
13/5/1987	0,990	1,00	1,011
14/6/1986	1,09	1,104	1,123
15/8/1987	0,99	0,981	1,017
14/2/1986	0,960	0,968	0,987
9/9/1990	1,001	1,010	1,031
4/5/1988	0,966	0,977	0,992
7/11/1986	0,961	0,975	0,991
18/11/1988	0,950	0,943	0,978
23/1/1987	0,960	0,977	0,992
1/8/1985	0,97	0,980	0,999
22/10/1989	0,98	0,988	0,989
11/11/1988	0,988	0,999	1,099
3/2/1988	0,944	0,955	0,971
9/8/1988	0,90	0,976	0,991
17/6/1986	1,003	1,015	1,048
1/8/1986	1,101	1,170	1,222
25/4/1989	0,949	0,944	0,976
29/3/1988	0,989	1,102	0,977
31/3/1989	0,949	0,941	0,977
14/12/1988	1,098	1,100	1,137
19/4/1988	0,947	0,942	0,976
22/4/1988	0,968	1,099	1,016
8/5/1988	1,000	1,009	1,029
18/4/1990	1,002	1,009	1,035
19/12/1986	1,083	1,189	1,201
25/7/1988	0,977	0,998	1,005
29/3/1988	0,989	1,102	0,977
8/9/1988	0,970	0,980	1,002
16/7/1989	0,993	1,022	1,032

excluded, or they retired from the study.

Recording history of participants

Each woman's medical history was recorded and

all information potentially useful for the completion of the study was gathered. The weight and height of participants using electronic scales and tape respectively were measured and the body mass index

was calculated. Gynaecological age, i.e. years from menarche, the type of menstruation, menstrual symptoms, physical activity, eating habits and the use of vitamin D were acquired.

Type and number of tests

Bone mineral density was measured of the lumbar spine [level O2-O4] and femur neck with a bone density scanner (DMS Challenger) using the Dual EnergyX Ray Absorptiometry (DEXA) method. The results were expressed as Bone Mineral Density (BMD), gr/cm². Identical measurements were repeated in both groups after 12 and 24 months.

Scale and accuracy of clinical parameters of bone density scanner

Bone density measurements using the bone density scanner can be applied to women aged between 15-95 years and weighting up to 200 kg. The measured value of BMD may range from 0.3 to 1.4 with accuracy $\pm 1,5\%$ in vivo ($\pm 1,0\%$ in vitro).

Results

1. Experimental and control groups

The number of women finally included in this study was sixty seven. Thirty seven did not take contraceptive pills, while thirty took the pill for the entire period of investigation. All women were 20-25 years old.

Women in both groups, experimental and control, were subjected to bone density measurements of the lumbar spine and femoral neck for two consequent years. The first measurement was performed at the beginning of the study and before the administration of oral contraceptives. The following measurements were performed once a year, for the next two years. The results of the three measurements of bone density in both anatomical areas, expressed as BMD (gr/cm²) are presented by group in the following tables.

The date of birth and the BMD (gr/cm²) at the begging of the study and at twelve and twenty four months afterwards, of the experimental group, are shown in Table 1.

In Table 2, similar results for the femoral neck are presented.

The date of birth and the BMD (gr/cm²) at the begging of the study and at twelve and twenty four months afterwards, of the control group, are shown in Table 3.

In Table 4, similar results of the control group for the femoral neck

2. Statistical treatment results

Statistical analysis of the measurements was made using the spss program.

2.1. Distribution normality check

Statistical Package of the SocialSciences (SPSS) 17.0 Software was used for the statistical analysis. Quantitative variables were tested for normal distribution by Kolmogorov- Smirnov Test.

The statistical normality test showed no significant difference. Therefore, it is concluded that the values of the measured parameters did not follow a normal distribution and thus nonparametric tests should be applied in order to perform statistical analysis of the results.

2.2. Bone's density changes check

The non-parametric test Wilcoxon Signed Ranks was applied, to check whether there is a statistically significant change in bone density during the two years of the survey for the two participant groups. Both groups appeared statistically significant increase in bone density, during each of the two years of study.

Specifically, twenty-seven women over thirty, of the experimental group showed an increase in their bone density during the two years of study.

All thirty seven women of the control group showed an increase in bone density during the same period.

Besides, the non-parametric Mann-Whitney test was applied to compare the increase of bone density between the experimental group and the control group.

The two groups compared with Mann-Whitney U test. The differences in the increase of bone density during the study were not statistically significant between the two groups.

Conclusions

The goal of this study was to check, whether the administration of hormonal contraception in women 20-25 years old, affects the bone density of the skeleton. This age was chosen because at that period the female skeleton reaches the maximum bone density values.

Originally surveyed 130 women aged 18 to 25. Participants divided into two groups, the control group and the experimental who received oral contraceptives according to the standard treatment. Finally, the examination of 67 women gave comprehensive and conclusive results. The 37 women were in the control group while 30 in the experimental group.

From the results and their statistical processing and analysis, it was concluded that:

All women who participated, whether they were treated with contraceptive tablet or not, showed in the majority, an increase of bone density during the two years following the start of the study. This result was expected, since according to the literature, all women 18-25 years old were at the age in which, the bone mineral density of the human skeleton is increasing.

In the vast majority, the increase of bone density was found in both measured anatomical regions.

The statistical check, whether the contraceptives caused a change in the bone density increase rates

resulted negative. The control group showed the same increase in bone density over two years with that of the experimental group.

Therefore, the use of birth control pills caused no inhibition or enhancement of the increase in bone density.

The results of this study involving young women between the ages of 20-35 are in full agreement with the international literature.

Conflict of interest

There is no conflict of interest.

References

1. Trémollières F. Impact of oral contraceptive on bone metabolism. *Best Pract Res Clin Endocrinol Metab* 2012; 27(1):47-53.
2. Gai L, Jia Y, Zhang M, Gai P, Wang S, Shi H, Yu X, Liu Y. Effect of two kinds of different combined oral contraceptives use on bone mineral density in adolescent women. *Contraception* 2012;86(4):332-6.
3. Di Carlo C, Gargano V, Sparice S, Tommaselli GA, Bifulco G, Schettino D, Nappi C. Short-term effects of an oral contraceptive containing oestradiol valerate and dienogest on bone metabolism and bone mineral density: an observational, preliminary study. *Eur J Contracept Reprod Health Care* 2013;18(5):388-93.
4. Sordal T, Grob P, Verhoeven C. Effects on bone mineral density of a monophasic combined oral contraceptive containing norgestrel acetate/17 β -estradiol in comparison to levonorgestrel/ethinylestradiol. *Acta Obstet Gynecol Scand* 2012;91(11):1279-85.
5. Wei S, Jones G, Thomson R, Dwyer T, Venn A. Oral contraceptive use and bone mass in women aged 26-36 years. *Osteoporos Int* 2010;22(1):351-5.
6. Wei S, Winzenberg T, Laslett LL, Venn A, Jones

G. Oral contraceptive use and bone. *Curr Osteoporos Rep* 2011;9(1):6-11.

7. Young D, Hopper JL, Nowson CA et al Determinants of bone mass in 10 to 26 year old females: A twin study. *J Bone Miner Res* 1995;10 : 558-67.

Received 19-1-2017

Revised 20-2-2017

Accepted 27-2-2017