The Effect of Oral Contraceptive Pill on Cortical Thickness and Bone Mineral Density of The Mandibular Mental and Gonial Regions in Premenopausal Females Using Spiral Computed Tomography

Israa K. Farhood B.D.S.D.D.S [1]
Ahlam A. Fatah B.D.S; MSc. [2]

ABSTRACT:

Background: Prolonged use of low-dose estrogen "20 micrograms or less" Combined oral contraceptive pill (that have estrogen and progesterone steroid hormone) had an effect on bone turnover .Bone mineral density is used in clinical medicine as an indirect indicator of osteoporosis and fracture risk.

The aim of the study: The aim of this study was to investigate the effect of low dose oral contraceptive pill on the cortical thickness (in millimeter) and bone mineral density at the mandibular cortex of mental and gonial regions in Hounsfield unit(HU) using spiral computed tomography.

Material and method: This prospective study was conducted on computed tomographic image of 100 women aged between (20-40) years .The collected sample includes patients attended for different diagnostic purposes to AL-Shaheed Al-Seder Teaching General Hospital of Al-Najaf AL-Ashraf from Julay, 2015 to May 2016.Data were grouped into two categories :group (1)control group (don't use combined oral contraceptive pill) (n=50);group(2)women taking low dose(20microgram) combined oral contraceptive pill for more than 2 years,(n=50).Cortical thickness measured in millimeter and Bone Mineral Density measured in Hounsfield unit both in mental foramen and gonial angle regions .Physical activity number of parity type of lactation were documented by questionnaire.

Result: There was a statically significant difference; in cortical thickness p=0.037 and bone mineral density P=0.007 in mental area between the two groups ;the lowest mean in group (2)and highest mean in group(1) . After adjustment for age ,number of parity, and physical activity measurement scores ,there was a significant difference p=0.001 in mean of bone mineral density and p=0.065 for cortical thickness of gonial angle between the two groups ;the highest mean in group (1) and lowest mean in group (2).

CONCLUSION: Computed tomography is a good diagnostic method to measure the value of cortical thickness and bone mineral density simultaneously in mental and gonial region of the mandible in premenopausal female using low dose combined oral contraceptive pill which have small effect on bone ;depended on the woman's age and the duration of using the pill ;that did not appear until about two years of use.

Keywords: combined oral contraceptive pill .Bone mineral density ,cortical thickness ,CT scan. **(J Bagh Coll Dentistry 2017; 29(4): 37-43)**

INTRODUCTION:

Estrogen and progesterone are both female hormones generated in the ovaries and play an important role in maintaining a healthy pregnancy and carrying the fetus to term The estrogenic hormones are accountable for the growth and development of female sexual characteristics, during adolescence and pregnancy**.** they participate significantly to bone health and preventing bone loss.[1]

Estrogen with well recognized beneficial effects on bone mass and plays a critical role in skeletal homoeostasis ;it exerts effects on the function of both osteoclast and osteoblast, at the cellular level, resulting in tonic inhibition of bone turnover and maintenance of the balance between bone resorpsion and bone formation[2]. Estrogen mediate indirect actions on bone through its effects on hormones, such as calcitonin , parathyroid hormone, cytokines and growth factors.[3].

Progesterone has bone-forming activity by binding to receptors on the osteoblasts ,it has the ability to increase osteoblast numbers as well as its effects to promote osteoblast maturation and differentiation .Progesterone appears to play physiological role in partnership with estrogen in achieving optimal peak bone mass. The effects of progesterone and estrogen on bone are synergistic and complementary to each other .[4]

(1) Master student, Department of Oral and maxillofacial Radiology, College of Dentistry, University of Baghdad.
(2) (2) Assist. Professor, Department Oral and maxillofacial Radiology, College of Dentistry, University of Baghdad.

A biological relationship of bone density to estrogen that is easily observed during menopause [5]. The relationship between estrogen deficiency and bone loss clearly suggests that hormonal contraceptive use may affect Bone Mineral Density (BMD) .[6]

Combined oral contraceptives pills (COCP) are the most popular form of reversible contraception today, which is a form of estrogen and progesterone, and used for different medical indication such as: Poly Cystic Ovary Syndrome, Endometriosis, Amenorrhea, Menstrual Cramps, Premenstrual Syndrome, Heavy Menstrual Periods, Acne. [7]

Bone mineral density is a medical term normally referring to the amount of mineral matter per square centimeter of bone .BMD is used as an indirect indicator of osteoporosis and fracture risk in clinical medicine.[8]

Computed Tomography (CT) is medical test that uses special x-ray equipment to produce multiple slices of the inside of the body and computer to join them together in cross-sectional views of the area being studied .CT is a technique that measures cortical thickness in millimeter and BMD with a calibration standard to convert Hounsfield Units (HU) of the CT image to bone mineral density value.[9]

The mandible is the largest ,strongest and lowest bone in the face it form the lower jaw and holds the lower teeth in place .The mental foramen(MF) is one of two holes(foramina) located on the anterior surface of the mandible ,it permits passage of the mental nerve and vessel, gonial angle (GA) is located at the junction of posterior and lower border of the ramus of the mandible.[10]

The current study is aimed to evaluate the effect of low dose COCP in cortical thickness and BMD at mandibular cortex of mental and gonial angle regions in millimeter (mm) and Hounsfield Unit (HU) using spiral computed tomography CT scan.

Aim of the study

Evaluation of the effect of low dose oral contraceptive pill (combined estrogen and progesterone hormone),on cortical thickness and bone mineral density value at the mandibular mental foramen and gonial angle regions among premenopausal females after two years of usage using spiral Computed tomographic scanning. (Iraqi study)

MATERIAL AND METHOD

Prospective Study of CT scan for 100 females, with age ranged from(20-40) attended the maxillofacial department at AL–Sheheed Al-Sadr General Hospital in AL- Najaf AL-Ashraf who admitted to have spiral CT scan for different purposes from July 2015 to May 2016. The study sample were divided into the following 2 groups; Group (1) 50 controlled females patient who don't take any type of contraceptive hormone. Group (2) 50 female patients who taking , contraceptive pills 20 mcg ethinyl estradiol (EE) and 75mcg gestodene ,one pill each day , for at least two years .

All of them asked about: number of parities, type of feeding ;breast or bottle feeding, history of abortion ,number of abortion, physical activity , type of exercise and body mass index(height and weight) .Any female with traumatic fracture in the examined area, metastatic tumor to the mandibular bone, taking another mode of contraceptive hormone, any female patients with diseases or taking medication that affected bone metabolism ,any female with family history of osteoporosis ,alcohol consumption and smoking were excluded.

All females asked about:1- body mass index; height and weight 2- Physical activity (daily work ,walking pace) scores; then by Computed tomography Scanner(Philip's Brilliance CT 64-slice scan) CT scan record the cortical thickness and bone mineral density in mental and gonial angle area.

Mental foramen area with Wical and Swoope technique mental area determined by tracing two lines; 1and 2: Parallel to the long axis of the mandible and tangential to the superior and inferior border of the mandibular cortex ;line 3 was performed Perpendicular to the tangential lines intersecting the inferior border of the mental foramen ;the distance between two parallel line represented the mandibular cortex and the BMD is measured at the midpoint of this distance on the third line. Measurement of the cortical thickness at the mental foramen region[11] as shown in fig1:

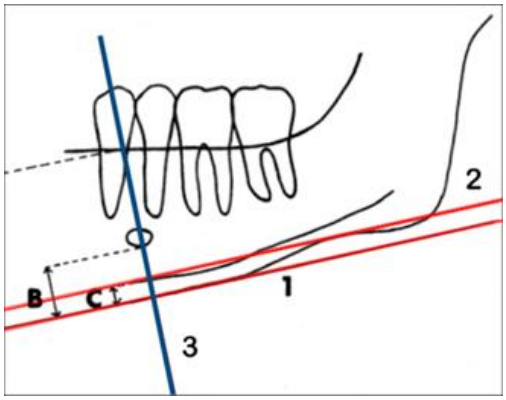

Fig1: Diagram show method of determination of cortical thickness in mental area.

Fig:2 Radiologic image showing the measurement of cortical thickness and BMD in mental foramen area.

Gonial angle: The angle of the mandible, is formed by the line tangent to the distal border of the ascending ramus and condyle and line tangent to the lower border of the mandible and by the line that bisectrix of the angle between the two tangent lines; the bone mineral density is measured at the middle area of the cortex with HU ,then the thickness of the cortical GA is measured in millimeter$_{(mm)}$[12]as shown in fig 3:

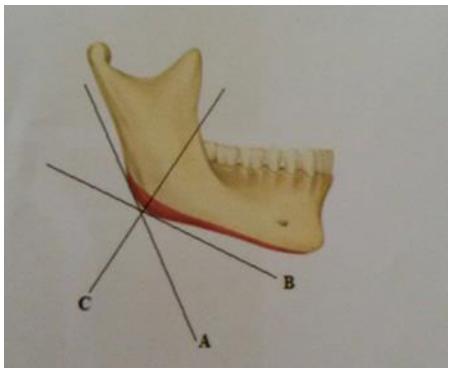

Fig 3: showing the measurement of cortical thickness and BMD in Gonial angle. A-tangential line to the distal border of ramus B-tangential line to the bottom of mandible C-Bisecting of the angle between A and B.

Fig 4:Radiographic image of CT scan (coronal section).
Showing the measurement of cortical thickness and BMD in gonial angle area.

RESULTS:

For each sample in the two study groups, the cortical thickness (in millimeter)and BMD in HU were recorded at both MF and GA area the data then statistically analysis ,there was significant difference p=0.037 between mean of cortical thickness and significant difference p= 0.007 between mean of BMD between control and user COCP group in mental foramen area but there was non-significant difference p= 0.15[NS]between cortical thickness &no significant difference p= 0.16[NS] between mean of Bone mineral density in gonial angle area between control and user of COCP as shown in table 1and fig5.

After adjusting with other explanatory variable that effect on cortical thickness and bone mineral density such as age ,duration of combined oral contraceptive usage ,number of parity and physical activity scores; there was a significant difference p=0.065 for cortical thickness and p=0.001 for bone mineral density between control and combined oral contraceptive user in gonial angle .table2and3.

Table1: The difference in mean cortical thickness and BMD at two selected mandibular location between users and non-users of COCP

		Controls (Non-users)	Cases (users COCP)	P (t-test)
1.	cortical thickness-Mental foramen			0.037
	Mean	4.94	4.76	
2.	cortical thickness-Gonial angle			0.15[NS]
	Mean	2.29	2.2	
3.	Bone mineral density-Mental foramen			0.007
	Mean	1620.4	1539.6	
4.	Bone mineral density-Gonial angle			0.16[NS]
	Mean	1404.4	1362.4	

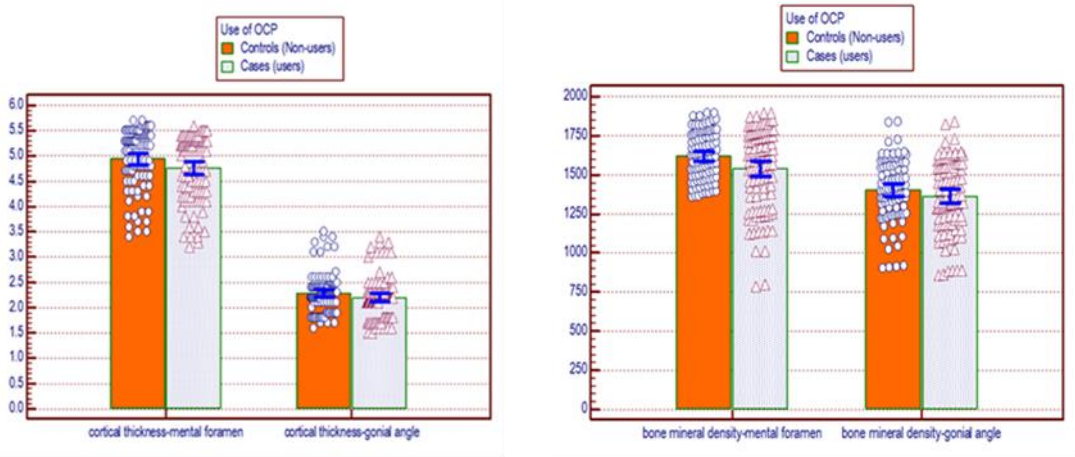

Fig 5: Error bar chart showing the difference in cortical thickness and BMD in mental and gonial angle between the two study groups.

Table 2: The effect of COCP on cortical thickness of Gonial angle after adjusting with other explanatory variable.

	Un Standardized Partial Regression Coefficient	P	Standardized Coefficients
(Constant)	2.578	0.001	
parity	-0.366	0.001	-0.498
Age (years)	-0.252	0.001	0.297
Walking pace	0.153	0.002	0.238
physical activity daily working	0.134	0.001	0.211
Duration of COCP use	-0.073	0.065	0.147

Table3: The effect of COCP on cortical thickness of Gonial angle after adjusting with other explanatory variable.

	Un Standardized Partial Regression Coefficient	P	Standardized Coefficients
(Constant)	1873.4	0.001	
Age (years)	-194	0.001	0.426
parity	-102.7	0.001	-0.261
Duration of COCP use	-56	0.001	-0.214
Walking pace	37.811	0.07	0.117
physical activity daily working	39.7	0.007	0.110

There is negative linear correlation and significant difference between the duration of combined oral contraceptive pill use and cortical thickness and BMD ;the highest mean as duration of use decrease and lowest mean as duration of use combined oral contraceptive increase.

In each two group there is a negative linear correlation and significant difference between age with cortical thickness and BMD the highest mean of cortical thickness and BMD in 20 years old age group and lowest in 40 years old age group, also there is negative linear correlation and significant difference between the number of parity with cortical thickness and BMD ;the highest mean of cortical thickness and BMD in the low number of parity and the lowest mean of cortical thickness and BMD in the 5 and more parity group .But there is a positive linear correlation between physical activity scores and cortical thickness and BMD in each two groups. The highest mean of cortical thickness and BMD in high scores physical activity and lowest mean in low score physical activity.

DISCUSION:

The sample was selected at age between 20-40 years old premenopausal ,since bone mass increases rapidly from birth, and during adolescence women will gain 40–50% of their skeletal mass[13] ·90% of total adult bone content will be accumulated by the age of 20 years [14] and the samples didn't exceed the age of 40 in order to avoid early menopause[15].

All the user of COCP are of a low-dose ,20 microgram(mcg) ethinyl estradiol and 75mcg gestoden ; Recommendations by the United States Food and Drug Administration (USFDA) that the dose of the estrogenic component of oral contraceptives be as low as possible ;otherwise sever risk side effect were happened such as deep venous thrombosis ,breast cancer and hypertensive[16]

The COCP had small impact on bone so the longer the duration of COCP use and at least two year; the effect of the pill on cortical thickness and BMD will be significant , current study agree with **Scholes et al. in 2010** who show that the duration of pill usage increased , the BMD decrease in a significant negative linear correlation ; and adults who had used oral contraceptives for 24 months or longer; the lower the mean BMD. [17]

Progestogen negative feedback reduce the pulse frequency of gonadotropin-releasing hormone released by the hypothalamus, which lowers the release of follicular stimulating hormone (FSH) and luteinizing hormone (LH) by the anterior pituitary. Diminished levels of FSH inhibit follicular development, preventing an increase in estradiol levels. Progestogen negative feedback and the lack of estrogen positive feedback on LH release prevent a mid-cycle LH surge. Suppression of follicular development and the absence of a LH surge inhibit ovulation.[18]

low estrogenic effects from lower dose COCP (~20 mcg EE)suppresses the mid-cycle estrogen peak that occurs with normal ovarian function[19].

Estrogens have multiple actions on bone that decreases bone turnover, which increases bone density; COCP may affect all these aspects of bone development; the small-estrogenic actions of COCP would be predicted to have negative, potentially age-related, effects on bone density[20]

The means of cortical thickness and BMD between two groups were significant in mental foramen area while not significant in gonial angle area only after adjusting with other explanatory variable(age, duration of COCP use ,number of parity, and physical activity measurement scores) that is because the mental index had greater sensitivity and specificity than gonial index which was least accurate due to the influence of the muscle attachment ,and continuous remodeling[21]

In current study all the mean of cortical thickness in COCP use was 4.76 for MF and 2.2 for GA area respectively ;and it is in in normal range ;**Devlin , 2007** suggest that patients with the thinnest mandibular cortices (≤3 mm)for MF and (1.2) for GA should be referred for further osteoporosis investigation,[22]

There was a statically negative linear correlation between age with cortical thickness and BMD ;as the age increase the cortical thickness and BMD decrease in the two group; **Aloia in 2010** showed that With aging and after menopause, fragmental calcium absorption has been reported to decline after 40 years of age. [23]

It is estimated by **Bachmann ,1987** ;that bone mass in women is lost at a rate of 0.75% to 1% per year from age 35 onwards, and this rate increases to 2% to 3% per year at menopause.[24]

There was significant negative linear correlation between number of parity and BMD in all the two study groups ;The mother adapts to meet the calcium demands of the fetus during pregnancy ; 2-3% of maternal calcium is transferred to fetus mostly in the second and third trimester when fetal bone development

peaks, If a pregnancy is followed by a period of breast-feeding, mother loses a further 300–400 mg calcium daily in the breast milk[25].

There was significant positive linear correlation between physical activity and BMD in all the two study groups ; Our present study agree with **Martyn et al. 2010** who stated that exercise programs that combine high-impact activity with high-magnitude resistance training appear effective in augmenting BMD in premenopausal women [26];bone is a living tissue that undergoes continuous remodeling adapts to the associated mechanical stresses, such as exercise, that are placed on it.[27] exercise may reduce the secretion of sclerostin by the osteocyte, thereby up regulating signaling and osteoblast genesis , that is, bone formation **(Schwab,2011)** [28]. Our result agree with **Hartard et al.,1997** who show ;there is no beneficial effect of exercise on BMD was found in the group with a long exercise period and long-term intake of COCP.[29]

CONCLUSION:

1-CT is a good diagnostic method to measure the effect of COCP on cortical thickness and BMD in MF and GA simultaneously.

2- Age had negative linear correlation with cortical thickness and BMD in all the study sample (user &non- user COCP)

3- Cortical thickness in mental and gonial area had a negative linear correlation with age in all two groups.

4-The effect of low dose COCP(20 mcg EE and 75mcg gestodene) on the density of bone ;negatively appear at least after two years of usage and as duration of use increased the loss of cortical thickness and BMD increased.

5-All the means of cortical thickness and BMD in each group of study sample with in the normal range ; but the mean of cortical thickness and BMD COCP use lower than that of control (non-user).

7-Number of pregnancy (including number of abortion)and parity have negative effect on cortical thickness and BMD specially more than 5 child.

8-Brest feeding (normal lactation) have reversible negative effect on BMD that return to normal value after discontinuation of lactation.

9-Physical activity daily working and walking pace cause significant increase in BMD, as physical activity scores increase the cortical thickness and BMD increase.

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تأثير حبوب منع الحمل على سمك وكثافة العظم في لحاء الحافة السفلى في منطقتي الثقب الذقني وزاوية الفك السفلي عند النساء قبل سن اليائس باستخدام جهاز المفراس الحلزوني

الخلاصة :

المقدمة: الاستعمال الطويل لحبوب منع الحمل منخفضة نسبة الأستروجين (20 ميكروغرام او اقل) و المركبة من هرموني الاستروجين والبروجسترون يؤثر على الايض الخلوي للعظم. كثافة معدن العظم مصطلح يستعمل في الطب السريري لقاس كثافة العظم وخطورة الكسر.

الهدف من البحث : فحص تأثير حبوب منع الحمل منخفضة نسبة الاستروجين على سمك لحاء الحافة السفلي للفك السفلي في منطقتي الثقب الذقني وزاوية الفك الاسفل بالملليمتر وكثافة العظم في وحدة قياس كثافة العظم الهاونسفيلد باستخدام جهاز المفراس الحلزوني.

العينات والمواد وطريقة العمل: هذه الدراسة الاستعادية موصولة بصور مقطعية بالمفراس الحلزوني ل100 امرأة تتراوح اعمارهم بين 20-40 سنة قصدت مستشفى الشهيد الصدر التعليمي العام. لمختلف اغراض تشخيصية من شهر تموز 2015 الى شهر ايار2016 . البيانات صنفت الى مجموعتين: المجموعة الاولى تتكون من 50 امرأة لا تتناول حبوب منع الحمل والمجموعة الثانية تتكون من 50 امرأة يأخذون حبوب منع الحمل منخفضة نسبة الاستروجين لمدة لا تقل عن سنتين . قياس سمك العظم بالملليمتر وكثافة العظم بوحدة الهاونسفيلد في منطقتي لحاء الحافة السفلية لفك السفلي في منطقتي ثقب الذقن وزاوية الفك السفلي, النشاطات الفيزيائية ,عدد الاطفال ونوع الرضاعة وثقت عن طريق ورقة استطلاعية.

النتائج: احصائيا وجد فرق ملحوظ القيمة المعنوية =0.037 في سمك لحاء الحافة السفلية وفرق ملحوظ القيمة المعنوية =0.007في كثافة العظم في منطقة الثقب الذقني بين المجموعتين حيث ان سمك وكثافة العظم هي الاعلى في المجموعة الاولى التي لا تستخدم حبوب منع الحمل منخفضة نسبة الاستروجين وفرق ملحوظ حيث القيمة المعنوية =0.001بالنسبة لكثافة العظم والقيمة المعنوية= 0.065بالنسبة لسمك العظم ولكن بعد تعديل النتائج مع العوامل الاخرى التي تؤثر على كثافة العظم مثل العمر ,عدد الاطفال, فترة استعمال الدواء ودرجات النشاط الفيزيائي(العمل اليومي وسرعة العمل) في سمك وكثافة العظم في زاوية الفك السفلي. ا لاستنتاجات :ا لمفراس الحلزوني هو طريقة تشخيصية جيدة لقياس سمك وكثافة العظم في ان واحد في منطقتي الثقب الذقني وزاوية الفك السفلي للنساء اللواتي يستخدمن حبوب منع الحمل منخفضة نسبة الاستروجين التي تؤثر تأثر خفيفا على العظم معتمدا على العمر ولفترة طويلة لا تقل عن سنتين لظهور الاعراض.