

The Effect of Hypertension and Beta-Blocker Antihypertensive Drug on Bone Mineral Density Value At the Mandibular Cortex in Mental and Gonial Regions in Hounsfield Unite Using Computed Tomographic Study

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Abstract:

Background: *Computed tomography is a medical technique that measures bone mineral density. Both hypertension and Beta-Blocker antihypertensive drug are associated with abnormality in calcium metabolism .The aim of this study was to study the effect of hypertension and Beta Blocker antihypertensive drug on bone mineral density in Hounsfield unite using computed tomography.*

Material and Method: *This prospective study was conducted on computed tomographic image of 150 men aged between (35- 85) years. Data were grouped into three categories according to their blood pressure: normotensive group (n=50), Hypertensive treated for > 8 months group (n=50) and Untreated hypertensive/recently*

diagnosed group (n=50).. Bone mineral densities were measured in each sample in both mental and gonial areas in Hounsfield unite.

Results: *There were a statically significant difference in bone mineral density in both mental and gonial area among the three study groups. Bone mineral density was highest in group 2 and lowest in group 3. P value was < 0.001 among the three study groups. There was a positive linear correlation between bone mineral density and the duration of antihypertensive drug used and there was a negative linear correlation between bone mineral density and duration of hypertension disease*

Conclusion: *Computed tomography is a good diagnostic method to measure the value of bone mineral density in hypertensive patients. Bone mineral density is highly affected by increasing blood pressure and by antihypertensive treatment and affected by duration of the disease and the treatment.*

Keywords: *Bone mineral density, hypertension, Beta-Blocker antihypertensive drugs.*

Introduction

Hypertension or high blood pressure, is a common chronic medical condition in which the blood pressure in the arteries is elevated.. Hypertension is classified as either primary (essential) hypertension which means high blood pressure with no obvious underlying medical cause, or secondary hypertension is caused by other conditions that affect the kidneys, arteries, heart or endocrine system [1].

Bone mineral density (BMD) is a medical term referring to the amount of mineral matter per square centimeter of bones. Increased bone resorption is based on the stimulation of both osteoclast formation and osteoclast activity. These effects are associated with beta-2 adrenergic activity present in both osteoblastic and osteoclastic cells [2].

Hypertension and BMD have a major pathophysiologic link between blood pressure regulation and calcium metabolism. High blood pressure is associated with abnormalities of calcium metabolism, which induces increased calcium leak from bone. The calcium leak from bone will be eventually excreted by kidney in the form of urine. [3, 4]

Antihypertensive are a class of drugs that are used to treat hypertension. There are many classes of antihypertensive, which lower the blood pressure by different means. Among the most important and most widely used drugs are beta blockers, Angiotensin-Converting Enzyme inhibitors, angiotensin II receptor antagonists, and calcium channel blockers [5].

Computed Tomography (CT) scan is a noninvasive medical test that uses special X-ray equipment to produce multiple images or pictures of the inside of the body. CT is a technique that measures (BMD) with a calibration standard to convert Hounsfield Units (HU) of the CT image to BMD values [6].

Materials and Methods

Prospective study of CT scan for 150 subjects, male with age ranged from (35-85 years) attended the maxillofacial department at AL-Shaheed AL-Sader General Hospital in Baghdad city who admitted to have spiral CT scan from November 2014 to February 2015. The samples were divided according to their medical history into 3 groups:

Group (1): normotensive patients with no sign and symptom of any systemic disease. (n=50). Group (2): Controlled hypertensive patients under treatment, they were treated with Beta-Blocker antihypertensive drug (Atenolol 50mg – 100mg daily

single dose) for more than 8 months. (n=50). Group (3): Untreated hypertensive and the recently diagnosed as hypertensive patients for at least one month (n=50). The excluded criteria including Any patient with fracture area or extracted teeth in the examined areas , smokers or alcoholic drinkers, patients had history of corticosteroid therapy or biphosphonate use, patients were on hormone replacement therapy , diabetic patients., patients with secondary. The entire participants have normal range of body mass index. Physical activity was determined according to Warren et al, 2010 [7].

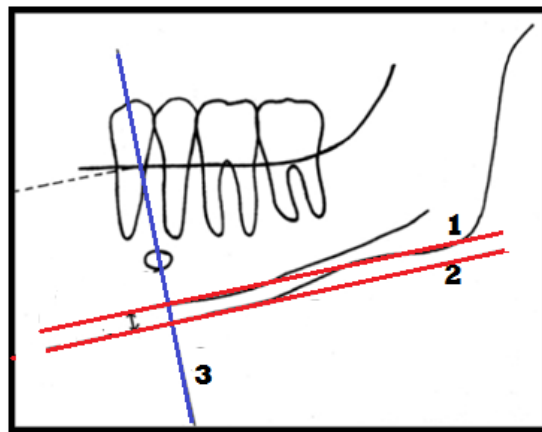


Figure 1: Diagram show method of determination of cortical thickness in mental area

- 1: Line parallel to the upper border of mandibular cortex (red line).**
- 2: Line parallel to the lower border of mandibular cortex (red line).**
- 3: Line perpendicular to line 1 and line 2 and pass at the middle of mental foramina (blue line).**

By using CT scan, BMD was measured. In mental area BMD was measured by drawing a line parallel to the upper border of mandibular cortex in mental foramina area and a line parallel to the lower border of mandibular cortex in mental foramina area, then draw a third line perpendicular to the previous two lines and pass throw the middle of mental foramina (blue line). The distance between two parallel lines represented the mandibular cortex and

the BMD is measured at the midpoint of this distance on the third line (8). As shown in figures 1 and 2.

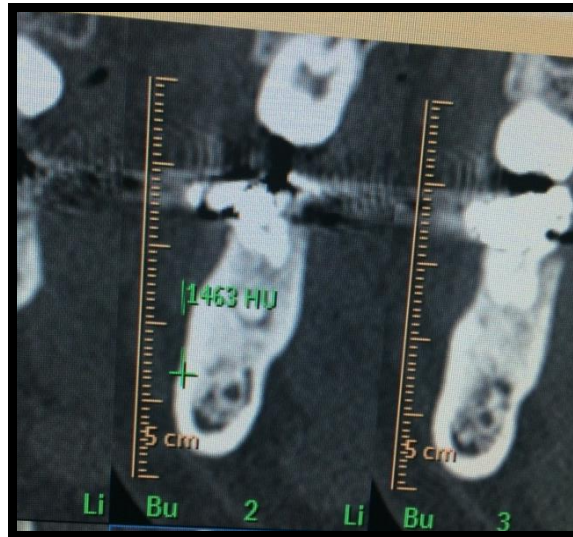


Figure 2: Radiographic image of CT showing the measurement of BMD in mental area in: sagittal view

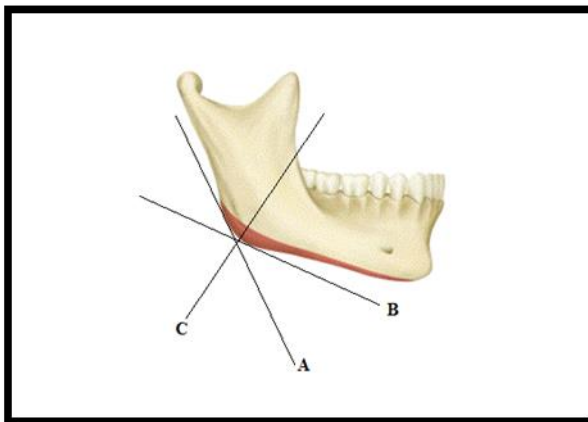


Figure 3: Diagram shows method of determination of cortical thickness in gonial region

- A. Tungsten line to the posterior border of ramus
- B. Tungsten line to the bottom of mandible
- C. Bisector of the angle between A and B

Gonial area is measured on the bisectrix of the angle between the tangent lines to the posterior border of the outer border of the ramus and the inferior border of the mandible [8] as shown in figures 3 and 4. Then the BMD is measured at the middle area of the cortex



Figure 4: Radiographic image of CT showing the measurement of BMD of gonial area in sagittal view

Results

There was a highly significant difference between the three groups as shown in table 1. P-value was <0.001 for both mental and gonial area. The mean of BMD was highest in group 2 for both mental and gonial areas, while BMD was lowest in group 3 for both mental and gonial area. The mean of BMD in group 2 was 1449.6 in mental area and 1404.1 in gonial area, while the mean of BMD in group 3 was 1027.2 in mental area and 952.7 in gonial area.

Age, duration of disease, duration of drugs and physical activity seem to be important factors that may effect on the value of BMD. There were a positive linear correlation between BMD and age for all the three groups. And there was a negative linear

correlation between duration of disease and BMD in group 3 and appositve linear correlation between duration of drug and BMD in group 2 and there was a positive linear correlation between BMD and the physical activity in all the three study groups.

After adjusting for age and selected measurement of physical activities duration of treatment for hypertension categories showing highly significant difference for BMD for both mental and gonial area. A higher magnitude of physical activities significantly increases BMD after adjusting for treatment duration and age for both mental and gonial areas. For each one year increase in age the BMD is expected to decrease by an average of 5.8 in mental area and decrease by an average of 3.3 in gonial area, after adjusting for the remaining explanatory variables included in the model as showing in table 2

Table 1 comparison between BMD in the 3 groups

	Study group			P (ANOVA)
	Healthy controls	Hypertensive treated for > 8 months	Untreated hypertensive/ recently diagnosed	
BMD-mental				<0.001
Range	(846 - 1486)	(990 - 1836)	(421 - 1296)	
Mean	1195.2	1449.6	1027.2	
SD	116.2	187	169.1	
N	100	100	100	
BMD-gonial				<0.001
Range	(783 - 1457)	(802 - 1827)	(505 - 1268)	
Mean	1137.2	1404.1	952.7	
SD	145.5	198.1	168.6	
N	100	100	100	

Table 2: Multiple linear regression model with BMD of mental and gonial areas as the dependent (response) variable and treatment for hypertension with its duration as the main explanatory variable after adjusting for age and selected measures of physical activity

BMD-mental	Unstandardized partial regression coefficient	P	Standardized Coefficients
Mental area:			
Duration of treatment for hypertension-categories			
<5 years duration of treatment compared to untreated hypertensive group	292.3	<0.001	0.344
5-10 years duration of treatment compared to untreated hypertensive group	492.8	<0.001	0.774
>10 years duration of treatment compared to untreated hypertensive group	581.8	<0.001	0.709
Related physical activities	35.1	0.011	0.144
Age (years)	-5.8	<0.001	-0.248
Gonial area			
<5 years duration of treatment compared to untreated hypertensive group	351.2	<0.001	0.393
5-10 years duration of treatment compared to untreated hypertensive group	513.1	<0.001	0.765
>10 years duration of treatment compared to untreated hypertensive group	674.6	<0.001	0.781
Related physical activities	35.0	0,013	0.136
Age (years)	-3.3	0.017	-0.136

Discussion

In current study, using CT scan, for determination significantly better BMD on mandible among 3 groups of study sample: healthy group, controlled hypertensive patient who had been receiving beta blocker treatment for at least 8 months and uncontrolled/ recently diagnosed hypertensive patient. Osteoporosis is a very important health problem especially because for increase the fracture risk, the effect of diseases and the treatment is of major importance. Moreover, osteoporosis and hypertension coexist in many patients; the use of antihypertensive drugs could influence the potential effect of this disease on the bones.

Effect of hypertension on BMD:

In this study there was a highly statistically significant difference in BMD between healthy controlled group and the uncontrolled hypertensive patients or recently diagnosed as hypertensive patients group (P value <0.001). The results showed also increasing the duration of disease would cause decreasing in the BMD in a highly significant negative linear correlation in which (P value<0.001) and this was similar to the results obtain by Cappuccio et al in 1999[9] who reported that hypertension was a significant predictor of BMD reduction in the femoral neck. It has been reported that, among hypertensive patients, there were various changes in calcium metabolism that led eventually to secondary hyperparathyroidism. Elevation of parathyroid hormone (PTH) accelerates bone turnover, reduces BMD, and changes bone quality. [10]

Effect of Beta Blocker treatment on BMD:

In the current study, there was a highly significant difference in BMD between healthy controlled group and the study group 2 who had been taken Beta Blocker antihypertensive treatment for more than 8 months. BMD was higher in group 2 than in group 1 in a highly significant difference where the P value <0.001. This agree with a study made by Bonnet et al in 2007[11], who

observed effects from use of B-blockers on bone metabolism by defining b-blocker users as those who had used the drug for 8 months or longer. Ducy et al in 2000,[12] demonstrated that, osteoblasts, which are multi-functional cells, control differentiation of osteoclasts. Signals of the sympathetic nervous system through B2-adrenaline receptors in osteoblasts control bone formation downstream of leptin. In other words and as explained by Elefteriou et al in 2005 [13], nerve pathways controlled by leptin are shown to control both of the bone remodeling processes and complete sympathetic nervous system signal transmission is necessary for an increase in bone, they had been suggested that leptin, which is considered a hormone that also inhibits bone formation, does not work directly on bone but acts through the central nervous system.

Effect of Physical Activity on BMD:

The physical activities had a clear effect on BMD. There was significant positive linear correlation between physical activities and BMD in all the three study groups, and the work related activity cause highly significant difference in BMD in all the three study groups where P value <0.001, this agree with Menkes et al, 1993 [14], who reported a possible justification for the increase in the BMD to the strength training is the bone piezoelectric effect. Continued training leads to continuous reactivating remodelling by replacing damaged and degraded bone tissue with new tissue and increases bone mineralization. [15, 16]

Effect of Age on BMD:

There was a statistically negative linear correlation between BMD and age in all the 3 study groups. Mazess and Barden in 2013 stated that, the bones lose calcium and other minerals with age; bones become more brittle and may break more easily..

Multiple Linear Regression Model with BMD for both Group 2 Treated Hypertensive Patients and Group 3 Uncontrolled Hypertensive/ Recently Diagnosed Hypertensive Patients:

BMD increased in treated hypertensive patients compared with untreated hypertensive patients after adjusting for duration of treatment, age and selected measure of physical activities and this is similar to the results of Turker et al in 2006 and Meisinger et al in 2007.[17, 18]. On the other hand, a study by Reid et al in 2005[19], disagree with the current study, they found that a statistically significant relationship between BMD and b-blocker use disappeared. Moreover, there was no difference in osteoporotic fracture risks by use of B-blockers that may reflect various effects of the sympathetic nervous system on bone-related local factors (such as mechanical loading), muscle mass and hormonal effects.

The current study has found that hypertension disease and Beta-Blocker antihypertensive drug effect clearly on BMD and their effect may effected by age, duration and physical activities.

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تأثير ارتفاع ضغط الدم نوع حاصرات (ب) على قيمة كثافة العظم في لحاء الحافة السفلى للفك الأسفل في منطقتي الثقب الذقني وزاوية الفك الأسفل بوحدة الهاونسفيلد باستخدام جهاز المفراس الحلزوني

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المستخلص

المفراس الحلزوني هو التقنيه الطبيه التي تقيس كثافة العظم بمقياس ثابت وبحول وحدة القياس في صورة المفراس الهاونسفيلد الى قيم كثافة العظم. ارتفاع ضغط الدم مرتبط بعدم انتظام الايض الخلوي للكالسيوم. استمرار فقدان الكالسيوم قد يؤدي الى زيادة نقصان معادن العظم عند الاشخاص ذوي ضغط الدم العالي. من جهة اخرى مضادات المستقبلات غير الانتقائيه (ب) كضري المنشأ لديها تأثير على الايض الخلوي للعظم. العديد من الدراسات اقترحت انه حاصرات (ب) تحفز تكوين العظم وتثبط امتزاز العظم.

هدف الدراسة: هو اكتشاف تأثير ارتفاع ضغط الدم والادويه المضادة لارتفاع ضغط الدم نوع حاصرات (ب) على قيمة كثافة العظم في لحاء الحافة السفلى للفك الاسفل في منطقتي الثقب الذقني وزاوية الفك الاسفل في وحدة قياس كثافة العظم الهاونسفيلد باستخدام جهاز المفراس. هذه الدراسة الاستعادية موصولة بصور مقطعيه بالمفراس الحلزوني لـ 150 رجل تتراوح اعمارهم بين 35 الى 85 سنة. البيانات صنفتم الى ثلاث مجاميع حسب ضغط الدم: طبيعي ضغط الدم (50 عينة) وذوي ضغط دم مرتفع يتناولون العلاج لأكثر من 8 أشهر (50 عينة) والمجموعه الثالثه ذوي ضغط دم عالي بدون علاج

أو المشخصين حديثا (50 عينة). مؤشر كتلة الجسم كان في معدلاتها الطبيعية لجميع العينات المأخوذة في الدراسة.

كثافة العظم تفحص لكل عينة في منطقتي الثقب الذقني وزاوية الفك الاسفل لوحدة هاونسفيلد لقياس كثافة العظم. النشاطات الفيزيائية وثقت عن طريق ورقة استطلاع. وجد احصائيا ان هناك فرق ملحوظ في كثافة العظم في منطقتي الثقب الذقني وزاوية الفك الاسفل بين المجاميع الدراسية الثلاثة. حيث ان كثافة العظم هي الاعلى في المجموعه الثانية والاقبل في المجموعه الثالثة. حيث ان القيمة المعنويه بين المجاميع الثلاثة عالية وكان هناك علاقة موجبه بين كثافة العظم ومدة استخدام الدواء المضاد لارتفاع ضغط الدم وهناك علاقة سالبة بين كثافة العظم ومدة الاصابة بمرض ارتفاع ضغط الدم بعد تثبيت العمر ومدة المرض ومدة استخدام العلاج والوظائف الفيزيائية فالقيمة المعنويه كانت عالية بين المجاميع الثانية والثالثة ووجد ان علاج ضغط الدم ومدته هما المؤشران القويان في كثافة العظم يليهما العمر ونوع العمل بمقياس الوظائف الفيزيائية.

الاستنتاج: كثافة العظم تتأثر جدا بارتفاع ضغط الدم وبالادوية المضادة لارتفاع ضغط الدم وتتأثر بمدة المرض والعلاج.

الكلمات الرئيسية: كثافة مادة العظم، ارتفاع ضغط الدم، ادوية ارتفاع ضغط الدم من نوع حاصرات ب.