

Alveolar Bone Density Changes in Postmenopausal Women with and without Hormone Replacement Therapy

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Abstract

Estrogen deficiency mostly results in a low bone mass in postmenopausal or bilateral oophorectomized women. Since evidence linking changes in alveolar bone density to estrogen status was lacking, this study aimed to compare alveolar bone density changes between postmenopausal or bilateral oophorectomized women with hormone replacement therapy (H+) and without hormone replacement therapy (H-). There were 13 H+ and 17 H- subjects completed this study. All were between 1-6 years after reaching menopause. They were in good periodontal health at entry and received regular 2- or 3-month oral prophylaxis during the study period. Intraoral radiographs were taken from lower posterior teeth using individual geometric standardized device under control of current, voltage, exposure time and film processing. Radiographs were converted into digital images. Alveolar bone density gain or loss between baseline and 12-month images were evaluated by intensity analysis software. The result indicated that H- group displayed a higher mean net loss in alveolar bone density when compared to H+ group at 12-month interval. However, differences between groups did not reach statistical significance ($p > .05$). Furthermore, H- group exhibited a higher number of sites demonstrating loss in bone density, while H+ group exhibited a higher number of sites demonstrating gain in bone density with Odds Ratio of 1.78 and 95% confidence interval of 1.48 – 2.14. Thus, estrogen status may influence a trend toward alveolar bone density changes in postmenopausal women who displayed healthy periodontal status.

Key words: bone density; estrogen; menopause

Introduction

Osteoporosis is metabolic bone disorder characterized by a generalized low bone mass and may lead to skeletal fragility and fractures which are devastating in terms of health care costs, loss of quality of life and increased mortality.¹⁻³ This disease mostly affects women with estrogen deficiency.^{1,4} Estrogens can enhance bone formation and mineralization,

and also affect bone metabolism in that they promote protein synthesis for bone matrix, and promote 1, 25-dihydroxycholecalciferol ($1,25-(OH)_2D_3$) formation in kidney, causing an increase in the efficiency of calcium absorption across the intestine. Estrogens also accelerate the mineralization of bone matrix by causing calcium and phosphate retention and increasing the rate of deposition of calcium and phosphate.^{5,6} Estrogens also exhibit their protective action on bone via an inhibition of osteoclastic bone resorption.⁷⁻¹⁰ Such estrogen deficiency results in bone loss in postmenopausal or bilateral oophorectomized women called postmenopausal osteoporosis.^{5,11} Most studies have confirmed that bone mass in women remains stable until the onset of ovarian failure.^{5,12} Marked bone loss in women starts about the menopause¹³ and the greatest amount of bone loss is observed within 7 years.¹⁴ The increased bone resorption in postmenopausal or oophorectomized women, however, was decreased after hormone replacement therapy.¹⁵⁻¹⁷

In a 5-year longitudinal study, the decrease in skeletal bone mineral density as determined by dual X-ray absorptiometry at the distal forearm were associated with the decrease in grey level value in the digitized radiographs of the mandibular alveolar process in dentate women, suggested that changes in the mandibular alveolar bone could reflect changes in the skeletal bone mineral density.¹⁸ In the osteoporotic women as diagnosed from radiographic evidence of vertebral compression fractures with no other metabolic bone disease, less mandibular bone mass and density, a thinner cortex at the gonion, a greater percentage of edentulous and greater tooth loss than the non-osteoporotic group have been found, indicated that image processing from dental radiographs could detect osteoporosis from the osteoporotic group.¹⁹ Tezal et al.²⁰ reported that interproximal alveolar bone loss was significantly correlated with skeletal bone loss in the trochanter, Ward's triangle, and total regions of the femur in postmenopausal women. Other investigators also suggested that dento-maxillofacial bone loss seem to be a part of generalized skeletal osteoporosis.²¹⁻²⁴ Since the alveolar bone has a higher rate of bone turnover, it is suggested that the osteoporosis may be manifested earlier in the alveolar process than in other bone of the body.²⁵⁻²⁸

While the alveolar process seems to be the sites of particular interest, direct evidence linking changes in alveolar bone density to estrogen status is lacking. Thus, this study aimed to compare alveolar bone density changes in a group of postmenopausal or bilateral oophorectomized women with or without hormone replacement therapy using conventional dental radiographs taken at baseline and 12 months and analyzed with intensity analysis software.

Materials and Methods

Subjects

The target population was consisted of 30 postmenopausal or bilateral oophorectomized Thai women. They were recruited from the Faculty of Dentistry, Mahidol University and Rajvithi Hospital. Subjects were divided into 2 groups, i.e., those who had received hormone replacement therapy before and during the study period (H+) and those who had never received hormone replacement therapy (H-) before and during the study period. Subjects had to meet the following criteria:

1. They were between 1-6 years after reaching menopause or after bilateral oophorectomy at baseline, because the greatest amounts of bone loss occurred within 7 years after menopause.¹⁰
2. They had more than one lower posterior teeth in the same sextant that contacted to each other and occluded with their opposing teeth. These teeth did not have an unable-to-restore carious or fractured lesion, poor restoration, periapical and root-surrounding radiographic lesions, food impaction or tooth mobility.

To eliminate smoking and periodontitis as confounders, subjects were non-smoker and had never smoked. They had probing pocket depth of less than 4 mm. Their periodontal status had been diagnosed as mild or moderate gingivitis. Additionally, in order to only recruit subjects that were healthy and not on medication known to alter phosphorus or calcium or bone metabolism during the previous 3 years, the following exclusion criteria were applied: endocrine abnormalities in parathyroid glands, thyroid glands and adrenals; malabsorption; malnutrition or obesity; renal, liver or bone diseases; previous partial or total gastrectomy; malignancy; diabetes mellitus; hysterectomy without bilateral oophorectomy; rheumatoid arthritis; premenopausal amenorrhea; hypogonadism; alcoholism; long-term immobilization; use of corticosteroids, thyroid hormone, calcitonin, anticonvulsive drugs, diuretics, anticoagulants, aluminium containing antacids, cytotoxic drugs, heparin, bisphosphonates or fluoride supplements.^{2,5,29-31} Subjects were informed about the purpose and the experimental design and were asked to sign the informed consent forms before entering the study.

Variables

1. Probing pocket depth (PPD) was measured with periodontal probe (Hu friedy® PCPUNC 15) from 6 sites in each tooth, i.e., mesiobuccal, mesiolingual, midbuccal, midlingual, distobuccal and distolingual site.

2. Full mouth Plaque Index (PII)³² was measured from mesiobuccal, buccal, lingual and distolingual surface from one representative tooth in each sextant (first molars or central incisors). If these teeth were not present or not able to be investigated, the neighboring one in the same sextant would be used. Mean PII were calculated for an individual subject.

3. Plaque Index³² of all study sites was measured from all experimental lower teeth. The plaque index of all study sites was derived from an average of plaque scores investigated from 4 interproximal tooth surfaces, i.e., distobuccal and distolingual tooth surfaces of the tooth in front of the interproximal area and mesiobuccal and mesiolingual tooth surfaces of the other tooth.

4. Full Mouth Gingival Index (GI)³³ was measured from the same tooth surfaces of the same representative tooth as used for PII. Mean GI for each individual subject was calculated.

5. Gingival Index³³ of all study sites was investigated from the same tooth surfaces as described in the method for investigation of PII for all study sites.

6. Alveolar bone density changes were derived from subtraction of mean intensity histogram between baseline and 12-month radiographic image using intensity analysis software (Image-Pro Plus, version 3.0, Media Cybernetics, MD, USA).

Prior to the study, all subjects were instructed in oral hygiene measures and received oral prophylaxis until individual full mouth GI, GI of all study sites, full mouth PII and PII of all study sites were ≤ 1 . Geometric standardized device was prepared for each individual subject (Fig. 1). Firstly, occlusal registration fitted to all study and their opposing teeth was made from self-cured acrylic resin. Two holds were prepared on the occlusal registration. These holes must be tightly fit to the 2 parallel stainless steel pins of the custom-made position indicating device. The occlusal registration was then connected with hard acrylic resin film placing pad. The custom-made position indicating device was then connected to the occlusal registration to make a geometric standardized device which could fix the position, distance and angulation of the x-ray's source, teeth and film.

At baseline, demographic information including age, postmenopausal years, type, dose and duration of hormone replacement therapy were collected by interviewing. The subjects' body weight (kg) and height (m) were examined. PPD, PII and GI were recorded. Then radiographs were taken by a single examiner using geometric standardized device (Fig. 2) and a dental x-ray film (Kodak ultraspeed DF 57, Eastman Kodak, NY, USA). A dental long cone x-ray machine (Gendex GX-1000, Gendex Corporation Dental Systems, IL, USA)

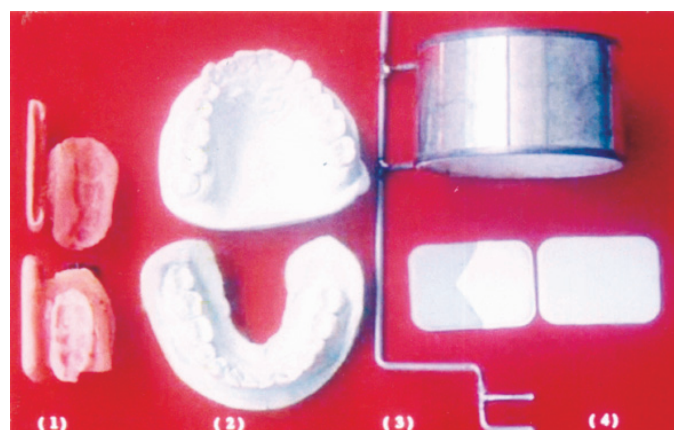


Fig. 1 Preparation of geometric standardized device

(1) Occlusal registration connected to film placing pads.

(2) Working models.

(3) Custom-made position indicating device

(4) Dental X-Ray films.

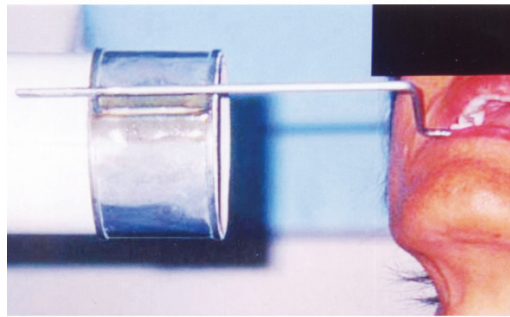
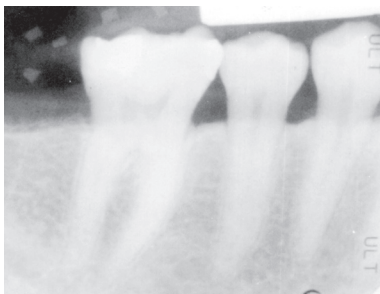
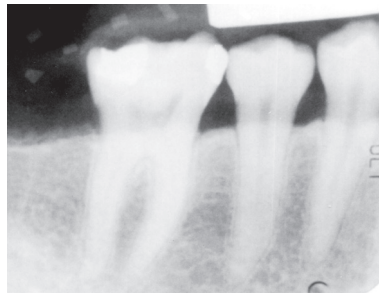


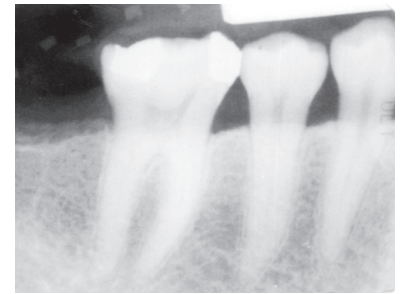
Fig. 2 Radiographic procedure using geometric standardized device



(3a) baseline image

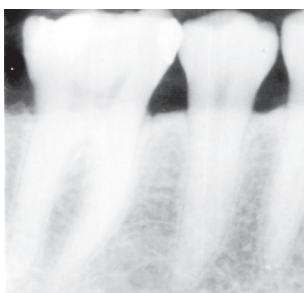


(3b) duplicate image

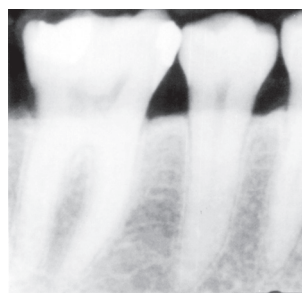


(3c) 12-month image

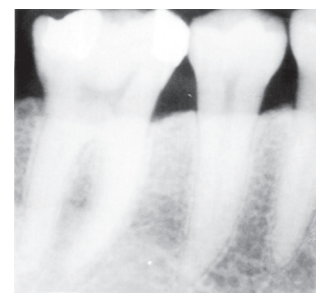
Fig. 3 Baseline and subsequent images demonstrated contrast discrepancies and distribution of grey values.



(4a) baseline image



(4b) duplicate image



(4c) 12-month image

Fig. 4 Baseline and subsequent images after intensity values were adjusted.



Fig. 5 Subtraction images between baseline and 12-month interval

Table 1 Demographic information of subjects in each group

Variable	Group	
	H- (n = 17)	H+ (n = 13)
Age (yr)	53.67 ± 2.77	51.74 ± 3.36
Menopausal age (yr)	4.18 ± 1.54	4.19 ± 1.63
Body weight (kg)	53.07 ± 7.78	57.32 ± 9.81
Body mass index (kg/m ²)	22.23 ± 3.31	23.59 ± 3.25

H- = No hormone replacement therapy; H+ = hormone replacement therapy

Table 2 Plaque index and gingival index for H- and H+ groups

Indices		group	Time interval		
			baseline	6 month	12 month
PII	Full mouth	H-	0.29 ± 0.06	0.28 ± 0.07	0.29 ± 0.05
		H+	0.32 ± 0.06	0.30 ± 0.06	0.27 ± 0.08
	All study sites	H-	0.23 ± 0.05	0.25 ± 0.05	0.25 ± 0.05
		H+	0.27 ± 0.06	0.27 ± 0.06	0.25 ± 0.07
GII	Full mouth	H-	0.18 ± 0.06	0.18 ± 0.06	0.19 ± 0.06
		H+	0.20 ± 0.05	0.20 ± 0.06	0.19 ± 0.06
	All study sites	H-	0.22 ± 0.05	0.22 ± 0.05	0.20 ± 0.05
		H+	0.27 ± 0.07	0.26 ± 0.06	0.24 ± 0.06

H- = No hormone replacement therapy; H+ = hormone replacement therapy

Table 3 Mean of different intensity values between baseline and 12-month images

ROI	group	No. of ROI	Mean of different intensity values (12 month – baseline)	p-value
Cervical zone	H-	234	-1.54 ± 3.17	0.49
	H+	126	-0.99 ± 3.22	
Middle zone	H-	233	-1.03 ± 2.19	0.63
	H+	126	-0.64 ± 1.96	
Apical zone	H-	195	-2.44 ± 3.73	0.27
	H+	119	-0.06 ± 2.54	

ROI = region of interest; H- = No hormone replacement therapy; H+ = hormone replacement therapy

Table 4 Number and percentage of alveolar bone ROI with bone density changes between baseline and 12-month images

ROI	group	No. of ROI		% of ROI	OR (95% CI)
		bone loss	bone gain	with bone loss	
Cervical zone	H-	158	76	67.52	1.83 (1.34 - 2.51)
	H+	67	59	53.17	
Middle zone	H-	137	96	58.80	1.47 (1.08 - 1.99)
	H+	62	64	49.21	
Apical zone	H-	141	54	72.31	2.24 (1.61 - 3.12)
	H+	64	55	53.78	
Total	H-	436	226	65.86	1.78 (1.48 - 2.14)
	H+	193	178	52.02	

ROI = region of interest; H- = No hormone replacement therapy; H+ = hormone replacement therapy; OR = Odds Ratio; CI = confidence interval.

was set at 10 mA, 65 kVp and 1.5 s exposure time. Radiographs were repeatedly taken at 30 minutes after the first one. These duplicates were used for the evaluation of the standardized geometry. All radiographs were developed in an automatic film processor (Durr Dental XR 24-II, Durr Dental Products, Germany) with developer and fixer (Kodak RP X-o mat developer replenisher; Kodak RP X-o mat LO fixer replenisher) in the same condition.

During the study period, subjects received maintenance programs every 2-3 months consisted of oral hygiene motivation and prophylaxis to ensure acceptable oral hygiene and gingival status.

PPD, PII, GI were recorded at 6-month and 12-month interval while standardized radiographs were taken at 12 months.

Intensity analysis

In order to process the image with a computer, the image must be converted into numeric form. This process, known as image digitization, divided the image into horizontal and vertical grids, of very small regions called "pixels". Each digitized image was then converted into intensity grey level, ranging from completely black with a grey value of 0, to completely white with a grey value of 255 in the pixel.

Thus, it could provide 256 different levels of grey value for each pixel compared to the human eyes that could distinguish less than 200 grey levels.³⁴ In this study, baseline, duplicate and 12-month radiographs were scanned and digitized by a blinded operator using a scanner (Nikon 210, Japan) with an output resolution of 100 pixels/mm and the scale of 10%. Although radiographs had been taken under control of current, voltage, exposure time and film processing, contrast discrepancies between baseline and subsequent images may occur. Thus, contrast correction was performed using standardized intensity references.

The digitized images were aligned with their baseline images using Image-Pro Plus. The regions of interest (ROI) were 16x16 pixels and were not touch with the tooth. The ROI was selected as much as possible at cervical 1/3, middle 1/3 and apical 1/3 of the alveolar process from the lower posterior interproximal sites. Each ROI from baseline image was outlined on the monitor and transferred to subsequent image with the same size and position as in its baseline image. Intensity in each ROI was calculated using histogram intensity analysis tool of the Image-Pro Plus. At least 30 ROI on the standardized intensity references were also outlined and histogram intensity analysis was performed in each image. The average of histogram intensity of each reference ROI were plotted and analyzed by regression analysis to run out a regression equation between baseline and duplicate image. Using the regression equation, data of alveolar bone ROI were corrected for the differences in grey value distribution between baseline and duplicate image. By the same way, the averages of histogram intensity obtained from 12-month image were corrected for the differences in grey values between baseline and 12-month image by a regression equation.

Statistical analysis

Statistical analysis was calculated by means of SPSS for Windows. The differences in initial characteristics including age, postmenopausal age, body weight (kg) and body mass index (kg/m^2) between groups were calculated by t-test. Comparisons between groups with respect to PII and GI were performed with ANOVA.

Comparison of histogram intensity value of each ROI from each pair of corrected baseline and duplicated image was evaluated by paired t-test. The different density value at each ROI was the result of the corrected density value of the 12-month image subtracted by that of baseline image. The different value might be a negative or positive integer, corresponding to a loss or gain in bone density, respectively. Comparison between groups with respect to the difference of each ROI was analyzed by t-test. The probability that

H- group demonstrated sites with bone density loss at 12-month following period was performed by Odds Ratio. The level of significance was set at $p < .05$.

Results

Demographic information of the subjects was shown in Table 1. When compared between groups, no statistically significant differences in age, postmenopausal age, body weight and body mass index were noted ($p > .05$). Full mouth and all study sites PII and GI measured at baseline, 6 and 12 months was shown in Table 2. All subjects maintained acceptable periodontal and oral hygiene status throughout the study period since favorable PII and GI scores were exhibited in both groups. When compared between groups, no significant differences at each time point were found ($p > .05$).

Baseline and subsequent images demonstrated contrast discrepancies and differences in overall distribution of grey values (Fig. 3). The regression equations that performed best fit to the graphs plotted from histogram intensity values of the standardized reference markers between baseline, duplicate images and 12-month images were all linear. Using the linear regression equations, the intensity values from subsequent images were adjusted (Fig. 4). Mean intensity values obtained from baseline and duplicate images were 90.07 ± 19.07 and 90.16 ± 19.00 , respectively. When the intensity values of each ROI measured from duplicate images were compared to that of baseline images, non significant differences were found ($p = .526$).

Subtraction images between baseline and 12-month images were shown in Fig. 5. A total of 1,033 ROI were chosen. Means of the different values between each pair of ROI from baseline and 12-month images in each group were demonstrated in Table 3. Although both groups demonstrated mean net loss in alveolar bone density, H- group displayed higher mean net loss from all zones of the alveolar process. However, the differences between groups did not reach statistical significance ($p < .05$).

As shown in Table 4, a loss in histogram intensity in this 12-month longitudinal study were 65.8% in H- group and 52.02% in H+ group. The H- group demonstrated ROI with a loss in bone density at 12-month interval with Odds Ratio of 1.78 and 95% confidence interval of 1.48–2.14. Separating interproximal sites into cervical, middle and apical zones, H- group also exhibited higher percentage of ROI with negative different intensity values compared to H+ group.

Discussion

In this 12-month longitudinal study, alveolar bone density changes were investigated in postmenopausal or total oophorectomized women who had received or had never received hormone replacement therapy before and during the study period. The 13 H+ and 17 H- subjects completed this study. However, 1 subject in the H+ group and 2 subjects in the H- group had shallow floor of mouth. As a result, the x-ray films could not be placed to cover the regions of interest at the middle and the apical zone. Thus, only the regions of interest at the cervical zone were compared in these subjects.

At baseline, both groups were homogeneous relative to age, postmenopausal age, body weight and body mass index, all were factors known to alter bone mineral density.^{5,12,35} They were also strictly selected with previously mentioned criteria in order to allow alveolar bone density changes be compared without confounding influences from those determinants.

The comparison of oral bone density changes using intraoral conventional radiographs is difficult due to the presence of a busy anatomical background including the teeth, the cortical and trabecular bone pattern. It has been found that at least 50% change in bone mass in a unit volume was required in order to be detected with an unaided eye.³⁶ Jeffcoat³⁷ also stated that such interpretative radiography was a relatively crude tool which did not register alveolar bone density changes until 30-50% of the bone mineral was destroyed. To provide a quantitative measurement of bone loss or gain, subtraction radiography was employed. Its principle is based on the decreasing of the structural noise (anatomic features other than those of diagnostic interest) and thus increasing the ability to detect fine changes occurring over time.³⁸ It was shown that less than 5% of bone change could be detected by computer image processing of high quality images with 90% sensitivity, specificity and overall accuracy.³⁴

Analysis of difference in density value between the images may have limitations due to discrepancies in projection geometry, contrast and density between 2 radiographs.³⁹ In this study, the reproduction of image geometry was created using an individual occlusal registration with film placing pad and position indicating device attached to the collimator. The device used had similar concept as positioning device recommended by Schmitt et al.⁴⁰ which showed a high angular reproduction with 89% of successful subtraction. The current, voltage, exposure time, and automatic film processing were also under control when radiographs were taken. Despite attempts to control these factors, contrast discrepancies still occurred. In this study, linear

regression equations derived from relationship in intensity values of reference markers between baseline images and their subsequent images were used in order to correct the discrepancies. Thus, the intensity values measured from each subsequent image were adjusted for differences in grey values between the images by the specific linear regression equation. When baseline images were compared with their duplicates, the intensity values of the images were not significantly different. These findings not only supported the reproducibility of the geometric standardized device, but also supported the efficiency of the specific linear regression equations in contrast correction.

In this study, means of different intensity values between baseline and 12-month images at cervical, middle and apical zones of the interproximal alveolar bone between H- and H+ group were not significantly different. The result of this study was not in agreement with that of Payne et al.¹⁴ who examined the association between estrogen status of postmenopausal women and alveolar bone density changes over a 1-year period. In that study, subjects who had periodontitis history and were undergoing periodontal supportive treatment were participated. Radiographs taken at baseline and 1 year were analysed by computer-assisted densitometric image analysis (CADIA), a version of subtraction radiography. They reported a significant difference in CADIA values between postmenopausal women with and without estrogen replacement and found that those with estrogen replacement displayed a mean net gain while those without estrogen replacement displayed a mean net loss in alveolar bone density. The discrepancy is probably due to the presence or absence of periodontitis in the study population. In our study, subjects with good oral health who received 2- to 3- month continual oral hygiene treatment were included. Changes in their alveolar bone density were most likely due to aging or to response to their estrogen status and were probably smaller than those due to periodontal disease. Furthermore, alveolar bone loss may be accelerated in estrogen-deficient women who exhibited pathologic inflammation.⁴¹ Reinhardt et al.⁴² also reported that estrogen deficiency was associated with increased crestal alveolar bone density loss only in subjects with periodontal progression. Additionally, the ability to detect true density loss might be reduced due to adjusting of the brightness and contrast of the follow-up images by gamma correction algorithm.¹⁴ In this study, contrast discrepancies of conventional radiographs were corrected by the linear regression analysis. The use of this correction, although necessary, may have resulted in underestimation of bone loss or gain.

In this study, H- subjects exhibited a higher percentage of sites demonstrating loss in alveolar bone density, while H+ subjects exhibited a higher percentage of sites demonstrating a gain in alveolar bone density with Odds Ratio of 1.78. Thus, estrogen status may influence a trend toward alveolar bone density changes in postmenopausal women who displayed healthy periodontal status.

Although estrogen is an important factor determining bone density changes, other factors, such as periodontal disease have to be taken into account. To determine whether estrogen status has a significant association with alveolar bone density changes in non-periodontitis subjects, further longitudinal studies with larger sample sizes are required.

Conclusion

Postmenopausal women without hormone replacement therapy displayed a higher mean net loss in alveolar bone density when compared to those with hormone replacement therapy, however, the differences did not reach statistical significance.

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บทวิทยาการ

การเปลี่ยนแปลงความหนาแน่นของกระดูกเบ้าฟันในหญิงวัยหมดระดูที่ได้รับและไม่ได้รับการบำบัดด้วยฮอร์โมนทดแทน

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บทคัดย่อ

การขาดฮอร์โมนเอสโตรเจนส่วนใหญ่ทำให้เกิดภาวะมวลกระดูกต่ำในหญิงวัยหมดระดูหรือหญิงที่ได้รับการผ่าตัดรังไข่ทั้งสองข้าง เนื่องจากยังขาดหลักฐานเชื่อมโยงการเปลี่ยนแปลงความหนาแน่นกระดูกเบ้าฟันกับสภาวะของเอสโตรเจน การศึกษานี้จึงมีวัตถุประสงค์เพื่อเปรียบเทียบการเปลี่ยนแปลงความหนาแน่นกระดูกเบ้าฟันในหญิงวัยหมดระดูหรือหญิงที่ได้รับการผ่าตัดรังไข่ทั้งสองข้างโดยได้รับหรือไม่ได้รับการบำบัดด้วยฮอร์โมนทดแทน อาสาสมัครที่ได้รับการบำบัดด้วยฮอร์โมนทดแทนจำนวน 13 คน และที่ไม่ได้รับการบำบัดด้วยฮอร์โมนทดแทนจำนวน 17 คน เข้าร่วมในการศึกษาจนเสร็จสิ้น อาสาสมัครอยู่ในระยะ 1-6 ปีหลังหมดระดู มีสุขภาพปริทันต์ดีเมื่อเริ่มต้นการศึกษาและได้รับการทำความสะอาดฟันทุก 2-3 เดือนตลอดการศึกษา ถ่ายภาพรังสีในปากจากฟันหลังล่างโดยใช้เครื่องมือกำหนดตำแหน่งและมุมเฉพาะบุคคลภายใต้การควบคุมกระแส ความต่างศักย์ ระยะเวลาในการถ่ายภาพ และกระบวนการล้างฟิล์ม แปลงภาพรังสีเป็นภาพดิจิทัล ประเมินความหนาแน่นกระดูกเบ้าฟันที่เพิ่มขึ้นหรือลดลงระหว่างภาพเริ่มต้นและภาพที่ถ่ายในเวลา 12 เดือนต่อมา โดยใช้ซอฟต์แวร์วิเคราะห์ความเข้ม ผลการทดลองพบว่ากลุ่มที่ไม่ได้รับการบำบัดด้วยฮอร์โมนทดแทนมีค่าเฉลี่ยความหนาแน่นกระดูกเบ้าฟันลดลงมากกว่าเมื่อเปรียบเทียบกับกลุ่มที่ได้รับการบำบัดด้วยฮอร์โมนทดแทนที่เวลา 12 เดือน อย่างไรก็ตาม ความแตกต่างนี้ไม่มีนัยสำคัญทางสถิติ ($p > .05$) นอกจากนี้ กลุ่มที่ไม่ได้รับการบำบัดด้วยฮอร์โมนทดแทนมีจำนวนบริเวณที่มีความหนาแน่นกระดูกลดลงมากกว่าในขณะที่กลุ่มที่ได้รับการบำบัดด้วยฮอร์โมนทดแทนมีจำนวนบริเวณที่มีความหนาแน่นกระดูกเพิ่มขึ้นมากกว่าด้วยอัตราเสี่ยงสัมพัทธ์ประมาณ 1.78 และช่วงความเชื่อมั่นร้อยละ 95 เท่ากับ 1.48-2.14 ดังนั้นสภาวะของเอสโตรเจนอาจมีอิทธิพลต่อแนวโน้มการเปลี่ยนแปลงความหนาแน่นกระดูกเบ้าฟันในประชากรกลุ่มนี้