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Bone Mineral Density Change Within 2 Years After Discontinuing Hormone Therapy In Postmenopausal Women

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ABSTRACT

Objective: To assess the rate of changes in vertebral and femoral BMD after hormone therapy (HT) cessation.

Design: Retrospective descriptive Study.

Setting: Menopause Clinic, Srinagarind Hospital, Khon Kaen, Thailand.

Materials and Methods: Medical records of 88 postmenopausal women who had taken HT for 1 to 5 years were reviewed. In all women, bone mineral density (BMD) was assessed within the last 6 months before HT withdrawal, then at least once within the first 24 months after treatment cessation. The rates of BMD changes were analyzed.

Results: Mean age of the assessed women was 54±5.6 years. Baselines BMD before starting HT were 0.979±0.130 g/cm^2 and 0.902±0.107 g/cm^2 at vertebral and femoral site, respectively. Mean vertebral BMD before and after discontinuation of HT were 1.004±0.134 g/cm^2 and 0.975±0.125 g/cm^2 while mean femoral BMD before and after discontinuation of HT were 0.903±0.108 g/cm^2 and 0.885±0.103 g/cm^2. After cessation of HT, the rates of vertebral and femoral BMD changes were -1.33 % and -0.99%, respectively. The numbers of postmenopausal women who had accelerated bone loss of at least 3% were 23.9% and 18.2% at lumbar spines and femur, respectively.

Conclusion: According to this study, average rate of bone loss were not accelerated within the first 2 years after cessation of HT.

Keywords: bone mineral density, hormone therapy, accelerated bone loss.

Introduction

Osteoporosis is common problem in postmenopausal women.[1] There are many modalities to prevent and treat osteoporosis such as life style modification or medication i.e. calcium, vitamin D, hormone therapy (HT) and bisphosphonate.[2-3]

The data from Woman Health Initiative (WHI) study in 2002, overall health risks exceeded benefits

from use of HT for an average 5.2 years. Although WHI is the first trial with definitive data supporting the ability of postmenopausal hormones to prevent fractures[4] but after publication, millions of regular HT users attempt to stop using HT.[5]

Bone mineral density (BMD) loss after HT is interesting subject. There were conflicting findings on the effect of discontinuing HT on bone mass. Both accelerated[6-9] and normal rates of bone loss.[10] Simon JA et al[6] presented a systematic review that showed bone loss after HT discontinuation was greater than those seen in placebo. Greendale GA et al[10] reported that the rate of BMD loss among postmenopausal women who had stopped HT was similar to that untreated women. Gallagher JC et al [11] found there had rapid bone loss in women who discontinued HT but total BMD of HT group were significant higher than the group had not used.

From literatures reviewed, there had been no study about this topic in Thailand and it is still controversial subject. For this reason the authors evaluated the rate of BMD change after stopped HT.

Materials and Methods

Study design was retrospective descriptive study which was approved by the Khon Kaen University ethics committee for human research. The target population was Thai women undergoing HT in Menopause clinic, Srinakarind Hospital from January 1997 to December 2007.

The objective of this study was to assess the rate of changes in vertebral and femoral BMD within 2 years after HT cessation.

We assessed postmenopausal women who had used hormone therapy for 1-5 years and discontinued HT for duration of less than 2 years. They were excluded if they had any chronic diseases such as chronic renal disease, chronic liver disease, metabolic bone disease or they had used drugs that affected BMD such as bisphosphonate, calcitonin, selective estrogen receptor modulators (SERM).

Sample size was calculated from prior study, Greenspan SL et al.[8] The mean of BMD was 0.8 g/cm², with standard deviation (SD) of 0.08 g/cm². This study defined accelerated rate of bone loss as decreasing of bone mineral density at least 3% per year. The mean difference (d) is 0.024 g/cm². The study had 95% power and type I error rate of 0.05. Under these conditions, 88 women were assessed.

Medical records of 88 postmenopausal women were reviewed. In all women, BMD had been assessed within the last 6 months before HT withdrawal, then at least once within the first 24 months after treatment cessation. The rate of BMD change was analyzed from these differences BMD.

All data were analyzed using SPSS software version 15.0, reported as mean values and percentage.

Results

Baseline characteristics of the women in the study were shown in Table 1. The mean age of the assessed women was 54$\pm$5.6 years. The mean age of menopause was 48.64±4.68 years. The average length of time for HT used was 3.01±1.28 years, and 48% of the participant had milk intake at least 1 glass/day.

Table 2 showed mean BMD in difference situations. Baselines BMD before starting HT were 0.979$\pm$0.130 g/cm^2 and 0.902$\pm$0.107 g/cm^2 at vertebral and femoral site, respectively. Mean vertebral BMD before and after discontinuation of HT were 1.004$\pm$0.134 g/cm^2 and 0.975$\pm$0.125 g/cm^2 while mean femoral BMD before and after discontinuation of HT were 0.903$\pm$0.108 g/cm^2 and 0.885$\pm$0.103 g/cm^2, respectively.

Among HT used, rate of BMD change rose 1.16% per year at vertebrae and 0.08% per year at femur. After cessation of HT, the rates of vertebral and femoral BMD changes were -1.33 % per year and -0.99% per year, respectively. (Table 3)

The numbers of postmenopausal women who had accelerated bone loss of at least 3% per year were 23.9% and 18.2% at lumbar spines and femur, respectively as shown in Table 4.

Table 1. Baseline characteristics (n = 88)

Variable	Mean	Standard Deviation
Age (yr)	54.4	5.6
BMI (kg/m^2)	24.4	2.9
Age of menopause (yr)	48.6	4.6
Length of time before start HT (yr)	5.6	5.3
Length of time for HT used (yr)	3.0	1.2
Length of time for cessation HT (yr)	1.4	0.5
Smokers (%)	5.7	
Alcohol consumption (%)	5.7	
Milk intake at least 1 glass/day (%)	48.9	

Table 2. Mean of bone mineral density (n = 88)

BMD (g/cm^2)	Mean (g/cm^2)	Standard Deviation
Baseline		
- L1-L4 spine	0.979	0.130
- Total femur	0.902	0.107
Before HT cessation		
- L1-L4 spine	1.004	0.134
- Total femur	0.903	0.108
After HT cessation		
- L1-L4 spine	0.975	0.125
- Total femur	0.885	0.103

Table 3. Rates of bone mineral density change (n = 88)

Rate of BMD change (% per yr)	Mean (% per yr)
After receiving HT	
- L1-L4 spine	1.16
- Total femur	0.08
After HT cessation	
- L1-L4 spine	-1.33
- Total femur	-0.99

Table 4. Number of bone mineral density change

Rate of bone loss after HT cessation	Frequency	Percent
L1-L4 spine		
- less than 3%	67	76.1
- at least 3%	21	23.9
Total femur		
- less than 3%	72	81.8
- at least 3%	16	18.2

Discussion

From this study, although postmenopausal women who stopped HT, had accelerated rate of bone loss, 21 cases (23.9%) at spine and 16 cases (18.2%) at femur but most of them did not have accelerated bone loss. The average rate of BMD loss was 1.33% per year at vertebrae and 0.99% per year at femur.

In previous studies, there had been inconsistent patterns of bone loss after hormone therapy withdrawal.[6-11] When comparing to other studies the rates of bone change in our study were similar to Greendale's study. The latter study showed that the rates of BMD loss among women who stopped HT did not differ significantly from those who did not receive HT.[10] Our results did not support the concept that accelerated bone loss arose after HT cessation.

In contrast, some previous studies found that accelerated bone loss was seen in the first few years after HT withdrawal.[8,9] In addition, women who had discontinued HT within 5 years had an increased risk of hip fracture when compared to never users.[7]

In present study, although mean BMD rose after receiving HT but after HT cessation means of BMD fell lower than baseline. This result had not correlated with Gallagher study[11] that reported residual effect on BMD after stop HT.

The limitation of our study was not designed to determine the benefits of HT on BMD. To answer this, we need to do a cohort study to compare BMD changes in postmenopausal women who had used HT with women who had not.

At Srinagarind hospital, many women came to menopause clinic because of their concern regarding vasomotor symptoms and osteoporosis. HT is an option for them. The results of our study can be used in advising women who want to receive or stop HT. In addition, it can be used as preliminary data for the other study.

Conclusion

Average rate of bone loss in most postmenopausal women were not accelerated within first 2 years after cessation of HT.

References

1. Limpaphayom KK, Taechakraichana N, Jaisamrarn U, Unyavejchevin S, Chaikittisilpa S, Poshyachinda M, et al. Prevalence of osteopenia and osteoporosis in Thai women. Menopause. 2001 Jan-Feb;8(1):65-9. PubMed PMID: 11201518.
2. Writing group for the PEPI Trial. Effects of hormone therapy on bone mineral density: results from the Postmenopausal Estrogen/Progestin Intervention (PEPI) trial. JAMA 1996;276:1389-96.
3. Cauley JA, Robbins J, Chen Z, Cummings SR. Effects of estrogen plus progestin on risk of fracture and bone mineral density: the women's health Initiative randomized controlled trial. JAMA 2003;290:1729-38.
4. Writing Group for Women's Health Initiative Investigator. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. JAMA 2002;288:321-33.
5. Ettinger B, Grady D, Tosteson ANA. Effect of the Women's Health Initiative on women's decisions to discontinue postmenopausal hormone therapy. Obstet Gynecol 2003;102:1225-32.

6. Simon JA, Wehren LE, Brynne H. Skeletal consequences of hormone therapy discontinuance: a systematic review. Obstet Gynecol Surv 2006;61:115-24.
7. Yates J, Barrett-Connor E, Barlas S. Rapid loss of hip fracture protection after estrogen cessation: evidence from the National Osteoporosis Risk Assessment. Obstet Gynecol 2004;103:440–6.
8. Greenspan SL, Emkey RD, Bone HG. Significant differential effects of alendronate, estrogen, or combination therapy on the rate of bone loss after discontinuation of treatment of postmenopausal osteoporosis: a randomized, double-blind, placebo-controlled trial. Ann Intern Med 2002;137:875–83.
9. Tremollieres FA, Pouilles JM, Ribot C. Withdrawal of hormone replacement therapy is associated with significant vertebral bone loss in postmenopausal women. Osteop Int 2001;12:385–90.
10. Greendale GA, Espeland MA, Slone S. Bone mass response to discontinuation of long-term hormone replacement therapy. Arch Intern Med 2002;162:665–72.
11. Gallagher JC, Rapuri PB, Haynatzki G. Effect of discontinuation of estrogen, calcitriol, and the combination of both on bone density and bone markers. J Clin Endocrinol Metab 2002;87:4914–23.

อัตราการเปลี่ยนแปลงความหนาแน่นกระดูกในผู้หญิงวัยหมดประจำเดือนที่หยุดใช้ฮอร์โมน

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วัตถุประสงค์ *: เพื่อศึกษาเกี่ยวกับอัตราการเปลี่ยนแปลงความหนาแน่นกระดูกของผู้หญิงวัยหมดประจำเดือนที่หยุดใช้ฮอร์โมน*

รูปแบบการวิจัย *: การวิจัยเชิงพรรณนา*

กลุ่มตัวอย่าง *: ผู้หญิงวัยหมดประจำเดือนที่มารับบริการที่คลินิกวัยทอง โรงพยาบาลศรีนครินทร์ คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น ในช่วงเวลาตั้งแต่ 1 ม.ค. 2540 – 31 ธ.ค. 2550 จำนวน 88 คน*

วัสดุและวิธีการ *: คัดเลือกผู้ที่เข้าเกณฑ์ของโครงการวิจัยโดยอาศัยข้อมูลจากบันทึกทางการแพทย์ รวบรวมข้อมูลพื้นฐาน ผลความหนาแน่นกระดูกในระยะเวลาไม่เกิน 6 เดือนก่อนหยุดใช้ฮอร์โมน ผลความหนาแน่นกระดูกหลังหยุดใช้ฮอร์โมนในระยะเวลา 2 ปี จากนั้นรวบรวมข้อมูลทั้งหมดมาคำนวณหาอัตราการเปลี่ยนแปลงของความหนาแน่นกระดูก*

ผลการวิจัย *: พบอัตราการลดลงของความหนาแน่นกระดูกสันหลังและต้นขาคิดเฉลี่ยเป็นร้อยละ 1.33 ต่อปีและร้อยละ 0.99 ต่อปี ตามลำดับ พบการลดลงอย่างรวดเร็วของความหนาแน่นกระดูกสันหลังและต้นขาคิดเป็นร้อยละ 23.9 และ ร้อยละ 18.2 ของกลุ่มประชากรศึกษา*

สรุป *: ในผู้หญิงวัยหมดประจำเดือนที่หยุดใช้ยาฮอร์โมนในระยะเวลา 2 ปี ส่วนมากไม่พบอัตราการลดลงอย่างรวดเร็วของความหนาแน่นกระดูก*