Effects of Differences in Polymorphism of Gene Encoding Enzyme Faenesyl Diphosphate Synthase (FDPS), *rs2297480*, on Bone Mineral Density and Biochemical Markers of Bone Turnover in Thai Postmenopausal Women

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Objective: *The purpose of this study was to find the frequency distribution of a SNP rs2297480 of the human FDPS gene and its influences on BMD and bone turnover markers in postmenopausal Thai women who never-use any anti-osteoporotic drugs.*
Material and Method: *One hundred and thirty-five postmenopausal women at the age of 40 or over, and having been menopause for at least 2 years were enrolled in the present study. The patients having chronic medical conditions and having a fracture in any bone within 3 months were excluded. All of the subjects never used any anti-osteoporotic drugs, steroid hormones and warfarin. Bone mineral density and bone turnover markers including N-MID osteocalcin and β-CTx were performed. Blood samplings for FDPS genotyping were collected and examined for rs2297480 SNP.*
Results: *The mean age of the patients was 60.4 (43-79) years old. The mean BMD T-score at all three major sites (Femoral neck, Lumbar spine, and Total hip) fell in the criteria of osteopenia. Twenty-four per cent of patients were diagnosed as osteoporosis (BMD T-score at one of three major sites was equal to or below -2.5 SD). One hundred and thirty-five patients whose data of rs2297480 SNP were defined as follows: AC genotype (45.1%), CC genotype (41.6%) and AA genotype (13.3%). Comparing among these three genotypes of rs2297480 SNP, the results showed no differences of BMD and BMTs among them. The absolute BMD after being adjusted to the same level of age and body weight and also β-CTx and N-MID OC between the group of AA + AC and the CC genotypes were also compared. No factors were statistically significant.*
Conclusion: *This is the first research investigating the gene FDPS rs2297480 SNP in postmenopausal Thai women. The frequency distribution of this SNP is the same as the distribution of the Asians but different from the Caucasians'. There are some small trends in the lower baseline of BMD at femoral neck and total hip in CC genotype group of these postmenopausal women although the results are not statistically significant. The effect of rs229748 SNP did not contribute to the baseline of BMD as well as the baseline of bone turnover markers before the treatment.*

Keywords: *FDPS gene, rs2997480, Bisphosphonates, Bone mineral density, Bone turnover markers*

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Osteoporosis is a skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissues which consequently increase bone fragility and the susceptibility to fracture[1]. In Caucasians, osteoporosis strikes one in four women over the age of 50 years[2]. In Thailand, the prevalence of osteoporosis defined by BMD among postmenopausal women is 21.4% (spine BMD) and 11.9% (hip BMD)[3]. The incidence of osteoporosis-related hip fractures in Thai women represented by the study of Phadungkiet et al[4] showed about 185 of fracture cases per 100,000 per year. This number is not as high as in Caucasian women. However, the one-year

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mortality associated with hip fractures among those women is 17%[5] which is the same as the one-year mortality rate after hip fracture of 20% mentioned by WHO[6]. It has been forecasted that hip fractures will increase most markedly all over the world to 6.26 million cases per year in 2050, and half of that number, *i.e.* 3 million cases will occur in Asia[7].

The most important current treatment strategy for prevention of osteoporotic fractures is antiresorptive therapy of which the leading agents are the nitrogen-containing bisphosphonates (N-BPs). All the N-BPs have a similar mode of action which leads to the reduction of the excessive bone turnover and increases in BMD that are the major factors associated with the risks for fractures. Once bisphosphonates are absorbed and distributed into the body, they not only localize at but also bind to bone mineral surfaces exposed by bone resorbing cells called osteoclasts as a part of the normal bone remodeling cycle[8]. Bisphosphonates reduce postmenopausal bone loss by inhibiting the osteoclast activity, reducing the rate of bone resorption and normalizing the mineralization process, subsequently, bone mass increases[9]. These effects can be monitored by measuring the levels of bone turnover markers in blood or urine and the changes in BMD by using DXA scans. Bisphosphonates also preserve the connectivity of trabecular bone and improve the structural properties[10-12] leading to increase bone strength and reduce fracture risks. BMD is an important surrogate measure of fracture risks. Wasnich and Miller[13] showed that greater increases in lumbar spine BMD caused larger reductions in vertebral fracture risks. Likewise, Hochberg et al[14] demonstrated that greater increase in lumbar spine BMD and greater increase in hip BMD result in larger reduction in non-vertebral fracture risks. Therefore, it can be expected that a bisphosphonate that significantly increases BMD will provide fracture prevention with a good correlation to the extent of BMD gain.

The studies to assess the efficacy of bisphosphonate preparations in improving BMD and bone turnover markers in osteoporotic Asian women are limited. Usually, the effective data and also the BMD response studied in the Caucasian population are used as references. A small short-term study of the postmenopausal Chinese women with osteoporosis in Hong Kong by Ho and Kung[15] reporting in 2005 demonstrated a large increase in BMD in these populations about 6.1% at L-spine, 5.6% at femoral neck and 3.5% at total hip in one year after the treatment with weekly dose (70 mg) of Alendronate. A short-term study in Caucasian Americans[16] reported in 2004 showed that the one-year increase in BMD at L-spine in the once-weekly Alendronate (70 mg) treated group was only 4.4%. Another one-year study done by Iwamoto et al[17] to determine the one-year BMD response in postmenopausal Japanese women with osteoporosis using half of recommended dose of Alendronate (5 mg/day) found the unexpected increase in L-spine BMD of 8.1% in 1 year.

In the HORIZON-PFT study[18], the researchers investigated a single dose once-yearly zoledronic acid infusion in postmenopausal women with osteoporosis. They found that Zoledronic acid could reduce risks of morphometric vertebral fracture by 70% and reduce risks of hip fracture by 41% during 3 years, when comparing with placebo. Zoledronic acid also reduced risks of non-vertebral fractures, and any clinical fractures by 25% and 33% respectively. Furthermore, it was associated with the increase of 6.71% in L-spine BMD as well as the increase of 6.02% in total hip BMD throughout 3 years. Surprisingly, the subgroup analysis of another study[19] according to the regions showed that in the Asian region (subpopulation of 1,090 cases) there was the highest rate of reduction in all fracture measurements. There was an 80% reduction in risks of vertebral fracture (RR = 0.20, 95% CI 0.35-0.11), 45% reduction in risks of any clinical fractures (RR = 0.55, 95% CI 0.94-0.32) and 67% reduction in risks of hip fracture (RR = 0.33, 95% CI 1.20-0.09 non-significance). As mentioned above, the responses to bisphosphonate treatment in postmenopausal Asian women with osteoporosis may be different from Caucasians in some extent. The individual factors such as low baseline of L-spine BMD, number of prevalence vertebral fractures, and high bone turnover women who show greater reduction in bone turnover markers at 6^{th} month are found to correlate with higher increase in L-spine BMD in the 1-year treatment with Alendronate in Japanese women[17]. Actually, the data concerning genetic determination of BMD response to anti-osteoporotic drugs in the Asian population are quite limited. The studies about Vitamin D receptor (VDR) gene polymorphisms that influence BMD response to calcium and vitamin D have been controversial[20]. A meta-analysis of 29 studies on the relationship of VDR genotype with BMD[21] concluded that VDR genotype was associated with BMD in the elderly subjects but with only 1-2% difference between the extreme genotypes. The estrogen receptor α-type (ERα) polymorphism with regard to the effect of hormone

replacement therapy on BMD has been studied. Kobayashi et al[22] found a significantly greater increase of BMD in women with the *pp* genotype than in those with the *Pp* or *PP* genotype in *Pvu*II polymorphisms of the ERα gene in postmenopausal Japanese women. In the present study, a genetic polymorphism within the *fdps* gene (*rs2297480)* which is the gene encoding for the enzyme farnesyl diphosphate synthase (FDPS) was explored. It is a key enzyme in the mevalonate pathway which is the main target for bisphosphonate to inhibit bone resorption[23]. A study in the Caucasian population[25] found that polymorphism in genotype of *fdps* gene contributed to BMD of postmenopausal women who were not included in the bisphosphonates treatment. This is the first study in Thailand to find the frequency distribution of this gene and its influences on BMD and common bone turnover markers in postmenopausal Thai women who have never used any anti-osteoporotic drugs.

Material and Method

The prospective comparative cohort study commenced at Phramongkutklao Hospital and College of Medicine, Bangkok, Thailand. One hundred and thirty-five postmenopausal women at the age of 40 years or over, and having been menopause for at least 2 years were enrolled in the present study. The patients who had a history or evidence of chronic medical conditions or metabolic bone diseases that may affect bone metabolism and also those who had a history or evidence of renal dysfunction, liver dysfunction were excluded. The patients with a history of cancer within 5 years, recent consumptions of an excess alcohol that was defined as more than 4 drinks per day, current smoking or drug abuse, and those who got a fracture in any bone within 3 months were also excluded. They must be able to walk independently and none of them engaged in any regular physical exercise programs. All of the subjects never used any anti-osteoporotic drugs such as bisphosphonates, strontium ranelate, teriparatide, hormone therapies, SERMs also steroid hormones and warfarin. Those taking any calcium and/or vitamin D supplement had to stop them for over a period of 3 months. The patients were asked to sign the informed consent on the first day of the research, then the medical examination, blood tests for screening of renal and hepatic impairment were performed. Bone mineral density (axial-DXA) and bone turn over markers (BTMs) including N-MID osteocalcin and β-CTx were conducted within 1 month after the consent was signed. Blood samplings for FDPS genotyping were collected and refrigerated at -20°C prior to the examination for FDPS polymorphism in the laboratory at Ramathibodi Hospital.

Bone Mineral Density Test

Bone mineral density of the lumbar spine (postero-anterior) and the hip (total hip, femoral neck) were measured by a dual-energy x-ray absorptiometry (DXA) machine in Phramongkutklao Hospital. Hologic QDR 4500A densitometer (Hologic Inc., Bedford, MA) the CVs for BMD measurements were 1.7% for the lumbar spine, 1.2% for the total hip, and 1.9% for the femoral neck[26].

Bone Turnover Markers Test

Bone turnover markers are further divided into the marker of bone resorption and the marker of bone formation which both reflect two essential parts of bone remodeling cycle. The effects of drugs or other factors on bone turnover are studied; at least one of both kinds of these markers is definitely done. The marker of bone resorption used in the present study is the serum C-telopeptide cross-linked of collagen type-1 (β-CTx) or beta-Crosslaps assay. It was assessed by using the electrochemiluminescence immunoassays (ECLIA) technique (Elecsys, Roche Diagnostics, Mannheim, Germany, ng/ml; intraassay CV 2.4-7.2%)[27,28]. For the marker of bone formation used in the present study was the serum N-MID Osteocalcin (N-MID OC) which, again, was assessed by using the ECLIA technique (Elecsys, Roche Diagnostics, Mannheim, Germany, ng/ml; intraassay CV 1.1-5.9%)[27,28]. Intact parathyroid hormone (iPTH) assay was also evaluated by the ECLIA technique (Elecsys, Roche Diagnostics, Mannheim, Germany, ng/ml; intraassay CV 1.7-5.5%)[27,28]. Serum for β-CTx, N-MID OC and iPTH assessment was collected in the morning at around 8.00 am, after an overnight 12-hour fasting and was frozen at -20°C. All specimens were sent to the central laboratory for the tests and quality control.

FDPS genotyping

DNA was isolated from the frozen buffy coats of whole blood by the standard method (3 ml, collected into EDTA)[29]. PCR reactions were performed. Amplifiction of *rs2297480* used forward primer 5'-AGGAATCCGTATCTGGGAAC-3' and reverse primer 5'-CAACTCTAGACACCCCCAGAAG-3' and genotypes assigned by fluorescence polarization[30]. The PCR cycling conditions and genotyping were run by the standard procedure according to the endocrine

laboratory in Ramathibodi Hospital as the following. DNA 20 ng was added into the PCR reaction consisting of TaqMan® Universal Master Mix (1x), TaqMan® MGB probes (1x) in a total volume of 10 mL. The real-time PCR reaction protocol was 10 min 95°C, and 40 cycles of 15 sec 92°C, 1 min 60° C using 7500 Real Time PCR System (Applied Biosystems, Foster City, CA).

Statistical Analysis

The analysis was performed by SPSS (version 17.0). Descriptive statistics was used to present the distribution of *rs2297480* A/C polymorphism in the AA, AC and CC genotypes among postmenopausal Thai women. The baseline of BMD, bone turnover markers and demographic data were processed to determine the mean, standard deviation and other descriptive statistics. The association between the baseline of BMD and bone turnover markers in three groups of *rs2297480* A/C polymorphism were analyzed by using one way ANOVA or Kruskal-Wallis test for the continuous data. A p-value of less than 0.05 was considered statistically significant.

Results

The characteristics of the BMD baseline, bone turnover markers and demographic data were shown in Table 1. The mean age of patients was 60.4 years old with the range between 43-79 years old. The mean BMD T-score at all three major sites (Femoral neck, Lumbar spine (L1-L4), and Total hip) fell in the criteria of osteopenia (T-score between -1 to -2.5, based on the National Osteoporosis Foundation [NOF] guideline)[31]. Thirty-two patients (24%) were diagnosed as osteoporosis as their BMD T-score at one of three major sites was equal to or below -2.5 SD and 24% of them had normal BMD as shown in Fig. 1.

One hundred and thirty five participants whose data of *rs2297480* A/C polymorphism were defined as follows: AC genotype (45.1%), CC genotype (41.6%) and AA genotype (13.3%) as shown in Fig. 2. After comparing the data of these three genotypes of *rs2297480* A/C polymorphism by using one way ANOVA or Kruskal-Wallis test for the continuous data, the results showed no differences of BMD and BMTs among the groups as shown in Table 2.

The authors compare the absolute BMD after being adjusted to the same level of age and body weight and also β-CTx and N-MID OC between the genotype groups of AA + AC and CC. Table 3 and 4 showed that no factors were statistically significant among the adjusted BMD, bCTx and N-MID OC

Discussion

At present, it is widely accepted that the molecular mechanism in which nitrogen-containing bisphosphonates inhibiting osteoclast activity is the

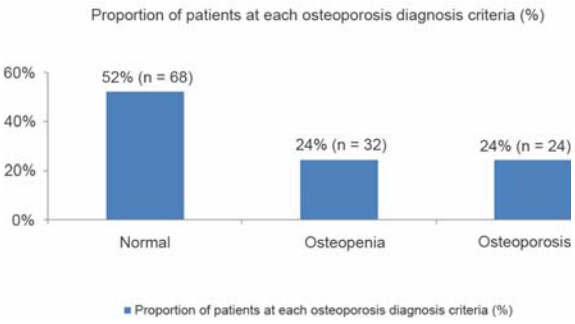

Fig. 1 Diagnosis criteria based on BMD T-score in post-menopausal Thai women (n = 132)

Table 1. Characteristics of the baseline BMD, bone turnover markers and demographic data among postmenopausal Thai women

Variables	n	mean (SD)	Minimum	Maximum
Age (yr)	134	60.41 (7.87)	43	79
β-CTx (ng/ml)	135	0.46 (0.24)	0.047	1.61
N-MID OC (ng/ml)	133	25.43 (10.01)	7	61
PTH (pg/ml)	134	48.99 (25.30)	16.28	254.90
L1-4 (g/cm^2)	132	0.82 (0.13)	0.497	1.115
L1-4 T-score	132	-1.56 (1.14)	-4.4	0.9
Neck (g/cm^2)	132	0.67 (0.10)	0.373	0.986
Neck T-score	132	-1.18 (1.04)	-4.0	1.7
Total hip (g/cm^2)	132	0.80 (0.11)	0.511	1.102
Hip T-score	132	-0.58 (1.03)	-3.1	2.2

Table 2. Examination of the association between the BMD baseline and bone turnover markers in three group of rs2297480 A/C polymorphism, using one way ANOVA or Kruskal-Wallis test

Variables	Genotype			p-value
	AA	CA	CC	
Age (n = 134)				0.288*
Mean (SD)	57.89 (7.36)	60.35 (7.77)	61.65 (8.03)	
Median (Min, Max)	57 (43, 71)	59 (46, 79)	60 (48, 79)	
β-CTx (ng/ml) (n = 135)				0.355**
Mean (SD)	0.45 (0.19)	0.44 (0.22)	0.5 (0.27)	
Median (Min, Max)	0.40 (0.20, 0.77)	0.42 (0.05, 1.08)	0.49 (0.06, 1.61)	
N-MID OC (ng/ml) (n = 133)				0.594**
Mean (SD)	27.39 (9.68)	24.9 (10.66)	25.62 (9.72)	
Median (Min, Max)	25.51 (7.79, 46.73)	25.05 (8.31, 61.42)	26.38 (7.38, 56.93)	
PTH (n = 134)				0.095*
Mean (SD)	45.2 (14.27)	46.19 (17.57)	54.28 (33.62)	
Median (Min, Max)	43.35 (25.59, 74.72)	42.75 (18.9, 100.9)	51.09 (16.28, 254.9)	
L1-4 (g/cm^2) (n = 132)				0.910**
Mean (SD)	0.81 (0.12)	0.82 (0.14)	0.83 (0.13)	
Median (Min, Max)	0.81 (0.63, 1.05)	0.82 (0.50, 1.12)	0.82 (0.55, 1.10)	
L1-4 T-score (n = 132)				0.843**
Mean (SD)	-1.67 (1.03)	-1.58 (1.16)	-1.50 (1.17)	
Median (Min, Max)	-1.70 (-3.20, 0.40)	-1.70 (-4.4, 0.9)	-1.60(-4.40, 0.80)	
Femoral neck (g/cm^2) (n = 132)				0.187**
Mean (SD)	0.69 (0.1)	0.69 (0.11)	0.65 (0.11)	
Median (Min, Max)	0.68 (0.56, 0.93)	0.68 (0.48, 0.99)	0.65 (0.37, 0.93)	
Femoral neck T-score (n = 132)				0.246**
Mean (SD)	-1.03 (0.90)	-1.05 (1.05)	-1.36 (1.09)	
Median (Min, Max)	-1.15 (-2.30, 1.20)	-1.10 (-3.10, 1.70)	-1.40 (-4.00, 1.20)	
Total hip (g/cm^2) (n = 132)				0.291**
Mean (SD)	0.82 (0.09)	0.81 (0.11)	0.78 (0.11)	
Median (Min, Max)	0.83 (0.62, 0.98)	0.81 (0.57, 1.10)	0.77 (0.51, 1.06)	
Total hip T-score (n = 132)				0.486**
Mean (SD)	-0.53 (0.93)	-0.44 (1.03)	-0.71 (1.07)	
Median (Min, Max)	-0.45 (-2.10, 1.10)	-0.50 (-2.80, 2.20)	-0.80 (-3.10, 1.80)	

* Kruskal-Wallis Test, ** One-Way ANOVA

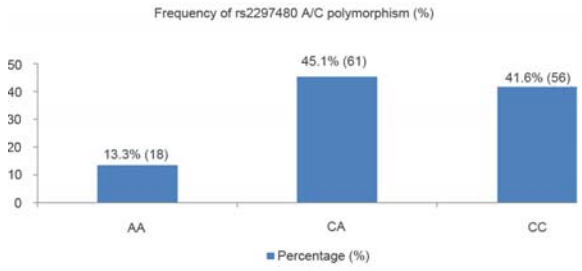

Fig. 2 Characteristic of rs2297480 A/C polymorphism in postmenopausal Thai women (n = 135)

action on mevalonate pathway. Farnesyl Diphosphate Synthase (FDPS), an indispensable enzyme for protein prenylation and activation of intracellular signaling proteins, is a key enzyme in the mevalonate pathway which is the main target for inhibition[23]. The disruption of this key enzyme function explains the loss of osteoclast activity and induction of apoptosis. There is a highly significant correlation between the order of potency of N-BPs for inhibiting human FDPS in vitro and their antiresorptive potency *in vivo* with the zoledronic acid which is an extremely potent inhibitor of FDPS. Importantly, minor modifications to the N-BPs side chain known to affect antiresorptive potency now have shown an effect on the ability to inhibit FDPS[24]. In the present study by Dunford et al[24], the order of potency for inhibiting enzyme FDPS were zoledronic acid > minodronate > risedronate > ibandronate > incadronate > alendronate > pamidronate.

Table 3. The difference of predicted variables (L1-4 g/cm^2, Neck g/cm^2 and Total HIP) comparing between the genetics CC and the AA + AC groups and the power of analysis was calculated

Variables	Comparison between AA + AC and CC genotypes			
	CC n = 56	AA + AC n = 79	p-value	Power
L1-4 g/cm^2			0.685	7.2%
Mean (SD)	0.83 (0.13)	0.82 (0.13)		
Median (Q1, Q3)	0.82 (0.73, 0.95)	0.82 (0.73, 0.9)		
NECK g/cm^2			0.070	54.2%
Mean (SD)	0.65 (0.11)	0.69 (0.1)		
Median (Q1, Q3)	0.65 (0.58, 0.72)	0.68 (0.61, 0.74)		
Total Hip			0.154	34%
Mean (SD)	0.78 (0.11)	0.81 (0.11)		
Median (Q1, Q3)	0.77 (0.7, 0.87)	0.81 (0.74, 0.87)		
β-TCx			0.155	28.1%
Mean (SD)	0.5 (0.27)	0.44 (0.21)		
Median (Q1, Q3)	0.49 (0.32, 0.67)	0.41 (0.3, 0.58)		
N-MID OC			0.859	5.4%
Mean (SD)	25.62 (9.72)	25.3 (10.27)		
Median (Q1, Q3)	26.38 (17.03, 32.23)	25.03 (16.86, 32.59)		

Table 4. The difference of predicted variables (L1-4 g/cm^2, Neck g/cm^2 and Total HIP) between the genotype CC group and the AA +AC group using multiple linear regression

Outcomes	CC and AA+AC (Predictor)			
	Coefficient	SE	95%CI	p-value
Model 1: L1-4 g/cm^2	-0.014	0.023	-0.06, 0.031	0.537*
Model 2: NECK g/cm^2	0.024	0.018	-0.011, 0.059	0.184*
Model 3: Total Hip	0.022	0.019	-0.016, 0.059	0.251*

*The age and body weight adjustments

Apart from the target for bisphosphonate therapy, Levy et al's research[25] also found that polymorphism in genotype of *fdps* gene certainly contributed to BMD of postmenopausal women who were not on the bisphosphonates treatment. They studied 373 Caucasian postmenopausal women and found a SNP (*rs2297480, A/C*) correlated with BMD. Among these women, 52.3% had the AA genotype, 42.8% had the AC genotype and 4.9% had the CC genotype. As finding from the electronic database of NCBI single nucleotide polymorphism (SNP) website[32], the reference SNP cluster report of *fdps rs2297480* gene found the population diversity in this gene was AA = 48.3%, AC = 41.7% and CC = 10% in the European population (n = 120) which was comparable with the frequency distribution of this gene found by Levy et al[25] in the American population. On the other hand, the frequency distributions of *rs2297480* in two reports of the Asian population from the International HapMap project were opposite[32]. These two studies reported the frequency distribution of AA = 6.7%, AC = 48.9% and CC = 44.4% in the Chinese population (n = 90) and also found the distribution of AA = 2.3%, AC = 36.4% and CC = 61.4% (n = 88) in the Japanese population[32]. This research found that the distribution of *fdps rs2297480* gene polymorphism in the postmenopausal Thai women were AA = 13.3%, AC = 45.1% and CC = 41.6% (n = 135). The result was the same as the Chinese population whose main genotype of this SNP was AC, but different from the Japanese and Caucasian populations whose main genotypes were CC and AA respectively.

The present study by Levy et al in 2007 in the Caucasian population showed that BMD was lower at all sites measured in women with the CC or AC

genotype compared to the AA genotype. However, the statistical significance was only seen in lumbar spine, trochanter and distal radius BMD[25]. In the present study, there were no statistical significances when BMD was shown by the absolute values and T-score which were lower in the CC genotype compared to the AA genotype in both femoral neck and total hip regions. Although the absolute values of BMD of both femoral neck and total hip regions after being adjusted to the baseline of age and body weight between the AA + AC genotype and the CC genotype to increase the number of subjects per group were done, there was still no statistical significance. These results were actually the same as Levy et al[25] which the statistical significance was only seen in lumbar spine, trochanter and distal radius regions but not in femoral neck and total hip regions. In the spine BMD, these results were not shown the trend in the lowest BMD in the CC genotype but they showed the reverse results. This event may occur due to the effect in spondylotic processes of the lumbar spine as the highest age group in the CC genotype was displayed (Table 2). Recently, there was a study of three single-nucleotide polymorphisms (SNPs) of FDPS in 1186 postmenopausal women in Spain[33]. There was only a marginally significant association of baseline hip BMD with *rs11264359* alleles (p = 0.043), but no significant difference with *rs2297480* of this gene took place. The present study also showed trends in the lower BMD response to bisphosphonates in the group of CC genotype of *rs2297480* SNP compared to the AA and AC genotypes. The BMD baseline result of the study by Olmos et al[33] was consistent with our result as the polymorphism of *fdps* gene *rs2297480* did not influence the BMD at the baseline but only contributed to the BMD responses after the bisphosphonate therapy.

Conclusion

This is the first study demonstrated in Thailand. It investigates the single-nucleotide polymorphisms (SNPs) of *fdps* gene, *rs2297480*, in postmenopausal Thai women. The frequency distributions of this SNP are AA = 13.3%, AC = 45.1% and CC = 41.6% (n = 135). They are the same as the distribution in the Chinese but opposite to the Caucasians. There are only small trends in the lower baseline of BMD at femoral neck and total hip in these postmenopausal women whose result analysis is not statistically significant. These results are occurred by a small number of subjects in the present study as well as the effect of this SNP (*rs2297480*) may not contribute to the baseline of BMD. As this *fdps* gene encodes the enzyme which is the main target for bisphosphonate action, they probably have the effect to the responses of BMD after the treatment with bisphosphonates.

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Potential conflicts of interest

None.

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ผลของความแตกต่างกันทางพันธุกรรมของจีนสำหรับเอนไซม์ฟาเนสซิลไดฟอสเฟตซินเทส (เอฟพีพีเอส) rs2297480 ต่อความหนาแน่นกระดูกและดัชนีชีวเคมีของการผลัดเปลี่ยนกระดูกในสตรีไทยวัยหมดระดู

ทวี ทรงพัฒนาศิลป์, สุวรรณี จันทร์ประเสริฐโยธิน

วัตถุประสงค์: *เพื่อหาความถี่ของการกระจายตัวของ polymorphism ของจีน rs 2297480 SNP ซึ่งเป็นจีนสำหรับเอนไซม์ ฟาเนสซิลไดฟอสเฟตซันเทส (เอฟดีพีเอส) และอิทธิพลของจีนนี้ต่อความหนาแน่นของกระดูกและดัชนีชีวเคมีของ การผลัดเปลี่ยนกระดูก ในสตรีไทยวัยหมดระดู ที่ไม่เคยได้รับยาใดๆ รักษาโรคกระดูกพรุน*

วัสดุและวิธีการ: *สตรีไทยวัยหมดระดูที่มีอายุเท่ากับหรือมากกว่า 40 ปี และหมดระดูแล้วอย่างน้อยสองปีขึ้นไป จำนวน 135 ราย ได้เข้าร่วมการศึกษานี้ สตรีที่มีปัญหาโรคเรื้อรังและเคยมีกระดูกหักในระยะน้อยกว่า 3 เดือน ได้รับการคัดออก ทุกคนไม่เคยได้รับยาใดๆ รักษาโรคกระดูกพรุน เช่นเดียวกับยาสเตียรอยด์และวาฟาริน ทั้งหมดนี้จะได้รับการตรวจวัดความหนาแน่นของกระดูก และเจาะเลือดตรวจวัดดัชนีชีวเคมีของการผลัดเปลี่ยนกระดูกซึ่งประกอบด้วย N-MID osteocalcin (OC) และ b-CTx รวมทั้งเจาะเลือดเพื่อตรวจหาความแตกต่างทางพันธุกรรมของจีน FDPS rs2297480*

ผลการศึกษา: *อายุเฉลี่ยของผู้เข้าร่วมการศึกษาคือ 60.4 (43-79) ปี ค่า T-score ของความหนาแน่นของกระดูกเฉลี่ยอยู่ในเกณฑ์กระดูกบางทั้งสามตำแหน่งหลัก (คอสะโพก, กระดูกสันหลัง และสะโพกรวม) 24% ของผู้เข้าร่วมการศึกษามีค่า T-score ของความหนาแน่นของกระดูกอยู่ในเกณฑ์เป็นโรคกระดูกพรุนที่ตำแหน่งใดตำแหน่งหนึ่งในสามตำแหน่งหลัก ความถี่ของการกระจายตัวของ polymorphism ของจีน rs2297480 SNP เป็น AC genotype 45.1% CC genotype 41.6% และ AA genotype 13.3% เมื่อเปรียบเทียบกันระหว่าง 3 genotypes ไม่พบความแตกต่าง ของความหนาแน่นของกระดูกและดัชนีชีวเคมีของการผลัดเปลี่ยนกระดูก อีกทั้งการเปรียบเทียบค่าความหนาแน่น ของกระดูกที่ได้ปรับด้วยน้ำหนักตัวและอายุ และค่าซีรัม N-MID OC และ β-CTx ระหว่างกลุ่ม AC+AA กับ CC genotypes ก็ไม่พบความแตกต่างอย่างมีนัยสำคัญทางสถิติ*

สรุป: *การศึกษานี้เป็นการศึกษาครั้งแรกเกี่ยวกับจีน เอฟดีพีเอส rs2297480 SNP ในสตรีไทยวัยหมดระดู ซึ่งมีความถี่ของการกระจายตัวของ polymorphism เช่นเดียวกับคนเอเชียแต่แตกต่างกับคนคอเคเซียน จีน เอฟดีพีเอส rs2297480 ไม่มีผลต่อความหนาแน่นกระดูก และดัชนีชีวเคมีของการผลัดเปลี่ยนกระดูกในสตรีไทยวัยหมดระดูที่ยังไม่ได้รับยาใดๆ รักษาโรคกระดูกพรุน*