Bone Mineral Density in Women Using Depot Medroxyprogesterone Acetate (DMPA) for at Least 2 Years Compared to a Control Group: A Cross Sectional Study

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Objective: *To compare the effect of long-term use of depot medroxyprogesterone acetate (DMPA) on bone mineral density (BMD) in Thai women compared to the control.*
Material and Method: *A cross sectional study was conducted on Thai women of reproductive age who used DMPA (50 subjects) for contraception for at least 2 years and non-hormonal users (50 subjects). BMD was measured at the lumbar spine, femur and distal radius, and ulna.*
Results: *There was significantly lower BMD at the lumbar spines in the DMPA group but there was no significant difference in BMD between groups at the femur, distal radius, and ulna.*
Conclusion: *Long-term use of DMPA has a negative impact on lumbar spine BMD.*

Keywords: *DMPA, Depo medroxyprogesterone acetate, BMD, Bone mineral density, Bone density, Lumbar, Femur, Distal radius, Ulna*

J Med Assoc Thai 2009; 92 (10): 1263-7
Full text. e-Journal: *http://www.mat.or.th/journal*

Depot medroxyprogesterone acetate (DMPA) has been widely used in Thailand as contraception for more than 30 years. It is well known for contraceptive effectiveness and convenience. However, DMPA induces a hypo-estrogenic state, and as a result, deterioration of bone could theoretically be harmful in long-term users. Consequently, based on the United States Food and Drug Administration, many practitioners suggest clients switch DMPA to other forms of contraception after 2 years use[1,2].

Nevertheless, available data on bone mineral density (BMD) and DMPA was controversial. Most published data showed a lower bone mass in DMPA users[3-11]. On the contrary, cross sectional studies in Thais revealed no difference in BMD of the forearm between users and the control group[12,13]. Furthermore, a recent study in Thai women found a negative impact of DMPA to vertebral bone mineral density, but no impact on the femur[14].

The purpose of the present study was to explore the BMD among Thai women with long-term use (≥ 24 months) of DMPA, compared to non-hormonal users.

Material and Method

One hundred healthy Thai women aged 15-45 years were recruited into the present study and divided equally into two groups: fifty women in the first group used DMPA and a control group used non-hormonal contraceptives. Women in the first group had used DMPA for at least two years. All of the subjects were healthy without any condition or drug use that might have interfered with their hormonal status and bone metabolism. Participants were enrolled

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into the present study in the year 2006, at the Family Planning Clinic, Maharaj Nakorn Chiang Mai Hospital, Thailand. BMD was measured by Dual Energy X-ray Absorptiometry (Hologic QDR-4500 C: DEXA) at the lumbar spine 1-4, greater trochanter of femur, Ward's triangle of femur, neck of femur, intertrochanteric of femur and total of proximal femur and distal radius and ulna (1/3 distal radius and ulna, middle distal radius and ulna, ultradistal radius and ulna and total distal radius and ulna). This was performed only once, immediately after enrollment.

Data were presented using the percentage, mean, standard deviation (SD) and 95% confidence interval (CI). Statistical analysis compared the difference in mean BMD between the two groups by using the t-test. A Chi-square test was used to compare the difference between the categorical data.

Results

One hundred Thai women were enrolled into the present study and divided into two groups, including 50 using DMPA for at least two years, and 50 non-hormonal contraception users. All of them lived in northern Thailand. Most participants in both groups were 21-45 years of age. Each group had a mean age of 34 years, menarche age of 13-14 years, parity of 0-4, and a mean body mass index (BMI) of 24.19 and 22.36, respectively. The demographic characteristics such as age, BMI, and parity were not significantly different as shown in Table 1. The mean ($\pm$ SD) duration of contraception for DMPA was 73.6 $\pm$ 56.0 months. The BMD (t-score) was classified according to WHO criteria at higher than or equal to -1.0 as normal, at equal -1.1 to -2.4 as osteopenia, and lesser than or equal to -2.5 as osteoporosis. The prevalence of osteopenia (t-score = -1.1 to -2.4) at the lumbar spine in the DMPA group in the present study of L1, L2, L3, L4, and total L1-L4 were 52%, 40%, 40%, 62%, and 52%, respectively higher than the non-hormonal group at all sites (Table 2).

The mean BMD at all sites of the lumbar spine (L1-L4) was compared with the non-hormonal contraceptive group. The present study revealed that there was significantly lower BMD in the DMPA group. However, there was no significant difference in BMD between DMPA users and the non-hormonal contraception group at the femur, distal radius, and ulna (Table 3).

Discussion

This cross sectional study reaffirms that the mean lumbar BMD in long-term DMPA users (24 months) was significantly lower than in the non-hormonal group, but there was no effect on BMD at other sites (femur, distal radius, and ulna). Theoretically, DMPA users had more hypo-estrogenic state than the control. Therefore, this effect induces a low BMD, especially in sensitive areas such as the vertebral column, which has more trabecular bones than other sites.

Although the present study does not test the serum estradiol level in the participants, this point is not an important issue, since the factors that influence the estrogenic states in the body (such as age of menarche, age, BMI, parity, smoking habit, race and habitat) were identical between groups.

Studies by Taneepanichskul[12] and Tharnpisarn[13] from Thailand did not find any adverse effect on bone. In their studies, however, distal radius and ulna were the only areas measured

Table 1. Demographic characteristic of participants

Characteristics	DMPA	Non-hormonal
Age (years)		
Mean $\pm$ SD (range)	34.18 $\pm$ 6.45 (21-45)	34.04 $\pm$ 7.83 (21-45)
BMI (kg/m^2)		
Mean $\pm$ SD (range)	24.19 $\pm$ 3.37 (17.91-34.31)	22.36 $\pm$ 3.40 (16.35-35.38)
Parity		
Median	1.0	1.0
Mean $\pm$ SD (range)	1.62 $\pm$ 0.88 (0-3)	1.26 $\pm$ 1.34 (0-4)
Duration of hormonal contraception (months)		
Minimum-maximum	24-268	0
Mean $\pm$ SD	73.62 $\pm$ 56.05	

Table 2. T-score at each site in each group

T-score	Lumbar: number (%)				
	L1	L2	L3	L4	L1-L4
DMPA					
-1.0 or higher	22 (44)	28 (56)	30 (60)	17 (34)	23 (46)
-1.1 to -2.4	26 (52)	20 (40)	20 (40)	31 (62)	26 (52)
-2.5 or less	2 (4)	2 (4)	0	2 (4)	1 (2)
Non hormonal					
-1.0 or higher	41 (82)	41 (82)	41 (82)	34 (68)	41 (82)
-1.1 to -2.4	8 (16)	9 (18)	9 (18)	16 (32)	9 (18)
-2.5 or less	1 (2)	0	0	0	0

	Femur: number (%)				
	Greater trochanter of femur	Ward's triangle of femur	Neck of femur	Intertro chanteric of femur	Total of proximal femur
DMPA					
-1.0 or higher	45 (90)	45 (90)	44 (88)	44 (88)	45 (90)
-1.1 to -2.4	5 (10)	5 (10)	6 (12)	6 (12)	5 (10)
-2.5 or less	0	0	0	0	0
Non hormonal					
-1.0 or higher	48 (96)	45 (90)	46 (92)	45 (90)	46 (92)
-1.1 to -2.4	2 (4)	5 (10)	4 (8)	5(10)	4 (8)
-2.5 or less	0	0	0	0	0

	Distal radius and ulna: number (%)		
	1/3 distal radius & ulna	Ultra distal radius & ulna	Total distal radius & ulna
DMPA			
-1.0 or higher	44 (88)	48 (96)	47 (94)
-1.1 to -2.4	6 (12)	2 (4)	3 (6)
-2.5 or less	0	0	0
Non hormonal			
-1.0 or higher	45 (90)	50 (100)	48 (96)
-1.1 to -2.4	5 (10)	0	2 (4)
-2.5 or less	0	0	0

by investigators. While the present study focused on all three sites of BMD, it found that DMPA had no effect on any of them except at the lumbar spines. The results of the present study were similar to those of Wanichsetakul[14].

In conclusion, DMPA has negative impact on bone at the lumbar spine, which is the most sensitive area due to a high content of trabecular bone.

Being cross sectional was a limitation of the present study. However, the authors can use the results in part of the counseling procedure to clients before DMPA use, especially in the high-risk group of osteopenia and osteoporosis.

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Table 3. Comparison of BMD (gm/cm^2) at each site between the DMPA and non-hormonal group

	DMPA Mean ± SD	Non hormonal Mean ± SD	p-value
Lumbar			
Lumbar 1	0.782 ± 0.101	0.844 ± 0.079	0.001
Lumbar 2	0.879 ± 0.102	0.937 ± 0.084	0.002
Lumbar 3	0.931 ± 0.093	0.993 ± 0.088	0.001
Lumbar 4	0.938 ± 0.096	1.006 ± 0.096	0.001
Lumbar 1-4	0.889 ± 0.092	0.951 ± 0.080	0.000
Femur			
Greater Trochanter of femur	0.652 ± 0.082	0.625 ± 0.077	0.096
Ward's triangle of femur	0.779 ± 0.106	0.790 ± 0.093	0.667
Neck of femur	0.779 ± 0.106	0.790 ± 0.093	0.574
Intertrochanteric of femur	0.972 ± 0.114	0.991 ± 0.102	0.380
Total of proximal femur	0.836 ± 0.097	0.855 ± 0.085	0.271
Distal radius and ulna			
1/3 distal radius and ulna	0.678 ± 0.039	0.679 ± 0.038	0.910
Ultra distal radius & ulna	0.429 ± 0.038	0.443 ± 0.039	0.063
Total distal radius and ulna	0.563 ± 0.033	0.572 ± 0.035	0.194

* Statistical singnificant $p < 0.05$
** Highly statistical significant $p < 0.001$

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ความหนาแน่นของมวลกระดูกในสตรีไทยที่ใช้ยาฉีดคุมกำเนิด DMPA อย่างน้อย 2 ปี เปรียบเทียบกับกลุ่มควบคุม: การศึกษาแบบตัดขวาง

สายพิณ พงษธา, มลฤดี เอกมหาชัย, สมศักดิ์ เชาว์วิศิษฐ์เสรี, นุชนาต สุนทรลิ้มศิริ, นันทนา มรกต

วัตถุประสงค์: *เพื่อศึกษาผลระยะยาวของการใช้ยาฉีดคุมกำเนิด DMPA ต่อความหนาแน่นมวลกระดูกในสตรีไทยเปรียบเทียบกับกลุ่มควบคุม*

วัสดุและวิธีการ: *การศึกษาแบบตัดขวางในสตรีไทยวัยเจริญพันธุ์ที่ใช้ยาฉีดคุมกำเนิด DMPA จำนวน 50 ราย อย่างน้อย 2 ปี กับกลุ่มควบคุมที่ไม่ได้ใช้ฮอร์โมนในการคุมกำเนิดจำนวน 50 ราย ทำการวัดความหนาแน่นมวลกระดูกที่ lumbar spines, femur, distal radius และ ulna*

ผลการศึกษา: *พบว่าความหนาแน่นมวลกระดูกที่ lumbar spines ในผู้ใช้ DMPA ต่ำกว่ากลุ่มควบคุมอย่างมีนัยสำคัญ แต่ที่ตำแหน่งอื่นไม่มีความแตกต่างกัน*

สรุป: *การใช้ DMPA ระยะยาวพบว่ามีผลลดความหนาแน่นมวลกระดูกที่ lumbar spines*