Bone Density in Women Receiving Norplant® Implants for Contraception

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Abstract

The aim of this study was to determine whether long-term Norplant® uses is associated with changes in bone density. The study group consisted of forty one healthy women aged 19-42 years who had used Norplant® for 31.1 ± 11.2 months with a minimum period of 12 months. Fifty current IUD users constituted the control group. The bone density was measured by dual energy X-ray absorptiometry (DEXA) at the non dominant distal and ultradistal forearm. Serum estradiol was measured by microparticle enzyme immunoassay technique. Age, parity, income, weight, height and body mass index (BMI) of both groups were no differences. Our analysis did not find any differences in bone mineral density of distal forearm and ultradistal forearm between Norplant® and IUD users (95% CI -0.01, -0.03 and -0.02, 0.02 respectively). Serum estradiol was not different in the two groups (95% CI -24.9,110). This study revealed that the Norplant® implants do not have any adverse effect on bone mineral density.

A worldwide trend towards increasing life expectancy has meant that osteoporosis is emerging as an important public health problem. Progestogen-only methods for contraception are often used for many years. These progestogens may affect the peak bone mass reached in adulthood and the amount of the premenopausal bone loss, both of which are important for fracture risk(1). Only a few papers have addressed the effect of different progestogens on bone mineral density(1,2). The results have often been contradictory.

The Norplant® , a levonorgestrel implants, have been used in The National Family Planning Program of Thailand since 1986(3). It is well accepted by Thai women with a relatively high continuation rate(4). The active users of Norplant® in December 1993 was 114,102 which was about 1.3 per cent of married women in the reproductive age(5). To establish the effect of Norplant® on bone density should benefit the family planning services. The aim of this study is to determine whether its use is associated with changes in bone mineral density or not.

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MATERIAL AND METHOD

Forty-one healthy women aged 19-42 years who had been using Norplant® for a minimum of 12 months and who attended the Family Planning Clinic, Department of Obstetrics and Gynaecology, Ramathibodi Hospital, Bangkok from 1st January 1996 to 31st December 1996 were recruited for this study. Another fifty healthy women who had been using the intrauterine device and had never used any hormonal contraceptives were selected as controls. An informed consent was obtained on all contraceptive acceptors. Both groups lived in Bangkok and are matched with age, parity, income, weight, height and body mass index (BMI). None had any history of smoking, alcohol intake, metabolic bone disease or had conditions or took drugs known to affect bone and mineral metabolism. Height was measured without shoes and weight was registered with light indoor clothing without shoes using the electronic Seca weighing machine. Bone mineral density was measured by dual energy X-ray absorptiometry (DEXA) at the non-dominant forearm using an Osteometer DTX200 (Osteometer A/S, Copenhagen, Denmark). Bone mineral density was analyzed at two regions, distal and ultradistal forearm. Distal(d) forearm corresponds to 24 mm of radius and ulna proximal to the place where the distance between radius and ulna is 8 mm. This site contains approximately 25 per cent trabecular bone and 75 per cent cortical bone(6). Ultradistal(ud) forearm corresponds to a 15 mm strip of radius distal to the point where the gap between the bones is 8 mm. This site contains approximately 65 per cent trabecular bone and 35 per cent cortical bone(6). The measurement and calculation procedures are fully automatic. In this study, the distal forearm was taken as cortical bone and the ultradistal forearm as trabecular bone. Bone mineral density (BMD) is expressed in gram per square centrimeter and was calculated separately for distal (BMDd) and ultradistal (BMD ud) measurements.

The serum estradiol concentration was obtained from each of these women within 5 days after cessation of menstruation and was measured by Microparticle Enzyme Immunoassay (MEIA) technique using the Abbott IMx® immunoassay automation, U.S.A. All data were collected, coded and analyzed by the investigators. SPSS/PC+ for windows and the CIA statistical package programme were used to analyze data with a PC microcomputer. Statistical values employed are mean, standard deviation, Student's *t* test and 95 per cent confidence interval(CI). The significance level considered was at 0.05.

RESULTS

The characteristics of Norplant® and IUD users are revealed in Table 1. There were no significant differences in age, parity, body weight, height and body mass index. The mean duration of Norplant® use was 31.1±11.2 months with minimum 12 months and maximum 48 months. The mean duration of IUD use was 47.7±31.3 months with the range 3-180 months Table 2 gives mean value for serum estradiol and bone mineral density of both groups. There were no differences in serum estradiol, BMD distal and ultradistal forearms between Norplant® and IUD users.

DISCUSSION

Norplant® , subdermal levonorgestrel contraceptive implants, has been one of the most significant additions to the available contraceptive method with worldwide approval and acceptability. Norplant® offers protection against pregnancy for at least 5 years. So it is important to study the safety of this method. Bone density data on women

Table 1. Characteristics of Norplant® and IUD users.

Characteristics	Norplant® users (n=41)	IUD users (n=50)	95% CI
Age	30.6±5.8	32.5±6.1	-4.38, 0.56
Parity	1.5±0.6	1.3±0.6	-0.15, 0.35
Body weight (kg)	55.9±9.1	55.7±6.3	-3.03, 3.41
Height (cm)	156.3±6.1	155.2±6.3	-1.56, 3.60
Body mass index (kg/m^2)	23.3±2.7	23.8±2.2	-1.6, 0.44

Table 2. Mean serum estradiol and bone mineral density.

Variables	Norplant® users (n=41)	IUD users (n=50)	95% CI
Serum estradiol (pg/ml)	189.9±217.2 (range 30.4-801.4)	147.5±91.9 (range 29.4-434.4)	-24.9, 110
Bone mineral density (g/cm^2) distal forearm	0.49±0.05 (range 0.38-0.62)	0.48±0.05 (range 0.38-0.64)	-0.01, 0.03
Ultradistal forearm	0.4±0.05 (range 0.31-0.51)	0.4±0.05 (range 0.3-0.59)	-0.02, 0.02

using Norplant® are scarce. In this study, it was shown that women who used Norplant® long term (mean 31.1±11.2 months) did not have any difference in bone mass density of distal and ultradistal forearm when compared to IUD users. While one prospective study demonstrated a 6 months increase in bone density in premenopansal women using Norplant® (1) and another prospective study of adolescent girls receiving Norplant® , bone density increased 2.5 per cent and 9.6 per cent after one and two years follow-up respectively(7). The difference in results may be due to different study designs and the number of acceptors.

This study is a control-trial study with large enough numbers of Norplant acceptors and long period of use, which is different from other studies(1,7). Its design intends to limit confounding factors by selected subjects and matching technique. Using the IUD users as the control group aimed at limiting the effect of hormonal exposure. The study group and the control group are matched with age, parity, income, weight, height and body mass index in order to control confounders in both groups. There are no statistical differences of these factors in both groups which mean effective matching procedures. The limitation of this study is that it could not explore the dietary and the exercise habits of both groups. However, all the subjects lived in Bangkok Metropolitan Areas and their monthly incomes were not different. All the subjects did not smoke cigarette or consume alcohol and drugs or have disease known to affect bone and mineral metabolism. It may be implied that the diet intake and exercise are not different between these two groups.

Concerning the technique of measuring the bone density, we used the dual energy X-ray absorptiometry (DEXA) which is reliable and reproducible(8). This low precision error of the bone density measurement method supports the validity of our findings. More over, DEXA forearm measurements are as predictive of the remainder of the skeleton(9).

Considering the serum estradiol level, it was shown that the serum estradiol levels were not different in the two study groups and their levels revealed no estrogen deficiency. Hypoestrogenism causes osteoporosis in post menopausal women and long term treatment with DMPA(2). This evidence was not demonstrable in Norplant® users. Consequently bone mineral density in these women were not effected by estrogen deficiency. Moreover, other studies have demonstrated broad, high peak of serum estrogen level or cycle fluctuation within a normal range in the majority of women using Norplant® (10,11). In conclusion, the long term use of Norplant® is not associated with significant reduction or increase in bone density of trabecular and cortical bone. Finally, this study revealed that Norplant® did not have any adverse effects on bone mineral density.

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ความหนาแน่นของกระดูกในสตรีที่ใช้ยาฝังคุมกำเนิด

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ได้ทำการวัดความหนาแน่นของกระดูกในสตรี 41 ราย ที่ได้รับการฝังยาคุมกำเนิดที่โรงพยาบาลรามาธิบดี เป็นเวลา 31.1 ± 11.2 เดือน เปรียบเทียบกับกลุ่มควบคุมซึ่งเป็นสตรีที่กำลังใช้ห่วงอนามัย 50 รายและไม่ได้รับฮอร์โมนคุมกำเนิด สตรีทั้งสองกลุ่มไม่มีความแตกต่างกันในด้านอายุ จำนวนบุตร น้ำหนักตัว ส่วนสูงและรายได้ พบว่าความหนาแน่นของกระดูกและระดับฮอร์โมนเอสโตรเจนในกระแสเลือดในสตรีทั้งสองกลุ่มไม่มีความแตกต่างกัน แสดงว่าการใช้ยาฝังคุมกำเนิดเป็นเวลานานกว่า 1 ปี ไม่น่าจะมีผลเสียต่อความหนาแน่นของกระดูก

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