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Estrogen–progestin contraceptive use during adolescence prevents bone mass acquisition: a 4-year follow-up study

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Abstract

Background: Estrogen–progestin contraception may affect estrogen production and alter the development of peak bone mass.
Study Design: A 4-year follow-up with 122 adolescent women aged 12-19 years. The data were divided into three groups based on estrogen–progestin contraceptive (EPC) use: (i) nonusers (n=52), (ii) 1–2 years of use (n=24) and (iii) use for more than 2 years (n=46). The estrogen dose of the preparations was ≤35 mcg. Height, weight, and the amount of exercise (ratio of work metabolic rate, h/week) as well as bone mineral content (BMC) of lumbar spine and femoral neck were measured repeatedly.
Results: There was a significant trend showing less of an increase in the mean adjusted BMC of lumbar spine in the group of adolescent women who had used EPC for more than 2 years compared with the two other groups. In the mean adjusted BMC of the femoral neck, there was a significant trend of a smaller increase in EPC users for more than 2 years compared with 1–2 years of use.
Conclusions: Long-term EPC with low-dose estrogen preparations seems to suppress normal bone mineral accrual in adolescent women.

Keywords: Adolescent woman; BMC; Estrogens; Estrogen-progestin contraceptives

1. Introduction

Osteoporosis is a skeletal disease affecting millions of people around the world. Genetic factors are thought to be the key determinants of bone mineral density (BMD) and bone mass, but environmental factors, such as physical activity, nutrition and, after puberty, sex steroid exposure, also influence the peak bone mass acquisition [1].

Estrogens and progesterone are known to have important effects on bone metabolism [2,3]. Estrogens, in particular, have an important impact on bone physiology: they participate in sexual dimorphism of the skeleton and in maintaining the bone mineral homeostasis during reproduction and play an essential role in maintaining the bone balance in adults [4]. Estrogen therapy is known to be beneficial to postmenopausal bone [5,6] and perimenopausal oral contraceptive (OC) use, even the low-dose formulations may prevent bone loss [7]. The skeletal effects of OCs in premenopausal women are not as evident. In general, it is believed that OCs are not harmful and might even be beneficial to the bone mass in premenopausal women [7,8]. However, there have recently been increasing concerns that hormonal contraception during adolescent years alters the normal peak bone mass development [9–11].

Reduced circulating estrogen concentrations have been established to be the main cause for reduction in BMD in postmenopausal [12] and premenopausal [13] hypoestrogenic women. Estrogen-progestin contraceptives with low-dose formulations modify the circulating estrogen level by maintaining constant concentrations low, similar to those measured during early follicular phase [14]. This suppression of ovarian estrogen production might be the mechanism by which the estrogen-progestin and other hormonal contra-

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ceptive methods cause deficits in bone mass. These changes are, however, considered to be reversible after discontinuation of the therapy in young women [15].

Maximizing the peak bone mass may contribute to less frequent later life fractures. Puberty is a crucial time in bone development, and during that time, in girls, estrogen produces a large increase in bone mass and changes in bone geometry [16]. Gain in bone mass also continues in healthy young women during the third decade of life, but it ends at a point close to the age of 30 years [17]. The hormonal contraceptives change the normal hormone balance of an organism and, thus, may influence the normal bone mass accumulation.

Approximately half of the Finnish female adolescent university students use hormonal contraception [18]. Most hormonal contraception supplies the body with both estrogen and progesterone to suppress ovulation. At the present, the estrogen dose used in combined hormonal contraception is usually 35 mcg ethinyl estradiol (EE) or less. The estrogen amount has been reduced because of the risk of complications, such as thromboembolia.

In a cross-sectional study, low-dose estrogen OC use in young women has been found to be associated with lower BMD, as compared with their controls [19]. Young starting age [11,20] and long duration of treatment [11] have been associated with lower BMD. Polatti et al. [10] found in a 5-year follow-up that long-term treatment with a monophasic pill containing 20 mcg EE and 150 mcg desogestrel prevented the physiologic occurrence of peak bone mass in 19–22-year-old adolescent women. The BMD of the control group increased 7.8% during the follow-up, while the BMD of the treatment group did not change [10]. Similar results have been established by others [20,21].

On the other hand, no significant effect of estrogen–progestin contraception on bone was found in two 3-year follow-ups in older study populations [22,23]. Some have found positive effects of oral contraceptive use on bone measurements in large population-based samples [24,25].

Because hormonal contraception is in common use and the data of its skeletal effects continues to be contradictory, we performed the analysis of our follow-up study data. The aim of this analysis was to investigate whether EPC does influence bone mass acquisition in a population of Finnish adolescent women. We also studied to see whether the duration of therapy will have an association with the development of bone mass.

2. Materials and methods

2.1. Participants

The study population was selected from the participants of a long-term health study with adolescent women since 1997. All participants who neither used hormonal contraception nor had a history of contraceptive use at the follow-up visit in 2000 were included in this study. The study population comprised 122 young women aged 12–19 years at inclusion. All participants were healthy and none had used any bone-affecting medication.

The participants were grouped after four follow-up years according to their EPC use into three groups: (i) no EPC (NC), (ii) EPC use for more than one year but less than two years (C1) and (iii) EPC use for more than 2 years (C2).

The ethics review committee of the Hospital District of Southwestern Finland approved the study protocol, and it was carried out in accordance with the declaration of Helsinki. Written informed consent was obtained from each participant as well as from her parent or guardian when the girl was under the age of 18 years.

2.2. Measurements

Follow-up visits were scheduled at baseline in 2000 and after a 4-year follow-up in 2004. At both follow-up visits, height was measured with a wall-mounted stadiometer (Harpenden Stadiometer, Holtain Crymych, UK) to the nearest 0.1 cm and weight recorded with an electronic scale (EKS exclusive, EKS International Sweden) to the nearest 0.1 kg in light clothing. The body mass index was calculated as kilograms per square meter.

The stages of pubertal development were individually evaluated with the Tanner's method [26] in each follow-up measurement. When discrepancies were evident between the breast and pubic hair stages, the degree of breast development was recorded.

The participants recorded their age at menarche, menstrual irregularities and use of hormonal contraceptives on a questionnaire. They were asked the number of days of menstruation and the number of days between the beginnings of two menstruations. They were also asked how many cycles they had per year. Only a few of the participants had menstrual irregularities. There were no differences between the three groups, and the menstrual irregularities were not significant in the analysis.

The same DXA scanner (Hologic QDR 4500C, Waltham, MA, USA; software version 12.3) was used to measure the bone mineral content (BMC, g) of the lumbar spine (L2–L4) and of the hip in the nondominant leg at baseline as well as in the fourth year of follow-up measurement. The same three trained radiographers performed all measurements and analyzed the data. They performed quality assurance by calibrating DXA with a spine phantom supplied by the manufacturer. The coefficients of variation for two consecutive measurements of 10 girls were 1.3% for the spine, 0.8% for the hip and 0.4% for the phantom for the total study period. The mean age of these girls was 15.7 years (S.D. 1.7) years (range 12.5–19.0 years) at baseline.

Participants filled out food frequency questionnaires at both visits. Calcium intake was estimated with a validated questionnaire. Vitamin D intake was estimated with another questionnaire. The questionnaire on Vitamin D intake was revised and updated for the follow-up visit because Vitamin D fortification in milk products increased in Finland in 2003.