The bone sparing effect of oral contraceptive use in non-smoking women

E. KITAI (*) - M. BLUM (**) - B. KAPLAN (***)

Summary: In a group of 30 women, mean age 23.7 years, we have examined the urinary calcium: creatinine ratio (Ca:Cr) as an indicator of bone resorption, before and 6.8 months after oral contraceptive (OC) use. Fasting Ca:Cr decreased significantly during OC use, being more pronounced in nonsmokers.

We agree with those who propose the use of OC in women also after 35 years of age, in view of their good effect on bone density.

Key words: Oral contraceptive; Bone density.

INTRODUCTION

The oral contraceptive (OC) pill is the most widely used means of contraception, as well as the most efficient. Although, the age of 35 years represents a limit after which OC is no longer recommended. Recently, some researches have been published which prove that OC use by healthy, nonsmoking women of this age is indicated ([1]). In USA, the FDA permitted the OC prescription up to the age of 45 years ([2]), in view of its effect in the reduction of endometrial carcinoma by 50%, and of the ovarian carcinoma by 40%. There is also a reduction in in benign breast diseases, ovarian cysts and ectopic pregnancy. OC use plays a role in the reduction of PID and, probably, also in the decrease of cases of endometriosis and osteoporosis ([1]).

The increase in bone density in OC users has been the subject of several works ([3-6]). Fasting urinary calcium/creatinin ratio (Ca/Cr) is a good, not expensive and rapid test showing accurately the bone resorption ([7]).

The aim of the present report is to show the good effect of OC use as a factor in the prevention of osteoporosis, as revealed by urinary Ca/Cr.

MATERIALS AND METHODS

The study group was composed of all the women who applied to us during the first three months of 1990 asking, for the first time, for advice about contraception methods to be used, to whom we prescribed the OC pill, since there was, according to our policy, no contraindication ([8]). Women with chronic diseases or receiving any medication were not included in the study. This group comprised 30 women, 15 to 31 years of age (mean age 23.7 years).

(*) The Neve Neeman Family Medical Clinic, Kupat Holim and Tel-Aviv University School, Israel

(**) The Family Planning Clinic, Mishmar Hayarden, Givataim, Kupat Holim, Dan District, Israel

(***) Dept. of Obs. Gyn., Beilinson Hosp., Petach-Tikva, and Tel-Aviv University Medical School, Israel

Table 1. — *Urine Calcium/Creatinin ratio before and during OC use.*

	Total population	Non smokers	Smokers	Significance of difference smokers Vs. non-smokers (unpaired t-test - 28 d. f.)
n	30	19	11	
Mean age (years)	23.7±3.9	23.5±4.2	24.1±3.4	N S D
Duration of OC use (months)	6.8±2.4	6.5±2.1	7.2±2.8	N S D
Urine Ca/Cr before OC use	0.120±0.038	0.112±0.019	0.134±0.057	N S D
Urine Ca/Cr during OC use	0.087±0.042	0.068±0.036	0.120±0.032	$P < 0.01$
Difference of Ca/Cr during OC use	–0.033	–0.044	–0.014	
Significance of difference Ca/Cr during OC use (paired t-test)	29 d. f. $p < 0.01$	18 d. f. $p < 0.01$	10 d. f. N S D	

d. f. = degrees of freedom.

After taking their medical history and after performing general, gynecologic and breast examinations, as well as laboratory routine tests, a fasting urine sample was taken from each woman for the determination of calcium level (by atomic absorption) and creatinine (by autoanalyzer). Calcium values expressed as mg/100 ml, were divided by those of creatinine (mg/100 ml) thus obtaining the Ca:Cr ratio.

Each of the 30 women received the same pill containing 0.03 mg ethynil estradiol and 0.15 mg levonorgestrel (Microgynon, Shering, Berlin).

On follow-up at the Family Planning Clinic, after the use of the pill for 3 to 12 months (mean time 6.8 months), we repeated the test for urinary Ca:Cr ratio.

The statistical comparison between Ca:Cr ratio before and during OC use was performed by the Paired Student's t test.

At the same time, the Ca:Cr values were compared between the group of non-smokers (19 women) and smokers (11 women), by the unpaired Student's t test.

RESULTS

From Table 1 one can see that urinary Ca/Cr decreased significantly in the study group after OC use, from 0.120 to 0.087. The smoking and non-smoking women were of identical age and the period of OC use was similar. The mean number of cigarettes smoked per day was 17.27. Urinary Ca/Cr before OC use was identical in both groups. After OC use, Ca/Cr decreased significantly in the non-smokers, as compared to smokers (Table 1).

COMMENT

The prolongation of life brought to light the fact that osteoporosis became an impediment from both medical and economic points of view. In some researches the frequency of fractures in women over 65 years of age reaches up to 30-40%.

Hormone replacement therapy during menopause proved to be useful in the prevention of osteoporosis and its complications ([10, 11]). The effect of estrogens on bone is not completely elucidated, since estrogen receptors were not found in bones ([12, 13]). It is presumed that estrogens help indirectly in the prevention of osteoporosis by increasing intestinal calcium absorption, by creation of serum calcitriol ([14]) and by secretion of calcitonin with inhibitory effect on bone resorption ([15]).

The use of OC was proved to increase bone mineral density ([3–6]) and from

the results of our study one can clearly see the decrease in Ca/Cr ratio after OC pill use.

We did not find a decrease in Ca/Cr ratio in smokers. It is known that smoking has an antiestrogenic effect which produces, among others, a premature menopause, as compared with the group of non-smokers ([16, 17]) and an acceleration of the process of osteoporosis ([18]). It is assumed that smoking accelerates the estrogen metabolism in the liver ([11, 19]).

Before OC use we found no differences in urinary Ca/Cr between smokers and non-smokers, and we assume that the antiestrogenic effect of smoking does not reach an expression in the young age such as that of our study group. But the pill containing 30 mcg estrogen did not prevent calcium loss in the smokers. Smoking increases the risk of cardiovascular disease in OC users ([20-23]), and therefore the use of contraceptive pills is not allowed in smokers over 35 years of age.

According to our results that Ca/Cr ratio does not decrease in smoking OC users, the contraceptive pill effect on the prevention of osteoporosis is much lower in smokers and in these women the old policy of not prescribing OC after 35 years of age is correct.

Our study is small and therefore our research will be continued also in the future.

REFERENCES

1) Speroff L.: « The use of oral contraceptives in women over 35 years old ». *Contemp. Obstet. Gynecol., 34*, 15-16, 1989.
2) Kleinman R. L.: « Oral contraceptives for older women ». *IPPf Med. Bull., 24*, 3, 1990.
3) Enzelberger H., Metka M., Heytmanek G., Huber J.: « The effect of oral contraceptives on bone density in climacteric females ». *Zentralbl. Gynakol., 111*, 967-973, 1989.
4) Stevenson J. C., Lees B., Devenport M., Cust M. P., Ganger K. F.: « Determinants of bone density in normal women: risk factors for future osteoporosis? ». *Br. Med. J., 298*, 924-928, 1989.
5) Enzelsberger H., Metka M., Heytmanek G., Schurz B., Kurtz C., Kusztrich M.: « Influence of oral contraceptive use on bone density in climacteric women». *Maturitas, 9*, 375-378, 1988.
6) Lindsay R., Thome J., Kanders B.: « The effect of oral contraceptive use on vertebral bone mass in pre- and post-menopausal women ». *Contraception, 34*, 333-340, 1986.
7) Nordin B. E. C., Gallagher J. C., Aaaron J. E., Horsman A.: « Post-menopausal osteopenia and osteoporosis ». *Front. Horm. Res., 3*, 133, 1975.
8) Blum M.: « One-year results using a risk scoring system in a family planning clinic ». *Adv. Contracep., 2*, 381-386, 1986.
9) Crilly R. G., Horsman A., Marshall D. H., Nordin B.E.C.: « Estrogen therapy ». *Front Horm. Res., 5*, 53-70, 1978.
10) Christiansen C., Christensen M. S., McNair P., Hagen C., Stocklund K., Transbol I. B.: « Prevention of early postmenopausal bone loss: controlled 2-year study in 315 normal females ». *Eur. J. Clin. Invest., 10*, 273-279, 1980.
11) Jensen J., Christiansen C., Rodbro P.: « Cigarette smoking, serum estrogens and bone loss during hormone-replacement therapy early after menopause ». *N. Engl. J. Med., 313*, 973-975, 1985.
12) Chen T. L., Feldman D.: « Distinction between alpha-fetoprotein and intracellular estrogen receptors: evidence against the presence of estradiol receptors in rat bone ». *Endocrinology, 102*, 236-244, 1978.
13) Van Paasen H. C., Poortman J., Borgart-Creutzburg I. H. C., Thijssen J. H. H., Dursma S. A.: « Estrogen binding proteins in bone cell cytosol ». *Calcif. Tissue Res., 25*, 249-254, 1978.
14) Gallagher J. C., Roggs B. L., De Luca H. F.: « Effect of estrogen on calcium absorption and serum vitamin D metabolits in postmenopausal osteoporosis ». *J. Clin. Endocrinol. Metab., 51*, 1359-1364, 1980.
15) Stevenson J. C., Abeyasekera G., Hillyard Hillyard C. J.: « Calcitonin and the calcium-regulating hormones in post-menopausal women: effect of estrogens ». *Lancet, 1*, 693-695, 1981.
16) Lindquist O., Bentsson C.: « Menopausal age in relation to smoking ». *Acta Med. Scand., 205*, 73-77, 1979.
17) Andersen F. S., Transbol I., Christiansen C.: « Is cigarette smoking a promotor of the menopause? ». *Acta Med. Scand., 212*, 137-139, 1982.

18) Daniell H. W.: « Osteoporosis of the slender smoker: vertebral compression, fractures and loss of metacarpal cortex in relation to postmenopausal cigarette smoking and lack of obesity ». *Arch. Intern. Med.*, *136*, 298-304, 1976.
19) Michnovicz J. J., Hershcopf R. J., Naganuma H., Bradlow H. L., Fishman J.: « Increased 2-hydroxylation of estradiol as a possible mechanism for the anti-estrogenic effect of cigarette smoking ». *N. Engl. J. Med.*, *315*, 1305-1309, 1986.
20) Mann J. I.: « Myocardial infarction in young women with special reference to oral contraceptive practice ». *Br. Med. J.*, *2*, 241-248, 1975.
21) Mann J. I.: « Oral contraceptive use in older women and fatal myocardial infarction ». *Br. Med. J.*, *2*, 445-447, 1976.
22) Jick H.: « Oral contraceptives and nonfatal myocardial infarction ». *JAMA*, *239*, 1403-1406, 1978.
23) Layde P. M., Beral V., Kay C. R.: « Further analyses of mortality in oral contraceptive users ». Royal College of General Practitioners' Study. *Lancet*, *1*, 541-546, 1981.

Address reprint requests to:
Dr. B. KAPLAN
14 Montifiori St.,
Kiryat-Ono, 55226, Israel