

The effect of gestanone and ethynyl estradiol on benign breast disease

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Summary: The evidence related to the effects of Ocs on the breast benign diseases and their secondary relation to malignancy is studied.

Our data are in concordance with other epidemiological studies, that showed no influence on breast mitosis and apoptosis and that there was a reduced incidence of benign breast disease; we also believe that it has a beneficial effect and that this method of contraception is the best.

INTRODUCTION

There has been a lot of publicity about the potential risks of oral contraceptive use. Although oral contraceptives offer numerous benefits – contraceptive and noncontraceptive – the media often spend substantially more time talking about risks than benefits.

Oral contraceptives (OCs) are known to have some side-effects but those related to the breast have caused controversy, particularly concerning the risk of breast cancer. This study is based on evidence, related to the effects of OCs on the breast, taken from the most important clinical, epidemiological, pathological and biological studies. Such studies have been concerned with benign diseases and their secondary relation to malignancy; for these

effects there are problems as well as answers ^(1,2).

Using the term “benign diseases” we mean two commonly accepted groups, of diseases that are divided into low and high risk ones, according to their conduction to malignancy (Tab. 1) ^(3,4).

MATERIALS, METHODS & RESULTS

During 1987-91, 6,752 women of reproductive age, mean age 29 ± 6.5 (sd), visited the Family Planning Clinic of the Dept. of Ob./Gyn. at the University of Patras, Greece. 50% of them used coitus interruption, 20% the rhythm method,

Table 1. — *Benign disease and breast cancer.*

– <i>Increased risk</i>
Epithelial hyperplasia
Atypical lobular hyperplasia
Duct papillomatosis
– <i>No increased risk</i>
Fibroadenoma
Cyst
Sclerosing adenosis
Blunt duct adenosis
Pink cell metaplasia
Duct ectasia
Fat necrosis

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Table 2. — 1987-1991 Dept. Ob./Gyn. University of Patras, Greece. Family Planning Unit. Birth control method used in 6,637 women.

Years	Coitus interruptus		Rhythm		Condom		O.C.		I.U.D.		Sterilization	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
1987	3578	53	1823	27	1080	16	135	2	66	1	4	0.06
1988	3714	55	1688	25	1013	15	199	3	135	2	7	0.1
1989	3452	52	1460	22	1057	15	408	8	199	3	4	0.05
1990	3318	50	1012	15	929	14	684	11	531	8	3	0.05
1991	2655	40	664	10	1012	15	1860	29	531	8	2	0.04
Total	3318	50	1327	20	1012	15	697	10.5	298	4.5	4	0.05

15% condoms, 9% oral contraception, 4% intrauterine devices and 2% sterilization (Tab. 2).

We used last generation oral contraceptives containing 30 mcg ethynyl estradiol and 75 mcg Gestadone. The purpose of our investigation was to study the effect of O.C. in 124 women with fibrocystic disease and mastodynia. The women studied had to have a mammographically confirmed glandular structure and/or cystic breast disease, associated with pronounced cyclical mastodynia lasting at least one week per cycle for more than 6 cycles.

Women were examined before taking O.C., after 1.3 and 6 months, and while being on O.C. An improvement both clinically and mammographically was observed in most cases.

We also divided the 124 women into 3 groups based on mammography readings. None of the groups differed in age at first child birth. We observed reduction of mastodynia and improvement of mammography in all 3 groups (Tab. 3).

Table 3. — Mean scores \pm SEM of mastodynia, palpable structure, and adenosis.

Study variable	Cycles of O.C. use	Mean Score \pm SEM
Cyclical Mastodynia score 0-3	0	2.75 \pm 0.06
	1	0.96 \pm 0.13
	3	0.38 \pm 0.09
	6	0.15 \pm 0.07
Palpable structure score 0-4	0	3.24 \pm 0.12
	3	1.26 \pm 0.13
	6	0.83 \pm 0.11
Adenosis (mammography) score 0-4	0	2.78 \pm 0.11
	3	2.24 \pm 0.10
	6	1.87 \pm 0.11

O.C. = oral contraception; O.C.S. = oral contraceptives.

DISCUSSION

It was found that there is a breast lobulus mitotic cycle variation for a day phase with a peak breast cell apoptosis which is related to the circulating hormones of the menstrual cycle. The responses in nulliparous and parous women were similar and although age had some influence in dampening the responses, the unexpected finding was that current OC users showed a response of mitosis and apoptosis equivalent to non-users. The hormonal environment of the breast during the artificial cycle would be expected to differ substantially from the natural cycle. Clearly this observation needs to be substantiated with larger numbers, but does emphasize our incomplete appreciation of breast parenchymal stimulation^(5, 6, 7, 8).

It is generally accepted that there is a reduced incidence of benign breast disease among O.C. users (Table 4 lists some of the comprehensive reports of the last 10 years which have examined this issue). Although the study groups were gathered in various ways, the conclusions showed that the incidence was decreased^(9, 10, 11, 12, 13, 14).

However, the problem here is the imprecise definition of the term "benign breast disease", an issue to which attention has been recently drawn⁽¹⁾. Some alterations of breast tissue prompting biopsy, which have a basis that is more phy-

Table 4. — OC Pill Effects on the Breast - Benign Disease Epidemiology.

Authors	Year	Study type	Effect
Kelsey <i>et al.</i>	1974	Case control	Decrease
Fasl and Paffenbarger	1975	Case control	Decrease
Vessey, Doll and Sutton	1972	Case control	Decrease
Ory, Cole, McMahon <i>et al.</i> . . .	1976	Postal enquiry	Decrease
Royal College GP Study	1977	Reporting rate	Decrease

siological than pathological, is a view gaining acceptance in both clinical and pathological practice (15, 16, 17, 18, 19, 20, 21).

(Table 4). Breast mitosis and apoptosis in the menstrual cycle (originally reproduced in the Journal of Obstetrics and Gynecology, Supplement 1984).

It has also been inferred that protection against benign breast disease may depend on the progestin content of the pill, with more progestin offering more protection. The Oxford University - Family Planning Association cohort study compared women using pills with the same amount of estrogen but with different amounts of the same progestin. Women using pills containing 2.5 or 3.0 mg norethindrone acetate had half the incidence of fibrocystic breast disease than women who used pills with 1.0 mg norethindrone acetate did. Since most pills now in use contain lower amounts of progestin, future studies may show a decrease in protection against benign breast disease (22, 23, 24, 25).

Our data are in concordance with the epidemiology studies that showed no influence on breast mitosis and apoptosis and that there was not only a reduced incidence of benign breast disease in women who were on O.C. treatment but also protection against it.

CONCLUSION

In conclusion, we believe that there is a beneficial effect of O.C. on the breast and O.C. is much more useful to women than other methods of contraception.

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