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# BIRTH CONTROL PILLS: RISKS AND BENEFITS

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It has been almost 20 years since the pill was approved by the FDA for use in the United States. It is estimated that about 10 million women are using the birth control pill in this country. Physicians and women became concerned when the early reports dealing with the cardiovascular complications were published. Recently, the continued research sponsored by NIH, Walnut Creek, and Boston Collaborative Study, has clarified many of the issues surrounding the question of safety of the pill.

There are various formulations of the birth control pill. The most common and most widely used is the combination type. In this type, each tablet contains an estrogen and a progestin. The estrogen is either ethinyl estradiol or mestranol. The latter has to be demethylated in the liver to ethinyl estradiol to be effective. So, essentially both ethinyl estradiol and mestranol have the same biologic potency. Nowadays, all the newly manufactured pills contain ethinyl estradiol as the estrogen fraction. The progestin part is a 19 nor testosterone derivative which is active orally and the androgenic potency is abolished to a major extent. The combination type pill is given for three weeks on and one week off to be effective.

Various changes occurred in the formulation of the birth control pill since its introduction. In the mid sixties, the estrogen fraction in the pill was reduced to 50 mcg, and in the mid seventies it was further reduced to less than 50 mcg, namely 30 and 35 mcg. In addition, the progestin component was reduced to 150 mcg. It has been realized that the low dose formulations are as effective as the high dose ones in prevention of pregnancy. In addition, these new formulations are associated with marked reduction in side effects.

The other varieties of the pill are: the sequential type in which the first 16 days of use are estrogen pills and the last 5 days are estrogen and progestin combination. This type of pill was taken off the market because of the reported cases of endometrial carcinoma associated with its use. The mini pill is a progestin pill and has no estrogen component. Its use is very minimal because the pregnancy rate is about 2—5 per 100 women per year.

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## MODE OF ACTION:

The combination type of pill leads to suppression of ovulation as the main action. This is due to suppression of mid cycle LH and FSH peaks as a result of the effect of both estrogen and progestin component on the hypothalamic pituitary axis. The mini pill leads to suppression of ovulation only in 25 percent of women users. In addition, due to the dominant progestin nature of the pill, the endometrium shows atrophy of the glands and thus, becomes unsuitable for implantation. Moreover, the cervical mucus becomes thickened and less permeable to the sperm.

## BIOLOGIC EFFECTS:

1. Carbohydrate metabolism: Studies have shown that the combination type pill leads to some deterioration in the glucose tolerance when the estrogen dose is 50 mcg or more.[1] The fasting blood sugar levels might not change, but there is an increase in the levels above normal during the two hour glucose tolerance test. This is also associated with an increase in serum insulin levels above the normal control levels. The effect on carbohydrate metabolism is not only due to estrogen fraction, but also due to the progestin component. Studies using progestins only have shown abnormalities in carbohydrate metabolism.[2] When low dose formulations are used with estrogens less than 50 mcg, the studies have shown no change in glucose tolerance and in some borderline diabetic patients an improvement was reported.[3] It is suggested that the pill should not be used in diabetic patients since their carbohydrate metabolism would deteriorate and control of their blood sugar levels might be somewhat difficult.

2. Lipid metabolism: There is an inverse relation between atherosclerosis and high density lipoproteins. There is also a positive correlation between concentration of low density lipoproteins and incidence of cardiovascular problems. Lipoproteins carry cholesterol and triglycerides in the circulation. Low density lipoproteins carry cholesterol to the peripheral tissues and enhance the formulation of atherosclerosis. On the other hand, high density lipoproteins carry cholesterol to the liver to be excreted, hence the protective function of high density lipoproteins against cardiovascular problems. During reproductive years cardiovascular and cerebrovascular accidents in women are significantly less

than in men. This is probably due to the effect of estrogens in women leading to an increase in high density lipoproteins. On the other hand, androgens are known to decrease high density lipoproteins. Birth control pills with estrogens 50 mcg or more have been shown to increase low density and very low density lipoproteins. It has also shown that pills with estrogens less than 50 mcg increase high density lipoproteins.[4]

3. Myocardial infarction and cerebrovascular accidents: Early reports have shown an increased risk in users compared to non-users. The problem with these studies was the fact that patients on the pill were at an older age group than nowadays. In addition, they were not screened for several predisposing factors. When these data were reanalyzed the risk factor was found to be minimal and not different from non-users in young patients below the age of 35 years.[5] The true increased risk is in women users above 35 years old and who have predisposing factors such as smoking, diabetes, hypertension, and hypercholesterolemia.[6] The risk is 1:20,000 to 1:30,000 users. This risk is decreased further when low dose pills are used. However, there is still an increase risk of thrombosis and embolism with pill use due to changes in coagulation factors. Precautions have to be taken in susceptible women.

4. Hypertension: The incidence of this problem in pill users is about 2 percent. The estrogen in the pill stimulates the liver to produce renin substrate (angiotensinogen). The action of renin on angiotensinogen leads to formation of Angiotensin I which is converted to Angiotensin II in the lungs. Angiotensin II leads to increased capillary tone and also increased aldosterone secretion. Both could lead to hypertension. However, hypertension occurs in only a very small percentage of pill users despite the changes in the renin angiotension aldosterone system. This might suggest a genetic predispostion. It is assuring to know that this hypertension is reversible when the pill use is discontinued.

5. Oncogenesis:

A. Endometrial carcinoma: Few cases have been reported in the mid seventies during the use of the sequential pill.[7] This was due to the effect of estrogen on the endometrium and the short duration of use of a weak progestin. These pills were withdrawn from the market and are not in use any more. The use of the combination pill reduces incidence of endometrial carcinoma by about 50 percent in users. The protective effect of pill use continued for five years following the discontinuation of pill use.[8]

B. Cervical dysplasia and cervical carcinoma: The recent data found no relation between pill use and carcinoma of the cervix.[9] It was also reported that dysplasia might show progress if the pill use extends to over seven years of use.[10] It is therefore essential to follow pill users with pap smears on a regular basis. Any dysplasia has to be corrected to avoid any possibility of further progress of such lesions.

C. Breast tumors: The use of birth control pills reduces the risk of development of benign breast lesions in women users.[11] As such, they reduce the premalignant lesions and thus, reducing incidence of malignancy in these patients. So far there is no relation between estrogen use and breast malignancies.[12] However, it is recommended that birth control pills should not be used in patients with a history of estrogen dependent malignant tumors.

D. Liver tumors: The incidence of liver adenomas is extremely low in pill users. However, physicians must be aware of the problem and a liver examination is to be done during the checkup or if the patient complains of pain over the liver region. If there is liver enlargement, a scan must be done to diagnose the condition. These tumors are benign and regress when the pill use is discontinued.[13]

E. Pituitary tumors: So far all the studies did not document any relation between prior pill use and the occurrence of pituitary tumors.[14]

6. Effect on subsequent fertility: Recent studies show that fertility is not affected after the pill use has been discontinued. There is no increase in fetal wastage, fetal growth, ectopic pregnancy, or fetal anomalies.[15 16]

Finally, maternal mortality for pill users have been shown to be 2—6 per 100,000 women which is significantly less than that for childbirth (20 per 100,000) in the United States. Thus, use of oral contraceptive pills is beneficial in reducing maternal mortality especially in developing and underdeveloped countries where the maternal mortality varies from 250 to 1,000 per 100,000 women.

In conclusion, the data presented suggest that the benefits outweigh the risks of pill use especially so, when the low dose formulations are used.

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