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Mini Review

Does Taking Oral Contraceptive Pills Increase your Risk for Breast Cancer? A Literature Review

Ibrar Anjum*, Amna Khalid, Farwa Eajaz and Syeda Sheharbano Jaffery

University Hospitals Cleveland Medical Center, Ohio, USA

***Corresponding Author**: Ibrar Anjum, University Hospitals Cleveland Medical Center, Ohio, USA.

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Abstract

Combination oral contraceptives (COCs) are the most common form of contraception available in the market. In addition to effectively preventing unplanned pregnancies, COCs help control other conditions such as acne, postmenopausal syndrome, menorrhagia, adenomyosis, endometriosis and mood swings.

Breast cancer is the most common cancer and cause of cancer-related deaths among women in the United States. It develops in breast tissues and is associated with many risk factors including a family history of breast cancer, prolonged use of COCs, alcohol consumption, obesity and older age. Several research studies have shown an increased risk of breast cancer in women using COCs especially in women with a history of chronic use. Estrogen plays the leading role in the pathophysiology of breast cancer. In this article, we will discuss the different research studies regarding the risk of breast cancer in women taking COCs.

Keywords: *Oral Contraceptive Pills; OCP and Breast Cancer; Birth Control Pills and Cancer*

Introduction and Background

Combination oral contraceptive (COC) use and its association with breast cancer are a concerning relationship as the incidence of breast cancer in the recent decades have been exponentially increasing around the globe. Moreover, the incidence of women using oral contraceptive pills (OCPs) at some point in their life has been increasing over time as well [1,2]. COCs are one of the most reliable forms of contraception available in the market [2,3]. They have a combination of estrogen and progestin components, with the most commonly used estrogen being ethinyl estradiol. Commonly used progestins include norethindrone, norethindrone acetate, levonorgestrel, and ethynodiol diacetate. COCs can be prescribed either as a monthly regimen or in an extended form [3]. Apart from its use as a form of contraception, COCs are also used to treat hyperandrogenism, dysmenorrhea, polycystic ovary syndrome, abnormal uterine bleeding, premenstrual syndrome (PMS) and premenstrual dysphoric disorder (PMDD) [4]. It has also been used in the treatment of symptoms seen in gynecologic disorders such as bleeding from leiomyomas, and pelvic pain seen in endometriosis. There is a benefit of COCs in the reduction of endometrial cancer, ovarian cancer, and colon cancer [3,5]. On the contrary, there have been side effects associated with COCs including breast tenderness, nausea, bloating, and abnormal uterine bleeding. However, these early side effects often resolve within the first few months. There is also a risk of venous thromboembolism and cardiovascular disease including myocardial infarction and stroke [3-5]. The theoretical failure rate of COCs is 0.1 percent while the actual failure rate is 2 - 3 percent due to non-compliance [4]. There is an increased risk of cervical cancer in women who used COCs however, the risk decreased after discontinuation and returned to that of non-users after 10 years of discontinuation [1,4].

The data regarding the association between COCs use and the risk of breast cancer in women is variable [4]. This association is significant since breast cancer is the most common cancer worldwide that affects women. Every year 1.4 million new cases are diagnosed [6]. Some studies show that COC use is associated with an increased risk of breast cancer [1-10]. Others depict no increased risk of breast cancer [11-14]. There have also been conflicting results about the current and past use of OCPs and their association with breast cancer [6,12]. It is speculated that OCP use is not associated with an overall increase in breast cancer risk although long-term use (greater than 10 years) can be associated with an increased risk, however, more extensive studies are needed to confirm this hypothesis [6]. Studies have shown that higher doses of estrogen and progestin OCPs are associated with an increased risk of breast cancer [1,2]. According to data from 54 epidemiologic studies, the most reliable predictor of breast cancer risk is the recent use of OCPs. The pooled data from all studies published until the mid-1990 by the Collaborative Group on Hormonal Factors in Breast Cancer expressed that current/recent use of COCs is associated with increased risk of breast cancer [1]. Short-term use has borderline risk whereas, long-term use is associated with a higher risk of breast cancer [8]. However, according to recent studies published in 2002 and 2013, there is no significant increase in breast cancer risk associated with OCP use [12,13].

Discussion

Oral contraceptive pills (OCPs) are an orally administered form of birth control. It comes in various combinations including estrogen and progesterone, progesterone alone, or estrogen alone. When taken correctly, it alters the menstrual cycle to eliminate ovulation and prevent pregnancy. The first OCP was made of progesterone and was created by the combined efforts of activist Margaret Sanger and Endocrinologist Gregory Pincus in 1953. They were the first approved form of contraception in the USA in 1960 and have quickly gained popularity over the years. Currently, 12 million women in the United States and over 100 million women worldwide use OCPs.

One of the most common uses of OCPs besides contraception is hormone replacement therapy (HRT) in postmenopausal women. The increased implementation of OCPs for off-label purposes led to the discovery of many side effects and risks including developing venous thromboembolism, early atherosclerosis, weight gain, depression and increased risk for cancers specifically endometrial and breast. The purpose of this discussion is to focus on the risk of breast cancer associated with the use of OCPs in any age group of women. Some studies showed a strong correlation between the development of breast cancer and the use of OCPs and some studies yielded minimal or no relationship between the two [15-21]. Even the studies that showed findings in association with the development of breast cancer varied from study to study depending on factors like age group, ethnicity, geographic dynamics, parity, menopausal and premenopausal status, type and dose of OCP used and time of exposure to OCPs in regards to the age of the women and the number of years of use.

One of the studies conducted by "The Collaborative Group on Hormonal Factors in Breast Cancer" that collected data from 54 studies in 25 countries, demonstrated that there is an increased risk of breast cancer in women using OCPs, however, this risk decreases 10 years after stopping OCPs is negligible after 10 years of cessation [22]. The Norwegian-Swedish Women's Lifestyle and Health Cohort Study showed an increased breast cancer risk among women who were current/recent users of OCPs of any type at the start of follow-up [RR,1.6; 96% confidence interval (CI), 1.2 - 2.1]. The risk was proportional to the duration of use of OCPs. Long-term users of OCPs were at a higher risk of getting breast cancer than never users [23].

Another study conducted by "The Collaborative Group on Hormonal Factors in Breast Cancer" focuses on the risk of patients using hormone replacement therapy (HRT). This study depicted how the risk of Breast cancer is increased in women using HRT and this risk is proportional to the duration of use. This risk decreased with cessation of use and almost disappeared after 5 years [24]. However, an increase in the risk of breast cancer with HRT in postmenopausal women is minimal when compared to the risk of COCs with estrogen-only preparation [25-27]. In some studies, the meta-analyzed risk of breast cancer in premenopausal women showed an increased risk in general but the association between COC use and breast cancer risk was most significant for parous women who used COCs for a duration of four or more years before their first full-term pregnancy [28-30]. Some meta-analysis studies also predicted that there may be a 20%

rise in the risk of breast cancer in younger nulliparous women along with chronic OCP users. Also, some studies showed that new preparation of low dose estrogen poses less risk as compared to older high dose preparations [31]. The protective effect of early menopause shows that ovarian hormones increase the risk of breast cancer because these hormones stimulate the mitotic activity in the breast cells. It is also noted that the mitotic activity is most significant during luteal phase than the follicular phase which gives rise to 2 hypothesis. One being that estrogen acts alone in a dose-dependent manner thereby increasing the risk and the other being progesterone acting in synergy with the estrogen to increase mitosis and thus to increase the risk. Both hypotheses suggest that the risk of breast cancer can be decreased by delaying the regular ovulatory menstrual cycles, therefore, minimizing the therapeutic use of estrogens and progestogens in postmenopausal women [32,33]. Progesterone can also cause a disruption in androgenic pathways which are protective against breast cancer and thus pose a risk for breast cancer due to its androgen opposing action as well [34]. Some studies showed that progesterone-only OCP use for greater than 5 years is associated with both Estrogen receptor+ (ER+) and estrogen receptor + /progesterone receptor+ (ER+/PR+) cancers [21]. The recent Danish cohort study reported a 20% increased risk of breast cancer among current and recent hormonal contraception users. These results are mostly consistent with previous studies [35].

To sum up this discussion, the evidence is conflicting on whether or not OCPs are a risk factor for breast cancer due to many studies suggesting that the implementation of OCPs for contraception or HRT pose a significant risk of breast cancer in different age groups of women. These studies demonstrate a strong relationship between the increase in risk for breast cancer and various factors including dose, duration of use, estrogen-only OCPs versus the combination of estrogen/progesterone OCPs. A large-scale study whose data was coordinated by the Center for Disease Control contradict these claims suggesting that either there is no risk or the risk is minimal [36-38].

There is a need to evaluate further the various factors that act together with OCPs to cause an increase in risk in some study groups and limited to no risk seen in other groups.

Conclusion

In this article, we have discussed the relationship between COCs and breast cancer at an epidemiological and pathophysiological level. We explored how estrogen and progesterone receptors in breast cancer cells can be affected by COCs leading to an increased number of cancer cells which can eventually metastasize to different organs in the body along with how breast cancer is more commonly seen in women with a prolonged history of OCP use. Although some studies may contradict, showing a minimal relationship between COCs and breast cancer, we have highlighted the risks that are associated with OCPs in this article while keeping in mind that some characteristics of breast cancer are still unknown, and more studies are required to prove this link between them.

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