The Effects of Oral Contraceptives on Risk and Prevention of Ovarian Cancer

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Abstract

Numerous studies have assessed potential prevention methods to reduce the risk of gynaecological cancers. The current study investigates how oral contraceptive use can decrease a woman's risk for ovarian cancer. The paper thoroughly explores the intricate relationship between oral contraceptives and ovarian cancer, the effects of dose and duration of use on said relationship, and the potential beneficial effects of oral contraceptive use for individuals at higher risk. The reviewed literature strongly supports that oral contraceptive use decreases women's risk for ovarian cancer. This knowledge can be applied to those in the at-risk populations as a preventative measure. Thus, the thesis that oral contraceptives protect against ovarian cancer is supported.

Keywords: contraception, dosage, long-term, hormones, ovulation, oncology

Numerous studies investigated the complexities of and explored prevention methods to reduce the risk for gynaecological cancers. Presently, there are five main types of gynaecological cancers: cervical, uterine, vaginal, vulvar, and ovarian. A study (Walker et al., 2015) asserted that ovarian cancer is the most lethal gynaecologic cancer. In 2015, the American Cancer Society estimated that 65% of women diagnosed with ovarian cancer would die of the disease. Similarly, Moorman et al. (2013) noted that ovarian cancer was ranked the fifth highest cancer for mortality in the US. These alarming statistics relating to ovarian cancer may be attributable to its stage distribution. Women are typically diagnosed at stage three or stage four cancer, when their disease has progressed extensively (Moorman et al., 2013). Physicians have fondly looked towards an early detection strategy; however, early-stage ovarian cancer is often asymptomatic or has nonspecific symptoms, proving early detection challenging. Therefore, there must be a shift from early detection to prevention.

Oral contraceptive pills are proposed as a possible prevention method for ovarian cancer. Women who use combined oral contraceptives (COCs), which contain estrogen and progestin, reduce their risk for ovarian cancer by 40% compared to non-users (Maia & Casoy, 2008). The protective effect of COCs is seen after three to six months and increases with the duration of use. Additionally, 80% risk reduction is achieved if used for more than ten years. Moreover, the lifetime risk of ovarian cancer is 1.4% for the general population, whereas the risk for women with a genetic predisposition to ovarian cancer is 11-39% (Moorman et al., 2013). This statistic highlights that the protective effect of COCs may be critical to women at an elevated risk. Exploring oral contraceptive effects, dose, duration of use, and application to high-risk populations are all critical areas of research to consider. This paper will investigate how oral contraceptive use can decrease a woman's risk for ovarian cancer.

Literature Review

Oral Contraceptive Consumption Effects

Numerous findings across reviewed literature supported that oral contraceptive use decreases a woman's risk of ovarian cancer and is a potential prevention method. Faber et al. (2013) suggested oral contraceptives reduced the risk of ovarian cancer through anovulation, suppression of gonadotropic hormones, and increased progestin levels. The study was a population-based case-control study conducted among women aged 35-79. The study matched 554 women with epithelial ovarian cancer and 1564 age-matched controls to analyse the protective effects of oral contraceptives against ovarian cancer. The study supported that anovulation prevents uninterrupted ovulations that cause micro-trauma to the ovarian surface, which may lead to cancer. In addition, Fathalla (2015) proposed that periodic suppression of ovulation may be beneficial among average women who are not using oral contraceptives. This recommendation was proposed as an intervention strategy as incessant ovulation has been supported to increase the probability of ovarian cancer. Suppression of ovulation can be achieved with nonsteroidal anti-inflammatory drugs, which pharmacologically produce a luteinized unruptured follicle. The production of a luteinized unruptured follicle was observed to simulate a normal cycle with steroid levels and cycle length unaltered. However, further research is needed to validate the potential of this approach.

Moreover, oral contraceptives were observed to achieve their protective effect by suppressing the secretion of the gonadotropic hormones, follicle-stimulating hormone (FSH), and luteinizing hormone (LH). These hormones were suggested to increase ovarian cancer risk by increasing cell growth and inhibiting cell death. Furthermore, increased progestin stimulation was also observed to contribute to COC's protective effect. This finding was supported by

experimental trials (Fathalla, 2015), where progestin inhibited ovarian cell growth, and synthetic progestin, levonorgestrel, induced cell death on the ovarian surface.Further studies may explore the possibilities of alternative forms of birth control as a prevention approach. Yang et al. (2013) examined the association between intrauterine device (IUD) use and ovarian cancer risk utilizing three population-based studies. Results proved insignificant, and IUD use was not supported to be associated with ovarian cancer risk. Similarly, Wheeler et al. (2019) explored the relationship between IUD use and the risk of ovarian cancer through a systematic literature review. In contrast to Yang et al. (2013), results indicated that IUD use is associated with a reduced incidence of ovarian cancer during a retrospective study. Additional research is needed to support the validity of IUD use as a prevention method for ovarian cancer.

Dose and Long-term Use

Havrilesky et al. (2013) reviewed citations to investigate the possible reduction in ovarian cancer risk associated with the use of oral contraceptive pills (OCPs). With this, the intricacies of use, formulation, and duration of use were thoroughly examined. Havrilesky et al. (2013) reported that the association between oral contraceptive use and the reduction of risk of ovarian cancer was significant and duration dependent. Women who used oral contraceptives long-term (for ten or more years) were found to have a 50% reduction in the incidence of ovarian cancer (Havrilesky et al., 2013). There was also a significant decrease in ovarian cancer incidence in ever users (women who have used OCs for at least three-four months) compared to never users. Furthermore, Faber et al. (2013) observed a decreased risk for ovarian cancer in both high (>35 ug estrogen) and low-dose (<35 ug estrogen) COCs compared with the never used control groups.

However, long-term use of oral contraceptives use may have some adverse effects on other aspects of health. Franco et al. (2008) stated that although oral contraceptives have protective effects for some cancers, such as ovarian cancer, long-term use was also associated with increased risk for breast and cervical cancers. Similarly, women who use oral contraceptives long-term were at a higher risk of developing blood clots or experiencing a stroke or heart attack.

High Risk Individuals

Moorman et al. (2013) reviewed numerous citations to understand the complex relationship between oral contraceptives and ovarian cancer and the possible implications for women at an elevated risk. The average woman's lifetime risk of ovarian cancer was reported at 1.4%. However, women with a family history of ovarian or breast cancer or carrying a BRCA1 or BRCA2 genetic mutation were at an 11-39% elevated risk (Moorman et al., 2013). Oral contraceptives were suggested as a viable prevention strategy for women at this high risk as data supported that COC use and risk are inversely related. Moorman et al. (2013) data supported that oral contraceptive use reduced the risk of ovarian cancer in BRCA1 and BRCA2 mutation carriers to a similar extent as observed in the general population. However, in women without known mutations but with a family history of breast or ovarian cancer, the data was inadequate to perform a meta-analysis of the effects of oral contraceptives on ovarian cancer. Nonetheless, there was no evidence to recommend against their use in these high-risk populations. Moreover, Fathalla (2015) suggested non-hormonal periodic interruption of consecutive ovulation for women at heightened risk for ovarian cancer. As previously mentioned, interruption of ovulation can be achieved by using pharmacological drugs such as nonsteroidal-inflammatory drugs.

Discussion

There is strong support that oral contraceptive use decreases a woman's risk for ovarian cancer. In the study by Faber et al. (2013), oral contraceptives are supported to protect against ovarian cancer through anovulation, suppressing gonadotropic hormone secretion, and increasing progestin levels. Combined oral contraceptives contain synthetic forms of progesterone and estrogen, which maintain consistent hormone levels designed to prevent ovulation and pregnancy. Ovulation occurs when a peak in estrogen signals the ovary to release an ovum. Anovulation occurs when hormone levels are maintained; therefore, an ovum is not released from the ovary. Repeated, uninterrupted ovulation during a woman's reproductive years causes micro-trauma to the ovarian surface, which can lead to a malignant transformation. Anovulation is supported to contribute to the protective effect of COCs as it prevents micro-trauma from occurring and therefore prevents the possibility of a malignant transformation.

Furthermore, oral contraceptives protect against ovarian cancer by suppressing gonadotropic hormone production from the pituitary gland (Faber et al., 2013). The gonadotropic hormones, FSH and LH are essential to female reproductive health as they instruct the ovaries to make estrogen and progesterone and stimulate the ovaries to produce eggs. However, these hormones increase ovarian cell growth and inhibit ovarian cell death, which may rapidly contribute to a malignant transformation. Progesterone, a common component of COCs facilitates a negative feedback loop to inhibit LH release, suppressing FSH and LH levels. This reduction in FSH and LH thereby prevents follicular development, ovulation, and malignant transformations.

As previously stated, COCs contain synthetic forms of progesterone called progestins. COCs contain progestins as they have numerous pregnancy-preventative effects, including

thickening the mucus in the cervix, which prevents the sperm from reaching the egg (Faber et al., 2013). Progestins are observed to reduce the risk of ovarian cancer as they inhibit ovarian cell growth by reducing the speed of ovarian cell mitosis and inducing ovarian cell death. For example, levonorgestrel, a synthetic progestin, causes cell death on the ovarian surface, contributing to malignant transformation prevention. A limitation to the reviewed literature is a lack of discussion on whether different types of progestin will have similar effects on cell growth and death and therefore, equally contribute to ovarian cancer prevention.

Moreover, there is evidence that the relationship between oral contraceptive (OC) use and its protective effect on ovarian cancer is not dose-dependent (Faber et al., 2013). A reduced risk was observed in both high and low-dose OC treatment groups (OC use for three-four months) when compared with the never use control groups. As lower doses do not mitigate OC's protective effect, numerous physicians and patients prefer using the lowest-dose oral contraceptive pill that will provide adequate cycle control and effectiveness. Another limitation is that most reviewed literature reported on COC use and lacks data on the effects of other OCs, such as the progestin-only pill and the continuous use pill. Further research is needed to accurately assess if all oral contraceptives protect against ovarian cancer equally.

Oral contraceptive protection is supported to be duration dependent. Havrilesky et al. (2013) highlight a significant reduction in ovarian cancer incidence in women who have used oral contraceptives for at least three to four months compared with women who have never used oral contraceptives. However, long-term use (ten or more years) of oral contraceptives appears to have benefits, including a significant reduction in the incidence of ovarian cancer and detriments and increased risk for breast and cervical cancers to a woman's health. Long-term use can also increase the risk of uncommon and extreme side effects, such as developing blood clots or

experiencing a stroke or heart attack. Oral contraceptives with higher doses of estrogen are considered to increase this risk as increased estrogen levels promote the formation of blood clots. In rare cases, increased estrogen levels may lead to increased clot formation as it increases the level of coagulation proteins and decreases anticoagulant proteins. These proteins influence the thickness of blood. A healthcare provider must carefully consider these adverse side effects and prescribe oral contraceptives on a case-by-case basis. A limitation to research on long-term use is that there needs to be more information found on the effects of long-term oral contraceptive use on future fertility, which may be a deciding factor for some patients.

Early detection of ovarian cancer is ineffective as symptoms tend to be nonspecific or unnoticed. A shift from early detection to prevention is needed, as ovarian cancer is the most lethal gynaecologic cancer. Nonsteroidal anti-inflammatory drugs have been explored as a potential prevention approach. However, as mentioned, further research is needed to verify the effectiveness of this approach. Moreover, alternative forms of birth control, such as the IUD, may affect a woman's risk of ovarian cancer; however, results prove inconsistent, and further research is recommended in this area. Overall, there is strong evidence supporting that oral contraceptive use decreases a woman's risk for ovarian cancer, but it is advised for physicians to prescribe it on a case-by-case basis.

Conclusion

In conclusion, there is strong support for oral contraceptives being an effective prevention method for ovarian cancer as they promote anovulation, suppression of gonadotropic hormones, and increased progestin levels. Health educators should provide women with accessible and comprehensive information on contraceptives' beneficial and adverse effects. This increased accessibility will foster well-informed decision-making about which contraceptive is

the best fit for the patient. Although significant evidence supports that OCs are protective against ovarian cancer, they also possess adverse effects. Physicians should prescribe oral contraceptives on a case-by-case basis as some women, such as high-risk populations, may benefit significantly. In contrast, others may find a different contraceptive method works best for them. The limitations of the literature were inconclusive on whether different types of oral contraceptives have a similar protective effect on ovarian cancer and if long-term use of oral contraceptives may affect a woman's fertility. Future studies may be conducted to review these topics more deeply. Future research may also be undertaken to review different types of contraception. For example, current research surrounding the association between IUD use and the risk of ovarian cancer indicates unclear and inconsistent results. Additional research may be conducted surrounding the relationship and duration of use relating to the IUD and the risk of ovarian cancer.

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