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# Running head: ORAL CONTRACEPTIVES IN PREVENTING OVARIAN CANCER

Protective Effects of Oral Contraceptives on Ovarian Cancer

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#### **PERMISSION**

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#### Abstract

Researchers have made great progress in understanding how certain mutations in DNA can cause normal cells to become cancerous. There are several theories regarding reasons for the development of ovarian cancer that include, but not limited to: genetic inheritance, increasing age, early onset of menstruation, never bearing a child, having a child after the age of 30, and no previous history of oral contraceptive use (Royer, 2002). There is insufficient evidence to conclude what may be the causative factor to the specifics in the development of ovarian cancer. The most consistently reported ovarian cancer risk factors were low parity and no oral contraceptive use. Research suggests that a correlation between the total number of menstrual cycles that occur throughout a woman's lifetime can directly affect her risk of developing ovarian cancer (Moorman et al., 2008). Using oral contraceptives decreases the risk of developing ovarian cancer by reducing the total number of times a woman ovulates.

To date, there are currently no standards or recommendations for the screening of ovarian cancer in asymptomatic women, making educational opportunities regarding risk reduction strategies a priority. Oral contraceptive use, in the only risk reduction strategy available for the prevention of ovarian cancer that a woman is able to initiate and also terminate based on her choosing. When women are informed that increasing their use of oral contraceptives can decrease their chances of ovarian cancer development, the likelihood of them incorporating these protective benefits will be increased based on their knowledge of this simple prevention strategy. The findings that follow, analyze the protective effects of oral

contraceptives that are associated with reducing the risk of ovarian cancer with consistent use.

# Background

Ovarian cancer is the fifth leading cause of cancer death in women and has a 5-year overall survival rate of just 44% (Guha,2013). With early detection methods so far showing no benefit in reducing ovarian cancer, the U.S. Preventative Services Task Force reaffirmed its guidance against routine screening for an average risk woman. So what does this mean in terms of decreasing the rate of ovarian cancer or increasing the prevention of ovarian cancer? Awareness. Healthcare providers and women of all ages need the knowledge regarding available resources to help decrease their risk of ovarian cancer and increase prevention strategies, since there are no current screening recommendations for asymptomatic women. Using oral contraceptives is one way that many women can greatly reduce their risk of developing ovarian cancer.

Women who used oral contraceptives for five or more years have been shown to have almost a 50% lower risk of developing ovarian cancer compared with women who never used oral contraceptives (Hillard, 2008). With these statistics existing, it is also important to question, how does oral contraceptive use compare with other preventable measures in reducing ones risk in the development of ovarian cancer? The data in the following sections will address these issues and provide rationale regarding the importance of oral contraceptives and their protective effects against the development of ovarian cancer in women.

## Case Report

<u>Identifying Information</u>: S.S. is a 20 year old female presenting to the clinic today to be started on "birth control".

Chief complaint: "I would like to be started on birth control".

<u>History of the Present Illness:</u> Pt reports she is heterosexual and has had a history of two prior sexual partners, both male. Pt denies any history of sexually transmitted infections (STI's) or known exposures. Pt denies any history of pregnancy or abortions, but did use an emergency contraceptive "Plan B" six months prior without any noted complications. Pt reports occasional dysuria with no other symptoms.

<u>Past Medical/Surgical History</u> Negative

<u>Family History:</u> Pt denies any history of heart disease or stroke. Reports father had a blood clot after surgical procedure (ankle surgery). Pt denies any familiar history of clotting disorders or cancer.

Personal and Social History: Pt currently a sophomore at the University of North Dakota were she is studying elementary education. Pt denies any concerns regarding her academics. Pt participates in moderate physical activity 2-3 times per week. Denies any concerns about her current weight and health. Pt denies the use of recreational street drugs, smoking, or the use of tobacco products. Pt reports occasional alcohol use of 2-3 drinks per week.

### Medications:

Xenadrine one tab daily Multivitamin one tab daily

Allergies: Penicillin

Immunizations: UTD including series of 3 Gardasil

#### **Review of Systems**

HEENT: Denies ear and eye pain. Denies post nasal drip, sore throat or difficulty swallowing.

Pulmonary: No shortness of breath or cough. No wheezing with exertion. Cardiovascular: Denies increasing heart rate, palpitations, or racing heart. Denies edema.

Gastrointestinal: Denies diarrhea, nausea or vomiting. Denies change in appetite or recent weight loss/gain. BM daily. No change in bowel habits.

Endocrine: Denies fatigue, excessive thirst, and changes in skin pigmentation. No fever.

Lymphatic: Denies bruising and recent blood transfusion.

Mental health: Denies suicidal/homicidal ideation. Denies anxiety and nervousness.

Musculoskeletal: Denies weakness, myalgia, arthritis, or recent fractures.

Genitourinary: Pt denies frequency or hematuria, but reports dysuria for three days. Pt reports yellow urine with no vaginal discharge or bleeding. No foul smell noted. No fever or suprapubic pain noted.

Gynecological: Pt reports regular 27-28 day cycle, with mild cramping noted on first day of menses. No heavy bleeding noted. Pt reports menarche at age 15.

Neurologic: Denies headaches, dizziness, or impaired speech. Denies history of migraines.

### Physical Examination

General Appearance: S.S is a 20 year old, Caucasian female who is well-groomed, answered questions respectfully and in an appropriate manner.

Vital signs: Height: 5 feet 6 inches, Weight: 110 lbs. BP: 122/74, HR: 82, Temperature: 98.5 F, RR 16, O2 SAT: 99%.

Integumentary: Skin appropriate for race. Warm and dry to touch, no rashes, nodules or vesicles noted.

HEENT: Head is normocephalic with symmetric facial features.

Eyes: Sclera white, not injected. Conjunctiva pink. No discharge evident. Pupils equal.

Ears: No pain with palpation to auricles, pinna, or mastoid process.

Nose: Symmetric, no discharge noted.

Throat and mouth: Lips pink and moist. No lesions noted.

Neck: Symmetric without masses, or palpations. No lymphadenopathy, thyromegaly or thyroid nodules.

Chest: Chest symmetric, respirations non-labored, no adventitious breath sounds.

Heart: normal rate, regular rhythm, normal S1, S2, no murmurs, rubs, clicks or gallops, normal rate and regular rhythm

Abdomen: Normal bowel sounds in all four quadrants. Unable to palpate spleen or liver.

Musculoskeletal system: Spine straight with sitting, normal gait. No costovertebral angle tenderness over bilateral kidneys.

Neurological system: Alert, oriented to person, place and time.

Gynecological: Pap deferred due to age.

### Plan:

1. Patient will be started on monophasic birth control. Pt does not smoke and has no family history of clotting disorders, so the risk of deep vein thrombosis and pulmonary embolism is low. Pt. reports "I don't want anything put in my arm and I don't want any shots". Pt. requests to "take a pill everyday".

- 2. Pt instructed that she may experience some of the following side effects, all of which are normal after starting an oral contraceptive.
  - a. mild weight gain of 2-3 pounds
  - b. nausea
  - c. breast discomfort/and or enlargement
  - d. change in her mood
  - e. decreased libido
  - f. irregular bleeding or spotting
- 3. Pt. instructed to try the monophasic birth control for three months. If any of the side affects are not tolerable to call the office and discuss with the provider. Pt educated that an adequate amount to try a new contraceptive is approximately three months, and after that time we will reevaluate if symptoms warrant an adjustment in medication.
- 4. Will check urinalysis due to symptoms of dysuria.
- 5. Will check urine pregnancy.
- 6. Pt instructed to seek nearest emergency department if she experiences a sudden onset of shortness of breath or heart palpitations or dizziness.
- 7. Pt verbalized that she is not concerned about her weight, and reports she will stop the xenadrine and will evaluate her weight in three months. Pt will continue with multivitamin.
- 8. Pt encouraged to continue with condom use for sexually transmitted infection prevention.
- 9. S.S. educated regarding recent data that has been studied between reducing the risk of developing ovarian cancer and the use of oral contraceptives.
- 10. By choosing the oral contraceptive method, S.S can potentially reduce her risk of developing ovarian cancer by 50%.

#### Literature Review

Decades of data show that oral contraceptive use reduces the risk of developing ovarian cancer. Ovarian cancer continues to be a silent killer. Most women have an advanced disease state by the time of diagnosis. Intensive efforts to develop effective screening strategies have been overturned, allowing ovarian cancers to progress to harmful stages due to failed efforts of early recognition and detection screening. According to the United States Preventative Services Task Force (USPSTF) Reaffirmation Recommendation Statement "There is no new evidence found on the benefits of screening for ovarian cancer. Screening asymptomatic women can result in unnecessary interventions, including surgery" (Ann Family Medicine 2012).

Why are these current recommendations alarming? Because ovarian cancer is rarely found in its early stages and often times by the time of diagnosis it is at an advanced stage. According to the USPSTF, ovarian cancer causes more deaths than any other cancer of the female reproductive system (Bellcross et al., 2013). Ovarian cancer has few symptoms warning a female patient to seek treatment or evaluation making the prognosis grim.

While advances in surgery, chemotherapy, and radiation therapy over the past 20 years have led to improved outcomes, the 5-year survival rate is only 42 percent for ovarian cancer compared with 88 percent for breast cancer and 63 percent for colorectal cancer as reported by the American Association for Cancer Research (Epidemiology & Biomarkers). The high mortality rate in women with ovarian cancer is largely attributed to the later stage of presentation at the time of

diagnosis compared with other common cancers. This has led to intensive research efforts in identify effective screening strategies for ovarian cancer, but results have been disappointing, due to the lack of government participation in providing leading forefront measures to increase protective measures in prevention.

As healthcare professionals, what does one do with these statistics and recommendations? The best answer would be to educate and inform health care providers and patients of the protective measures with the use of oral contraceptives in the prevention of ovarian cancer. Oral contraceptive use has consistently been found to be associated with a reduced risk of ovarian cancer. The likelihood for the development of ovarian cancer was reduced with longer use. The risk decreased by 10-12 percent after 1 year of use, and by approximately 50 percent after 5 years of use (Jatoi et al., 2015). Because there are no current screening recommendations, it is important to participate in preventative measures to help reduce a female's risk of ovarian cancer.

A variety of biological explanations have been offered regarding the protective effects of oral contraceptives on ovarian cancer risk. These include: (1) excessive ovulation promotes risk; (2) elevated steroid hormone levels increase risk; (3) unopposed estrogen increases risk; and (4) pelvic inflammation increases risk (Tsilidis et al., 2011). Through analysis of the data, the sooner a female is started on oral contraceptives, the earlier one may receive the protective benefits in the prevention of ovarian cancer.

Women may begin to ovulate in their teenage years requiring the use of properly functioning ovaries for potentially decades. With the use of oral

contraceptives in their teenage and early reproductive years, the chances for the development of ovarian cancer in woman who participate in oral contraceptive use have chosen to protect their ovaries and help to reduce their risk in the development of ovarian cancer in later years. As providers who deliver healthcare, it is imperative that the discussion of the protective benefits of oral contraceptives occurs at each visit to all women of childbearing age.

Researchers have studied how the amount or type of hormones in oral contraceptives affect ones ovarian cancer risk. A recent data analysis extracted from the Cancer and Steroid Hormone (CASH) study indicated that oral contraceptive formulations with higher levels of progestin were associated with a lower risk of ovarian cancer than formulations with low progestin levels The change of a higher dose of the progesterone component within the oral contraceptive suggests that this may be the protective mechanism in preventing ovarian cancer that have been seen with the estrogen-progestin formulations of oral contraceptive (Allen, 2005). As deliverers of healthcare, this is an important consideration to remember when choosing to start a female patient on an oral contraceptive.

According to the research presented by Jatoi et al., (2015) the approximated risk reduction for the development of ovarian cancer is significant among women who have used oral contraceptives for 10 years or longer at any point in their lives. According to research studied at the Mayo Clinic in Rochester, Minnesota "Continuous ovulation is thought to predispose to ovarian epithelial cell DNA damage, which in turn gives rise to carcinogenesis, thus providing mechanistic plausibility to how cessation of ovulation from oral contraceptives might lead to

lower cancer risk" (p.137). Oral Contraceptive use has been studied along with several proven biologically plausible mechanisms for their protective effect, which should direct practitioners and consumers towards the use of oral contraceptives for the prevention of ovarian cancer.

More than 23,000 cases of ovarian cancer are diagnosed in the Unites States annually, with a median age at diagnosis of 63 years. Although more than two thirds of ovarian cancer cases are diagnosed among postmenopausal women, most known risk factors are characteristics related to reproduction that occur primarily when women are in their twenties and thirties (Havrilesky, 2013). The choices that a female patient makes in her 20s and 30s may have a lasting and overall protective effect on reducing her chances of developing ovarian cancer in her later years.

Within this literature review it is evident that oral contraceptive use has been proven effective for the risk reduction of ovarian cancer, which makes it also important to compare oral contraceptive use with other preventable measures and modifiable risk factors in prevention. If a genetic history is common among a family, a woman may choose to continue with genetic testing to determine her likelihood of being a carrier of the BRCA gene. This gene is known to be genetically linked to an increased chance of developing ovarian cancer (Robinson, 2015). So far, what is known about risk factors has not translated into practical ways to prevent most cases of ovarian cancer. Both tubal ligation and hysterectomy with oophorectomy may reduce the chance of developing ovarian cancer in carriers of the BRCA gene, but experts agree that these operations should only be done for medical reasonsnot for their effect on ovarian cancer prevention (Menkiszak, 2016).

A large European studied examined reproductive variables in the development of ovarian cancer. The examination consisted of an analysis of woman who conceived a child compared with those who did not. Women who had given birth (parity) had a 29% lower risk of ovarian cancer with a progressive reduction in risk with each additional pregnancy. This study confirms the strong protective association of oral contraceptive use and parity in reducing the risk of ovarian cancer. No other significant associations with risk reduction were found for age at menarche, age at first full-term pregnancy, incomplete pregnancies or breastfeeding (Tsilidis, 2011). Although there is no proven way that one can completely prevent this disease; one is clearly able to lower their risk of developing ovarian cancer through the use of oral contraceptives and an increasing number of times a female conceives a child. The seemingly obvious factor that a woman is able to control and actively regulate is oral contraceptive use. It seems to have the strongest correlation with risk reduction in ovarian cancer, and although child bearing does lessen your chance of developing ovarian cancer, this risk reduction factor is not always ideal for all women.

Many women worry about oral contraceptives increasing their risk of other cancers. According to Bui and associates "For women who are pre-menopausal and normally would have estrogen and progesterone in their system, taking the birth control pill does not increase the risk of breast cancer. For post-menopausal women, long-term use of hormones, especially combining estrogen and progesterone can slightly increase the risk of developing breast cancer, but not the risk of dying from breast cancer" (p.230). With these statistics present, reassurance and misconception

regarding the topics of increasing other types of cancer with oral contraceptives should be discussed with each patient. The benefits and risk reduction of the prevention of ovarian cancer out weigh the risks and have proven to be beneficial in lessening ones chance of ovarian cancer, due to the lack of preventive testing being reinforced.

Several of the health benefits and risks associated with the oral contraceptive pill are particularly relevant to women at risk of ovarian cancer. In a recent study published regarding women's beliefs on oral contraceptives, Fifty-three percent of women had positive attitudes towards oral contraceptives. Most women felt confident with their use in consuming oral contraceptives and felt this may have the largest predictability in reducing their cancer risks (Crane, 2011).

As healthcare providers, the mission should be to educate and inform women of their risk factors for the development of ovarian cancer and preventative measures that can reduce their lifetime risk of ovarian cancer which include the use of oral contraceptives. Through a combined effort of education and implemented prevention strategies from healthcare providers to female patients, the likelihood for the development of ovarian cancer can be decreased.

# **Learning Points**

- Ovarian cancer continues to be a silent killer of women. Most women have an
  advanced disease at the time of their diagnosis due to a lack of screening
  measures and prevention strategies. The protective effects of oral
  contraceptive pills have been well documented and studied, and their use
  should be encouraged to help decrease ones risk of ovarian cancer.
- The most consistently reported ovarian cancer risk factors are nulliparity, low parity and no oral contraceptive use. With these factors in mind, education regarding oral contraceptive use should begin in early reproductive years as the choices that a female makes during this time can supply protective effects from the development of ovarian cancer well into a woman's later years.
- The research reviewed not only supported preventative measures in reducing ovarian cancer rates, it favored an association between prior oral contraceptive use and an improved overall survival rate among those women diagnosed with ovarian cancer at a later age.
- A greater than 20% relative risk reduction appears to occur for every 5 years
  a woman reports taking oral contraceptives. This risk reduction for the
  development of ovarian cancer is significant among women who have used
  oral contraceptives for 10 years or longer at any point in their lives.
- Oral contraceptives represent a promising primary prevention strategy for ovarian cancer and healthcare providers should encourage their use as ovarian cancers progress rapidly, due to a lack of early detection screening

and their protective benefits should be brought to the attentions of all female patients. The change of a higher dose of the progesterone component within the oral contraceptive suggests that this may be the protective mechanism in preventing ovarian cancer that have been seen with the estrogen-progestin formulations of oral contraceptive.

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