

Literature Review

Contraception in Malignancies**Kontrasepsi pada Keganasan****Tricia D Anggraeni, Yosep Sutandar**

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Abstract

Along with the development of cancer diagnosis and treatment, the life expectancy of women in reproductive age who suffer from cancer are also higher. Women with cancer still have the possibility to be pregnant and have a child during or after completion of therapy. Taking this into consideration, the guideline for contraception in special circumstances like this is needed. After reviewing the safety and effectiveness of contraceptive methods available for women with cancer, The Society of Family Planning urged not to use combination hormonal contraceptives (estrogen and progestin). Hormonal contraceptive use in cancer patients may increase the risk of venous thromboembolism (Level A). T380A IUD, which has a high effectiveness, reversible, long-term, and hormone-free contraception should be considered as the primary choice in patients with breast cancer (Level A). In women who received tamoxifen therapy, the use of IUD containing Levonorgestrel can be considered as a second choice (Level B) because it can decrease the proliferation endometrium. Women with anemia due to chemotherapy may be given contraceptive containing progestin (Level A). Women with osteopenia or osteoporosis after chemotherapy should avoid progestin contraceptive injection (Level A). Currently, there are no data to evaluate the risk of venous thromboembolism in progestin contraceptive use. Further information is also needed to determine the effect of the use of IUD that contains Levonorgestrel against breast cancer recurrence and the effect of hormonal contraceptives on breast cancer in women who received chest wall radiotherapy.

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Keywords: cancer, contraception, malignancy

Abstrak

Seiring dengan perkembangan diagnosis dan terapi kanker yang semakin baik, angka harapan hidup wanita usia reproduksi yang menderita kanker juga semakin tinggi. Wanita penderita kanker masih mungkin hamil dan memiliki anak selama atau setelah menyelesaikan terapi. Dengan begitu, diperlukan pedoman kontrasepsi dalam keadaan khusus seperti ini. Setelah melakukan tinjauan keamanan dan efektivitas metode kontrasepsi yang tersedia untuk wanita penderita kanker, Society of Family Planning menghimbau untuk tidak menggunakan kontrasepsi hormonal kombinasi (estrogen dan progestin). Penggunaan kontrasepsi hormonal pada penderita kanker dapat meningkatkan risiko terjadinya tromboemboli vena (Level A). AKDR T380A yang memiliki efektivitas tinggi, reversibel, jangka panjang, dan bebas hormon harus dipertimbangkan sebagai kontrasepsi pilihan utama pada penderita kanker payudara (Level A). Pada wanita yang mendapat terapi Tamoxifen, penggunaan AKDR yang mengandung Levonorgestrel dapat dipertimbangkan sebagai pilihan kedua (Level B) karena dapat menurunkan proliferasi endometrium. Wanita dengan anemia karena kemoterapi dapat diberikan kontrasepsi yang mengandung progestin (Level A). Wanita dengan osteopenia atau osteoporosis setelah kemoterapi harus menghindari injeksi kontrasepsi progestin (Level A). Saat ini, belum ada data untuk evaluasi risiko tromboemboli vena pada penggunaan kontrasepsi progestin. Diperlukan juga Informasi lebih jauh untuk mengetahui pengaruh penggunaan AKDR yang mengandung Levonorgestrel terhadap rekurensi kanker payudara dan pengaruh kontrasepsi hormonal pada penderita kanker payudara pada wanita yang mendapatkan radioterapi di dinding dada.

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Kata kunci: kanker, keganasan, kontrasepsi

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INTRODUCTION

Malignancies are typically diagnosed later in life, but it does not mean that the disease cannot be sustained in young age. There are several types of malignancies that can affect children and young adults.

Cancer therapy has evolved significantly in recent decades. With a better understanding of the pathophysiology of the disease, screening tests are becoming increasingly effective in diagnosing ma-

lignancy in human so that it can be diagnosed at an earlier stage. Early diagnosis aided by conservative treatment can increase the life expectancy of cancer patients.¹

At present, therapy for advanced-stage malignancies has also become better. Radiotherapy can localize specific organ or tumor so healthy tissue damage can be minimized. Currently available chemotherapy has minimal side effects, and surgery nowadays has become more conservative. The de-

velopment of diagnosis and treatment resulted in an increase of life expectancy for cancer patients. A woman of reproductive age suffering from cancer and undergoing treatment can remain fertile during therapy and thereafter. For that, pregnancy and birth control are still necessary issues, as well as family planning.

Another problem in family planning that needs to be considered in patients with cancer is the teratogenic effects of chemotherapy and radiotherapy. Therefore, contraception must be used during treatment and for up to six months after completion of chemotherapy or radiotherapy. Contraceptive methods available today vary widely and each has different side effects. The effectiveness and side effects of each contraceptive may guide clinicians in making decisions for contraceptive use in cancer patients.²

Advanced Research

Contraception Choices

There are six classes of contraceptive methods: behavioral methods, barrier methods, estrogen-containing methods, progestin-only methods, intrauterine devices (IUD), and surgical sterilization. There are pros and cons to each of these methods. Although contraceptive efficacy is frequently discussed in the context of 1-year failure rates, it is a very important consideration for women who require long-term contraception. In the long term, IUDs, contraceptive implants, and sterilization are significantly more effective than barrier methods or birth control pills. Unfortunately, birth control pills are still the most frequently chosen methods.^{3,4}

Family Planning Association has issued guidelines for contraceptive options for women with cancer. Although in some cases, chemotherapy and radiotherapy can reduce fertility, many women are still fertile. Anti-Mullerian hormone test is a diagnostic tool to determine the appropriate number of follicles that are still available.

Hormones play an important role in the development of breast cancer. Therefore, the use of combined oral contraceptives or progestin pills are not recommended in patients with breast cancer. In women with breast cancer, intrauterine device

(IUD) is the best contraceptive choice. For women receiving tamoxifen therapy as part of treatment regimens, contraceptive intrauterine systems (IUS) provide the most benefits. This contraceptive works against proliferative effects of tamoxifen on the endometrium.

Cancer increases the risk of venous thromboembolism. Therefore, the combination contraceptive of estrogen/progestin is not recommended in patients with cancer. However, this type of contraception can still be used in cancer patients with anemia because it can reduce blood loss during menstruation.^{5,6}

Assessment of Fertility in Patients with Cancer

Pregnancy has been reported in patients who survive from cancer although they are suffering from amenorrhea with menopausal FSH levels.^{7,8} This suggests that the absence of menstruation is not an indication of diminished ovarian function.⁹ Therefore, a variety of biochemical tests (including the level of FSH, inhibin A or B level, or the Anti-Mullerian hormone) and biophysical tests (transvaginal ultrasound) should be used to estimate the ovarian reserve. Today, anti-Mullerian hormone levels are considered to be the best predictor of a woman's fertility. Ways to identify whether a woman is still fertile after chemotherapy is still under investigation at this time.¹⁰⁻¹²

Primary Cancer Affecting the Selection of Contraception

Several types of cancers can affect the selection of contraception, especially in patients with breast cancer or other cancers that are hormone mediated. In women with breast cancer, exogenous estrogen and progesterone are not recommended because it increases the risk of recurrence. Estrogen and progestin receptor status influence tumor growth and thus estrogen receptor blockade is a main component of breast cancer treatment. Tamoxifen therapies can cause endometrial proliferation and endometrial cancer. Therefore, contraceptive intrauterine system containing Levonorgestrel is the most favorable choice because it can reduce endometrial proliferation.¹³

Selection of Contraception in Gynecologic Malignancies

Gestational Trophoblastic Disease

In patients with gestational trophoblastic disease, patients are encouraged to delay pregnancy until therapy is completed. Patients receiving chemotherapy is recommended to postpone pregnancy until one year after completion of therapy. Therefore, contraception is required to delay pregnancy. Women with gestational trophoblastic disease is recommended to use barrier method of contraception since the time of diagnosis until β -hCG levels became normal. When β -hCG reaches normal levels, contraception can be continued using combination contraceptive pills. There is strong evidence that progesterone pill has a better effect than combination pill.¹⁴

Germinal Ovarian Cancer Cells

The prevalence of ovarian germ cell tumors is 20-25% of all ovarian neoplasia with only about 3% turning out to be malignant. Since the mid 1980's, fertility-preserving surgery, which entails removing the affected ovary and preserving the contralateral ovary and the uterus, followed by combination chemotherapy has become the standard procedure for early stages and selected advanced malignant germ cell tumors of the ovary. The main advantage of this therapy is that patients with malignant germ cell tumors of the ovary could conserve their reproductive function after effective treatment. Low et al. reported 74 patients with germ cell ovarian cancer who received conservative surgery, 47 patients of whom received adjuvant chemotherapy, 20 patients attempted conception, and 19 patients were successful.^{15,16} However, conception should be avoided during chemotherapy because of the teratogenic side effects of chemotherapy. The recommended contraception is combination pill or progesterone only pill.¹⁷

The Risk of Venous Thromboembolism Affecting the Selection of Contraception

Both cancer and estrogen are independent risk factors for the occurrence of venous thromboembolism. Cancer patients with venous thromboembolism have doubled risk of mortality compared to those without venous thromboembolism. It is obvious that thromboembolism is one of the causes

of death in cancer patients. Lung, lymphatic system, gynecologic, and genitourinary cancers have a high risk for venous thromboembolism.¹⁸

Due to the increased risk of venous thromboembolism, the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) recommend that women with active cancer or who have been treated for cancer in the last 6 months avoid combined hormonal contraceptive methods (Category 4). Progestin-only contraceptives increase the risk of venous thromboembolism much less than estrogen-containing products,¹⁹ and the CDC suggests that the benefits outweigh the perceived risks (Category 2). The available literature is insufficient to determine if progestin-only contraceptives increase the likelihood of venous thromboembolism among high-risk women.²⁰

Complications of Cancer Treatment Affecting the Selection of Contraception

Anemia

Hormonal contraceptive use in cancer patients with anemia may be warranted. The incidence of anemia in cancer patients is quite high, especially in women with lung cancer (77% suffer from anemia), and patients with gynecological cancer (81% suffer from anemia). As women with cancer-induced anemia have decreased functional capacity and quality of life and shorter survival, efforts to minimize menstrual blood loss with the use of progestin-containing contraceptive, particularly the levonorgestrel IUS, may be warranted.²¹ The Copper T380A may increase menstrual blood loss in some women.²² The implant may cause an unpredictable bleeding profile throughout the course of its use.²³

Osteoporosis

Osteoporosis is a common complication of chemotherapy. For patients with pre-existing bone density loss, the use of DMPA should be considered with extreme caution even though the effect of DMPA on bone mineral density have been found to be reversible. One database study conducted in the United Kingdom, concluded that the use of DMPA is associated with a slight increase in the risk of fracture. The use of contraceptive implants affects the decrease in bone mineral density of the radius and ulna, although no increased risk of frac-

ture was confirmed. In contrast, the use of estrogen-containing contraceptives may have an advantage in osteopenic women although these studies are still contradictory.²³

Immunosuppression

There are limited data on IUD use by women with immunosuppression due to cancer treatment. However, the WHO and the CDC state that IUD contraception is safe and can be used in women who are immunosuppressed due to cancer treatment.²⁴

Chest-Wall Radiation

Women who have received radiotherapy to the chest-wall (Hodgkin's lymphoma) have an increased risk of developing breast cancer. Therefore, these patients should avoid the potential risk of exogenous estrogen or progestin.²⁵ Nevertheless, some clinicians still consider the use of combination hormonal contraceptives containing low-dose estrogen or use of progestin-only contraceptives in this case. This is based on the absence of studies that conclude the effect of the use of contraceptives containing estrogen and progestin leading to an increased risk of breast cancer. T380A IUD contraceptive use remains the primary choice in women who received radiotherapy to the chest-wall, with the levonorgestrel-containing IUS, which produce the lowest serum hormone levels, as the second choice.^{26,27}

CONCLUSION

The information and education of contraception should be provided for any woman considering contraception. In women with cancer, it is recommended that the use of contraception is reversible and highly effective, such as IUD or implantable contraceptive. Any type of contraception can be used in women who have been free of cancer for at least 6 months and had no history of hormone-mediated cancers, not receiving chest-wall radiation, no anemia, no osteoporosis and not experiencing venous thromboembolism.

The following recommendations are based on good clinical evidence and consistent (Level A): The Combined hormonal contraceptive methods (containing estrogen and progestin) should be

avoided by women with active cancer or have been treated for cancer in the last 6 months due to high risk for venous thromboembolism. The use of T380A IUD, highly effective, hormone-free method is recommended for women with a history of breast cancer. Moreover, Levonorgestrel-containing IUS may be used to minimize menstrual blood loss.

The following recommendations are based on limited or inconsistent scientific evidence (Level B): Levonorgestrel-containing IUS has high efficacy and decrease the risk of endometrial cancer without breast cancer recurrence, and is recommended in women who received tamoxifen. Among women with a history of chest-wall radiation, use of total systemic estrogen and progesterone contraceptives should be avoided. Injectable progestin-only contraception should be avoided in women with osteopenia or osteoporosis. The use of estrogen-containing contraception may be beneficial in women with osteopenia or osteoporosis. Intrauterine contraceptive use is quite safe in women with immunosuppression due to chemotherapy.

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