

Primary Prevention of Gynecologic Cancers

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Pendahuluan: Terdapat tiga jenis kanker yang banyak diderita oleh wanita dalam bidang ginekologi, yaitu kanker serviks, kanker ovarium dan kanker endometrium. Patofisiologi kanker serviks hampir dikenal dengan baik, sedangkan patofisiologi kanker ovarium mulai terbuka, dan patofisiologi kanker endometrium juga mulai diketahui. Dengan dasar tersebut dilakukan penelitian terhadap faktor risiko timbulnya kanker ginekologi. Pengenalan faktor risiko yang didapat dari penelitian epidemiologi menjadi dasar untuk melakukan upaya pencegahan primer kanker ginekologi. Pencegahan primer dilakukan dengan memberikan nasihat dan terapi yang mempunyai pengaruh menurunkan risiko timbulnya kanker ginekologi.

Tujuan: Menyampaikan kebijakan pencegahan primer kanker ginekologi berdasarkan hasil penelitian epidemiologi.

Bahan dan cara kerja: Kajian pustaka.

Hasil: Kanker serviks risikonya dapat diturunkan dengan menghindari pola pasangan ganda, menghindari merokok, mengonsumsi makanan yang kaya vitamin C. Kanker ovarium risikonya dapat diturunkan dengan memberi kontrasepsi oral, menyusui, sterilisasi ataupun histerektomi. Kanker endometrium dapat diturunkan risikonya dengan memberikan kontrasepsi oral kombinasi, menurunkan berat badan.

Kesimpulan: Dapat dilakukan upaya menurunkan risiko timbulnya kanker ginekologi melalui pencegahan primer.

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Kata kunci: pencegahan primer, kanker ginekologi

Introduction: There are three types of cancer commonly suffered by women in the field of gynecology, i.e. cervical cancer, ovarian cancer, and endometrial cancer. Pathophysiology of cervical cancers is almost well known, while pathophysiology of ovarian cancer has begun to unfold, and so has the pathophysiology of endometrial cancer. Based on such understanding, studies were conducted of the risk factors of the occurrence of gynecological cancers. Identification of risk factors obtained from epidemiological studies served as the foundation for undertaking primary prevention of gynecological cancer. Primary prevention could be performed by providing advice and therapy aimed at reducing the risk for the incidence of gynecological cancers.

Objective: To present the policies in primary preventions of gynecological cancers based on the results of epidemiological studies.

Material and methods: Literature review.

Results: The risks of cervical cancer could be reduced by refraining from multiple sexual partnership, smoking, and by consuming foods rich in vitamin C. The risks of ovarian cancers could be reduced by providing oral contraceptives, breastfeeding, sterilization, or hysterectomy. The risks of endometrial cancer could be reduced by providing combined oral contraceptives, and reducing body weight.

Conclusions: Efforts could be made to reduce the risks of gynecological cancers through primary prevention.

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Keywords: primary prevention, gynecological cancer

INTRODUCTION

There are three types of gynecological cancers that require special attention for their primary prevention, i.e. uterine cervical cancer, ovarian cancer, and endometrial cancer. These three cancers constitute the three most frequently encountered cancers in the world in general, and in Indonesia in particular. Primary preventive efforts required data obtained from epidemiological studies on the factors contributing to the onset of malignancy. Primary prevention generally is not an invasive intervention, although over the last decade there have been some developments concerning malignancy and preventive surgery. A great many women did not provide special attention to the prevention of primary malignancy, such as avoiding risk factors, undergoing periodic examinations for early detection of malig-

nancy. In addition, medical personnel tended to overlook the efforts at primary prevention, and the selection of and policies in administering therapy. The selection of contraceptives should be tailored to the policies of primary prevention, in addition to serving their primary purposes. This will be of great benefits to the high-risk patients suffering from malignancy. This paper aimed to raise the awareness of physicians in participating in the efforts of primary prevention in gynecological cancers.

Cervical Cancer

There are a number of risk factors in cervical cancer, either the risks of the onset of cervical cancer or the risks of aggravation and precipitation of the incidence of cervical cancer or degeneration into invasive cervical cancer.

It has been known that HPV (human papilloma virus) is a vector that plays a major role in the incidence of cervical cancer of the uterus, and this virus is responsible for sexually transmitted diseases in the sense that the majority of transmissions occur by way of sexual intercourse. Therefore, the primary preventive initiative should be aimed at avoiding multiple partnership for both women and men. Pap smear examinations performed to discover cases at the stage of pre-cancerous lesion constitute the efforts to provide early detection and immediate treatment to prevent its further degeneration into cervical cancer.^{1,2,3}

- Smoking habit. It has been known that smoking increases the risk of cervical cancer twice as high, with odds ratio ranging from 1.8 to 10.1. In addition, there is a trend of growing risks with the increase of smoking dosage, i.e. the higher the smoking dosage, the higher the risk for developing cervical cancer.^{4,5}
- Dietary habit also plays a role in the risk for developing cervical cancer of the uterus. Case-control studies showed that diet of high vitamin C was associated with lower risks for developing cervical cancer, i.e. 31% lower with odds ratio of 0.7% than those who had dietary habit with low vitamin C. Thus, dietary habit with vitamin C intake plays a part in preventing cervical malignancy. The efficacy of vitamin C in preventing malignancy was also evident among smokers. The risk of developing cervical cancer among smokers with dietary intake of low vitamin C will increase 2.2 times as high. (1.1 - 4.4).^{6,7}
- The use of oral contraceptives, as shown by some studies, proved to increase the risk of developing cervical cancer by up to 60%, with odds ratio of 1.5 - 1.8, and the risk will increase in proportion to the longer use of these contraceptives. In women with HPV infection and using oral contraceptives for five years, the risk of developing cervical cancer increased 1.3 times and 1.7 times for a use of five to nine years. There is a strong correlation between the incidence of cervical adenocarcinoma and the use of oral contraceptives, since the use of oral contraceptives will increase the risk for developing cervical adenocarcinoma in women with HPV infection 6 - 12.6 times.⁸ Therefore, in the group of high-risk women, it is advisable that the administration of oral contraceptives be avoided.^{9,10,11}

- As shown by some studies, the use of diaphragm contraceptives in women did not produce adverse effects, or preventive effects, on the incidence of cervical cancer of the uterus (odds ratio 0.2 - 1.2). Similarly, the use of condom as a contraceptive method in these studies provided a variety of results, with odds ratio ranging between 0.2 and 0.9.^{11,12} On the other hand, these studies showed that vaginal spermicide was efficacious in providing preventive effects with odds ratio of 0.1 - 0.7. It may be concluded then that the use of spermicide will reduce the risks of cervical cancer of the uterus.^{11,12}

Endometrial Cancer

Endometrial cancers are comprised of both hormonal-dependent and nonhormonal-dependent endometrial cancers. However, epidemiological studies did not divide the cases of endometrial cancers clinically. A number of factors have been implicated as the risk factors, such as obesity, hypertension, diabetes mellitus, and unovulated cycles. Estrogen factor or estrogen receptor factor was still considered as the basis for the incidence of endometrial cancer, with odds ratio of 0.1 - 0.6, and most of the studies found odds ratio at 0.5.

- Normal body weight is a very significant indication of primary prevention of endometrial cancer, since obesity obviously increases the risk for developing endometrial cancer with odds ratio of 1.0-20.3. Thus, the effort to reduce body weight in high-risk women is the most appropriate option.¹³
- Oral contraceptives. The use of combined oral contraceptives proved to provide protective effects for patients against the possible development of endometrial cancer. Protection will particularly occur with the use of oral contraceptives for one year.^{14,15,16,17}

Ovarian Cancer

Ovarian cancer has been widely known to carry risks or to belong to the series of family cancers. The risks for developing ovarian cancer and breast cancer are noted in the families possessing BRCA 1 or BRCA 2. Inclusion cyst, which was considered the precursor of ovarian cancer resulting from ovulation trauma, is regarded as a risk factor. The triggering of ovulation will increase the risk for developing inclusion cyst or ovarian cyst, or ovarian cancer.

- Prevention of ovulation is an important step in primary prevention, because by doing so the possible occurrence of inclusion cyst is averted, which may degenerate into ovarian tumor and ovarian cancer. Oral contraceptives that are efficacious in preventing ovulation have proved to be effective in reducing the risks for the occurrence of ovarian cancer. Almost all epidemiological studies showed the benefits of oral contraceptives in preventing the occurrence of ovarian cancer. With relative risk of 0.3 - 0.6 and the outcome of 0.6 in meta-analysis, the benefits of oral contraceptives as a means of preventing primary ovarian cancer have been proven.^{18,19}
- Breastfeeding has been shown to reduce the risk for the occurrence of ovarian cancer with odds ratio of 0.7. The effects of breastfeeding in lowering the risks of ovarian cancer may be due to the fact that the ovulated menstrual cycles are disrupted.
- Sterilization intervention. In epidemiological studies, sterilization interventions have been shown to be effective in reducing the risk of ovarian malignancy with a relative risk of 0.3. Sterilization intervention is associated with the disconnection of relationship between ovaries and the outside world through fallopian tube, such that carcinogen substances that may enter through the vagina and tube will be averted by sterilization intervention. This result did not differ from that achieved by women through hysterectomy. It was reported that in women who underwent hysterectomy the risk for developing ovarian cancer was reduced.²⁰

With a reference to the data obtained from epidemiological studies, the efforts at primary prevention can be made by taking into account the risk factors of patients. The selection of contraceptive methods, and changes of dietary habits to support the preventive effects should be made carefully. The ideas which are based on such data will definitely change the mindset of physicians in administering therapy or providing advice during consultation. Such efforts should be made in a case-by-case manner by taking into account risk factors.

CONCLUSIONS

The risks for the occurrence of cervical cancers could be reduced by avoiding the lifestyle of multiple partnerships, smoking, and by consuming vitamin C-rich foods. Contraceptive pills could increase the risk for developing cervical cancer of the

uterus. The risks for developing ovarian cancer could be reduced by administering oral contraceptives, breastfeeding, and sterilization or hysterectomy. Meanwhile, the risks for the occurrence of endometrial cancers could be reduced by providing combined oral contraceptives and by reducing body weight appropriately.

REFERENCES

1. Shin B, Dubeau L. Cell cycle abnormalities in squamous cell carcinoma of the cervix. *CME Gynecol Oncol* 2001; 6: 167-72
2. Park TW, Fujiwara H, Wright TC. Molecular Biology of cervical Cancer and Its Precursors. *Cancer* 1995; 76: 1902-13
3. Southern SA, Herrington CS. Disruption of cell cycle control by humanpapillomaviruses with special reference to cervical carcinoma. *Int J Gynecol Cancer* 2000; 10: 263-74
4. Winkelstein W Jr. Smoking and cervical cancer-current status: a review. *Am J Epidemiol* 1990; 131: 945-57
5. La Vecchia C, Franceschi S, Decarli A, Fasoli M, Gentile A, Tognoni G. Cigarette smoking and the risk of cervical neoplasia. *Am J Epidemiol* 1986; 123: 22-9
6. Potischman N. Nutritional epidemiology of cervical neoplasia. *J Nutr* 1993; 123: 424-9
7. Block G, Patterson B, Subar A. Fruit, vegetables, and cancer prevention: a review of the epidemiological evidence. *Nutr Cancer* 1992; 18: 1-29
8. Lacey JV Jr, Brinton LA, Abbas FM. Oral contraceptives as risk factors for cervical adenocarcinomas and squamous cell carcinomas. *Cancer Epidemiol Biomarkers Prev* 1999; 8(12): 1079-85
9. Brinton LA. Oral contraceptives and cervical neoplasia. *Contraception* 1991; 43: 581-95
10. Parazinni F, La Vecchia C, Negri E, Maggi R. Oral contraceptive use and invasive cervical cancer. *Int J Epidemiol* 1990; 19: 259-63
11. Thomas DB. The WHO collaborative study of neoplasia and steroid contraceptives: the influence of combined oral contraceptive on risk of neoplasms in developing and developed countries. *Contraception* 1991; 43: 695-710
12. Hildesheim A, Brinton LA, Malin K. Barrier and spermicidal contraceptive methods and risk of invasive cervical cancer. *Epidemiology* 1990; 1: 266-72
13. Koumantaki Y, Tzonou A, Koumantakis E, Kaklamani E, Aravantinos D, Trichopoulos D. A case-control study of cancer of the endometrium in Athens. *Int J Cancer* 1989; 43: 795-9
14. Weiss NS, Sayvetz TA. Incidence of endometrial cancer in relation to the use of oral contraceptives. *N Engl J Med* 1980; 303: 1045-7
15. Hulka BS, Chambless LE, Kaufman DG, Fowler WC Jr, Greenberg BG. Protection against endometrial carcinoma by combination-product oral contraceptives. *JAMA* 1982; 247: 475-7

16. Jick SS, Walker AM, Jick H. Oral contraceptives and endometrial cancer. *Obstet Gynecol* 1993; 82: 931-5
17. Villard L, Murphy M. Endometrial cancer trends in England and Wales: a possible protective effect of oral contraception. *Int J Epidemiol* 1990; 19: 255-8
18. Parazzini F, La Vecchia C, Negri E, Bocciolone L, Fedele L, Franceschi S. Oral contraceptive use and the risk of ovarian cancer: an Italian case-control study. *Eur J Cancer* 1991; 27: 594-8
19. Hankinson SE, Colditz GA, Hunter DJ, Spencer TL, Rosner B, Stampfer MJ. A quantitative assessment of oral contraceptive use and risk of ovarian cancer. *Obstet Gynecol* 1992; 80: 708-14
20. Irwin KL, Weiss NS, Lee NC, Peterson HB. Tubal sterilization, hysterectomy, and the subsequent occurrence of epithelial ovarian cancer. *Am J Epidemiol* 1991; 134: 362-9