Analgesic Use and Ovarian Cancer Risk

Through authoring this collaborative advisory with AHA, ACOG has alerted OB/GYN specialists and subspecialists to pay attention to one of the most important threats to women's health. The risk assessment and counseling steps being advocated are straightforward. The AHA's Life's Simple 7 tool can be completed by patients before their visits (even privately in the waiting room). The results can identify patients' specific risks to enable efficient use of the face-to-face visit. Fortunately, even brief messages from physicians repeated over time can be effective. Universal implementation of the advisory recommendations by the OB/GYN community is an important step toward reducing cardiovascular morbidity and premature death in women.—LAL)

Analgesic Use and Ovarian Cancer Risk: An Analysis in the Ovarian Cancer Cohort Consortium

Britton Trabert, Elizabeth M. Poole, Emily White, Kala Visvanathan, Hans-Olov Adami, Garnet L. Anderson, Theodore M. Brasky, Louise A. Brinton, Renee T. Fortner, Mia Gaudet, Patricia Hartge, Judith Hoffman-Bolton, Michael Jones, James V. Lacey, Jr, Susanna C. Larsson, Gerardo G. Mackenzie, Leo J. Schouten, Dale P. Sandler, Katie O'Brien, Alpa V. Patel, Ulrike Peters, Anna Prizment, Kim Robien, Wendy V. Setiawan, Anthony Swerdlow, Piet A. van den Brandt, Elisabete Weiderpass, Lynne R. Wilkens, Alicja Wolk, Nicolas Wentzensen, and Shelley S. Tworoger, on behalf of the Ovarian Cancer Cohort Consortium (OC3)

Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD (B.T., L.A.B., P.H., N.W.); Brigham and Women's Hospital and Harvard Medical School, Boston, MA (E.M.P.); Cancer Prevention Program, Fred Hutchinson Cancer Research Center, Seattle, WA (E. White, G.L.A., U.P.); Johns Hopkins Bloomberg School of Public Health, Baltimore, MD (K.V., J.H.-B.); Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden (E. White, H.-O.A.); Clinical Effectiveness Research Group, Institute of Health and Society, University of Oslo, Oslo, Norway (H.-O.A.); Division of Cancer Prevention and Control, College of Medicine, The Ohio State University, Columbus, OH (T.M.B.); Division of Cancer Epidemiology, German Cancer Research Center, Heidelberg, Germany (R.T.F.); Epidemiology Research Program, American Cancer Society, Atlanta, GA (M.G., A.V.P.); Division of Genetics and Epidemiology and Division of Breast Cancer Research, The Institute of Cancer Research, London, United Kingdom (M.J., A.S.); City of Hope, Duarte, CA (J.V.L.); Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden (S.C.L., A.W.); Department of Nutrition, University of California Davis, Davis, CA (G.G.M.); Department of Epidemiology, GROW-School for Oncology and Developmental Biology, Maastricht University, Maastricht, the Netherlands (L.J.S., P.A.v.d.B.); National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, NC (D.P.S., K.O.); Division of Epidemiology and Community Health, School of Public Health, and Masonic Cancer Center, University of Minnesota, Minneapolis, MN (A.P.); Department of Exercise and Nutrition Sciences, Milken Institute School of Public Health, George Washington University, Washington, DC (K.R.); University of Southern California, Los Angeles, CA (W.V.S.); Department of Community Medicine, Faculty of Health Sciences, University of Tromsø, The Arctic University of Norway, Tromsø (E. Weiderpass); Department of Research, Cancer Registry of Norway, Institute of Population Based Cancer Research, Oslo (E. Weiderpass), Norway; Genetic Epidemiology Group, Folkhälsan Research Center, Helsinki, Finland (E. Weiderpass); University of Hawaii Cancer Center, Honolulu, HI (L.R.W.); Department of Epidemiology, Harvard T. H. Chan School of Public Health, Boston, MA (S.S.T.); and Department of Cancer Epidemiology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL (S.S.T.)

J Natl Cancer Inst 2018; doi: 10.1093/jnci/djy100

ABSTRACT

The most fatal gynecologic cancer is ovarian cancer. This is largely due to its delayed symptom presentation and lack of early detection strategies. Although chemoprevention for this cancer has not been widely studied, it may present approaches to reduce ovarian cancer burden. It has suggested that chronic inflammation has a key role in ovarian carcinogenesis. Previous studies have reported an association between aspirin use and reduced risk of several cancers. In a recent pooled analysis of 12 case-control studies in the Ovarian Cancer Association Consortium, there was a 10% decrease in risk of ovarian cancer with regular aspirin use, which was stronger for daily use and with low doses.

Any increased or decreased cancer risk of aspirin, nonaspirin nonsteroidal anti-inflammatory drugs (NSAIDs), and acetaminophen may have important public health implications because of their wide use. Use of high-dose NSAIDs, but not acetaminophen, has been associated with lower ovarian risk. The few prospective observational studies conducted between aspirin or other NSAID use and ovarian cancer risk had inconsistent results.

The aim of this prospective cohort study was to investigate associations of analgesic use with ovarian cancer. The association between frequent aspirin, nonaspirin NSAIDs, and acetaminophen use with ovarian cancer risk was assessed using pooled data in 13 studies from the Ovarian Cancer Cohort Consortium. A total of 758,829 women were included, who self-reported analgesic use over at least a 6-month period; 3514 of these women developed ovarian cancer. Associations between frequent medication use and risk of ovarian cancer were assessed using Cox regression. Dose and duration of use were also evaluated. Frequent use was defined as at least 4 to 5 times per week, and very frequent use was defined as 6 or 7 days per week.

Compared with infrequent/nonusers, women who used aspirin daily or almost daily use (≥6 d/wk) had a 10% reduction in ovarian cancer risk; the rate ratio (RR) was 0.90, with a 95% confidence interval (CI) of 0.82 to 1.00; $P = 0.05$. No increased ovarian cancer risk was found with frequent use (≥4 d/wk) of aspirin (RR, 0.95; 95% CI, 0.88–1.03), nonaspirin NSAIDs (RR, 1.00; 95% CI, 0.90–1.11), or acetaminophen (RR, 1.05; 95% CI, 0.88–1.24). Risk of ovarian cancer was elevated with daily acetaminophen use (RR, 1.28; 95% CI, 1.00–1.65; $P = 0.05$). There was a small statistically insignificant increase in risk for frequent, long-term (10+ years) use of aspirin (RR, 1.15; 95% CI, 0.98–1.34) and nonaspirin NSAIDs (RR, 1.19; 95% CI, 0.84–1.68).

The findings of this large, prospective study suggests that daily use of aspirin slightly lowers risk of developing ovarian cancer (10% lower than infrequent/nonuse), which is similar to that observed in case-control analyses. Further studies are required because the observed potential elevated risks for 10+ years of frequent aspirin and NSAID use could be due to confounding by medical indications for use or variation in drug dosing.

EDITORIAL COMMENT

(Aspirin is the workhorse of all drugs. It has been used for various ailments for more than 2000 years. Related to derivatives found in the willow tree, Bayer coined the name aspirin in 1899. The World Health Organization lists aspirin as one of the world's essential medicines, and its cost is measured in pennies. Aspirin is effective for treatment of pain, inflammation, fever, and headache and plays a role in mitigating cardiac abnormalities due to myocardial infarction. Relevant to cancer, the US Preventive Services Task Force recommends "…initiating low-dose aspirin use for the primary prevention of cardiovascular disease (CVD) and colorectal cancer in adults aged 50–59 years who have a 10% or greater 10-year CVD risk, are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years." There are no solid recommendations for taking aspirin for prevention of other cancers. The Women's Health Study evaluated every-other-day use of low-dose aspirin and did not see a reduction in cancer in 40,000 women 40 years or older.

The current study was undertaken by Dr Trabert and colleagues of the Ovarian Cancer Cohort Consortium, a multidisciplinary collection of experts situated in the National Cancer Institute whose goal is to study ovarian cancer from pooled data. In this analysis of 13 studies, women who took aspirin were evaluated for the risk of ovarian cancer. Studies were collected from North America and Europe, and data were collected on aspirin as well as nonaspirin, nonsteroidal, and acetaminophen use over a 6-month period. Medication use was self-reported by patients based on memory and recollection. A diagnosis of ovarian cancer was expanded to include all histologies. The group reported that taking aspirin more than 4 days a week ("frequent") was not associated with lowering the risk of developing ovarian cancer. However, if patients expanded their use to more than 6 days a week ("daily"), they experienced a 10% reduction in ovarian cancer. It is also notable that if patients took aspirin daily for more than 10 years there was a slightly increased risk of developing ovarian cancer. The authors cite the strengths of their study to include a large sample size and the availability of detailed history regarding risk factors for ovarian cancer and the ability to track patient outcome such as death. Limitations are notable for the self-reported nature of the data, lack of information regarding low-dose use, and fewer data on health conditions and medical indications for using analgesia. One of the reasons to not use aspirin is the potential adverse effect, gastrointestinal bleeding, a particular concern in the older patient. There is no information about adverse effects in this study. Given our updated

understanding that ovarian cancers differ (high-grade histology, low-grade serous, clear cell histology all differ), it would have been interesting to evaluate the relationship between aspirin, outcome, and ovarian cancer histology.

Aspirin is cheap and cures many ills. However, conclusions regarding its utility in cancer prevention have been slow in coming. It took the US Preventive Services Task Force years to make recommendations about aspirin use to prevent colon cancer. In the current study, 6 days of aspirin use made a difference; however, 4 days did not, and taking aspirin too long (>10 years) was detrimental. Inasmuch as aspirin use was self-reported, was there underreporting or overreporting and would that make a difference in the conclusion? Although it would be amazing, stupendous, and wonderful if an inexpensive, commonly available medication such as aspirin could reduce the risk of developing ovarian cancer and improve mortality, the role of aspirin in ovarian cancer risk needs further study.—LVL)

Evidence-Based Improvisation: Facing the Challenges of Cervical Cancer Care in Uganda

Megan Swanson, Stefanie Ueda, Lee-May Chen, Megan J. Huchko, Carol Nakisige, and Jane Namugga

Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, University of California at San Francisco, San Francisco, CA (M.S., S.U., L.-M.C.); Department of Obstetrics and Gynecology, Duke Global Health Institute, Durham, NC (M.J.H.); and Division of Gynaecologic Oncology, Uganda Cancer Institute (C.N.), and Division of Gynaecologic Oncology, Mulago National Referral Hospital (J.N.), Makerere University College for Health Sciences School of Medicine, Kampala, Uganda

Gynecol Oncol Rep 2018;24:30–35

ABSTRACT

In 2012, cervical cancer accounted for more than a half million new cases and 250,000 deaths worldwide. This cancer is the most common malignancy in Uganda and is responsible for the greatest cancer-related mortality among women in that country. A wide disparity exists between high-resource and poor-resource counties in the prevalence of cervical cancer. Low- and middle-income countries (LMICs) shoulder a disproportionate share of disease incidence and a much greater proportion of morbidity and mortality. There is an inverse relationship among developing and developed countries between per-capita income and available resources for diagnosis, treatment, and palliation of cervical and other cancers. Only 6% of total resources spent on cancer care globally are in less-developed countries. This gross discrepancy in funding (together with the advanced-stage diagnosis of cervical cancer) severely limits available treatment and contributes to the high mortality rates in LMICs.

The incidence of this disease has decreased in developed countries in large part because of widespread uptake of screening and vaccination. However, its incidence in Uganda and neighboring countries has increased because fewer than 10% of women in these LMICs have ever been screened. Diagnosis is also limited by costs and the lack of magnetic resonance imaging and positron emission tomography machines. Although prevention and screening of cervical cancer remain public health priorities, given the large number of women in LMICs affected by this cancer, expanding treatment capacity should be included in any evidence-based intervention plan. Cervical dysplasia and early cancers are treatable, and there is improved survival with treatment; local control palliates symptoms cost-effectively.

Uganda serves as a representative case study for challenges of diagnosis and access to treatment for women in sub-Saharan Africa. At least 80% of cervical tumors in Uganda are diagnosed at an advanced stage, and 5-year overall survival is low (approximately 18%). In addition to late-stage presentation for care, challenges facing patients and providers in Uganda include limited opportunities for provider training, prohibitive cost of diagnostic studies, limited access to criterion-standard treatment, and underuse of palliative care services. There are few specialty-trained surgical and medical gynecologic oncologists in Uganda and other African countries, as well as few radiation oncologists, pathologists, radiation therapists, nurses, and other staff.