Effect of aspirin, NSAIDs on colorectal cancer risk may differ from genetic variations

March 17 2015

Coated aspirin tablets. Image: Wikimedia Commons.

Among approximately 19,000 individuals, the use of aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs) was associated with an overall lower risk of colorectal cancer, although this association differed according to certain genetic variations, according to a study in the March 17 issue of *JAMA*.

Considerable evidence demonstrates that use of aspirin and other NSAIDs is associated with a lower risk of colorectal cancer. However, the mechanisms behind this association are not well understood. Routine use of aspirin, NSAIDs, or both for prevention of cancer is not currently recommended because of uncertainty about the risk-benefit profile. Understanding the relationship between genetic markers and use of

aspirin and NSAIDs, also known as gene by environment interactions, can help to identify population subgroups defined by genetic background that may benefit most from use of these agents to prevent cancer, according to background information in the article.

Andrew T. Chan, M.D., M.P.H., of Massachusetts General Hospital, Boston, Li Hsu, Ph.D., of the Fred Hutchinson Cancer Research Center, Seattle, and colleagues conducted a genome-wide analysis of gene by environment interactions between regular use of aspirin, NSAIDs, or both and single-nucleotide polymorphisms (SNPs; genetic variations) in relation to risk of colorectal cancer. The researchers used data from 5 case-control and 5 cohort studies initiated between 1976 and 2003 across the United States, Canada, Australia, and Germany and included colorectal cancer case patients (n = 8,634) and matched controls (n = 8,553) ascertained between 1976 and 2011. Participants were all of European descent.

An analysis of the overall data indicated that regular use of aspirin and/or NSAIDs was associated with lower risk of colorectal cancer compared with nonregular use. But among individuals with two less common genotypes of rs16973225 (AC or CC, 9 percent of participants), no association was found between regular use and risk of colorectal cancer. And among participants with two rare genotypes of rs2965667 (TA or AA, 4 percent of participants), aspirin and/or NSAID use was associated with a higher risk of colorectal cancer.

In this genome-wide investigation of gene by environment interactions, "use of aspirin, NSAIDs, or both was associated with lower risk of colorectal cancer, and the association of these medications with colorectal cancer risk differed according to genetic variation at 2 SNPs at chromosomes 12 and 15. Validation of these findings in additional populations may facilitate targeted colorectal cancer prevention strategies," the authors write.

"In the not-too-distant future it will be possible to affordably and efficiently conduct genetic testing in healthy individuals to more accurately define benefits and risks of interventions intended to decrease risk of disease," writes Richard C. Wender, M.D., of the American Cancer Society, Atlanta, in an accompanying editorial.

"It will be important for primary care clinicians to understand genetic risk and to have informed, clear, literacy-adjusted, culturally competent discussions with their patients about how to use this information; otherwise, the goal of using genetic information to enhance decision making about prevention will remain elusive. Research needs to test different approaches to translating this complex information into practical methods to share information and improve clinical decisions. The ability to translate genetic profiling into tailored preventive care plans for individuals is still years away, but with the study by Nan et al, the road, arduous as it may be, is more clearly illuminated."

More information: doi:10.1001/jama.2015.1815
doi:10.1001/jama.2015.1032

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