

Does aspirin really reduce the colorectal cancer risk?

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Cancer is the leading cause of death in developed countries and the second leading cause of death in developing countries, where the cancer burden is rising.¹ Colorectal cancer is the third most commonly diagnosed cancer in males and the second in females, with over 1.2 million new cancer cases and 608,700 deaths estimated to have occurred in 2008.¹ Eliminating exposure to carcinogens, such as tobacco, has been a well-established approach to the cancer prevention, but active intervention with the agents that expected to reduce the risk of cancer is becoming increasingly accepted.^{2,3}

Among several chemopreventive interventions, aspirin is perhaps the agent with the strongest body of evidence that significantly reduces the population burden of colorectal cancer (CRC). Aspirin, which is a nonsteroidal anti-inflammatory drug, has been shown to reduce the risk of cancer, particularly of CRC, by complicated mechanisms through the signaling pathway. Aspirin blocks proliferation of colorectal cancer cells and causes them to self destruct by inhibiting the mechanistic target of rapamycin (mTOR).⁴ Many signaling pathways are dysregulated in cancer cells, including phosphoinositide-3-kinase (PI3K) signaling via mTOR—a serine/threonine kinase that controls cell survival and regulates cell metabolism. The mTOR is overexpressed in colorectal cancer cells, and the tumor suppressor phosphatase and tensin homolog (PTEN), which down-regulates mTOR, is inactivated in 30%–40% of colorectal tumors. It is proposed that Aspirin activates adenosine monophosphate-activated protein kinase (AMPK), which inhibits mTOR signaling and through these pathways, aspirin affects cell signaling pathways involved in mRNA stability, cell cycle, autophagy, protein translation, and ribosome biogenesis.⁴ Further studies are needed to determine the complex effects of aspirin on cancer cell.

The cancer-preventive effect of aspirin has been tested in the multiple trials and it was shown that in patients with a history of a previous CRC or a history of colorectal adenomas, the incidence of new colorectal adenomas was reduced in those taking aspirin versus those taking no aspirin.⁵⁻⁷ In another study of patients with hereditary CRC (Lynch syndrome), using an intention-to-treat analysis, the hazard ratio (HR) of long-term effects of aspirin was found to be 0.63 (95% CI=0.35–1.13; p=0.12).⁸ Multiple

Accepted on

December 26th, 2012

DOI Name

10.3126/jaim.v2i1.7627

Keywords

Aspirin, colorectal cancer, prevention

Citation

Shrestha UK. Does aspirin really reduce the colorectal cancer risk? *Journal of Advances in Internal Medicine* 2013;02(01):1-2.

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randomized clinical trials that were originally designed with non-cancer end points found that, after a minimum of 5 years of follow-up, trial participants who took aspirin daily, regardless of dose, for a mean of 4 years, had a 44% reduction in cancer mortality compared with participants who took a placebo, and the largest reduction in risk was found for gastrointestinal cancers (esophageal and colorectal adenocarcinoma).⁹⁻¹¹ Data also showed a lower risk of cancer-associated mortality after 20 years of follow-up.⁹ Together, these studies strongly suggest a role of aspirin in colon cancer risk reduction.

Low dose aspirin has long been established for its use to treat and prevent cardiovascular disease, including heart attack, stroke, and peripheral artery disease and people with a higher risk of heart attack definitely have a greater potential for benefit. However, the cardiovascular benefits of aspirin must be weighed against its possible gastrointestinal side effects. The similar situation might be true for its anti-cancer use in the prevention of CRC. Since aspirin can substantially increase the risk of serious gastrointestinal bleeding, the chemoprevention for CRC may be decided only on an individual basis depending upon the high-risk group for CRC with less potentiality of gastrointestinal side effects. Though the evidence of anti-cancer activity of aspirin is becoming stronger, further research is needed to substantiate a guideline to use aspirin for the prevention of CRC.

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