Does aspirin use reduce the risk for cancer?

Usman Iqbal,[1,2] Hsuan-Chia Yang,[2,3] Wen-Shan Jian,[2,4] Yun Yen,[5,6] Yu-Chuan (Jack) Li[2,5,7]

[1]Masters Program in Global Health and Development Department, College of Public Health, Taipei Medical University, Taipei, Taiwan
[2]International Center for Health Information Technology, Taipei, Taiwan
[3]Institute of Biomedical Informatics, National Yang Ming University, Taipei, Taiwan
[4]School of Health Care Administration, College of Management, Taipei Medical University, Taipei, Taiwan
[5]College of Medical Science and Technology, Taipei Medical University, Taipei, Taiwan
[6]City of Hope, Duarte, California, USA
[7]Department of Dermatology, Wan Fang Hospital, Taipei, Taiwan

Correspondence to
Professor Yu-Chuan (Jack) Li, College of Medical Science and Technology (CoMST), Taipei Medical University, Department of Dermatology, Wan Fang Hospital, Taipei, Taiwan; jack@tmu.edu.tw

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ABSTRACT

Recently, studies have reported that aspirin has chemopreventive properties. In this study, we used the Taiwan NHI database, which covers a population of 23 million (99.99%) Taiwanese from 2001 to 2011. This was a case–control study which identified 601,733 patients using ICD-9-CM codes who were diagnosed with cancer. Each case with 4 eligible controls was matched for age, sex, and index date and adjusted for confounding factors. The observed overall cancer risk (adjusted OR (AOR), 0.95; 95% CI 0.94 to 0.96) reduced with aspirin use, specifically, colorectal (AOR, 0.97; 95% CI 0.94 to 0.99) and digestive system (AOR, 0.96; 95% CI 0.94 to 0.98) cancers. Findings from the Asian population would contribute to the discussion on aspirin's safety profile.

INTRODUCTION

Aspirin is the most commonly prescribed medication around the world. Several studies reported that aspirin has chemopreventive properties as it plays an important role in reducing overall cancer incidence,[1 2] including a recent one from the USA.[3] We were interested to see whether these findings are also generalizable to the Asian population or not.

MATERIALS AND METHODS

We used the Taiwan National Health Insurance research (NHI) database, which covers a population of 23 million (99.99%) Taiwanese from 2001 to 2011. We designed a case–control study which identified 601,733 patients by using the ICD-9-CM (140–208) codes (International Classification of Diseases, Ninth Revision, and Clinical Modification) who were aged over 20 years and who were newly diagnosed with cancer during 2004–2011. We matched each case with four eligible controls (2,406,932) for age, sex, and the index date (ie, free of any cancer at the same date of case diagnosis) by using a propensity score.

For case and control, we defined case as all patients who were diagnosed with any cancer for the first time and we used the date of cancer diagnosis as the index date. We define control as, for each case, we selected four controls randomly among all individuals in the sample population, and a propensity score was matched for sex, age at cancer diagnosis, and year of diagnosis. Controls were assigned an index date identical to the date of diagnosis for the corresponding case. Outcomes: Aspirin exposure (yes/no users).

Data were adjusted for confounding factors like age, sex, Charlson comorbidity index, and medications such as statin, metformin, ACE inhibitors, and Angiotensin II receptor blockers during the study period to mimic bias. Aspirin exposure was calculated from prescriptions using ATC (Anatomical Therapeutic Chemical) drug classification codes (B01AC06). Exposure was defined as patients having had aspirin prescribed at least for 2 months during the 3-year period before the initial cancer diagnosis.

In Taiwan, health behavior is very different from that in the USA or other countries. Although patients can purchase aspirin from pharmacies in Taiwan, it is rarely used to treat fever, pain, and inflammation because most commonly people use panadol, ibuprofen, or diclofenac. So, its short-term use is very rare.

It is also important to note that aspirin is prescribed for long-term use to treat cardiovascular disease in Taiwan. So, it is often prescribed within hospitals by physicians only. Moreover, aspirin is covered by Taiwan NHI; therefore, people also avoid buying it from pharmacies and prefer getting it from hospitals. Thus, the long-term use of aspirin in Taiwan is for preventing myocardial infarction instead of treating fever, pain, and inflammation.

RESULTS

Interestingly, we found that overall cancer risk (adjusted OR (AOR), 0.95; 95% CI 0.94 to 0.96) was reduced with aspirin use, specifically, colorectal cancer (AOR, 0.97; 95% CI 0.94 to 0.99) and digestive system cancers (AOR, 0.96; 95% CI 0.94 to 0.98), as presented in table 1. However, we observed that the risk for gastric cancer (AOR, 0.96; 95% CI 0.92 to 1.00), prostate, and breast cancer was not statistically significant.

DISCUSSION

Studies recently reported the chemopreventive effect of aspirin. Choi *et al*[4] observed a 2.7 to 3.6-fold decreased risk for cholangiocarcinoma in aspirin users. Drew *et al*[1] provided evidence demonstrating that aspirin has potential for the prevention of cancer, particularly colorectal cancer. Erichsen *et al*[2] reported that aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) may reduce colorectal cancer risk. Nan *et al*,[5] who reported genome-wide investigation of gene–environment interactions, found that the

Table 1 Association between aspirin use and cancer risk

	Cases (n=601,733) Exposed/unexposed	Controls (n=2,406,932) Exposed/unexposed	Unadjusted odds ratio (95% CI)	p Value	Adjusted odds ratio* (95% CI)	p Value
Cancers						
Overall	88,153/513,580	353,001/2,053,931	1.00 (0.99 to 1.01)	0.74	0.95 (0.94 to 0.96)	<0.001
Colorectal	14,850/71,747	58,175/288,213	1.03 (1.01 to 1.05)	0.01	0.97 (0.94 to 0.99)	0.004
Digestive	20,575/10,1359	82,717/405,019	0.99 (0.98 to 1.01)	0.46	0.96 (0.94 to 0.98)	<0.001
Gastric	4,158/18,416	17,096/73,200	0.96 (0.93 to 1.00)	0.07	0.96 (0.92 to 1.00)	0.057
Breast	4,853/60,638	192,662/242,702	1.01 (0.98 to 1.04)	0.60	0.99 (0.96 to 1.03)	0.757
Lung	12,999/55,410	52,528/221,108	0.99 (0.97 to 1.01)	0.23	0.95 (0.92 to 0.97)	<0.001
Prostate	7,946/24,473	30,473/99,203	1.06 (1.03 to 1.09)	0.00	1.03 (0.99 to 1.06)	0.104

p<0.001.
*Adjusted ORs were adjusted for the confounders such as comorbid conditions and other drugs in the analysis.

use of aspirin and/or NSAIDs was associated with lower colorectal cancer risk.

In animal models of cancer, aspirin showed a chemopreventive effect, also with regard to chemically induced lung and colon cancer, and human cancer xenografts. Regardless of the poor in vitro potency of aspirin, it has shown significant efficacy in humans as well.[6] Rüschoff *et al*[7] observed that the exposure of cultured cells to aspirin reduces microsatellite instability in mismatch repair-deficient colon cancer cells.

Randomized trials have also shown that aspirin contains a moderate chemopreventive effect as its use is associated with reduction in large bowel adenomas.[8 9]

Our findings are supported by all these studies and we believe that these findings from the Asian population would contribute to the discussion on aspirin's safety profile. It is important to emphasize the importance of observational health data for pharmacoepidemiology because of its lower cost, greater timeliness, and a broader range of patients.[10] However, this study has known limitations which need to be mentioned before drawing definitive conclusions; it is always of lower quality than randomized control trial studies as NHI data serve for administrative billing and not for scientific validation purposes. Moreover, the hypothesis drawn from observational health data could play an important role for reverse translation to translational medicine. Further studies, including randomized clinical trials for aspirin, are needed to demonstrate any association with biological mechanisms contributing to morbidity and mortality.

Contributors Y-CL, UI, and H-CY designed the study, enrolled patients, interpreted data, wrote the report, and approved the final draft. UI, H-CY, and W-SJ designed the study, searched the published work, analyzed and interpreted data, reviewed the manuscript, and approved the final draft. Y-CL, W-SJ, and YY interpreted data, reviewed the report, and approved the final draft.

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Competing interests None declared.

Ethics approval Ethical approval was not required as we used anonymous data.

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