

ACE Inhibitors May Cut Risk of Some GI Cancers

Analyses of a large veterans' database show fewer cases of colon, pancreatic, and esophageal cancers.

BY MARY ELLEN SCHNEIDER
Senior Writer

LOS ANGELES — The use of angiotensin-converting enzyme inhibitors is associated with a significantly lower risk of developing esophageal, pancreatic, and colon cancers, according to research presented at the annual Digestive Disease Week.

Three case-control analyses of more than 480,000 veterans living in eight states in the south-central United States showed that patients who used ACE inhibitors were less likely to develop certain cancers. Patients taking ACE inhibitors were 53% less likely to develop colon cancer, 52% less likely to develop pancreatic cancer, and 46% less likely to develop esophageal cancer than patients who did not take the drugs.

ACE inhibitors may exert this risk-reduction effect by suppressing vascular endothelial growth factor (VEGF), which many researchers believe plays a significant role in the angiogenesis of human tumors, said lead study author Dr. Vikas Khurana of the Overton Brooks VA Medical Center in Shreveport, La. Dr. Khurana is on the

speakers' bureau for AstraZeneca.

Dr. Khurana and his colleagues performed three retrospective analyses of the Veterans Integrated Service Network 16 database, looking at 483,733 patients who made regular visits to a VA medical center clinic from October 1998 to June 2004.

Of those patients, 184,743 (38%) were using ACE inhibitors. A total of 6,697 patients in the VA database (1.5%) had colon cancer, 475 patients (0.1%) had pancreatic cancer, and 659 patients (0.14%) had esophageal cancer.

The data were adjusted for age, race, gender, body mass index, smoking, alcohol use, diabetes, and statin use. The protective effect of ACE inhibitor use was independent of statin use for all three cancers, Dr. Khurana said. However, the investigators did not factor the dose, duration, or type of ACE inhibitor into their analysis.

But Dr. Khurana does not recommend a change in prescribing patterns based on the results of this study, since it was a case-control analysis. "We need to have randomized controlled trials before we use these agents as chemopreventive agents," he said. ■

Moderate Drinking May Help Prevent Colorectal Adenoma

BY MARY ELLEN SCHNEIDER
Senior Writer

LOS ANGELES — Individuals who consume moderate amounts of alcohol have a lower risk of developing colorectal adenomas compared with heavy drinkers, according to research presented at the annual Digestive Disease Week.

Also, moderate alcohol consumption—between two and seven drinks per week—may actually protect against the disease, compared with teetotalism, said lead investigator Dr.

Greg Austin of the University of North Carolina at Chapel Hill.

He and his colleagues performed a case-control analysis of 203 patients and 522 controls; all underwent a full colonoscopy and completed the National Cancer Institute's food frequency questionnaire.

Individuals who reported consuming an average of less than two drinks a week or between two and seven drinks per week had the lowest probability of developing colorectal adenoma. Moderate drinkers—those who reported consuming between two and seven drinks—were used as a ref-

erence group in the study. The researchers controlled for potential confounding factors including sex, age, body mass index, race, smoking, and the use of nonsteroidal anti-inflammatory medications.

Those who abstained from alcohol use, the largest group in the study, had about a 40% increased risk, compared with moderate drinkers.

Heavier drinkers had the highest risk. Individuals who consumed between 7 and 14 drinks per week had about a 60% increased risk of developing adenoma compared with moderate drinkers, and those who consumed 14 drinks or more had a 150% increased risk.

"A moderate level of alcohol consumption certainly isn't harmful," and it may be protective, Dr. Austin said.

The preliminary results lack statistical power to show that limited alcohol intake is better than abstention, commented Dr. Lee Kaplan, director of the Massachusetts General Hospital Weight Center, Boston.

But the findings clearly show that moderate alcohol consumption is better than heavy consumption, said Dr. Kaplan, who was not involved in the study. ■

Diet, Exercise, Common Drugs Lower Colorectal Cancer Risk

BY BETSY BATES
Los Angeles Bureau

SAN FRANCISCO — Colorectal cancer risk reduction has been found to be highly associated with the use of several over-the-counter and prescription drugs, as well as with exercise and consumption of vegetables, in a large ongoing chemoprevention study in Israel.

Low-dose aspirin and statins, for example, each appeared to be protective in the case-control Molecular Epidemiology of Colorectal Cancer (MECC) study.

Combined, the protective benefit of the two drugs appeared to be even more powerful, reducing by 60% the relative risk of colorectal cancer in healthy adults, said Dr. Gad Rennert, director of the CHS National Israeli Cancer Control Center in Haifa.

Case-control studies do not produce strong evidence of an association, as would be seen in a randomized, controlled trial, Dr. Rennert noted at a symposium sponsored by the American Society of Clinical Oncology. But large studies such as MECC can examine multiple potential contributors to cancer risk—factors that are common to many people in the population. Fairly good evidence of an association can be seen if there are sharp differences in factors such as lifestyle or prescribed drugs between controls and people diagnosed with cancer.

In the MECC study, there was a lower relative risk of colorectal cancer in people taking aspirin and other nonsteroidal anti-inflammatory drugs, statins, allopurinol, and thyroxine, compared with people who were not using such agents. Those interventions were associated with even greater reductions in relative risk in a high-risk group: carriers of the APC 11307K genetic mutation, which is linked to a twofold elevation in risk of colorectal cancer in Ashkenazi Jews. (See box.)

"We see strong associations with very narrow confidence intervals—pretty much the dream of an epidemiologist," Dr. Rennert said. The largest risk reductions were seen among subjects who participated in sports, ate five or more vegetables a day, and took either a statin

or an aspirin or NSAID daily. These subjects had a relative risk of colorectal cancer of 0.22—a reduction of nearly 80%, compared with people with none of these protective factors. In the high-risk group, the protective factors combined to confer an 84% reduction in risk.

Referring to colorectal cancer as "a highly preventable disease," Dr. Rennert said the MECC findings might ultimately point to preventive strategies for healthy people and, especially, those at high risk for the disease. The MECC

study is a collaboration between Dr. Stephen B. Gruber of the University of Michigan, Ann Arbor, and Dr. Rennert in Israel. The research is funded by the National Institutes of Health.

More than 6,000 subjects have been enrolled, with one control for each patient newly diagnosed with colorectal cancer. The study draws on clinical and pharmacy records, pathology reports, and biopsy studies, as well as thorough interviews covering lifestyle and nutrition issues.

Applying the findings to preventive efforts becomes tricky, since any intervention must be weighed against possible harm. "Side effects are extremely important when you're talking about healthy people," he noted. In people with a high risk for colorectal cancer because of a personal or family history or genetic profile, the balance may tip more in favor of preventive intervention.

There is little hope of ever studying the preventive benefit of low-dose aspirin or statins in a randomized, placebo-controlled trial, Dr. Rennert said, because the drugs are so commonly used that it would be hard to enroll an unbiased sample and ensure that results were not contaminated.

But the "very strong evidence" in the MECC case-control study suggests that these agents, when used for other indications by a wide variety of people, may reduce colorectal cancer rates in the future.

"Time will say whether this is the case or not," he said at the meeting, which was also sponsored by the American Gastroenterological Association, the American Society for Therapeutic Radiology and Oncology, and the Society of Surgical Oncology. ■



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DR. RENNERT

Relative Risk of Colorectal Cancer by Medication Use

Intervention	In average-risk population	In high-risk group*
Aspirin or NSAIDs	0.57	0.34
Statins	0.47	0.25
Allopurinol	0.48	0.35
Thyroxine	0.51	0.35
Aspirin + statin	0.36	Data not yet available

*Relative risks are based on comparison with other persons with similar risk.
Sources: Dr. Rennert, Dr. Gruber