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Personal Health (A Special Report); The Hidden Dangers of Heartburn: How a common health problem is quietly becoming an unsuspected killer

By Tara Parker-Pope, The Wall Street Journal, 2359 words Oct 10, 2005

Document Text

FEW HEALTH PROBLEMS are as ubiquitous as heartburn. An estimated 100 million Americans suffer from it every month; about 15 million battle it at least once a day.

In fact, heartburn is so common that most people don't worry about it.

But they should.

There's a growing uneasiness in the medical community about the hidden dangers of heartburn. The condition is linked with debilitating sleep problems, chronic cough and even asthma. Worse, years of chronic heartburn can turn deadly, leading to an aggressive esophageal cancer that few survive. The disease typically kills its victims within a year of diagnosis.

At a time when most cancer rates are falling, esophageal adenocarcinoma -- the type linked with heartburn -- has jumped fivefold in the past 30 years. Although esophageal cancer remains relatively rare -- about 14,000 people were diagnosed last year -- it has the dubious distinction of being the fastest-growing cancer in the country. And many health experts worry that this is just the beginning.

"There may be only 14,000 cases now, but if you keep up that rate of rise, it's going to pass them all," says Scott Swanson, chief of thoracic surgery at Mount Sinai School of Medicine in New York. "If it continues, we're going to be dealing with a real epidemic."

Even more troubling are the theories about why esophageal cancer due to heartburn is gaining ground at such an alarming rate. Although obesity and poor dietary habits are likely culprits, there's mounting evidence that the way doctors and patients treat heartburn symptoms may also be making things worse.

Some preliminary research suggests that the use of acid-suppressing drugs such as proton-pump inhibitors or PPIs -- which are highly effective in curbing heartburn symptoms -- may play a role in the rise of esophageal cancer. While the drugs themselves are viewed as safe, the concern is that long-term use of acid-reducing drugs alters the environment in the digestive

tract in a way that allows cancer to take hold in certain patients. In addition, while the drugs clearly make patients feel better, studies show that stopping symptoms may not be enough to stop continuing damage to the esophagus.

"There's an explosion of the use of these drugs to treat reflux disease," says Jeffrey Hagen, associate professor of surgery at the Keck School of Medicine of the University of Southern California. "If we're right about [reflux drugs], then what you've seen over the past decade may only be the tip of the iceberg. Esophageal cancer is not going to be so rare anymore -- it's going to be huge numbers."

PPIs, which include AstraZeneca PLC's Nexium, Wyeth's Protonix and Tap Pharmaceutical Products Inc.'s Prevacid, account for nearly \$13 billion in drug sales each year, making PPIs the second most popular drug type, after cholesterol drugs. Prescriptions for PPIs have nearly doubled from 50 million in 1999 to more than 93 million last year, according to pharmaceutical sales research firm IMS Health.

Despite questions about the long-term effects of acid-suppressing drugs, the solution isn't necessarily to stop taking them. Rather, many doctors believe more aggressive monitoring of PPI users is needed, to ensure that the underlying problem is being treated along with the symptoms.

Heartburn symptoms show up in a variety of ways -- as a burning pain behind the breastbone, indigestion, or a sour or burning taste in the back of the throat. It happens when stomach juices -- acids, bile and digestive enzymes -- slosh onto the lining of the esophagus. A valve at the lower end of the esophagus usually keeps the acid and other corrosive liquids in the stomach where they belong. But frequent heartburn sufferers often have gastro-esophageal reflux disease, or GERD, which occurs when the valve doesn't work right, allowing stomach acids and other corrosive liquids to flow backward into the esophagus.

While this malfunction leads to regular bouts of heartburn, it also can take a dramatic toll on the esophagus, leaving it inflamed and irritated. Healthy esophageal tissue resembles the smooth, gummy lining of the cheek, but years of exposure to digestive fluids can transform it into the pale, cobblestone appearance of the stomach. Only about 12% of GERD sufferers develop this condition, known as Barrett's esophagus. But once the transformation takes place, risk for esophageal cancer increases by 40 times. While most Barrett's patients never get cancer -- lifetime risk is estimated at 5% depending on the age of diagnosis -- there's no way to know who is most at risk.

Although reflux and heartburn have been around for centuries, doctors say the toll reflux disease takes on the esophagus is different now. Doctors say heartburn sufferers 20 years ago often showed up with esophageal ulcers, narrowed passages that interfered with swallowing and other complications directly related to exposure to stomach acid. Today, acid-suppressing drugs do such a good job of controlling stomach acids that heartburn sufferers don't show up with such grisly complications. "Now we see malignant

complications," says Dr. Hagen.

The reason may have something to do with how we're treating reflux. Although antacids have long been used to neutralize stomach acid, the introduction in the late 1970s of H-2 blockers such as Tagamet, Pepcid and Zantac revolutionized heartburn treatment. Instead of just neutralizing the acid that was already there, the H-2 blockers worked by limiting the production of stomach acid. In 1989, the FDA approved Prilosec, the first proton-pump inhibitor, which worked by suppressing even more acid production.

But while the acid suppressors work wonders on relieving painful heartburn, some scientists believe there is a potential downside. The concern is that by suppressing acid, these drugs aren't really solving the underlying reflux problem. Instead, the fear is that the drug therapy just changes the chemical makeup of the gastric juice being refluxed. So instead of being exposed to acid, the esophagus is bathed in bile -- an alkaline and potentially more injurious gastric fluid.

Last year, a study in the Journal of Gastrointestinal Surgery monitored gastric reflux in six patients before and after Prilosec therapy. In the study, Prilosec use didn't change the overall number of reflux episodes; it just shifted the chemical makeup of the reflux from acid to alkaline.

And when acid is suppressed, two important changes occur in the gut. First, suppressing the acid may result in an overgrowth of bacteria in the digestive tract, a change that can lead to a higher proportion of a particularly damaging form of bile. In addition, pH levels -- that's the balance between acid and alkaline -- are also changed in the stomach by acid-suppressing drugs. The altered pH creates an environment where damaging bile salts can do even more harm.

But in the battle against heartburn, the focus is almost entirely on acid reflux, with little attention paid to bile or alkaline reflux. Alkaline substances, though, are dangerous, too. Drano, for instance, is alkaline.

"If you expose the lower esophagus to alkaline secretions, you will get a more severe injury and destruction than if you expose it to acid alone," says Nasser Altorki, director of the division of thoracic surgery at New York Presbyterian-Weill Cornell Medical Center.

And even though antacids and acid-reducing drugs may cure symptoms, some studies show that patients can still experience bile reflux and even low levels of acid reflux that they aren't aware of. Last year, a British study in the Archives of Surgery followed 32 patients with Barrett's esophagus who had cured their heartburn and reflux symptoms with PPI drugs. Using special monitoring devices, the researchers found that two-thirds of the patients still had bile reflux or abnormal acid reflux, even though medications were controlling the obvious symptoms. "You don't want to make people think it's all fine because they don't feel the heartburn," says Dr. Swanson.

Makers of PPI drugs say there's no real evidence that the treatments play any role in esophageal cancer and point out that the first spike in cancer

cases started in the early 1980s, about 10 years before PPIs were even introduced. Long-term safety and monitoring data have also never flagged any concerns.

And some studies have even suggested that PPIs may have a protective effect against cellular changes that lead to cancer, says Mark Sostek, senior director of clinical research for AstraZeneca. Dr. Sostek says the company is funding research to better understand the reasons for the rise in esophageal cancer.

The data are conflicting and confusing. And other factors almost certainly are contributing to the rise in esophageal-cancer rates.

Studies show that weight gain and being overweight are linked to heartburn, reflux and the development of Barrett's esophagus. Changes in eating habits and a shift to large portions of fried and fatty foods most likely play a role. Even the trend toward fast food and eating on the run may contribute to the rise in heartburn. One study showed that having one or more carbonated soft drinks a day raised risk for nighttime heartburn by 31%. A Swedish study suggested a link between esophageal-cancer rates and certain blood-pressure medications, sleeping pills, anti-anxiety drugs and other medicines that are known to relax the valve between the esophagus and stomach. And there's some evidence that treatments to eradicate *Helicobacter pylori* bacteria, which cause stomach ulcers, have paradoxically led to an increase in reflux problems.

Until more is known about the reasons for the rise in esophageal cancer, experts say, there needs to be a dramatic shift in the way patients and doctors deal with heartburn. Right now, patients take drugs until they feel better. But the only way to find out if a PPI is really working and determine the best dose is by monitoring and analyzing gastric fluids -- something that is rarely done.

One solution may be to actually increase the dose of acid-suppressing drugs. While a lower dose may control obvious symptoms, a higher dose may be needed to counter all of the acid reflux. Higher doses also have the potential to further alter a patient's pH level in a way that limits the damage caused by bile (intermediate pH levels cause the most damage, so more-alkaline levels probably would be less harmful).

An alternative to drug treatment is antireflux surgery, a procedure that reinforces the leaky valve so gastric fluids can't wash back up into the esophagus. Unlike drug treatments, which just suppress acid, the surgery keeps all gastric fluids, including both acid and bile, away from the esophagus and in the stomach where they belong. Although the data on whether surgical procedures can reduce risk for esophageal cancer also aren't conclusive, a few studies do suggest it may make a difference, while others say it has no impact.

But all surgeries carry risks. Side effects of antireflux surgery include bloating and diarrhea. And even after surgery, heartburn symptoms can return over time, particularly in patients who don't make the necessary lifestyle

and dietary changes that probably caused reflux to develop in the first place. And questions remain about whether patients who undergo antireflux surgery should be regularly monitored or even put back on acid-suppression drugs.

Indeed, one of the biggest worries about heartburn, GERD and cancer is the shocking lack of patient screening, monitoring and follow-up by the medical community. And it's only getting worse. The Food and Drug Administration two years ago allowed Prilosec to be sold over-the-counter, a move that has countless patients taking acid-suppression therapy without ever consulting a doctor.

Even those patients who seek prescription treatments are rarely given a screening endoscopy or follow-up monitoring. The problem is that the PPIs usually make patients feel so much better that neither patients nor doctors are particularly motivated to take a closer look to determine if the drug therapy is really helping control GERD inside the body or whether it's just relieving the most obvious outward symptoms.

And the top medical authorities are divided on whether patients with chronic heartburn should be screened at all for esophageal-cancer risk. Screening is expensive, costing about \$1,000 a test, and involves putting a lighted scope down the throat of a sedated patient to view the esophagus for precancerous changes. Because esophageal cancer remains relatively rare and most heartburn sufferers will never develop cancer, many experts say the cost and risk of screening endoscopies can't be justified.

But because esophageal cancer is so deadly, other experts believe patients with a long history of reflux should be given cancer screening before starting long-term use of acid-suppressing drugs. Even though the risk of cancer remains low, "chronic heartburn merits an endoscopy," says David H. Ilson, an oncologist at Memorial Sloan-Kettering Cancer Center in New York who specializes in gastrointestinal cancers.

In addition, with the number of esophageal-cancer cases on the rise, the cost-effectiveness equation is likely to change. Even if it doesn't, screening can make a dramatic difference for those few people who are able to catch esophageal cancer before it spreads. The overall five-year survival rate for esophageal cancer is only about 15%, but when the cancer is found early, surgical removal of the esophagus and chemotherapy can improve five-year survival to about 70%. The vast majority of cases, however, are diagnosed at later stages, when survival is only about 5%.

The American College of Gastroenterology suggests a screening endoscopy for men over 50 if they have a history of five years or more of chronic reflux and reflux symptoms at least twice a week. Patients diagnosed with Barrett's esophagus are checked more often. But the guidelines miss large numbers of people at risk. One in eight esophageal-cancer patients are women. And some GERD patients don't have typical symptoms, suffering from chronic cough rather than typical reflux.

Even though the debate continues about the value of screening heartburn

patients, many experts agree that patients and doctors, overall, need to treat the disease far more aggressively than they do now. "Taking something until you feel good is not enough," says Dr. Hagen, the USC surgeon. "If heartburn is incompletely controlled, it may make things worse."

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