Bisphosphonates and Gastrointestinal Cancer: Is There a Link?

Preclinical studies have shown that bisphosphonates, one of the treatments for osteoporosis, have antitumor properties, but other studies have sounded a warning about esophageal cancer. To find out whether adverse effects on the gastrointestinal (GI) tract, such as mucosal irritation, could lead to ulceration and possibly cancer, researchers from University Park in Nottingham, United Kingdom, designed a series of nested case-control studies using the 2 largest population databases in the United Kingdom. They matched patients aged ≥ 50 years who had a diagnosis of primary GI cancer with up to 5 controls.

The researchers found no overall association between the use of bisphosphonates and the risk of esophageal, gastric, or colorectal cancer. One database showed a small, but significantly increased risk of gastric cancer associated with alendronate. The risk, which was restricted to short-term users, was nearly double for those who used alendronate for < 1 year. The researchers say this is unlikely to be a causal relation, since there was no association with long-term use.

The 2 databases were nearly identical in number of cancer cases. Within the 14-year study period, 20,106 patients in one database developed colorectal cancer, 5,364 developed esophageal cancer, and 3,155 developed gastric cancer. In the second database, 19,035 patients developed colorectal cancer, 5,132 developed esophageal cancer, and 3,157 developed gastric cancer.

The researchers point out that the study group had a higher proportion of patients taking acid-lowering drugs and corticosteroids; those patients are more likely to develop secondary osteoporosis. Also, a heightened rate of upper GI disorders before osteoporosis treatment has been reported elsewhere. While upper GI disorders and use of acid-lowering drugs could be important confounders, the researchers suggest, they might also lie on the causal pathway. Removing them from the adjusted analyses, however, did not noticeably change the results. ●

Source: Vinogradova Y, Coupland C, Hippisley-Cox J. *BMJ.* 2013;346:f114. doi: 10.1136/bmj.f114.