Proton Pump Inhibitors May Raise Liver Cancer Risk

Use of medications like Prilosec and Nexium were associated with a higher liver cancer rate in a recent large study.

September 17, 2018 By Benjamin Ryan

The use of proton pump inhibitor (PPI) medications such as Prilosec (omeprazole) and Nexium (esomeprazole) is associated with an increased risk of hepatocellular carcinoma (HCC, the most common form of liver cancer). In a recent large study this increased risk was dose dependent, meaning that longer use of PPIs was tied to a higher risk of liver cancer.

Publishing their findings in Alimentary Pharmacology & Therapeutics, researchers conducted a nested case-control study in which they analyzed data drawn from the Taiwan National Health Insurance Research Database about people without viral hepatitis in the Southeast Asian nation between 2000 and 2013.

The researchers established a cohort of 29,473 individuals who were diagnosed with liver cancer at least one year after the beginning of their follow-up. They also created a cohort of 294,508 matched controls who did not have liver cancer.

More than half of those in both study groups were older than 60 years old at the outset of their follow-up. The mean follow-up time was 60 months.

The study did not include those with hepatitis B or C virus (HBV/HCV) because these infections are themselves so strongly associated with liver cancer risk and the researchers wanted to be able to better isolate PPI use as a potential contributing factor.

The investigators considered the cohort members' cumulative days of use of PPIs during follow-up. A total of 2,448 of those with liver cancer and 7,840 of the matched controls used PPIs for more than 28 cumulative days. A respective 27,133 and 287,134 members of each group used PPIs for zero to 28 cumulative days.

After adjusting the data for various factors, the researchers found that using PPIs for more than 28 cumulative days, compared with zero to 28 days of cumulative use, was associated with a 2.86-fold increased risk of liver cancer.

Stratifying cumulative PPI use, the researchers found that compared with zero to 27 days of use, 29 to 180 days, 181 to 240 days, 241 to 300 days and more than 300 daysof use was associated with a respective 2.74-fold, 2.98-fold, 3.23-fold and 3.43-fold increased risk of liver cancer after adjusting the data for various factors.

The association between PPI use and an increased risk of liver cancer remained consistent among those with or without cirrhosis, diabetes and high blood lipids, as well as those who did or did not receive an ulcer treatment called H. pylorieradication therapy. This indicated that PPI use is an independent risk factor for liver cancer among such individuals.

Among those with gastroesophageal reflux disease (GERD), taking PPIs was not associated with an increased risk of liver cancer after the researchers adjusted the data for other risk factors. Among those without GERD, PPI use was associated with a 2.97-fold increased risk of liver cancer.

Nevertheless, the researchers concluded: “Our study results raise concerns regarding the safety of long-term PPI use, particularly in patients with gastric acid–related disorders such as GERD who might take a PPI indefinitely.”

To read the study abstract, click here.

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