Proton Pump Inhibitors Linked to Advanced Liver Disease in Those With Hep C

Use of drugs like Nexium or Prilosec is tied to progression to cirrhosis, decompensated cirrhosis and liver cancer in this population.

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People with hepatitis C virus (HCV) who take proton pump inhibitors (PPIs) have a higher risk of developing cirrhosis, decompensated cirrhosis (the more severe stage of the advanced liver disease) and hepatocellular carcinoma (HCC, the most common form of liver cancer).

PPIs are over-the-counter drugs used to treat conditions such as acid reflux and peptic ulcers and include medications such as Nexium (esomeprazole) and Prilosec (omeprazole).

Publishing their findings in Alimentary Pharmacology & Therapeutics, researchers analyzed medical records data on 11,526 individuals (5,752 PPI users and 5,773 nonusers) included in the ERCHIVES database of HCV-positive U.S. veterans. The individuals included in the overall database tested positive for the virus between 2001 and 2015.

Individuals were included in the cohort if they had received at least two weeks of treatment for hep C. They were excluded if they had HIV, tested positive for hepatitis B surface antigen (HBsAg), had been diagnosed with cirrhosis or had experienced a health event associated with decompensated cirrhosis before entering the cohort, or had gastroesophageal varices (abnormal veins in the lower part of the tube running from the throat to the stomach) or liver cancer at any point stretching back to six months prior to entering the cohort.

The median follow-up length for the members of the study cohort was 93.4 months among PPI users and 89.5 months among nonusers. Among those who used PPIs, the median exposure to the class of drug was 27.3 months.

After adjusting the study data to account for various risk factors for the development of cirrhosis, the investigators found that the following factors were associated with a modulated risk of developing the advanced liver condition: taking more than a cumulative 900 daily recommended doses of PPIs over time, compared with taking no PPIs (associated with a 1.32-fold greater risk of cirrhosis); each relative additional 10 years in age (1.4-fold greater risk); diabetes (1.41-fold

greater risk); having a history of alcohol abuse, compared with no history of alcohol abuse (1.31-fold greater risk); every relative increase of 10 international units per milliliter in baseline ALT liver enzyme level (4 percent reduced risk); every relative increase of 10 IU/mL in baseline AST liver enzyme level (1.11-fold increased risk); statin use (40 percent reduced risk); and being treated and cured of hep C, compared with being treated and not cured (42 percent reduced risk).

After adjusting the study data to account for risk factors for cirrhosis and risk factors for using PPIs, the investigators found that a cumulative 181 to 540 doses, 541 to 900 doses and greater than 900 daily recommended doses of PPIs were associated with a respective 3.46-fold, 3.72-fold and 3.79-fold increased risk of developing decompensated cirrhosis. Additionally, every relative increase of 10 IU/mL in baseline AST liver enzyme level was associated with a 1.14-fold increased risk of developing the advanced form of cirrhosis.

Lastly, after adjusting the study data to account for risk factors for developing liver cancer, the investigators found that the following factors modulated the risk of developing that form of liver disease: each relative additional 10 years of age (1.44-fold increased risk); a cumulative 181 to 540 doses and more than 900 daily recommended doses of PPIs (a respective 2.15-fold and 2.01-fold increased risk); each relative 10 IU/mL increase in baseline AST level (1.06-fold increased risk); and being cured of hep C, compared with not being cured (65 percent reduced risk).

The study authors concluded that PPIs were associated with a dose-dependent risk of progression of chronic liver disease to cirrhosis, meaning that a greater cumulative use of the drug class over time was associated with a greater risk of the liver condition, and that PPIs are also associated with an increased risk of the development of decompensated cirrhosis and liver cancer.

To read the study abstract, click here.

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