Good Old Aspirin Might Protect Against Liver Fibrosis

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BOSTON — Will wonder drugs never cease? Aspirin, already touted for its cardiovascular and anti-inflammatory prowess, seems to be flexing its muscles against liver fibrosis, particularly in people at risk for chronic liver disease, according to new research.

"Clinical equipoise is emerging that may justify prospective randomized trials of aspirin and, potentially, other antiplatelet drugs such as antifibrotic agents," Gordon Jiang, MD, a gastroenterology fellow at the Beth Israel Deaconess Medical Center in Boston, and colleagues state in a scientific poster here at The Liver Meeting 2014.

In a population-based cross-sectional study of more than 14,000 adults, there was "a consistent association between aspirin use and less liver fibrosis," Dr. Jiang and colleagues report.

The team drew on the National Health and Nutrition Examination Survey (NHANES) III to look at the association between aspirin, ibuprofen, and liver fibrosis. Fibrosis was measured with four validated noninvasive indices: Fibrosis-4, the nonalcoholic fatty liver disease fibrosis score, the aspartate aminotransferase/platelet ratio index, and the Forns Index.

To see if the association between aspirin and fibrosis protection is stronger in patients most at risk for fibrosis, they did additional analyses in patients with viral hepatitis, heavy drinkers, and patients with fatty liver disease.

On the four measures, the use of aspirin was consistently associated with lower stages of liver fibrosis. In contrast, there was virtually no link between ibuprofen use and liver fibrosis.

Similarly, in an analysis of patients with and without chronic liver disease (hepatitis B or C infection, more than 5 alcoholic drinks per day, or suspected nonalcoholic steatohepatitis), aspirin but not ibuprofen was consistently associated with lower stages of fibrosis.

For patients with or at risk for liver disease, compared with those without risk factors, there was about a 5-fold increase in the negative coefficient for the interaction between aspirin use and liver fibrosis. This suggests that the protective effect of aspirin is much larger in patients with chronic liver disease, said researcher Yury Popov, MD, PhD, assistant professor of medicine at the Beth Israel Deaconess Medical Center.

The researchers acknowledge that the study was limited by the observational design, and by that fact that the NHANES III data were limited to 1 month of drug use, "whereas the protection against liver fibrosis likely requires long-term use."

They speculate that the antiplatelet activity of aspirin, rather than its anti-inflammatory properties, likely account for its positive effects on fibrosis.

"Our observations support emerging experimental and clinical evidence for a pathologic link between platelet activation and liver fibrosis," they write.

In a separate study, also presented here, another group of researchers report that "platelets drive liver fibrosis through the direct activation of hepatic stellate cells in chronically injured liver."

"We also found that aspirin in the long term, at the low dose — the antiplatelet dose — is reducing — well actually, preventing — fibrosis in the mouse model," Dr. Popov, who was involved in both studies, told Medscape Medical News.

More potent antiplatelet agents — such as clopidogrel (Plavix), prasugrel (Effient), and others currently in the pipeline — could have an even stronger effect against fibrosis, said Athan Kuliopulos, MD, PhD, professor of medicine at the Tufts University Sackler School of Biomedical Sciences in Boston, who was not involved with the study.

"And this is just liver fibrosis," he told Medscape Medical News. "What does it mean for outcome?"

He said that if, as he and his colleagues theorize, platelet activation or action is a primary cause of fibrosis, it might be possible to "bypass the platelet entirely," and target the factor Xa protease.

Dr. Jiang has disclosed no relevant financial relationships. Dr. Popov reports consulting for and receiving research grants from Gilead Sciences. Dr. Kuliopulos is the CEO of Oasis Pharmaceuticals.

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