Adjunct PPI Confers Effective Gastroprotection

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Adding a proton pump inhibitor to a nonsteroidal anti-inflammatory drug provides as much protection against NSAID-induced gastropathy as a cyclooxygenase-2 inhibitor (coxib), according to a new study September 2007 issue of the journal Gastroenterology.

Adding a proton pump inhibitor (PPI) to a coxib may provide some additional protection, but in recent years some coxibs have been shown to cause serious cardiovascular disease, wrote Wayne A. Ray, Ph.D., and his colleagues at Vanderbilt University, Nashville, Tenn.

The observational study used data from TennCare, the state of Tennessee's Medicaid program. Patients aged 40 years and older with a new episode of prescribed NSAID or coxib use between 1996 and 2004 were included. After excluding patients with serious illnesses such as cancer, HIV infection, cirrhosis, and chronic alcoholism, and those with less than 2 years of baseline data, the study included 234,010 new episodes of NSAID use and 48,710 new episodes of coxib use, with a total of 363,037 person-years of follow-up.

The investigators adjusted for a large number of demographic variables; prior history of peptic ulcer disease; use of low-dose aspirin, other antiplatelet drugs, anticoagulants, or systemic corticosteroids; new residence in a nursing home; and new nongastrointestinal hospital admission.

They found that the use of NSAIDs without gastroprotective cotherapy was associated with 5.65 peptic ulcer hospitalizations per 1,000 person-years, which is 2.8 times the incidence for comparable patients who were former users of either NSAIDs or coxibs.

Use of a PPI, a double-dose histamine-2 receptor antagonist, or misoprostol along with an NSAID reduced the risk of peptic ulcer hospitalization by 39%. Of the various gastroprotective therapies, PPIs were associated with the greatest risk reduction—54%—among NSAID users.

Unprotected use of a coxib resulted in a 40% reduction in the risk of peptic ulcer hospitalization, compared with unprotected use of an NSAID. Using a gastroprotective therapy in addition to a coxib resulted in a further 10% reduction in risk (for a total of 50%), with no statistically significant advantage for PPIs over other gastroprotective therapies.

Of all of the various gastroprotective therapies, proton pump inhibitors were associated with the greatest risk reduction—54%—among NSAID users.

In a subanalysis adjusted for dose, naproxen proved to be associated with the highest risk of peptic ulcer hospitalization, with an adjusted rate of 7.8 per 1,000 patient-years. Ibuprofen, rofecoxib, and celecoxib all were associated with significantly lower risks of hospitalization.

Another subgroup analysis showed that an NSAID with gastroprotection was significantly better for several patient groups than an NSAID alone. These groups included patients over the age of 65 years and those with a history of previous ulcers.

In other subgroups with medical comorbidities, those taking low-dose aspirin, and those on antiplatelet or anticoagulant therapy, gastroprotection had no statistically significant improvement over unprotected NSAIDs. The researchers said this was partly because of relatively small numbers of patients in some of the subgroups.

The study was supported by the Agency for Healthcare Research and Quality, and the investigators stated that they received no support from any pharmaceutical company. "[It] is increasingly unlikely that large clinical trials of gastroprotective cotherapy in NSAID users will be conducted," they wrote. "Proton pump inhibitors are available generically, which limits the incentives for pharmaceutical manufacturers to fund such studies. Furthermore, because NSAID-induced gastropathy is frequent and potentially life threatening, the ethics of randomizing patients to NSAID use without gastroprotective cotherapy are questionable."

The researchers recommended future trials directly comparing coxibs to NSAIDs with a PPI, and said additional investigation is "urgently needed" to study the benefits of adding a PPI to celecoxib and other coxibs. ■