Drug Monitor

Teratogenic Medications and Adherence to Oral Contraception

Many women who are taking teratogenic medications (and whose pregnancies would thus be at risk) may not be adhering to prescribed oral contraception.

Researchers from Medco Health Solutions in Franklin Lakes, New Jersey, evaluated prescription medication claims and refill patterns for more than 6 million women aged 18 to 44 years. Among the 2,355,790 women who were taking 1 or more long-term medications to treat a chronic disease, 146,758 (6%) were taking medication classified as Category X—of whom 26,136 (18%) were also taking an oral contraceptive. Nearly all (97%) of the Category X prescriptions fell into 1 of 4 classes: sedative hypnotic, antineoplastic, retinoid, or statin. More than two-thirds of the women were receiving 5 or more medications (chronic and acute) during the study period.

Adherence was defined as 95% or greater and adherence levels were defined as low, moderate, and adherent. About 40% of women who received Category X medications and oral contraception had refill patterns suggesting suboptimal adherence to their oral contraception—a percentage no better than that of the general population.

The greater the number of total prescribed medications, the less likely the woman was to be adherent to her oral contraception. Women who received statins were more adherent, while those who were taking antineoplastic, retinoid, or sedative hypnotics were less adherent. Adherence was highest among women whose contraception was prescribed by a primary care provider. Those whose prescribers were obstetricians/gynecologists were about as adherent as the general population, and those whose prescribers were dermatologists were least adherent. Older, better educated women were more adherent as compared to women who were single and had a lower-income.

In discussing reasons for the lack of adherence, the researchers cited a CDC study that found only 1 in 5 women correctly interpreted the teratogen warning symbol to mean that they should not get pregnant while taking the medication. But the researchers also note that it's possible that women who received Category X drugs were not well advised about teratogenic risks. Research has suggested, they say, that physicians do not routinely counsel patients about the risks or the need for contraception. One study, for instance, found that half of women who filled a Category X medication prescription had no documentation of contraceptive counseling or contraception dispensed within the 2 years before filling the Category X prescription.

In addition to aiming more educational efforts at women who are less likely to be adherent, the researchers suggest other ways to help improve compliance, including electronic reminders for physicians at the time of prescribing and pharmacy alerts about women who are late in filling their oral contraception prescription.

Source: *Am J Med.* 2010;123(1):929–934. doi:10.1016/j.amjmed.2010.05.009.

H Pylori Infection: Test and Treat Older Patients

Although *Helicobacter pylori* (HP) infection is very common among older patients (more than 70% in patients with HP–related pathologies and more than 50% in asymptomatic patients), they aren't screened proportionately, say researchers from University of Palermo in Italy. The researchers propose, however, that a test-and-treat strategy can not only be effective in eradicating HP, but also in helping prevent peptic disease, gastric cancer, and even death. They note that older patients are at high risk for death due to peptic ulcer disease and its complications, with mortality rates of about 200 per million at age 70, compared with 1 per million at age 20.

In the study, 140 of 195 older patients had positive results on the C^{13}-urea breath test. Incidence of erosive or micro-erosive pathology (such as erosive gastritis, erosive duodenitis, and erosive gastroduodenitis), gastric or duodenal ulcer, and reflux esophagitis were similar among subjects with or without dyspeptic symptoms. Symptoms were not linked to any specific organic pathology. Micro-erosive and peptic lesions were associated with both nonspecific symptoms and a wide variety of symptom combinations. Symptoms were also variable and nonspecific in patients without any lesion at gastric endoscopic exploration. Hence, the researchers say, the data confirm that in older patients, it is not possible to formulate an accurate differential diagnosis between organic pathology and functional disorders of the upper gastrointestinal tract based only on symptoms. None of the patients with specific symptoms with or without organic pathology had different responsiveness to HP-eradicating treatment. It is "noteworthy," the researchers say, that even the asymptomatic group had a high

frequency of organic pathology, similar to that of the symptomatic group. Thus, they point out, HP-positivity may entail damage even in the absence of clinical manifestation.

All HP-positive patients were treated with omeprazole 20 mg bid, clarithromycin 500 mg bid, and amoxicillin 1 g bid, for 1 week. After 4 weeks, the patients were again evaluated with the C^{13}-urea breath test. In both the symptomatic and asymptomatic groups, *H pylori* infection was eradicated in 88% of patients with minimal secondary effects. Seven patients dropped out for nonmedical reasons.

The researchers say their findings of well-tolerated treatment with a high rate of eradication suggest that it can be initiated promptly and safely in older patients, regardless of the endoscopic diagnosis.

Source: *Arch Gerontol Geriatr.* 2010;51(3):237–240. doi:10.1016/j.archger.2009.11.006

GI Bleeding After PCI: First 30 Days Are Most Dangerous

Gastrointestinal bleeding (GIB), while an uncommon complication of percutaneous coronary intervention (PCI), is of concern because of the accompanying dramatic increase in mortality. But the risk factors for GIB that complicate PCI and ischemic outcomes are poorly studied, say researchers from Washington Hospital Center in Washington, DC. They looked at the impact of GIB on 30-day mortality and 1-year major adverse cardiac events, comparing 147 patients with in-hospital GIB with 20,474 patients without in-hospital GIB.

In-hospital GIB was associated with a "remarkably high" mortality rate of 20.5% at 30 days, compared with only 2.4% at 30 days in the non-GIB group. Rates of other cardiovascular outcomes, including target vessel revascularization, Q-wave myocardial infarction, and stent thrombosis, were similar between the 2 patient groups.

After adjusting for variables, in-hospital GIB remained significantly associated with 30-day mortality. Importantly, the researchers say, the interaction term between GIB and presentation with cardiogenic shock was highly significant.

Of the study patients, 56 with in-hospital GIB and 8,445 without in-hospital GIB survived to discharge and were available for follow up at 1 year. Despite its link to early mortality, the researchers say GIB did not appear to influence mortality or thrombotic outcomes in patients who survived to discharge, although unadjusted rates of mortality (18% vs 5% among patients without GIB) and major adverse cardiac events (25% vs 13%) were significantly higher in patients with GIB. And, again, rates of target vessel revascularization, Q-wave MI, and stent thrombosis were similar in the 2 groups. However, at 1 year, the interaction term between GIB and shock was no longer significant. This may be explained, the researchers say, by the fact that patients who present in shock and survive long enough to develop in-hospital GIB are, by default, at lower risk than patients who do not survive shock (and thus don't live long enough to develop GIB).

The finding that GIB seemingly had no effect on mortality if a patient survived to discharge is an important observation, the researchers say, because it "speaks to potential mechanisms of death in patients with GIB." They point out that some researchers have postulated that patients with bleeding have higher mortality because they are more likely to stop antiplatelet medications prematurely. Their data suggest that such an outcome is limited to inpatients; they did not, for instance, observe an increase in ischemic outcomes at 1 year that would be expected in patients who prematurely discontinue clopidogrel. However, although all patients in the study were treated with clopidogrel and aspirin initially, the researchers did not have information about subsequent treatment and could not assess the relationship of in-hospital GIB and premature discontinuation.

Clinical factors associated with GIB in PCI patients are not well described, the researchers say, but older age appears to be the most consistent predictor, as well as presentation with shock. Patients who receive a proton pump inhibitor after PCI may have a lower risk of GIB. Their study draws attention, however, to the unequal effect of antiplatelet and antithrombotic medications on GIB. GIB was more likely with glycoprotein IIb/IIIa inhibitors and less likely with bivalirudin, and not associated with heparin or thrombolytics. The fact that heparin and thrombolytics did not have a significant effect suggests that "antiplatelet medications play a more prominent role in the genesis of GIB complicating PCI." Other studies have also found higher rates of overall major bleeding with glycoprotein IIb/IIIa inhibitors plus heparin compared with bivalirudin. It would thus seem reasonable, say the researchers of this study, to use bivalirudin for patients at higher risk of GIB.

Source: *Am J Cardiol.* 2010;106(8):1069–1074. doi:10.1016/j.amjcard.2010.06.011.