MedicalXpress

Proton-pump inhibitors and birth defects -- some reassurances, but more needed warns epidemiologist

November 24 2010

Despite the reassurances of Pasternak and Hviid in their study, "Use of Proton-Pump Inhibitors (PPI) in Early Pregnancy and the Risk of Birth Defects," featured in the Nov. 24 issue of the *New England Journal of Medicine*, an epidemiologist from Boston University School of Medicine (BUSM) believes that further studies are needed.

The original study found that on the basis of data from more than 840,000 live births in Denmark, there was no evidence to suggest that the use of the most common PPIs (omeprazole, lansoprazole, and esomeprazole) anytime during pregnancy increased the risk of birth defects overall, and in the case of omeprazole, the PPI used most commonly during pregnancy, they found no evidence of a risk among selected subgroups of major birth defects. "These findings, together with earlier reports that were based on smaller numbers of pregnant women exposed to PPIs, are important in providing some reassurance about the safety of these drugs when they are taken during pregnancy," said editorial author Allen A. Mitchell, MD, director of BUSM's Slone Epidemiology Center. "However, as the authors acknowledge, these data provide only a broad — and incomplete —overview," he added.

According to Mitchell, drugs that cause birth defects, called teratogens, tend to increase the risks of specific birth defects, not birth defects overall. Secondly, although medications in the same class (e.g., PPIs) share pharmacologic effects, they may have very different effects on the

fetus. Of particular importance, Mitchell points out that despite the large size of this study population, "it was still too small to consider the risks of specific birth defects in relation to specific PPIs, which is what we need to know." One finding of possible concern is that women who took PPIs in the weeks just before pregnancy—but not during pregnancy—seemed to have an increased risk of birth defects, and this observation needs to be understood; the one PPI that did not show any increased risk during these weeks before pregnancy was omeprazole.

Lastly, despite the richness of the data sources used for the Danish study, Mitchell notes that they lack information on important variables that could themselves account for possible associations between medications and birth defects, including the reasons for the use of PPIs. They also lack information on exposures to over-the-counter medications; among this latter group, for example, it is critical to know whether women were taking folic-acid around the time of conception, since folic acid has been repeatedly shown to reduce the risk of a number of birth defects.

Mitchell points out that the report by Pasternak and Hviid represents the best available data on the possible risk of birth defects associated with the use of PPIs during pregnancy, and it supports two conclusions. First, the PPIs most commonly represented in the study do not appear to carry major risks of birth defects when they are taken during the first trimester or later in pregnancy. Second, the modestly increased risk during the period before conception that was observed with PPIs as a group was not seen with omeprazole.

Further studies using a case–control design are needed to consider specific defects in relation to individual PPIs, and future analyses must also include information on critical additional variables, such as use of folic acid supplements around the time of conception. "Until such studies are available, the current findings, although reassuring, must be considered far from definitive," stressed Mitchell.

Provided by Boston University Medical Center