

# PPIs Might Raise Risk of Cardiac Birth Defects

BY HEIDI SPLETE

FROM THE ANNUAL DIGESTIVE  
DISEASE WEEK

NEW ORLEANS – Pregnant women who used proton pump inhibitors for gastroesophageal reflux during the first trimester of pregnancy were more than twice as likely to have babies with cardiac defects than were pregnant women who did not use PPIs, based on a retrospective study of 200,000 women.

Previous data have indicated a non-significant trend toward an association between use of proton pump inhibitors (PPIs) early in pregnancy and cardiac malformations, Dr. Andrew D. Rhim of the University of Pennsylvania in Philadelphia said in his presentation.

“Before this study, there were very limited human data [on risk], and this study suggests a possible increased risk of cardiovascular defects,” Dr. Jennifer Niebyl of the University of Iowa, Iowa City, said in an interview. A prospective study is needed to confirm these results, which are hampered by uncertainties surrounding the trimester of exposure and possible selection bias.

## Timing Is Very Important

Retrospective case-control studies can show associations, but they cannot determine if the associations are causal. Moreover, such studies have major limitations, including selection bias, recall bias, and timing of exposures. Timing is very important. For example, closure of the ventricular septum occurs by 6 weeks post conception, so an exposure that causes a ventricular septal defect (VSD) must occur before 6 weeks.

Consider the animal reproduction data included by manufacturers in package inserts. None of the six PPIs in the United States (dexlansoprazole [Dexilant], esomeprazole [Nexium], lansoprazole [Prevacid], omeprazole [Prilosec], pantoprazole [Protonix], and rabeprazole [Aciphex]) cause structural defects in animals. This is important: With only two exceptions, all known human teratogens also are teratogenic in animals.

I know of no studies that have shown a significant association between PPIs and cardiac defects. Atrial septal defects and VSDs are among the most common cardiac defects. VSDs are among the most common birth defects.

GERALD BRIGGS is clinical professor of pharmacy at the University of California, San Francisco.

Dr. Niebyl and her colleagues conducted a study of 3,458 women that suggested metoclopramide may be a safe option for pregnant women (N. Engl. J. Med. 2009;360:2528-35). She advised that pregnant women avoid PPIs during the first trimester.

From a database of 208,951 pregnancies, Dr. Rhim and his colleagues identified 2,445 cases of cardiac malformations in newborns and compared them with

19,530 matched controls. All the newborns were registered between 2000 and 2008 in The Health Improvement Network, a database of information collected by general practitioners in the United Kingdom. “We found 130 instances of a PPI being prescribed within the first trimester” in the women who gave birth to infants with cardiac birth defects, Dr. Rhim said. After adjustment for multiple variables including maternal BMI, smok-

ing status, alcohol use, and use of other medications, the risk for cardiac birth defects remained significant (odds ratio, 2.14). A history of cardiac malformations or diabetes in the mother was associated with a significantly increased risk of a cardiac defect in the baby.

The researchers identified septal, left ventricular, and right ventricular defects.

Dr. Rhim said that he had no financial conflicts to disclose. ■



Visit [www.obgynnewsnetwork.com](http://www.obgynnewsnetwork.com)  
for the latest advances from key symposia at the

## 39<sup>TH</sup> GLOBAL CONGRESS OF MINIMALLY INVASIVE GYNECOLOGY

Las Vegas, Nevada  
November 8-12, 2010



[www.obgynnewsnetwork.com](http://www.obgynnewsnetwork.com)

**OB.GYN. NEWS NETWORK Custom Conference Coverage provides onsite coverage of selected key sessions from the 39<sup>th</sup> Global Congress of Minimally Invasive Gynecology. Stay up-to-date on the latest developments in the field by reading about key clinical findings and watching interviews with some of the top researchers and clinicians who presented at this year's meeting.**

This news site is brought to you by the Custom Conference Coverage Department of Ob.GYN. NEWS Network, and is not an official site of the Congress nor its sponsor, the American Association of Gynecologic Laparoscopists (AAGL).