Off-label morning sickness drug deemed safe for fetuses

June 11 2009

Metoclopramide, a drug approved in the U.S. for nausea, vomiting and heartburn poses no significant risks for the fetus according to a large cohort study published in the *New England Journal of Medicine*.

According to the pediatrician and clinical pharmacologist, principal investigator Dr. Rafael Gorodischer, prof. emeritus at Ben-Gurion University of the Negev, "Metoclopramide is the drug of choice in Europe and Israel for "morning sickness-like" symptoms of nausea and vomiting, which are common in pregnant women. In the U.S. however, it is only used in the most severe cases, as it is an "off-label" use for nausea and vomiting during pregnancy. The findings of this very large cohort study examining infants born to mothers who were exposed to metoclopramide during the first trimester provide significant reassurance for the safety of the fetus when the drug is given to women to relieve nausea and vomiting during pregnancy."

Between 50 percent to 80 percent of pregnant women experience nausea and vomiting during the first trimester and beyond, which can be severe.

This study is collaboration between Ben-Gurion University of the Negev, Soroka University Medical Center and Clalit Health Services -- all in Beer-Sheva, Israel -- along with the Division of Pharmacology, Hospital for Sick Children in Toronto, Canada. The study is part of the doctoral thesis of Ilan Matok and was conducted by the three Israeli entities as part of the BeMORE collaboration (Ben-Gurion MotheRisk Obstetric Registry of Exposure). The study of the safety of other medications

commonly used off-label in pregnancy is an ongoing project of BeMORE investigators in large cohorts of women in Southern Israel.

According to principal investigator epidemiologist Dr. Amalia Levy of the BGU Faculty of Health Sciences, and chairwoman of the BeMORE collaboration, "of the vast majority of medications approved for use, there is insufficient data from human studies to determine whether the benefits of therapy exceed the risk to the fetus. Medicines are approved for use only after there is sufficient scientific evidence demonstrating the drug safety and effectiveness for its intended uses. There is extensive experience with the use of this medication in non-pregnant persons, with evidence of overall low rates of adverse effects when it is used as recommended."

The safety of metoclopramide use during the first trimester of pregnancy was investigated by linking a database of medications dispensed over 10 years to all women registered in Clalit Health Services in the Sothern District of Israel, with databases containing maternal and infant hospital records of Soroka University Medical Center, during the same period. In the study, 3,458 (or 4.2 percent) were exposed to metoclopramide during the first trimester of pregnancy of the 81,703 infants born to mothers during the study period.

The rate of major congenital malformations identified in the group that was exposed to metoclopramide during the first trimester was 5.3 percent% (182 of 3458 infants), as compared with a rate of 4.9 percent (3834 of 78,245 infants).

As a result, exposure to metoclopramide among this group was not associated with significantly increased risks of major congenital malformations. The results were unchanged when therapeutic abortions of exposed fetuses were included in the analysis. In addition, infants exposed in utero had no increased risk of perinatal mortality, low birth

weight or premature birth.

Data of this study support the labeling of metoclopramide for nausea and vomiting during pregnancy.

Source: American Associates, Ben-Gurion University of the Negev (news : web)