

Pasternak B, Svanstrom H, Molgaard-Nielsen D, et al. **Metoclopramide** in Pregnancy and Risk of Major Congenital Malformations and Fetal Death. JAMA. 2013 Oct 16;310(15):1601-1611. (Original) PMID: 24129464

IMPORTANCE Metoclopramide, a drug frequently used for nausea and vomiting in pregnancy, is thought to be safe, but information on the risk of specific malformations and fetal death is lacking. **OBJECTIVE** To investigate the safety of metoclopramide use in pregnancy. **DESIGN, SETTING, AND PARTICIPANTS** Register-based cohort study in Denmark, 1997-2011. From a cohort of 1 222 503 pregnancies, metoclopramide-exposed and unexposed women were matched (1:4 ratio) on the basis of age, calendar year, and propensity scores. **MAIN OUTCOMES AND MEASURES** Primary outcomes were major congenital malformations overall, 20 individual malformation categories (selected according to power criteria), spontaneous abortion, and stillbirth. In matched analyses, logistic regression was used to estimate prevalence odds ratios of malformations and Cox regression to estimate hazard ratios (HRs) of spontaneous abortion. **RESULTS** Among 28 486 women exposed to metoclopramide in the first trimester, 721 had an infant with a major congenital malformation (25.3 [95% CI, 23.5-27.1] cases per 1000 births), compared with 3024 among 113 698 unexposed women (26.6 [95% CI, 25.7-27.5] per 1000 births). There were no significant associations between metoclopramide use and malformations overall (prevalence odds ratio, 0.93 [95% CI, 0.86-1.02]) or any of the 20 individual malformation categories, eg, neural tube defects, transposition of great vessels, ventricular septal defect, atrial septal defect, tetralogy of Fallot, coarctation of the aorta, cleft lip, cleft palate, anorectal atresia/stenosis, and limb reduction (upper limit of 95% CI below 2.0 for 17 of 20 categories). Metoclopramide was not associated with increased risk of spontaneous abortion (757 cases [20.0 {95% CI, 18.5-21.4} per 1000] among 37 946 metoclopramide-exposed women and 9414 cases [62.1 {95% CI, 60.9-63.3} per 1000] among 151 661 unexposed women; HR, 0.35 [95% CI, 0.33-0.38]) and stillbirth (142 cases [3.5 {95% CI, 2.9-4.1} per 1000] among 40 306 metoclopramide-exposed women and 634 cases [3.9 {95% CI, 3.6-4.2} per 1000] among 161 098 unexposed women; HR, 0.90 [95% CI, 0.74-1.08]). **CONCLUSIONS AND RELEVANCE** Metoclopramide use in pregnancy was not associated with increased risk of major congenital malformations overall, any of the 20 individual malformation categories assessed, spontaneous abortion, or stillbirth. These safety data may help inform decision making when treatment with metoclopramide is considered in pregnancy.

Comments from Clinical Raters

General Internal Medicine-Primary Care(US)

Very useful. I am surprised and perhaps worried that there were better results in the metoclopramide group. Perhaps an unmeasured confounder? Benefit of treatment?

Pediatric Neonatology

This is an important nation-wide study that includes a very large cohort of cases. It provides as definitive an answer as possible that metoclopramide use during pregnancy neither increases fetal congenital malformation or rate of abortion. A fact that is well known, but this study provides great reassurance.