Use of Zofran in Pregnancy: An Update

Concerns Over Fetal Defects From Zofran Use During Pregnancy: important facts to know.

1. No medications are approved for treating hyperemesis gravidarum due to ethics and liability.
2. Nearly all research studies, large and small, find little if any increase in the number of cases of birth defects after mothers use Zofran. (see table below)
3. Other concerns about the safety of Zofran involve giving a large, single dose or multiple medications with serotonin effects simultaneously, neither of which typically are given for HG.
4. The lawsuit associated with Zofran just filed in Massachusetts has not yet been litigated in court. Other than cardiac defects, the multiple birth defects cited in the baby have not been found or suggested to be associated with Zofran in any of the published studies.
5. One of the studies cited by attorneys as the strongest evidence in support of the litigation refers to an UNPUBLISHED study. To our knowledge, this research has not undergone peer review to determine its validity.
6. GSK did not market Zofran for HG. The 2012 settlement GSK accepted to avoid further litigation focused on 3 other drugs. Zofran's small contribution to the settlement reimbursed the US government for health care charges arising from the use of Zofran off-label.
7. Congenital cardiac defects are structural heart problems present at birth, and occur before 10 weeks, often before the mother knows she is pregnant. They range from minor (septal) to complex.
8. About 15% of over 2.3 million pregnancies take Zofran during pregnancy. (Taylor, 2017)
9. About 3% of all babies in the US are born with major birth defects and 70% of pregnant women take at least one prescription medication during pregnancy.
10. Prematurity and other health problems associated with malnutrition during pregnancy may result in diagnosis of more defects in children born to mothers with HG.
11. It is likely that many babies born to HG mothers would not be here without medications that effectively minimize nausea and vomiting.

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New England Journal of Med 2013;368:814-23.	1970 Mothers who took Zofran during the first trimester in Denmark.	"Receipt of ondansetron was NOT associated with - significantly increased risk of spontaneous abortion - significantly increased risk of stillbirth - any major birth defect, preterm delivery, delivery of a low-birth-weight infant, or delivery of a small-for-gestational-age infant." "Ondansetron taken during pregnancy was not associated with a significantly increased risk of adverse fetal outcomes."
BioMed Research International. 2013;2013:909860.	251 Mothers who took Zofran during pregnancy in Western Australia, 2002–2005.	"Our study did not detect any adverse outcomes from the use of ondansetron in pregnancy but could not conclude that ondansetron is safe to use in pregnancy."
Reproductive Toxicology. 2014 Dec;50:134-7.	1349 Infants of women who took ondansetron in early pregnancy between 1998-2012 in Sweden.	"No statistically significantly increased risk for a major malformation was found… The teratogenic risk with ondansetron is low but an increased risk for a cardiac septum defect is likely." Note: There were 17 septum (cardiac) defects out of 1349 (<1%) women exposed to Zofran (aka cases) compared to their control group where 315 septum defects were identified out of 41,388 (<1%) pregnancies exposed to meclizine. In both cases and controls approximately 99% of exposed babies did NOT have a cardiac septum defect.
Birth defects research. Part A, Clinical and molecular teratology.2012 January;94(1): 22–30.	514 Mothers who took Zofran in United States.	"Nausea and vomiting of pregnancy was not observed to be associated with an increased risk of birth defects, but possible risks related to three treatments (i.e. proton pump inhibitors, steroids and ondansetron), which could be chance findings, warrant further investigation." Note: The increased risk was very small statistically.
Ondansetron Use in Pregnancy and Birth Defects: A Systematic Review. *Obstet Gynecol*. 2016;127(5):878-883.	423 records across all databases	"Data from the various studies were conflicting: whereas the three largest studies showed no increased risk of birth defects as a whole (36 malformations, 1,233 exposed compared with 141 malformations and 4,932 unexposed; 58/1,248 exposed compared with 31,357/895,770 unexposed; and 38/1,349 exposed compared with 43,620/1,500,085 unexposed… two of these studies demonstrated a slightly increased risk of cardiac defects." "The overall risk of birth defects associated with ondansetron exposure appears to be low. There may be a small increase in the incidence of cardiac abnormalities in ondansetron-exposed neonates."

"There are numerous limitations in the current literature on ondansetron safety including exposure to the medication is not limited to sensitive windows of organogenesis, there is a lack of information on dosing and compliance, self-reports of exposure are commonly used, an inadequate accounting exists for other factors that may explain the relationship between ondansetron exposure and the adverse outcome, and there exists a lack of biologic plausibility by which ondansetron might cause harm. It is the authors' opinion that current data do not support a reluctance to treat women with ondansetron in clinical practice."
Obstet Gynecol. 2016 May;127(5):873-7.

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