

Einarson A et al. The safety of ondansetron for nausea and vomiting of pregnancy: a prospective comparative study. *Br J Obstet Gynaecol*, 2004, 111, 940-3

Type of study	Prospective cohort
Where	Canada-Australia
When	Not indicated
Characteristics of the starting cohort	Pregnant women who contacted Helpline or Teratogen Information Services
Ascertainment of drug exposure	Standardised intake form used by both centers (information about any concurrent antiemetic or other medication)
Exposure definition	Intake during the first trimester of pregnancy
Size of the studied cohort	Exposed to the studied drug women: 188 recruited, 176 in follow up, 169 infants born Exposed to other anti-emetics women: recruited, 176 in follow up, 161 infants born Unexposed reference group women: recruited, 176 in follow up, 162 infants born
Exposed cohort	Newborns exposed to a specific drug
Control cohort	Newborns not exposed to the studied drug: - exposed to other anti-emetics (doxylamine+vitamin B6, metoclopramide, phenothiazines, ginger) - exposed to drugs considered safe in pregnancy or not exposed to drugs
Malformations ascertainment	Prospective ascertainment with follow-up interview, similar in exposed/nonexposed groups: women contacted 4-6 months after delivery to obtain outcome data using a standardised follow up form. Subsequently, the interviewer sent a letter to the caller's physician to verify the mothers' information
Malformations definition	Major malformation: definition not indicated
Prevalence of malformations among control offspring	Exposed to other drugs group: 1.8% Unexposed reference group: 1.8%
Analysis	Outcome endpoints compared using χ^2 , Fishers exact, ANOVA statistical tests
Strengths	- Internal reference group - Exposures were ascertained few days after the intake and outcomes were ascertained prospectively - Both centers used similar operating procedures for data collection, exposure assessment, follow up - No differentiated recall bias between the exposed and non exposed groups - The time of the interview after delivery was similar in the groups - Evaluation of the study's power analyses - The first epidemiological study about this drug
Weaknesses	- Women were self-selected by calling the Service for counselling - Exposure and outcome self-reported by women - Not indicated if the staff at the follow up interview was unaware of the exposure status of the women - This sample size had only a 20% power to show observed sixfold difference in hypospadias
Main results	Ondansetron does not appear to be associated with an increased risk for major malformations above baseline (3.6%, 6 cases: 3 hypospadias, double urinary collecting system in kidney, mild

pulmonary stenosis, duodenal atresia). There were no statistical differences in any of the study endpoints between the comparison groups. There was a low rate (2.9%) of miscarriages in the ondansetron group compared with others (7.5% - 8%)