

Ondansetron use in early pregnancy and the risk of congenital malformations – a register based nationwide cohort study

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Background

Ondansetron is an effective antiemetic in hyperemesis gravidarum. It acts as a 5-hydroxytryptamine receptor antagonist, a receptor which plays a role in the development of emesis and nausea. Only limited data concerning the safety of ondansetron in pregnancy is available.

Therefore we conducted a nationwide cohort study testing the hypothesis use of ondansetron during the first trimester was associated with a higher prevalence of congenital malformations.

Methods

The study included all women giving birth in Denmark 1997 and 2010. The Medical Birth Registry was used to identify all women giving birth and the National Hospital Register was used to identify all offspring with a record of congenital malformation. Prescription data was obtained from the National Prescription Register. The primary outcome was the prevalence of major congenital malformations according to the EUROCAT classification system and subgrouping among first trimester users of ondansetron compared to non-users. Exposure was defined redemption of one prescription of ondansetron in the first trimester of pregnancy.

Results

We identified 897 018 births in the study period. 1248 women redeemed a prescription of ondansetron in the first trimester of which 58 (4.7%) had offspring with a congenital malformation compared to 31357 (3.5 %) in the unexposed group. The odds ratio (OR) of having an offspring with a major malformation after exposure to ondansetron was 1.3 (CI95% 1.0-1.7). This was mainly caused by an increased prevalence of heart defects (OR=2.0 (CI95% 1.3-3.1). To rule out confounding by indication we also tested the risk of another drug frequently used in hyperemesis

gravidarum, metoclopramide. There was no association with first trimester exposure and having an offspring with a congenital malformation (OR=1.0 (CI95% 0.95-1.1). Furthermore we found no increased OR in any of the EUROCAT subgrouping among women exposed metoclopramide.

Conclusion

We found a doubling in the prevalence of major congenital heart defects in children whose mothers redeemed a prescription of ondansetron in the first trimester of pregnancy.