

Czeizel AE et al. Vaginal treatment with povidone-iodine suppositories during pregnancy. *Int J Gynecol Obstet* 2004, 84, 83-5

Type of study	Population-based case-control (Hungarian Case-Control Surveillance of Congenital Abnormalities-HCCSCA)
Where	Hungary
When	1980-1996
Cases	22,843 newborns or fetuses with congenital abnormalities (CAs). Cases with isolated CAs and multiple CAs of the HCCSCA were identified from the data set of the Hungarian Congenital Abnormality Registry (HCAR) reported in the first 3 months after births or termination of pregnancies. These cases comprised 77% of the HCAR. Three mild CAs (such as congenital dislocation of the hip based on the Ortolani click, congenital inguinal hernia, and hemangiomas), minor variants (eg umbilical hernia), and CA syndromes of Mendelian and chromosomal origin were excluded
Case prevalence among the population	The total recorded prevalence of cases with CA diagnosed from the 2 nd trimester of pregnancy through to the age of one year was 35 per 1,000 informative offspring (liveborn infants, stillborn fetuses and malformed fetuses after elective termination of pregnancy). Approximately 90% of major CAs were reported to the HCAR during the study period
Controls	38,151 newborns without any defects. Controls without CA were selected from the National Birth Registry of the Central Statistical Office, followed by 1-2 months of case notification. Two newborns were matched to every case according to sex, week of birth and district of parents' residence
Exposure definition	- Vaginal povidone-iodine suppositories during pregnancy - Mean duration of treatment: 12.4/12.5 days
Ascertainment of drug exposure	The data regarding exposure were obtained prospectively through antenatal care logbooks and retrospectively by questionnaires completed by mothers. Exposure information available for 80% cases and 70% controls
Prevalence of exposure among controls	0.11%
Analysis	- Adjusted prevalence OR and 95%CI were estimated (McNemar test and logistic regression to control for potential confounders: maternal age, birth order, marital/employment status, acute infectious/chronic maternal diseases, other drugs). Analysis considered treatment in the entire pregnancy or in the 2 nd and 3 rd month of gestation
Strengths	- Large, population-based data set - Standardized answers (structured questionnaire, list of drugs and diseases) - Thorough search of exposure data - Good characterization of cases - The first controlled epidemiological study about this drug
Weaknesses	- Control infants with no birth defects (risk of recall bias) - Despite the size of the population-based data set there were no cases or only a limited number of cases in some CA groups - The number of drug users was limited - Incomplete exposure information (risk of selection bias) (Information available for a total of 96.3% cases, 83.1% controls: the response rate was somewhat lower in the controls than in the cases (risk

	<p>of selection bias)</p> <ul style="list-style-type: none">- Active follow up for all non respondents in the case group, but only 200 families in the control group (risk of selection bias)- The mean time between birth and return of the questionnaire was different in the two groups (1.6 vs 3.5 months)
Main results	<p>The findings suggest that vaginal treatment of pregnant women with povidone-iodine in the usual therapeutic doses does not increase the risk of CAs in newborns. A higher mean birthweight after treatment (141g, $t=2.01$, $P=0.04$) offers an important argument against possible fetotoxic effect</p>