

**Pastuszak AL et al.** Use of misoprostol during pregnancy and Mobius' syndrome in infants. *N Engl J Med* 338, 1881-5, 1998

Type of study	Case-control
Where	Brazil (7 hospitals)
When	1990-1996
Cases	96 infants with Mobius' syndrome (time of the diagnosis by geneticists 16 months: range 0.5-78): bilateral or unilateral facial-nerve paralysis (paralysis of cranial nerve VII), with or without other neurologic signs or malformations. Infants were excluded if they had muscular dystrophy, myopathy, or generalized neuropathy, Mobius' syndrome due to dominant inheritance. The diagnosis in the infant was extracted from the records by personnel using a standardized form
Case prevalence among the population	Not available (not recorded in current registries of birth defects in Brazil)
Controls	96 randomly chosen infants born during the same period who were given a diagnosis of a neural-tube defects (meningocele, meningomyelocele, anencephaly, encephalocele) by the same clinical geneticists at the same hospitals within the first week of life. Infants with neural-tube defects due to amniotic-band sequence were excluded
Exposure definition	Intake during the first trimester of pregnancy: orally (47%), orally and vaginally (47%), vaginally (7%)
Ascertainment of drug exposure	At the time of clinical diagnosis, the geneticists interviewed the mothers and recorded information about misoprostol treatment (indication, route, dose, duration, complications)
Prevalence of exposure among controls	3%
Analysis	OR and 95% CI were estimated with stratification according to route of administration and date of clinical diagnosis
Strengths	<ul style="list-style-type: none"> <li>- Control infants with birth defects (reduced risk of recall bias)</li> <li>- Good characterization of cases and controls</li> <li>- Standardized interviews</li> <li>- Detailed information on studied drug use</li> <li>- Evaluation of the study's power analyses</li> </ul>
Weaknesses	<ul style="list-style-type: none"> <li>- It is possible an under-registration of use (illegal use)</li> <li>- The time of the interview after delivery in case and control groups was different, with a wide range in the cases: the exact timing of prenatal exposure to studied drug was difficult to determine in many cases</li> <li>- Drug intake based on maternal report (risk of recall bias)</li> <li>- Not indicated if the interviewers were aware of the case and control status</li> </ul>
Main results	Among the case group, 47 mothers (49%) had used misoprostol in the first trimester of pregnancy, as compared with 3 (3%) of the mothers among the controls (OR 29.7, 95% CI 11.6-76.0). Attempted abortion with misoprostol is associated with an increased risk of Mobius' syndrome in infants

