



Title:

Pregnancy Registries: The Importance of Inclusion and Exclusion Criteria. Holmes LB.

Abstract:

Introduction: Pregnancy registries have been proposed as a method for improving the speed of determining whether or not exposure during pregnancy to a “new” drug is teratogenic. The outcome evaluated typically is malformations identified at birth. One definition of a malformation is a structural abnormality with surgical, medical or cosmetic importance.

Methods: To maintain consistency in including specific abnormalities, a decision tree is developed as new outcomes are identified in exposed and unexposed newborn infants. The exclusions in the North American AED (antiepileptic drug) Pregnancy Registry are: a) minor anomalies (transverse palmar crease; b) birth marks (hemangioma); c) positional deformities (torticollis); d) effects of prematurity (PDA in infant below 37 wks gest age); e) hereditary disorders (postaxial polydactyly, type B); f) chromosome abnormalities (Down Syndrome); g) abnormalities identified by prenatal ultrasound but not by pediatrician (unilateral renal agenesis); h) minor findings by echocardiogram (ASD <0.4mm); i) abnormality identified in newborn screening (abnormal hemoglobin or cystic fibrosis).

Results: The review of the medical reports on 149 valproate-exposed and 77 phenobarbital-exposed newborns showed that 17% had physical features that were excluded in comparison to 10.7% and 7.7% major malformations respectively (Ungar L et al: BDR [Part A]: 76:373, 2006). The review process of specific features benefits from having photographs of features and the reports from consultations with specialists.

Conclusions: To identify an increase in the frequency of malformations in drug-exposed newborn infants, it is essential that the same inclusion and exclusion criteria be used for both the exposed and unexposed comparison groups. The findings in different pregnancy registries can be compared if each uses the same time period (e.g. birth or up to age 1 yr) and inclusion/exclusion criteria.

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