Affect of Seizures During Gestation on Pregnancy Outcomes in Women with Epilepsy

Affect of Seizures During Gestation on Pregnancy Outcomes in Women with Epilepsy. Chen YH, Chiou HY, Lin HC, Lin HL. *Arch Neurol* 2009;66(8):979–984. OBJECTIVE: To assess whether seizures in women with epilepsy during pregnancy contribute to adverse pregnancy outcomes. DESIGN: A retrospective cross-sectional study. SETTING: Taiwan. PATIENTS: This study linked 2 nationwide population-based data sets: Taiwan's birth certificate registry and the Taiwan National Health Insurance Research Data set. A total of 1,016 women with epilepsy were selected who had single births from 2001 to 2003 and who had been diagnosed with epilepsy within 2 years prior to their index delivery, together with 8,128 matched women without chronic disease as a comparison cohort. Women with epilepsy were further stratified into 2 groups for analysis: women who did and did not have seizures during pregnancy. MAIN OUTCOME MEASURES: Low-birth-weight infants, preterm delivery, and infants who are small for gestational age (SGA). RESULTS: Compared with women without epilepsy, epileptic seizures during pregnancy were independently associated with a 1.36-fold (95% confidence interval [CI], 1.01–1.88), 1.63-fold (95% CI, 1.21–2.19), and 1.37-fold (95% CI, 1.09–1.70) increased risk of low-birth-weight infants, preterm delivery, and SGA, respectively, after adjusting for family income and parental and infant characteristics. Further, the risk of SGA increased significantly (odds ratio, 1.34; 95% CI, 1.01–1.84) for women with seizures during pregnancy compared with women with epilepsy who did not have seizures during pregnancy. CONCLUSION: We suggest preventing seizures during pregnancy as an essential step to reduce risk of adverse pregnancy outcomes.

COMMENTARY

This amazing study by Chen et al. of neonates born to mothers with epilepsy shows an association between the risk of being small for gestational age (SGA) and the occurrence of seizures during pregnancy. Women with epilepsy who did not have seizures during pregnancy did not have an increased risk of SGA offspring compared to the offspring of healthy control mothers. Their findings reveal an important and clinically meaningful adverse outcome for neonates born to women with epilepsy. In the absence of maternal infection or illicit drug use, which are known causes of SGA, an evaluation for potential genetic causes of SGA and increased vigilance for perinatal complications, such as perinatal asphyxia, meconium aspiration, and hypoglycemia, are warranted in this patient population.

Identifying an association between SGA and seizures during pregnancy is novel. An association between women with epilepsy taking antiepileptic drugs (AEDs) and a doubled risk for SGA among in utero AED-exposed offspring has been found (1). Remarkably, the usual confounder for similar trials—maternal AED use—was not present in the Chen et al. investigation, since many women in this geographic region are untreated, and women with epilepsy who were taking medications were excluded from the group used for analysis (2). The study was performed by cross-referencing two national databases in Taiwan, those of women who had single births and those of women who were diagnosed with epilepsy between 2001 and 2003. The diagnosis of epilepsy in this subset of women was supported by documentation that included at least three consensus diagnoses of epilepsy or convulsions within the 2 years prior to the index delivery.

The risk of SGA among the offspring of women with epilepsy who had seizures during pregnancy, compared to women with epilepsy who did not have seizures during pregnancy, was mildly elevated, at an odds ratio of 1.34. Even the fairly tight 95% confidence intervals (i.e., 1.01–1.84) do not exclude the possibility of a moderate risk for an increased rate of SGA, although they do exclude a doubled risk. The authors also compared the women with epilepsy and a healthy control group and found an increased risk of low birth weight and preterm delivery among the women who had seizures, even after controlling for socioeconomic factors. Again, AED use was not a potential confounder; in fact, 84% of the women with epilepsy in this study (850 out of 1,016) were not taking AEDs. This dataset is one that likely would not be available in other parts of the world where similar surveillance of pregnant women with epilepsy is ongoing (e.g., the European Pregnancy Registry [EURAP] study and the North American Pregnancy Registry), as most patients in these trials are taking AEDs.

Additional valuable data could come from this dataset, such as whether there is a risk of birth defects related to seizures and epilepsy during pregnancy—a question that has long been unsatisfactorily answered, because the data have been confounded by the risks imparted by AEDs or by the likelihood that the epilepsy in the untreated group is mild or even questionable, making the comparison groups fundamentally different at baseline. Of note, previous studies have shown a lower risk

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of adverse pregnancy outcomes in untreated women, but the data have been confounded by the possibility that these women had less severe epilepsy. This study adds credence to this theory, since it appears that women without seizures (i.e., with milder epilepsy) did better than those with severe (active) epilepsy. The finding indicating that epilepsy, itself, is an adverse factor for pregnancy outcomes, in comparison to healthy controls, is provocative and needs further investigation and clarification.

This study provides additional evidence that can be used to counsel patients that it is best to try to maintain seizure control during pregnancy. These data are sorely needed, given that clinicians still struggle to communicate effectively with pregnant women with epilepsy to impress upon them exactly why preventing seizures during pregnancy is important, as prospective mothers usually are instead focused primarily on the risks to the fetus associated with AED use.

by Cynthia Harden, MD

References

1. Harden CL, Meador KJ, Pennell PB, Hauser WA, Gronseth GS, French JA, Wiebe S, Thurman D, Koppel BS, Kaplan PW, Robinson JN, Hopp J, Ting TY, Gidal B, Hovinga CA, Wilner AN, Vazquez B, Holmes L, Krumholz A, Finnell R, Hirtz D, Le Guen C. Management issues for women with epilepsy-Focus on pregnancy (an evidence-based review): II. Teratogenesis and perinatal outcomes: report of the Quality Standards Subcommittee and Therapeutics and Technology Subcommittee of the American Academy of Neurology and the American Epilepsy Society. *Epilepsia* 2009;50:1237–1246.
2. Mbuba CK, Ngugi AK, Newton CR, Carter JA. The epilepsy treatment gap in developing countries: a systematic review of the magnitude, causes, and intervention strategies. *Epilepsia* 2008;49: 1491–1503.