Epilepsy Currents
2021, Vol. 21(4) 252–254

DOI: 10.1177/1535759721012026
journals.sagepub.com/home/epi
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Like Mother, Like Child. Keeping Control of Seizures During Pregnancy

Changes in Seizure Frequency and Antiepileptic Therapy During Pregnancy

Pennell PB, French JA, May RC, et al. *N Engl J Med*. 2020;383(26):2547-2556. doi:10.1056/NEJMoa2008663

Background: Among women with epilepsy, studies regarding changes in seizure frequency during pregnancy have been limited by the lack of an appropriate nonpregnant comparator group to provide data on the natural course of seizure frequency in both groups. Methods: In this prospective, observational, multicenter cohort study, we compared the frequency of seizures during pregnancy through the peripartum period (the first 6 weeks after birth) (epoch 1) with the frequency during the postpartum period (the following 7.5 months after pregnancy; epoch 2). Nonpregnant women with epilepsy were enrolled as controls and had similar follow-up during an 18-month period. The primary outcome was the percentage of women who had a higher frequency of seizures that impaired awareness during epoch 1 than during epoch 2. We also compared changes in the doses of antiepileptic drugs that were administered in the 2 groups during the first 9 months of epoch 1. Results: We enrolled 351 pregnant women and 109 controls with epilepsy. Among the 299 pregnant women and 93 controls who had a history of seizures that impaired awareness and who had available data for the 2 epochs, seizure frequency was higher during epoch 1 than during epoch 2 in 70 (23%) pregnant women and in 23 (25%) controls (odds ratio, 0.93; 95% CI, 0.54-1.60). During pregnancy, the dose of an antiepileptic drug was changed at least once in 74% of pregnant women and in 31% of controls (odds ratio, 6.36; 95% CI, 3.82-10.59). Conclusions: Among women with epilepsy, the percentage who had a higher incidence of seizures during pregnancy than during the postpartum period was similar to that in women who were not pregnant during the corresponding epochs. Changes in doses of antiepileptic drugs occurred more frequently in pregnant women than in nonpregnant women during similar time periods. (Funded by the National Institutes of Health; MONEAD ClinicalTrials.gov number, NCT01730170.).

Commentary

Embarking on the adventure of pregnancy and motherhood presents unique challenges to every woman. Physiologic, social, and economic changes and risks of common medical complications take the forefront during pregnancy like in no other time in life. For women with epilepsy (WWE) the challenges are even greater. Mothers and families must evaluate the possibilities of increased risks of fetal malformations in relation to the diagnosis of epilepsy and to anti-seizure medications (ASM). Women worry about the risks of seizures during pregnancy for their own health and for the well-being of their unborn child. They consider the possibility of their kids developing epilepsy at birth or later in life.

Partnering with a health care team that understands the challenges and stands ready to inform the family and monitor and support the mother during pregnancy, and the postpartum period is key to achieving healthy outcomes for the mother and newborn child. The epilepsy community does not have answers to some questions that WWE have about pregnancy. However, much progress has been achieved in recent years, allowing us to inform prospective mothers of the actual risks and benefits of decisions during pregnancy and protocols which would improve the outcomes of pregnancy for mothers and babies alike.

A very active research group has provided much needed answers. The NEAD[1] study evaluated the effects of ASM in the neurodevelopment of children born to WWE at birth and up to 6 years of age, while the MONEAD collaboration continues to provide answers regarding the maternal outcomes of pregnancies exposed to ASM.[2-4]

The risk of seizures during pregnancy is one issue that deserved special attention. Is pregnancy by itself a risk factor for increased seizure frequency? What are the consequences of having seizures during pregnancy for the mother and fetus? What can we do to mitigate that risk and improve the chances for a healthy and seizure-free pregnancy? The highlighted study by Pennell et al[5] certainly provides some answers.

The study compared the seizure frequency of pregnant WWE with a control group of nonpregnant WWE. The pregnant group was followed during pregnancy and the immediate postpartum period and for 9 months following childbirth, while the control group was followed for 18 consecutive months. Seizure frequency during the pregnancy and immediate (6 week) postpartum period (epoch 1) was compared to the following 7.5 months (epoch 2) in the pregnant women group. Seizure frequency in the control group was also followed in 2 epochs of similar duration (epoch 1 of 10.5 months and epoch 2 of 7.5 months). Adjustments in medication doses during the observed time, the actual medications received, and potential risk factors for seizure frequency were followed in both groups during the time of observation.

The authors found no difference in the proportion of women who had increased frequency of seizures during the peri-pregnancy period or epoch 1 and epoch 2 within the pregnant WWE (23%) as compared to control WWE (25%). They did find however that more pregnant WWE underwent ASM dose adjustment at least once during pregnancy (74%) as compared to the control group (31%). These results highlight the fact that, with adequate follow-up and medication adjustments, pregnant WWE do not have a higher risk of having seizures during pregnancy and within the immediate postpartum period.

The risk of seizures during pregnancy was addressed recently by the International League Against Epilepsy Task Force on Women and Pregnancy.[6] Seizures during pregnancy represent a risk to the fetus resulting from blunt trauma, hypoxemia, and possibly other factors which could result in pregnancy loss, fetal injury, intrauterine growth retardation, and preterm delivery. Seizures during pregnancy should be prevented and the strategies for prevention need to be balanced against the known risks for fetal malformations and other challenges associated with ASM.

All women of childbearing age should be counseled regarding pregnancy-related risks and management. Birth control and pregnancy planning—including the interaction of ASM with hormonal treatments for birth control and the benefits of folic acid to decrease the risks of birth defects and other cognitive problems in children born to WWE[7]—should be discussed at every visit. We should strive for seizure freedom as it is, as shown again in the present study, an excellent predictor for seizure control during pregnancy. We should choose medications with low risk of fetal malformations and neurocognitive problems and favor monotherapy if possible.

Neurologists, obstetricians, and primary care providers need to be aware of known pharmacokinetic changes that affect the metabolism of ASM during pregnancy. These include a larger volume of distribution and increased renal clearance and hepatic metabolism. For medications that have measurable serum levels; it is generally advisable to establish the prepregnancy level at which the patient is controlled and actively match it during the pregnancy by adjusting ASM doses.

Following delivery, ASM doses can be rapidly adjusted to prepregnancy doses in a 2-step decrease occurring at second day and second week postpartum to prevent side effects or medication toxicity; this depends on the route of elimination of the specific ASM.

Having a neurologist or epilepsy expert following along during the pregnancy results in better communication with the obstetrics and fetal medicine teams and a more satisfying experience for the mother and the health care team. The present study showcases the fact that when perinatal epilepsy care for WWE is done right there is no increased seizure frequency during pregnancy. This is amazing news to share with our patients and families.

Unfortunately, the model of care described is not the one most WWE experience. Looking carefully through the demographics of the study, it is easy to notice an overrepresentation of white, highly educated women under the care of health care providers practicing in highly subspecialized clinics with specific interest in the care of WWE and pregnancy. Our challenge as a community devoted to the care and well-being of all people living with epilepsy is to educate more providers at general neurology and even primary care levels to identify the challenges of WWE of childbearing age and pregnant WWE. The described strategies are of relatively low cost and can make a big difference. Our goal should be to offer similar standards of care to all mothers and children living with epilepsy in our community.

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