

Estrogen, Progesterone, and Epilepsy: What's the Relationship?

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Background

Approximately one third of women with intractable focal epilepsy have seizures related to their menstrual cycle, also known as "catamenial epilepsy."^[1] Among their many biological effects, ovarian hormones may be neuroactive. Estrogen lowers seizure threshold while progesterone raises it, supporting a hormonal influence on seizure frequency that may underlie catamenial epilepsy.^[1] Catamenial epilepsy can be diagnosed in women who experience at least twice their usual seizure frequency at a specific time around their menses.^[1] Three patterns of catamenial epilepsy have been proposed, based on the timing of seizure exacerbation: (1) perimenstrual, (2) periovulatory, and (3) during the second half of an anovulatory cycle.^[1]

Study Design and Baseline Characteristics

To evaluate the seizure course of patients with catamenial epilepsy during pregnancy, Cagnetti and colleagues^[2] prospectively followed 274 women before and during pregnancy, of whom 59 had catamenial epilepsy and 215 had noncatamenial epilepsy.^[2] For each participant, seizure frequency observed during pregnancy was compared with the 9-month period prior to pregnancy.

The two groups of participants had comparable baseline characteristics. Mean age at epilepsy onset was 16.7 years for the catamenial epilepsy group and 15.5 years for the noncatamenial epilepsy group. Mean age at pregnancy was 30.3 years for the catamenial epilepsy group and 30.7 years for the noncatamenial epilepsy group. With respect to epilepsy type, 45.8% of the catamenial epilepsy group had cryptogenic epilepsy vs 47.9% of the noncatamenial epilepsy group; 33.9% of the catamenial epilepsy group had idiopathic epilepsy vs 31.2% of the noncatamenial epilepsy group; and 20.3% of the catamenial epilepsy group had symptomatic epilepsy vs 20.9% of the noncatamenial epilepsy group. Focal seizures were the most common seizure type in both groups, occurring in 62.7% of participants in the catamenial epilepsy group and 53.5% of participants in the noncatamenial epilepsy group. Generalized seizures were less common and occurred in 33.9% of the catamenial epilepsy group and 41.9% of the noncatamenial epilepsy group. Undetermined seizure types occurred in 3.4% of the catamenial epilepsy group and 4.7% of the noncatamenial epilepsy group. Nearly all women in both groups were receiving antiepileptic drug (AED) treatment, with 96.6% of participants in the catamenial epilepsy group and 89.3% in the noncatamenial epilepsy group receiving at least one AED.

Results

Forty-seven (79.7%) women with catamenial epilepsy were seizure free during pregnancy compared with 48 (22.3%) women with noncatamenial epilepsy (odds ratio [OR], 2.6; 95% confidence interval [CI], 1.9-3.3; $P < .001$). Thirty (50.8%) women with catamenial epilepsy vs 18 (8.4%) women with noncatamenial epilepsy experienced reduced seizure frequency during pregnancy (OR, 2.4; 95% CI, 1.7-3.1; $P < .001$). Ten (16.9%) women with catamenial epilepsy and 54 (25.1%) women with noncatamenial epilepsy had an increase in seizure frequency during pregnancy ($P =$ not significant).

Discussion

In this study, women with catamenial epilepsy were significantly more likely to be seizure free and experience a reduction in seizure frequency during pregnancy compared with women with noncatamenial epilepsy. During pregnancy, cyclic hormonal changes are replaced by an increase in circulating progesterone levels, which may be responsible for improved seizure control in women with catamenial epilepsy. This is consistent with nonpregnant women who have increased seizure frequency when progesterone levels are lower or when the estrogen/progesterone ratio is higher.^[3]

One of the most troubling characteristics of epilepsy is the unpredictable occurrence of seizures. Even if relatively infrequent, the fact that a seizure may occur without warning at any time may significantly restrict activities such as driving, working with machinery or at heights, swimming, and many social activities. Clinicians should instruct women with epilepsy to keep accurate and detailed seizure diaries to try to identify the occurrence of one of the three patterns of catamenial epilepsy. Greater attention to AED levels, adequate sleep, and adjunctive therapy are all therapeutic approaches that may improve seizure

control during these vulnerable times. In addition, patients should be particularly attentive to safety precautions when at heightened risk for increased seizures. Progesterone therapy may be effective for catamenial epilepsy but has not been widely used.^[4,5]

Conclusions

Women with catamenial epilepsy are more likely to become seizure free or experience improved seizure control during pregnancy compared with women with noncatamenial epilepsy. Elevated progesterone levels during pregnancy may be at least partially responsible for improved seizure control in women with catamenial epilepsy. Hormonal, metabolic, and physiologic changes during pregnancy in women with epilepsy need to be further studied, which may lead to improved antiepileptic therapy.

References

1. Herzog AG, Klein P, Ransil BJ. Three patterns of catamenial epilepsy. *Epilepsia*. 1997;38:1082-1088. [Abstract](#)
2. Cagnetti C, Lattanzi S, Foschi N, Provinciali L, Silvestrini M. Seizure course during pregnancy in catamenial epilepsy. *Neurology*. 2014;83:339-344. [Abstract](#)
3. Backstrom T. Epileptic seizures in women related to plasma estrogen and progesterone during the menstrual cycle. *Acta Neurol Scand*. 1976;54:321-347. [Abstract](#)
4. Herzog AG. Progesterone therapy in women with complex partial and secondary generalized seizures. *Neurology*. 1995;45:1660-1662. [Abstract](#)
5. Najafi M, Sadeghi MM, Mehvari J, Zare M, Akbari M. Progesterone therapy in women with intractable catamenial epilepsy. *Adv Biomed Res*. 2013;2:8.

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