Issues for Women with Epilepsy

Naymeé J. Vélez-Ruiz, MD[a,*], Page B. Pennell, MD[b,c]

KEYWORDS

• Women • Epilepsy • Catamenial • Pregnancy • Antiepileptic drugs • Contraception

KEY POINTS

- Women with epilepsy may experience seizure patterns related to the menstrual cycle and are at risk of reproductive abnormalities and pregnancy complications.
- There are bidirectional pharmacokinetic interactions between antiepileptic drugs (AEDs) and hormonal contraceptives, which may result in reduced efficacy of either one.
- AED treatment during pregnancy is a balancing act between teratogenic risks to the fetus and maintaining maternal seizure control.
- Folic acid supplementation prior to and during pregnancy has been associated with a risk reduction in the occurrence of congenital malformations and cognitive teratogenesis.
- Estimates of AED exposure from breast milk suggest that it is low for many AEDs.

INTRODUCTION

Epilepsy is one of the most common chronic conditions affecting women. Although the prevalence of epilepsy and treatment approaches are similar for women and men, women are more likely to experience seizure patterns related to hormonal cycles and are at risk of reproductive alterations and pregnancy complications.

NEUROSTEROIDS

Neurosteroids are molecules that modulate brain excitability and, therefore, can affect the occurrence of seizures. Estrogen and progesterone, the primary reproductive

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[a] Division of Epilepsy, Department of Neurology, University of Miami, 1120 Northwest, 14th Street, Suite 1329, Miami, FL 33136, USA; [b] Division of Epilepsy, Department of Neurology, Brigham and Women's Hospital, Harvard Medical School, Harvard University, 75 Francis Street, Boston, MA 02115, USA; [c] Division of Women's Health, Brigham and Women's Hospital, Harvard Medical School, Harvard University, 75 Francis Street, Boston, MA 02115, USA
* Corresponding author.
E-mail address: nxv146@med.miami.edu

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hormones for women, both affect neuronal excitability. The actions of neurosteroids on neuroexcitability occur via 2 mechanisms. The first is a short latency, nongenomic effect mediated by the neuronal membrane.[1,2] The second is a long-latency (hours to days) genomic effect.[2,3] Estrogen has been suggested as neuroexcitatory, and some women with epilepsy might be susceptible to its proconvulsant effect.[2] Progesterone, on the other hand, promotes neuroinhibition, primarily through the action of its metabolite, allopregnanolone, which acts as a positive allosteric modulator of γ-aminobutyric acid conductance.[2,4,5]

SEX STEROID HORMONE AXIS

Release of female reproductive steroid hormones is controlled by the hypothalamic-pituitary-ovarian axis through a bidirectional feedback loop, as shown in **Fig. 1**.[6] Gonadotropin-releasing hormone (GnRH) is secreted by the hypothalamus and stimulates release of follicle-stimulating hormone (FSH) by the pituitary. FSH stimulates formation of the ovarian follicles, which secrete estradiol (the main estrogen in women). Midcycle, a surge of luteinizing hormone (LH) induces oocyte maturation, ovulation, and conversion of the follicle into the corpus luteum. This marks the end of the follicular phase and the beginning of the luteal phase. After ovulation, the corpus luteum secretes progesterone. Progesterone inhibits secretion of GnRH, FSH, and LH. If there is no pregnancy, the corpus luteum regresses and production of progesterone and estradiol declines. When progesterone secretion tapers off and GnRH inhibition decreases, the cycle repeats.

CATAMENIAL EPILEPSY

The pattern of seizure clustering during certain parts of the menstrual cycle is termed *catamenial*, derived from the Greek, *katamenios*, meaning monthly.[2] The reported prevalence of catamenial epilepsy depends on the specific definition used during quantification. Menstrual seizure exacerbations have been reported in up to 70% of women with epilepsy, although a more strict definition used by Herzog and colleagues[7] in their 1997 study suggested that this pattern was present in approximately one-third of women with epilepsy.

Menstrual Cycle

The average menstrual cycle is 28 (24–35) days, with day 1 the first day of menses and ovulation occurring on day 14 (or day −14 to adjust for cycle lengths other than

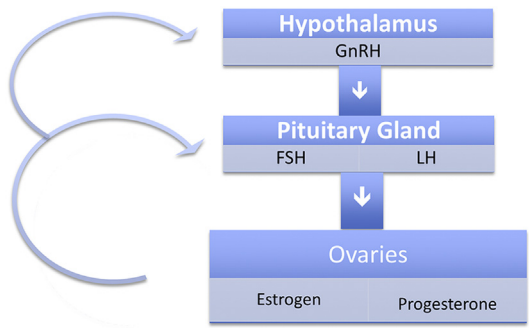

Fig. 1. Hypothalamic-pituitary-ovarian axis.