OPINION

Treatment and care for epileptic women prior to, during, and after pregnancy

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Slate J. Treatment and care for epileptic women prior to, during, and after pregnancy. J Neuropathol. 2022; 2(4):36-7.

ABSTRACT

Women with Epilypsy (WWE) who want to have a child are a highly relevant subset of epilepsy patients. The treating epileptologist must define the epilepsy syndrome and select the appropriate Anti-Seizure Medication (ASM) while keeping in mind the main goal of seizure freedom, teratogenic risks, changes in drug metabolism during and after pregnancy, and the need for up-titration during and after pregnancy. This review also covers folic acid and vitamin K supplements, as well as breastfeeding. Teratogenic potential is lowest for lamotrigine and levetiracetam. Oxcarbazepine has a favourable teratogenic risk profile, whereas topiramate has an unfavorable profile. Valproate requires special attention. It is most effective in generalized seizures, but it should be avoided as much as possible due to teratogenic effects and a negative impact on neuropsychological development.

Key Words: *Neuropsychological development*

INTRODUCTION

Valproate is still justified in patients who have not achieved seizure freedom with other ASMs or if a woman chooses or is unable to become pregnant for any reason. When valproate is the best treatment option, the patient and caregiver must be fully informed of the risks of using it during pregnancy. To reduce the risk of major congenital malformations, folate supplementation is advised. However, there is insufficient data to determine the optimal dose, and it is unclear whether higher doses provide more protection. There is currently no consensus on peripartum vitamin K prophylaxis. Most ASMs (e.g., lamotrigine, oxcarbazepine, and levetiracetam) must be increased during pregnancy to compensate for the drop in serum levels; valproate and carbamazepine are exceptions. Women of childbearing age with epilepsy are a relevant subgroup of epilepsy patients, accounting for approximately 15 million patients worldwide. Their special needs are diverse and include contraception, the desire to have children, folic acid supplementation, teratogenic risks, and seizure control during pregnancy, changes in Anti-Seizure Medication (ASM) serum levels during pregnancy and postpartum, birth mode, puerperium, and breast feeding. After thorough counselling with the patient, the epileptologist should consider these issues in conjunction with the underlying epilepsy syndrome and select the appropriate ASM. WWE management and care begin in the preconception phase with pregnancy, childbirth, postpartum, and breastfeeding planning.

The ASM should be appropriate for the epilepsy syndrome and should take into account the drug's teratogenic potential. Valproate and other ASMs with a high potential for teratogenicity should be avoided. Individualized ASM baseline concentrations should be established in monotherapy using the lowest effective dose. If an appropriate ASM monotherapy is prescribed, the teratogenic risk remains low, and most WWE will give birth to a healthy child. Although folate supplementation is strongly recommended to prevent NTDs, clear dosing guidelines are lacking. Aside from teratogenicity, the child's neurocognitive outcome is still a concern. Despite the risk of autism spectrum disorders, lamotrigine and levetiracetam are the two most preferred ASMs for WWE due to their MCM safety profile. During pregnancy, gynecologists, obstetricians, and geneticists are involved in the care. If seizures are stable, we recommend at least three clinical visits. During pregnancy, increased ASM clearance causes significant fluctuations in several ASMs, including levetiracetam and lamotrigine. To avoid seizures, it is necessary to gradually increase the dose. The goal is to strike a balance between challenging teratogenicity while preventing (tonic-clonic) seizures. Recent evidence shows that careful clinical decision making in drug dosing is as effective as serum sampling. ASMs that have been up titrated during pregnancy can be empirically reduced by 50% within the first 3 days postpartum, reaching preconception dosages after about 1 week. To address sleep deprivation, it may be necessary to keep the dosage slightly higher than preconception. Data on lamotrigine are plentiful, but rarely prescribed ASMs (e.g.,

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Received: 2 July 2022, Manuscript No. PULNP-22-5188; Editor assigned: 4 July 2022, PreQC No. PULNP-22-5188 (PQ); Reviewed: 17 July 2022, QC No. PULNP-22-5188 (Q); Revised: 18 July 2022, Manuscript No. PULNP-22-5188 (R); Published: 26 July 2022, DOI: 10.37532/pulnp.2022.2(4).36-7

pregabalin) necessitate individual decision making when titrated during pregnancy. Sleep deprivation raises the risk of seizure recurrence. As a result, the immediate postpartum period is critical. The risk of seizure-related injuries for mother and child can be reduced by a variety of lifestyle changes. For example, a sleep-deprived mother should not carry her newborn free, but rather move it indoors in a bedside cot on wheels. Second, instead of carrying the baby in a baby sling outside, use a baby stroller, and third, use escalators instead of stairs. Furthermore, changing diapers on a floor pad rather than a baby changing table reduces the risk of dropping. Babies do not require a bath on a daily basis. Instead, washing with a facecloth on a pad reduces the risk of drowning. The bathtub should be saved for future generations. However, recent findings from a prospective, observational cohort study indicate that therapeutic drug monitoring should begin early in pregnancy, and that increasing doses of these anticonvulsants may be required throughout the pregnancy. The EURAP, NAARP, and UKIEPR registries provide the majority of information on teratogenic effects. Valproate, whether used alone or in combination, is associated with the highest risk of negative neurodevelopmental outcomes.

Morphologic ultra-sonographic evaluation is advised before conception and once during each trimester. If available, more detailed sonography (organ screening) is advised. Recent evidence does not support the use of peripartum vitamin K prophylaxis. Vaginal delivery is generally advised. Cesarean sections are indicated when poor seizure control during pregnancy and a high risk of seizures during labor threaten delivery and increase the risk of complications.

After discharge, serum ASM concentrations return to preconception levels in 14 days to 21 days. We recommend empirically reducing the dose by roughly twice the up-titrated dose within half a week and nearly to preconception levels after one week. We recommend repeated drug monitoring during the first week after delivery to adjust ASM dosages and weekly controls within the first four weeks. To account for the potential effect of sleep deprivation during breastfeeding, it may be prudent to keep the ASM dosage slightly higher than preconception levels. Most ASMs are compatible with breastfeeding and have a low to moderate risk of side effects in the infant; however, it is critical to observe the infant and monitor the possibility of side effects; in these cases, consider mixed nutrition with formula.