

Seizures in Pregnancy

The following section is entitled “**Seizures in Pregnancy**”. This section deals with some of the basic concepts important in caring for epilepsy during pregnancy. The section begins with a *learner handout* with space for the learner to make their own notes. The *learner handout* is following by the *teaching script* for the educator. The section then concludes with several cases for discussion and a brief bibliography for this topic.

SEIZURES IN PREGNANCY

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Incidence

Seizures complicate 1% of pregnancies

Association with Congenital Defects

Maternal epilepsy is associated with a two-fold increase in the incidence of congenital abnormalities.

Anticonvulsant therapy may contribute to the incidence of congenital abnormalities in the children of epileptics, but some increased risk is present regardless of therapy.

Justification for Treatment

However, anticonvulsant therapy in pregnancy is justified to prevent uncontrolled generalized seizures.

Specific Anticonvulsants Used

Phenytoin (Dilantin®) carbamazepine (Tegretol®) have been used successfully in pregnancy.

Phenobarbital may be associated with a higher rate of congenital anomalies.

Valproic acid (Depakote®) has also been used but has a 1% risk of neural tube defects associated with it.

Anticonvulsant Levels

Total blood levels of anticonvulsants tend to go down in pregnancy due to increased hepatic and renal clearance and an increased volume of distribution.

This is partially counteracted by the fact that free (and therefore active) drug levels may increase due to a normal decrease on the concentration of serum proteins that occurs in pregnancy.

Anticonvulsant Management

Serum blood levels should be checked monthly in pregnant women and anticonvulsant dose adjusted accordingly.

Some clinicians prefer to follow their patients clinically and monitor levels and adjust dosing only if seizures occur.

Effect of Pregnancy on the Course Of Epilepsy

Approximately 20% of epileptic women have increased seizure frequency during pregnancy, mostly due to poor compliance with anticonvulsant therapy, but also due to nausea and vomiting and sleep deprivation.

Acute Seizure Management

Acute management of a seizure during pregnancy is the same as it is for the nonpregnant individual but, remember that maintaining maternal oxygenation is paramount to the fetus, and that not all seizures in pregnancy are from epilepsy (but not all of them are from eclampsia either.)

Peripartum Management

Vitamin K administration in the last month of pregnancy probably decreases the risk of hemorrhagic disease of the newborn and postpartum hemorrhage in the mother.

Postpartum Management

After delivery, mothers with seizure disorders can be sent home on a dose halfway between their pre-pregnancy dose and their most recent pregnancy dose. They can go back to their pre-pregnancy dosing by two weeks postpartum.

Mothers with seizure disorders should be given some practical advice about safely caring for their newborns.

Breast Feeding

All anticonvulsants are compatible with breast feeding.

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Teaching Script

Seizure disorders complicate approximately 1% of all pregnancies.

Risks of epilepsy and anticonvulsant therapy in pregnancy

Maternal epilepsy is associated with a two-fold increase in the incidence of congenital anomalies in children born to women with epilepsy. Some of this increase in the incidence of congenital anomalies appears to occur even in the absence of anticonvulsant medication. There is even some evidence that paternal epilepsy is associated with an increased incidence of congenital abnormalities. Anticonvulsant therapy does appear to further increase the incidence of congenital abnormalities in children of epileptics, particularly with polypharmacy, but it is important to emphasize that some increased risk is present regardless of therapy when counseling epileptics about pregnancy.

Despite the increased risk of congenital anomalies that may be associated with anticonvulsant therapy, it is generally accepted that anticonvulsive therapy is warranted during pregnancy because of the danger that both the potential physical trauma and the periods of maternal apnea associated with a grand mal seizure can present to the fetus.

Phenytoin (Dilantin®) and Carbamazepine (Tegretol®) have both been used successfully to control seizures in pregnancy and appear to be associated with a similar risk of congenital anomalies. Congenital anomalies most commonly associated with these medications and epilepsy include facial abnormalities (such as cleft palate and cleft lip) and cardiac abnormalities (such as ventricular septal defects and atrial septal defects). Phenobarbital (Phenobarb®) has been associated with a higher risk of congenital anomalies than the other anticonvulsant

medications and is also associated with possible impaired intellectual development of children following *in utero* exposure. Valproic acid (Depakote®) has also been used to control seizures in pregnancy but carries with it a 1% risk of neural tube defects. The mildest form of neural tube defects is spina bifida occulta, but its most severe form is anencephaly. Although high dose folate in the range of 4 mg per day may decrease the risk of neural tube defects in mothers whose offspring are at risk, it is best, when possible, to avoid the use of valproic acid during the first trimester.

Management of Anticonvulsant Therapy in Pregnancy

If a pregnant woman is maintained on the same dose of an anticonvulsant throughout pregnancy, total blood levels of the anticonvulsant will tend to go down during the pregnancy due to a pregnancy related increase in hepatic and renal clearance of the drug and a pregnancy related increase in the volume of distribution of the drug (this effect is least for carbamazepine). This drop in total blood levels is partially counteracted by the fact that free (and, therefore, active) drug levels may increase due to a normal decrease in the concentration of serum protein that occurs in pregnancy. Therefore, for any given total drug level there is likely to be more free drug available during pregnancy than there would be in a nonpregnant individual.

Because of the difficulty in interpreting serum drug levels of anticonvulsants during pregnancy, it is advisable to check total serum drug levels if available monthly in pregnant women and adjust their dose accordingly.

In the circumstance that seizures are occurring and there is concern about the meaning of a particular total serum drug level, free drug levels can be obtained at many laboratories. It is best to use the least number of drugs at the lowest dose possible to prevent seizures.

Some clinicians prefer to do less monitoring of drug levels in pregnancy and to adjust anticonvulsant dose primarily on the basis of seizure activity. We feel that such an approach

places the patient and her fetus under some additional risk.

Course of Epilepsy in Pregnancy

It appears that, overall, seizure frequency increases in approximately 20% of patients during pregnancy. The most important predictor of an individual patient's frequency of seizures during pregnancy is the frequency of seizures for that patient in the year prior to conception. This suggests that for the most part epilepsy manifests itself similarly in the pregnant woman as it does in the non-pregnant woman.

Individuals who have an increased frequency of seizures during pregnancy should be questioned about both sleep deprivation and compliance. It has been our observation that the sleep deprivation associated with pregnancy (occurring for such diverse reasons as difficulty in getting comfortable at night in the third trimester, and frequent nocturia) may be responsible for increased seizure activity in some individuals. Lifestyle modifications that increase the hours of sleep the patient is getting may therefore improve seizure control. Also, because of the possible fetal effects of anticonvulsants, compliance with these drugs can be a problem in pregnancy and needs to be carefully addressed as a possible cause of seizure activity and/or sub-therapeutic anticonvulsant levels.

Acute Management of a Seizure in Pregnancy

The acute management of the seizure during pregnancy is the same as for the non-pregnant individual except for the fact that in pregnancy it is important to remember that maintaining maternal oxygenation is of paramount importance to the fetus. Although the brief nature of most seizures means that hypoxia is unlikely to present a major problem to the nonpregnant adult who has a seizure, brief periods of hypoxia in a mother can be associated with dramatic fetal hypoxia (due to the uniqueness of the fetal hemoglobin oxygen dissociation curve). Benzodiazepines such as Lorazepam (Ativan®) and Diazepam (Valium®) can be given intravenously acutely. The patient can then be loaded with Phenytoin (Dilantin®). If seizures

persist, Phenobarbital would be used next, just as would be done for the management of a seizure in a non-pregnant woman.

It is very important to remember that not all seizures in pregnancy are from epilepsy. There are reports of seizures due to Wernickes encephalopathy secondary to thiamine deficiency related to hyperemesis gravidarum. Epileptic women, although at no proven increased risk for an eclamptic seizure, will on occasion develop preeclampsia/eclampsia. Therefore, preeclampsia/eclampsia should be part of the differential diagnosis of any seizure occurring in the third trimester. Likewise, it is important to remember that not all first time seizures occurring in the third trimester are preeclampsia/eclampsia. It is said that up to 10% of epileptic women will present for the time during pregnancy.

Vitamin K Therapy to Decrease the Risk of HDN and Postpartum Hemorrhage

Pregnancy appears to cause some depletion in maternal vitamin K stores and this depletion appears to be worse in women on any anticonvulsant other than valproic acid. Vitamin K administration to epileptic women is recommended for the last month of pregnancy because there is evidence to suggest that building up vitamin K stores in the mother will decrease the incidence of Hemorrhagic Disease of the Newborn and postpartum hemorrhage in the mother. The exact mechanism of this is poorly understood. The vitamin K is usually given orally as a 10 mg per day dose from 36 weeks gestation until delivery.

Postpartum Management

After delivery we usually send the woman home on a dose halfway between her pre-pregnancy dose of anticonvulsants and her most recent pregnancy dose. We maintain her on this level of anticonvulsant for two weeks before returning her to her previous pre-pregnancy dose of anticonvulsants. This is done in recognition of the gradually decreasing volume of distribution and the gradual resumption of the normal level of hepatic and renal clearance that occurs during

the postpartum period. Safety precautions such as not bathing infants alone and changing baby on the floor rather than a change table should be suggested to all new mothers with seizure disorders.

Despite concerns often expressed by mothers and pediatricians, women on anticonvulsants should be encouraged to breast feed. Although anticonvulsants do appear in breast milk, they are found at low levels that are not likely to have a significant effect upon the newborn. If concerns arise about anticonvulsant toxicity in the breast feeding newborn, neonatal drug levels can be readily measured.

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Case Discussion

Case #1

Adapted from ACP workshop syllabus

A 21-year old G₁ P₀ with tonic clonic seizures is surprised to find out that she is 6 weeks pregnant after missing only one birth control pill. She was on Phenytoin (Dilantin®) and Valproic Acid for seizure control but stopped them yesterday when she found out she was pregnant. She is very fearful of the effects her medications may have on her fetus and wants to be switched to the safest antiepileptic drug. Although she wants to keep the pregnancy, she would elect a termination if a major problem was found.

What should be done about her AEDS and why?

What are the chances of her baby being affected with a major abnormality?

Is there a preferred AED in pregnancy?

What can be done to minimize the risk of malformations?

What screening tests should you offer her?

She feels reassured enough after talking to you to resume her medications. However, she is now worried about whether her epilepsy might worsen with the pregnancy and wanted to know how you will take care of her during the pregnancy.

What is the effect of pregnancy on seizure frequency?

How will you follow her AED medication during her pregnancy?

She has read that AEDs can cause bleeding in the mother and fetus after a delivery and wants to know if this is true.

What do you tell her?

She calls you back that same afternoon and is worried about whether she will be able to breast feed with this medicine.

What do you tell her?

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Case Discussion

Case #2

Adapted from ACP workshop syllabus

A 34-year old G₅ P₄ at 38 weeks gestation presents to the emergency department after being brought in by her husband who found her at home on the floor semi-conscious. She has no known history of seizure disorders or syncope and by the time she has arrived at the hospital she seems back to normal but has no memory of the event.

What questions would you ask to determine if this was a seizure?

What causes of seizure would you consider?

How would you investigate the possible diagnosis of eclampsia?

While in the emergency department she has another sudden loss of consciousness with seizure like activity.

What medications would you use to stop the seizure?

What additional precautions would you take to protect the patient and the fetus?

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Case Discussion

Case #3

Adapted from ACP workshop syllabus

A 21-year old G₁P₀ at 22 weeks gestation with known epilepsy is brought in by her family to the emergency department because she has had a seizure at home. She is being managed on Phenytoin (Dilantin®) 300 mg a day and her last level was therapeutic at 15.

What laboratory tests would you order on this patient?

What reason might there be for her to be having seizures now, when they were previously well controlled?

You check her Dilantin® level and it is 6, which is well below therapeutic: why might this be and what would you do about it?

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