

Epilepsy and Neurological Disorders in Pregnancy: An Insight into Etiopathogenesis.

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Abstract: It complicates 1 in 200 pregnancies and is an important cause of seizures. It is defined as a paroxysmal disorder of the central nervous system with an abnormal neuronal discharge with or without loss of consciousness. 17-33% of Seizure frequency increases during pregnancies. Generalized tonic-clonic seizures during pregnancy can lead to increased maternal trauma. If the maternal trauma involves the abdomen, a theoretical risk of abruption exists, possibly leading to fetal hypoxia or death. Furthermore, the risk of maternal aspiration can lead to maternal hypoxia, which can also lead to fetal hypoxia.

Women with epilepsy appear to have a greater baseline risk of fetal malformations, which is further increased with the use of antiepileptic drugs (AEDs). First-trimester use of even a single AED is associated with a 2- to 5-fold increase in major malformations. Furthermore, there is an increase in fetal malformations with AED polytherapy. **Preconceptual management of women with epilepsy** is to decrease pharmacotherapy to monotherapy, preconception genetic counseling. Supplement the diet with folate at 4 mg/d.

INTRODUCTION

Epilepsy complicates 1 in 200 pregnancies and is an important cause of seizures. The condition defined as a paroxysmal disorder of the central nervous system with an abnormal neuronal discharge with or without loss of consciousness. In epilepsy there is predisposition to recurrent unprovoked seizures. Epilepsy syndromes include partial seizure or generalized seizures.

EFFECT OF PREGNANCY ON EPILEPSY

Seizure frequency during pregnancy varies from 17-33% ; possible etiologies include

1. Increased levels of circulating estrogen during pregnancy increase the function of the P-450 enzymes, which leads to more rapid hepatic metabolism of the AEDs.
2. Renal function increases during pregnancy, with a 50% rise in creatinine clearance, which impacts the metabolism of carbamazepine, primidone, and benzodiazepines.
3. The increase in total blood volume and a concomitant rise in the volume of distribution also lead to decreased levels of circulating AEDs. In contrast, the decrease in albumin and circulating plasma proteins likely increases the free component of the AEDs in serum.
4. Estrogen has been shown to be epileptogenic, decreasing the seizure threshold. Thus, the rising estrogen levels in pregnancy, which peak in the third trimester, may have some impact on the observed increase in seizure frequency. Conversely, progesterone seems to have an antiepileptic effect, and women with seizure disorders have been observed to have fewer seizures during the luteal phase of the menstrual cycle.
5. The increased stress, hormonal changes, and decreased sleep during pregnancy likely lower the seizure threshold and have been shown to increase seizure frequency in patients who are not pregnant.
6. Many women have decreased compliance with taking AEDs because of concerns regarding the effects on their fetuses.

Generalized tonic-clonic seizures during pregnancy can lead to increased maternal trauma. If the maternal trauma involves the abdomen, a theoretical risk of abruption exists, possibly leading to fetal hypoxia or death. Furthermore, the risk of maternal aspiration can lead to maternal hypoxia, which can also lead to fetal hypoxia.

The workup of these patients should involve a neurologic examination, consultation with a neurologist, CBC count, chemistry panel (particularly

for electrolytes), head MRI versus CT scan, and EEG

AED levels should be monitored monthly during pregnancy, with adjustment of dosing based on these levels and the clinical manifestations of seizure frequency.

Management of women with epilepsy during labor and delivery

- Check levels of antiepileptic drugs (AEDs).
- Inform all care providers, including nurses, anesthesiologists, and pediatricians, that the patient has epilepsy.
- Consider seizure prophylaxis with intravenous benzodiazepines or phenytoin.
- Manage seizures acutely with intravenous benzodiazepines (1-2 mg of diazepam), then load phenytoin (1 g loaded over 1 h).
- Labor management should be based on routine standards of care.
- Start administration of vitamin K for the infant, and send the cord blood for clotting studies.

Management of a pregnant patient in status epilepticus

- Establish the ABCs, and check vital signs, including oxygenation.
- Assess the fetal heart rate or fetal status.
- Rule out eclampsia.
- Administer a bolus of lorazepam (0.1 mg/kg, ie, 5-10 mg) at no faster than 2 mg/min.
- Load phenytoin (20 mg/kg, ie, 1-2 g) at no faster than 50 mg/min, with cardiac monitoring.
- If this is not successful, load phenobarbital (20 mg/kg, ie, 1-2 g) at no faster than 100 mg/min.
- Check laboratory findings, including electrolytes, AED levels, glucose, and toxicology screen.
- If fetal testing results are nonreassuring, move to emergent delivery.

EFFECT OF EPILEPSY ON PREGNANCY

Women with epilepsy appear to have a greater baseline risk of fetal malformations, which is further increased with the use of antiepileptic drugs (AEDs). First-trimester use of even a single AED is associated with a 2- to 5-fold increase in major malformations. Furthermore, there is an increase in fetal malformations with AED polytherapy.

Specific increases in congenital abnormalities observed in infants born to mothers with epilepsy include a 4-fold increase in cleft lip and palate and a 3- to 4-fold increase in cardiac anomalies. An increase in the rate of neural tube defects is also observed in the offspring of patients with epilepsy who are using carbamazepine or valproic acid. Long-term studies on neurodevelopment show higher rates of abnormal EEG findings, higher rates of developmentally delayed children, and lower intelligence quotient

Fetal Anomaly	Phenytoin	Phenobarbital	Primidone	Valproate	Carbamazepine	Trimethadione
Neural tube defects	X	X	...
Intrauterine growth restriction	X	X
Microcephaly	X	X
Low IQ	X	...	X
Distal digital hypoplasia	X	X
Low-set ears	X	X	X
Epicantal fold	X	X	...	X	X	X
Short nose	X	X	...	X	X	...
Long philtrum	X	...	X	...
Lip abnormalities	X	X	X	X
Hypertelorism	X	X
Developmental delay	...	X	X	X
Other	Ptosis	Ptosis	Hirsute forehead	...	Hypoplastic nails	Cardiac anomalies

(IQ) scores.

The mechanisms of teratogenicity of the AEDs have not been fully characterized. Phenobarbital, primidone, and phenytoin act as folate antagonists. Certainly, a folate deficiency appears to lead to an increase in congenital malformations, particularly neural tube defects; thus, folate administration prior to conception has been recommended for prophylaxis.

PRECONCEPTUAL MANAGEMENT OF WOMEN WITH EPILEPSY

- Attempt to decrease pharmacotherapy to monotherapy.
- Taper dosages of AEDs to the lowest possible dose.
- In women who have not had a seizure for 2-5 years, attempt complete withdrawal of pharmacotherapy.
- Establish the level of total and free AEDs necessary for achieving good clinical control.
- Consider preconceptual genetic counseling.
- Supplement the diet with folate at 4 mg/d.

MANAGEMENT OF WOMEN WITH EPILEPSY DURING PREGNANCY

- Check total and free levels of AEDs monthly.
- Consider early genetic counseling.
- Check maternal MSAFP levels and perform a level II fetal survey and ultrasonography at 19-20 weeks' gestation.
- Consider amniocentesis for alpha-fetoprotein and acetylcholinesterase.

MULTIPLE SCLEROSIS (MS) IN PREGNANCY

It is a multifocal autoimmune disease of the central nervous system (CNS). It is characterized by relapsing and remitting natural history with inflammation, demyelination and axonal damage in the CNS. Exact aetiology is not known but genetic predisposition and viral infection do play a role. Patient may present with optic neuritis (loss of vision, diplopia), muscle weakness, dysarthria, ataxia, hyperreflexia, bladder dysfunction.

EFFECT ON PREGNANCY

Various studies confirm that pregnancy does not accelerate the course of MS in pregnancy and infant may have protective effect. However, relapses are more common in puerperium. Women may fatigue easily and urinary

infections are common in women with bladder dysfunction.

Management of MS During Pregnancy

It's tailored for individual patients. For moderate to severe relapses, intravenous high dose prednisolone followed by a tapering course of oral steroids is given. Imipramine is useful for urinary urgency. Baclofen may be given for spasticity and paroxysmal pain and anticonvulsant drugs for epilepsy.

Beta interferon therapy reduces the development of brain lesions and lowers the frequency of relapses but is very expensive. There is not enough data of its safety in pregnancy, but it doesn't appear to be teratogenic. Cyclophosphamide and azathioprine are less effective than interferon but are cheaper.

Vaginal delivery is allowed except when serious disability may make vaginal delivery impractical in which case cesarean delivery should be performed. Epidural anesthesia can be given. Breast feeding is avoided during interferon therapy.

MYASTHENIA GRAVIS

It's an immune mediated neuromuscular disorder of unknown etiology in which IgG mediated destruction of postsynaptic striated muscle acetylcholine receptors. There is easy fatigability of facial, oropharyngeal, extraocular and limb muscles. The disease is marked by exacerbations and remissions. Exacerbation may be precipitated by systemic disease, concurrent infections and emotional upsets. There may be thymic hyperplasia or thymoma in upto 75 percent women and may need thymectomy. Treatment is with longer acting acetyl cholinesterase inhibitors like neostigmine and pyridostigmine which are the first line drug and can be given in pregnancy. Immunosuppressive therapy (steroids, azathioprine and methotrexate) are second line drugs. Plasmapheresis and intravenous immunoglobulin infusions are used for serious exacerbations.

Pregnancy doesn't affect the course of myasthenia gravis. They can deliver vaginally and epidural analgesia can be given. Acetylcholine receptor IgG antibody have been detected in maternal serum. They cross the placenta and can cause neonatal effects like feeble cry, poor suckling and depression of respiration.

Pregnancy should be managed in association with neurologist. During labor, anesthetist and neonatologist should be involved. Regular fetal monitoring is recommended. In second stage, there may be fatigue of skeletal muscles necessitating instrumental delivery. Magnesium sulphate is contraindicated for treatment of hypertension or eclampsia in such women.

Neonate should be observed for any signs of myasthenia gravis and breast feeding is given with caution if anticholinesterase drugs are given.

RECOMMENDED READING

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