Epilepsy in pregnancy

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Epilepsy is the most common neurologic condition in pregnancy. Therefore all doctors involved should know how to counsel women with epilepsy as they are considering pregnancy. Over 90 percent of women with epilepsy have a normal pregnancy. This should be emphasized to the patient who is likely to have many fears and anxieties regarding the risks. The management of pregnancy and epilepsy will be discussed here.

Preconception management

Preconception counseling is important for all women of child bearing years because many pregnancies are unplanned and the risks of complications can be minimized by interventions before and early in pregnancy.

Contraception

Women with epilepsy should be aware that hormonal contraceptive failure may occur with antiepileptic drugs (AEDs) which are inducers of the hepatic cytochrome P-450 system (phenytoin, phenobarbital, carbamazepine, oxcarbazepine, primidone, topiramate).

Folic acid supplementation

Low serum folate levels in women with epilepsy are independently associated with an increased risk of major fetal malformations. It has not yet been conclusively determined if folic acid supplementation prevents neural tube defects in women receiving AEDs. An observational study in women with epilepsy found that the incidence of neural tube defects were similar in women who reported preconceptual use of folic acid compared to those who reported to have begun folic acid supplementation later in pregnancy. The 2009 American Academy of Neurology and American Epilepsy Society guidelines state that data are insufficient to determine whether doses higher than 0.4 mg offer greater protective benefits. The American College of Obstetricians and Gynecologists recommend 4.0 mg of folic acid daily for women at risk of having an offspring with neural tube defects (including women taking AEDs).

Choice of antiepileptic drug

If it is felt that medications cannot be withdrawn, the patient should take the most suitable medication for the seizure type. The optimal treatment of women with epilepsy who are of childbearing age is unclear. As it would be problematic to perform randomized controlled trials assigning women with epilepsy to various anticonvulsant choices prior to pregnancy, most of the available data regarding outcome of pregnancy on anticonvulsants come from matched cohort observational studies such as pregnancy registries.

Since there is no agreement as to which AED is most or least teratogenic, the AED that stops seizures in a given patient is the one that should be used. An exception is valproate. Early results from pregnancy registries and most recent cohort studies suggest a trend toward higher teratogenicity with valproate than with other AEDs. It is reasonable to avoid valproate in women planning to become pregnant whose seizures can be adequately controlled with other AEDs. If valproate is used, high plasma levels (>70 μg/mL) should be avoided unless necessary to control seizures, and the drug should be given in three/four divided doses daily.

Other recommendations:

- The AED should be administered at the lowest dose and lowest plasma level that protects against seizures.
- The plasma drug level should be monitored regularly during pregnancy including, if available, the physiologically important free or unbound drug concentration.
- Polypharmacy should be avoided where possible.
- In established pregnancy, decisions to alternate AED therapy should not be undertaken solely to reduce teratogenic risk, but for other reasons. Changing AEDs may precipitate seizures. Overlapping AEDs during the change exposes the fetus to effects of an additional AED and polypharmacy. There is limited advantage in changing AEDs if pregnancy has already been established.

Management in pregnancy and delivery

While all the usual recommendations for women of child bearing potential apply, including preconceptual and ongoing use of folic acid, calcium and Vitamin D, additional consideration must be given to the need for adjustment of anticonvulsant therapy. Many women who experience increased seizure frequency during pregnancy are sleep-deprived or noncompliant because of concerns about the effects of the medication on the developing fetus. Preconception counseling may play a role in minimizing this risk. It is important to emphasize the importance of adequate sleep, medical compliance, and minimizing stress and other factors known to precipitate seizures.

Screening for malformations

Screening for major anomalies pro-

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Competing interests: None

March 2013 Sri Lanka Journal of Obstetrics and Gynaecology 1
vides the patient with the opportunity to terminate the pregnancy if a malfor-
mation is present. Even if the patient
would not consider termination, it
may be helpful to know if a major
defect is present in order to plan the
optimum mode of delivery and to refer
the patient to a center with specialty
pediatric services for delivery.

Drug levels and dose adjustment
Pregnancy is accompanied by many
alterations in drug metabolism,
including increased liver metabolism,
renal clearance, and volume of distri-
bution, and decreased gastroin-
testinal absorption and plasma protein
binding8. For example, for AEDs that
are highly protein bound such as
phenytoin, valproate, the total plasma
drug level may decrease with impai-
red protein binding, but the physiolo-
gically important free or unbound
drug concentration may not change.
As a result, free drug levels for these
AEDs may be more reliable during
pregnancy. However, medication
dosage should be adjusted if the patient's seizures are not controlled,
not relying solely on the free or total
level that has decreased.

Vitamin K supplementation
The 2009 AAN AES guidelines con-
cluded that there was not sufficient
evidence to recommend for or against
this practice5. Most physicians recom-
mand administration of prophylactic
vitamin K (10 to 20 mg/d) during
the last month of pregnancy to women
treated with AEDs to protect the child
against severe postnatal bleeding due
to a deficiency in vitamin K-dependent
clotting factors8.

At delivery
Most women have a normal vaginal
delivery10. However, elective cesarean
section may be justified in women
with frequent seizures during the
third trimester or a history of status
epilepticus during severe stress11.
Doses must not be missed during the
period of labor. Convulsive seizures
during labor and delivery should be
treated promptly with intravenous
benzodiazepines; lorazepam is con-
sidered the drug of choice10. Magnesium
sulfate is not an appropriate alter-
native for epileptic seizures. However,
when seizures first present during the
third trimester of pregnancy or the
early postpartum period, it may be
difficult to distinguish eclampsia from
a new onset or late relapse of epilepsy.
In these cases, treatment of eclampsia
and evaluation of other etiologies for
the seizure is warranted.

Management in the postpartum
period
If the AED dose has been altered
during pregnancy, a return to prepreg-
nancy levels should be considered
during the first few weeks after
delivery. The mother needs to be
advised of the importance of adequate
rest, sleep and compliance with drug
therapy. Precautions need to be taken
to protect the infant if the mother has
a seizure. It is prudent, for example,
to have another person present when
the mother bathes the child. In
addition, the baby should be changed
on the floor or an alternative safe
position.

Breast feeding
There is no evidence to determine
whether this form of AED exposure
has clinical effects on the newborn9.
Most experts believe that taking AEDs
does not generally contraindicate
breast feeding, as probable benefits
outweigh risks1.

Problems tend to occur only with
the sedative drugs, such as phenobar-
bital, primidone, or benzodiazepines.
Exposure to these drugs may cause
the child to become irritable, fall
asleep shortly after beginning to
nurse, or fail to thrive. If this occurs,
breast feeding may need to be
discontinued but can be retried one
week later.

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