

Epilepsy in Pregnancy: An Evidence- Based Management



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Background



Epilepsy is a group of neurological diseases characterized by epileptic seizures that can vary from brief and nearly undetectable to long periods of vigorous shaking. (WHO 2016)

Epilepsy is one of the most common neurological conditions in pregnancy, with a prevalence of 0.5–1%. (Edey S, et al 2014)

Background

- 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.

Background

- **Phenytoin** (Dilantin[®]) and **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.



Diagnosis of epilepsy in pregnancy

- Diagnosis of epilepsy **should be** made by a *neurologist*.
- Women with epilepsy (WWE), their families and healthcare professionals *should be aware of the different types of epilepsy and their presentation* to assess the specific risks to the mother and baby.
Table (1)

Table 1. Clinical presentation of various seizures types and their effects on the mother and baby

Common types of epilepsy/seizures	Clinical presentation	Effects on mother and baby
Tonic-clonic seizures (previously known as grand mal)	Dramatic events with stiffening, then bilateral jerking and a post-seizure state of confusion and sleepiness.	Sudden loss of consciousness with an uncontrolled fall without prior warning. Associated with a variable period of fetal hypoxia. ²² This seizure type is associated with the highest risk of SUDEP.
Absence seizures	Generalised seizures that consist of brief blank spells associated with unresponsiveness, which are followed by rapid recovery.	Effects mediated through brief loss of awareness although physiological effects are modest. Worsening absence seizures place the woman at high risk of tonic-clonic seizures.
Juvenile myoclonic epilepsy	Myoclonic jerks are the key feature of this form of epilepsy and often precede a tonic-clonic convulsion. These jerks present as sudden and unpredictable movements and represent a generalised seizure.	Occurs more frequently after sleep deprivation and in the period soon after waking or when tired. The sudden jerks may lead to falls or to dropping of objects, including the baby.
Focal seizures (previously defined as 'complex partial' if seizures impair consciousness and 'simple partial' if consciousness not impaired)	Symptoms are variable depending on the regions and networks of the brain affected. Within an individual, the attacks are recognisable and stereotypical. Seizures may impair consciousness. Primary focal seizures can undergo secondary generalisation. An aura is a primary focal seizure.	Impairment of consciousness increases risk of injury such as long bone fracture, dental or head injury, electrocution or burns compared with if consciousness is retained (an epileptic aura only). They can be associated with a variable period of hypoxia and risk of SUDEP.

Differential diagnosis

- **Eclampsia** : pregnant women presenting with seizures in the second half of pregnancy which cannot be clearly attributed to epilepsy, *immediate treatment should follow existing protocols for eclampsia management* until a definitive diagnosis is made by a full neurological assessment. (✓)

Differential diagnosis

- **Other conditions should be considered; (✓)**
 - Cardiac conditions
 - Metabolic disorders
 - Intracranial conditions
 - Neuropsychiatric conditions including non-epileptic attack disorder.

Pre-Conception Counseling





Pre-conception counseling

1- Follow-up by a *clinician competent* in the management of epilepsy take responsibility for sharing decisions around **choice** and **dose** of AEDs, based on the risk to the fetus and control of seizures.



Pre-conceptional counsel.

2. WWE; reassured that most mothers have normal healthy babies and the *risk of congenital malformations is low* if they are *not* exposed to AEDs in the *peri-conception period*.

3. WWE Should be informed that the *risk of congenital abnormalities in the fetus is dependent on the type, number and dose* of AEDs.

Anti-Epileptic Drugs (AEDs)



ENZYME-INDUCING AEDs	NON ENZYME-INDUCING AEDs
<ol style="list-style-type: none">1. Carbamazepine,2. phenytoin,3. Phenobarbital,4. Primi-done,5. Oxcarba-zepine,6. Topira-mate7. Esli-carbazepine	<ol style="list-style-type: none">1. Sodium valproate,2. Levetira-cetam,3. Gabapentin,4. Viga-batrin,5. Tia-gabine6. Pre-gabalin

Table 2: fetal anomalies associated with AEDs

Fetal Anomaly	<u>Phenytoin</u>	<u>Phenobarbital</u>	<u>Primidone</u>	Valproate	Carbamazepine	Trimethadione
Neural tube defects	X	X	...
IUGR	X	X
Microcephaly	X	X
Low IQ	X	...	X	X
Distal digital hypoplasia	X	X	X
Low-set ears	X	X	X
Epicanthal fold	X	X	...	X	X	X
Short nose	X	X	...	X	X	...
Long philtrum	X	...	X	...
Lip abnormality	X	X	X	X
Hypertelorism	X	X
Developmental delay	...	X	X	X
Other	Ptosis	Ptosis	Hirsute forehead	...	Hypoplastic nails	Cardiac anomalies

Minimizing Congenital Abnormalities in WWE



1. **5 mg/day of folic acid** prior to conception and to continue the intake until at least the end of the first trimester to reduce the incidence of major congenital malformation especially **cognitive** deficits .
2. The **lowest** effective dose of the most appropriate AED should be used .

Minimizing Congenital Abnormalities in WWE

3. Exposure to *sodium valproate* and other AED poly-therapy should be **minimized** by changing the medication prior to conception, as recommended by an epilepsy specialist after a careful evaluation of the potential risks and benefits.

Polytherapy  monotherapy

Pregnancy Management



Antepartum Management; ...counseling...



- Two-thirds of WWE will **not** have seizure deterioration in pregnancy.
- Pregnant women who have experienced seizures in the **year** prior to conception require **close** monitoring for their epilepsy.

Antepartum Management; ...counseling...



- WWE should be provided with verbal and written information on:
 1. prenatal screening and its implications,
 2. the risks of self-discontinuation of AEDs
 3. effects of seizures and AEDs on the fetus and on the pregnancy, breastfeeding and contraception.

Antepartum Management; ...counseling...



- Healthcare professionals need to be aware of the **small** but **significant** increase in obstetric risks to WWE and those exposed to AEDs.
- Introduction of a few **safety precautions** may significantly reduce the risk of accidents and minimize anxiety.
- Healthcare professionals should **acknowledge** the **concerns** of WWE and be aware of the effect of such concerns on their adherence to AEDs.

Antenatal management: *...the settings...*



- Access to **regular planned** antenatal care with a designated epilepsy care team.
- WWE taking AEDs who become **unexpectedly** pregnant should be able to discuss therapy with an **epilepsy specialist** on an urgent basis. It is **never** recommended to **stop** or change AEDs abruptly without an informed discussion.



Antepartum management

-Screening for fetal anomalies-

- Early pregnancy can be an opportunity to screen for ***structural abnormalities***. The fetal anomaly scan **at 18⁺⁰–20⁺⁶ weeks** of gestation can identify major cardiac defects in addition to neural tube defects.
- All WWE should be offered a detailed ultrasound.

Antepartum management

Monitoring AEDs



- Based on current evidence, **routine** monitoring of serum AED levels in pregnancy is **not** recommended *although individual circumstances may be taken into account.*
- We should be alert to signs of **depression, anxiety** and any **neuropsychiatric** symptoms in mothers exposed to AEDs.

Antepartum management

-Monitoring pregnancy-



- **WWE are regularly assessed for the following:**
 - Risk factors for *seizures*, such as sleep deprivation and stress;
 - Adherence to AEDs; and
 - Seizure type and frequency.
- **WWE at reasonable risk of seizures should be accommodated in an environment that allows for continuous observation .**

Antepartum management

Monitoring pregnancy (cont.)



- Serial **growth** scans are required for detection of small-for-gestational-age babies and to plan further management in WWE exposed to AEDs.
- There is **no** role for *routine* antepartum fetal surveillance with CTG in WWE taking AED

Antepartum management



Role of vitamin K

- All **babies** born to WWE taking *enzyme-inducing AEDs* should be offered **1 mg** of intramuscular vitamin K to prevent hemorrhagic disease of the newborn.
- There is **insufficient** evidence to recommend routine **maternal** use of oral vitamin K to prevent hemorrhagic disease of the newborn in WWE taking enzyme-inducing AEDs.
- There is **insufficient** evidence to recommend giving vitamin K to WWE to prevent **postpartum** hemorrhage.

Antepartum management

Antenatal Corticosteroids



- **Doubling** of the antenatal corticosteroid dose for prophylaxis against respiratory distress syndrome in the newborn is **not routinely recommended** in WWE taking enzyme-inducing AEDs who are at risk of **preterm** delivery.

WHEN & HOW TO DELIVER

- WWE should be reassured that most will have an uncomplicated labor and delivery.
- The diagnosis of epilepsy per se is **not** an indication for planned **cesarean** section or induction of labor.
- There are **no known** contraindications to use of any **induction agents** in WWE taking AEDs.

WHERE TO DELIVER

- *Delivery should be in a consultant-led unit with facilities for one-to-one obstetric care and maternal and neonatal resuscitation.*
- WWE who are not taking AEDs and who have been seizure free for a significant period may be *offered a water birth (on request)* after discussion with their epilepsy specialist.



INTRAPARTUM CARE

- WWE should be counseled that the risk of seizures in labor is **low**.
- Adequate analgesia and appropriate care in labor should be provided to minimize risk factors for seizures such as *insomnia*, *stress* and *dehydration*.
- Long-acting **benzodiazepines** such as **clobazam** can be considered if there is a **very** high risk of seizures in the peripartum period.
- AED intake should be **continued** during **labor**. If this cannot be tolerated orally, a *parenteral alternative* should be administered.



INTRAPARTUM CARE

MANAGEMENT OF EPILEPTIC SIZURE IN LABOR

- Seizures in labor should be terminated as *soon as possible* to avoid maternal and fetal hypoxia and fetal acidosis. **Benzodiazepines** are the drugs of **choice**.
- Continuous fetal monitoring is **recommended** in women at high risk of a seizure in labor, and following an intra-partum seizure.

INTRAPARTUM CARE



ANALGESIA


- Pain relief in labor should be **priority** in WWE, with options including **transcutaneous** electrical nerve stimulation (TENS), nitrous oxide and oxygen (**Entonox[®]**), and regional analgesia.
- **Pethidine** should be used with **caution** in WWE for analgesia in labor. **Diamorphine** should be used in preference to pethidine.



POSTPARTUM CARE

- Although the overall chance of seizures during and immediately after delivery is **low**, it is relatively **higher** than during pregnancy.
- AEDs should be continued **postnatal**.
- Mothers should be well supported in the postnatal period to ensure that ***triggers of seizure*** deterioration such as sleep deprivation, stress and pain are minimized.

POSTPARTUM CARE

- If the AED dose was increased in pregnancy, *it should be reviewed within 10 days* of delivery to avoid postpartum toxicity.
- Neonates born to WWE taking AEDs should be monitored for *adverse effects associated with AED exposure in utero*. 
- WWE who are taking AEDs in pregnancy should be *encouraged to breastfeed*.
- Based on current evidence, mothers should be informed that the risk of adverse *cognitive* outcomes is **not increased** in children exposed to AEDs through breast milk.

POSTPARTUM CARE

- Postpartum *safety advice and strategies* should be part of the antenatal and postnatal discussions with the mother alongside breastfeeding, seizure deterioration and AED intake.
- Postpartum *continuous observation should be offered* to mothers with epilepsy at reasonable risk of seizures.
- WWE should be *screened for depressive disorder* in the puerperium.

CONTRACEPTION

- WWE should be offered effective contraception to *avoid unplanned* pregnancies.
- The risks of contraceptive failure and the short- and long-term adverse effects of each contraceptive method should be carefully explained to the woman.
- Effective contraception is extremely important with regard to stabilization of epilepsy and planning of pregnancy to optimize outcomes.

CONTRACEPTION

- Copper intrauterine devices (IUDs), the levonorgestrel-releasing intrauterine system (LNG-IUS) and medroxyprogesterone acetate injections *should be promoted* as reliable methods of contraception that are *not affected* by enzyme-inducing AEDs.
- Women taking enzyme-inducing AEDs should be counseled about the risk of failure with some hormonal contraceptives.

CONTRACEPTION

- Women should be counseled that the efficacy of **oral** contraceptives (combined hormonal contraception, progestin-only **pills**), transdermal **patches**, vaginal **ring** and progestin-**only** implants may be **affected** if they are taking enzyme-inducing AEDs .
- **All methods** of contraception may be offered to women taking **non-enzyme-inducing** AEDs.



CONTRACEPTION

Special Situations

- WWE taking enzyme-inducing AEDs should be informed that a **copper IUD** is the preferred choice for **emergency contraception**.
- Emergency contraception **pills** with levonorgestrel and ulipristal acetate are **affected** by enzyme-inducing AEDs.
- Women taking **lamotrigine** monotherapy and estrogen-containing contraceptives should be informed of the potential *increase in seizures due to a fall in the levels of lamotrigine*.

THANK YOU
FOR YOUR
ATTENTION

References:

- Green-top Guideline No. 68 June 2016
- Uptodate: **Seizure Disorders in Pregnancy**: Author: Aaron B Caughey, MD, MPH, PhD; Chief Editor: Ronald M Ramus, MD -Updated: May 02, 2016