Epilepsy in Pregnancy

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Key Amendments

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4th June 2024	Document extended for another 12 months whilst under review	Maternity Governance
12th February 2025	Document updated with amendments	Maternity Governance Meeting and Medicines Safety Committee

Introduction

Epilepsy affects approximately 0.5–1.0% of women of childbearing age and it is the most common serious neurological condition affecting women of childbearing age (Joint Epilepsy Council 2011).

It can be generalised (tonic-clonic or absence) or focal (which can be accompanied by sensory aura). **Occasionally it can arise secondary to an epileptogenic focus after brain injury, stroke or tumour.**

Non-epileptic attack disorder (NEAD) is a separate often challenging condition. The principles of management for this are included at the end of this guideline.

The rate of indirect maternal deaths has remained static. The most recent MBRRACE report lists neurological causes (i.e. epilepsy and strokes) as the second most prevalent cause of maternal death. Maternal deaths from epilepsy are usually from SUDEP (Sudden Unexpected Death in Epilepsy), status epilepticus or accidents such as drowning. There is increasing evidence around the importance of pre-conception counselling and antenatal care with an MDT approach to reduce morbidity and mortality.

Most women will have pre-existing diagnosis of epilepsy in pregnancy and de novo diagnosis is rare.

Consideration for midwifery led care can be advised if:

1. Seizure free for 10 years and off AED (Anti-Epileptic Drugs) for >5 years
2. Childhood diagnosis of seizure disorder and treatment and seizure free in adult life

Impact of pregnancy on Epilepsy

- Two thirds of people with epilepsy will remain stable in pregnancy or see seizure control improve.
- If seizure free for 12 months prior to conception, 90% will remain seizure free during pregnancy.

- Remaining third of people will experience deterioration in seizure control. This is more commonly seen in women with poor control prior to pregnancy or for those on polypharmacy.

- Peripartum poses the highest risk for seizures, with 1-4% occurring in labour and 24 hours after delivery.

- Pregnancy may affect AED levels. Lamotrigine is the most affected with the potential for levels to drop by 70%. Levetiracetam can drop by 40% and Topiramate by 30%. Advise women of this pre-conceptionally and emphasise the importance of continuing with prescribed medications, whilst reassuring that it may be necessary to increase dosage in pregnancy to achieve control.

Impact of epilepsy and AED on pregnancy

Women with epilepsy are naturally anxious regarding the use of AED in pregnancy. MBBRACE is clear that AEDs should not be abruptly discontinued with careful consideration by neurology teams.

Background risk of congenital malformations is 2-3%. AED increases the risk to 4-10%. The risk increases with higher dosages and polypharmacy.

Congenital malformations include:

- Neural tube defects (Valproate, Carbamazepine)
- Congenital heart defects (Phenobarbitals, Phenytoin)
- Orofacial cleft (Carbamazepine, Phenytoin)

Levetiracetam (1.77%), Lamotrigine (2.31%) and Carbamazepine (3.0%) have the lowest rates of teratogenicity when used as a monotherapy. In addition, reassure women that there is no evidence of neurodevelopmental delay in children exposed in utero to these AEDs.

Sodium Valproate (Epilim) has a high teratogenic potential. Exposed fetuses have up to 11% risk of congenital malformation and 30-40% risk of neurodevelopmental disorder which may lead to permanent disability. Valproate should not be used for women <55 years of age unless two specialists experienced in the management of epilepsy or bi-polar disorder independently consider and document that there is no other effective or tolerated treatment.

Topiramate use during pregnancy can increase the risk to the fetus of congenital malformation (4-9 per 100), low birth weight, 2 to 3 times increased risks of intellectual disability, autistic spectrum disorder and attention deficit hyperactivity disorder. Topiramate should not be used in women of childbearing potential unless the conditions of the Pregnancy Prevention Programme are fulfilled.

Women should be made aware that deteriorating seizure control is detrimental to fetal development, growth and child IQ, mainly through impaired oxygen delivery and uterine trauma. It is therefore imperative to impress on WWE the importance of good AED compliance.

Advise women that epilepsy is not an indication for planned caesarean. The majority of WWE will have an uncomplicated pregnancy and delivery. There is however a small increase in the risk of APH, PPH, pre-eclampsia, preterm birth, IOL and caesarean section. There is also a significantly increased risk of postnatal depression.

Maternal mortality in context of epilepsy is rare. SUDEP increases 10x in pregnancy and is more common where there is a history of nocturnal seizures or where there is an abrupt discontinuation of AED or poor compliance with medication.

Because enzyme inducing AEDs can disrupt neonatal clotting and increase the risk of haemorrhagic disease of the newborn, intramuscular vitamin K should be offer for the newborn.

Vitamin K dosage:

- 1milligrams IM for babies ≥1.5kg
- 0.5milligrams IM for babies <1.5kg

There is no evidence to support the use of oral vitamin K in this clinical scenario.

Antenatal management

- Ideally WWE should be managed in a combined obstetric seizure clinic. Whilst waiting for this to be established in WAHT, good MDT liaison is key for the successful management of these patients.
- Review early in first trimester
- Perform routine dating scan and routine 1st trimester screening
- Discuss with women:
    - Seizure type
    - Frequency of seizures
    - Which AED woman is taking and document dose and compliance
    - Where women have abruptly stopped their AED without discussion urgent referral to Maternal Medicine clinic is required. Epilepsy teams should also be made aware.
    - If taking Levetiracetam, Lamotrigine or Oxcarbazepine should have AED levels taken at booking, at 28 weeks and if there is any increase in frequency of seizures.
    - The AED level should be in the normal range as per the lab reference. Any concerns about AED levels or frequency of seizures or patients on more than one AED, patients should be referred to neurology team through Badgernet referrals. **Only monitor levels for other AED if non-compliance is suspected.**
- Offer inclusion on the UK Epilepsy and Pregnancy Register www.epilepsyandpregnancy.co.uk
- Discuss risks for seizures such as sleep deprivation and stress
- Give general advice regarding coping with morning sickness and avoiding seizure triggers. Threshold for anti-emetics should be low to minimise the risk of poor absorption which might impact on seizure control.
- Risks of baths should be discussed and strategies such as showers with unlocked bathroom door considered.
- Sign post women to these support groups: www.EpilepsyAction.co.uk and www.womenwithepilepsy.co.uk
- Ensure Paediatric Alert added to Badger if woman is taking AEDs.
- Advise to call 999/present to A&E if they are having prolonged seizures lasting >5 minutes or more than 3 seizures in 1 hour.

Owing to the association between AEDs, epilepsy and FGR, organise serial growth scans. Where there is good epileptic control and no additional risk factors, growth scans at 32 and 36 weeks is acceptable. Where there is poor control and/or polypharmacy, start growth scans at from 28 weeks.

It is important to remember that WWE may have poor mental health or additional needs e.g. learning difficulties. Where appropriate offer perinatal mental health referral or additional support.

If admitting to the antenatal ward for any reason, aim to care for the woman in an open bay to avoid risk of lone seizures.

Discuss postnatal care of baby:

- Changing nappies on floor
- Feeding on floor
- Avoiding bathing baby when alone
- Avoid co-sleeping
- Placing baby in carry seat when using stairs

Delivery Planning

Discuss birth preferences, analgesic options and precautions in labour around 36 weeks gestation. Epilepsy is not a contraindication to normal vaginal birth.

In the absence of fetal growth concerns, deteriorating seizure control or any other concerns, epilepsy is not an indication for routine IOL. Since seizure control can be more challenging in the 3rd trimester, it is not unreasonable to offer IOL around term where control is problematic. Clobazam and Clonazepam can be useful adjuncts around term and intrapartum where control is poor.

There is a 1-4% chance of seizure activity intrapartum, hence women should be informed of the importance of continuing AED throughout labour and postnatally.

Avoid prolongation of latent phase as this can lower the seizure threshold through sleep deprivation.

Recommend delivery on consultant-led unit and avoid birthing pools.

In the absence of other risk factors, it is acceptable for well controlled epilepsy, a well grown baby and spontaneous onset of labour to receive intermittent auscultation.

IV access should be considered due to 1-4% risk of Intrapartum seizure.

Continue normal administration of AED in labour

Ensure good hydration in labour.

Poor epileptic control is associated with placental insufficiency and therefore CEFM in labour should be recommended.

Pain, stress and lack of sleep are all seizure triggers. Women can be offered TENS, Entonox and PCA remifentanil infusions. Epidural is also a good option. Pethidine should be avoided since it has an epileptogenic metabolite and will therefore lower seizure thresholds.

Breastfeeding whilst on AEDs is generally safe. This is especially true for levetiracetam and lamotrigine. Breastfeeding should therefore be encouraged as optimum feeding method for baby. Women on a high dose of Lamotrigine (>850milligrams/daily) should be made aware that there are some reports of neonatal rashes and drowsiness.

The infants of mothers who have been taking levetiracetam during pregnancy, should be monitored for sedation, poor feeding, adequate weight gain and developmental milestones.

Withdrawal effects may happen in infants of mothers who have suddenly stopped breastfeeding, especially if she was taking phenobarbital, primidone or lamotrigine.

If a woman on AEDs delivers preterm and wants to breastfeed, it is important to liaise with neonatal teams. Infant metabolism in preterm infants is slower in the pre-term and so there is the potential for drug accumulation and toxicity. Lamotrigine is especially likely to accumulate.

Encourage women to express breast milk, to enable partners to support feeding with breast milk, enabling women to get adequate rest at night.

Postnatal care

- If epilepsy is well controlled, discharge can be performed within 24 hours, following obstetric review.
- 1–2% will have a seizure within 24 hours of delivery
- Where there has been an increase in AED during pregnancy, they will need to be reduced postnatally to avoid toxicity. Arrange follow up with the epilepsy specialist nurse 6 weeks postnatal for review.
- Reiterate the messages around safety with newborn.
- Reiterate the importance of rest, hydration ad AED compliance.
- Reiterate bath and shower safety messages.
- Offer Vitamin K to baby as detailed above.
- Consider contraception in accordance with FSRH. AED may alter efficacy of various methods. Furthermore, AED levels can be affected by various contraceptive agents.

NEAD (Non-Epileptic Attack Disorder)

- NEAD are self-limiting, involuntary movements with no epileptiform changes seen n EEG.
- They may result in tongue biting, urinary or faecal incontinence, hence confusion with true epilepsy.
- There is a strong association with major depressive disorders, personality disorders and post-traumatic stress disorder
- Management includes CBT and reassurance around pregnancy outcomes.
- In context of seizure activity, reassure the woman, adopt the recovery position and remove any hazards.
- Discuss importance of minimising postnatal stress and need for rest.

Pre-pregnancy counselling

It is good practice to ensure that women with epilepsy (WWE) who are considering a pregnancy be offered the opportunity to engage in pre-pregnancy counselling, to ensure optimisation of both fetal and maternal wellbeing.

A history should be taken to determine the type of epilepsy, timing of last seizure, seizure frequency and any AED medication history.

There should be a discussion regarding the impact of pregnancy on the epilepsy and the impact of the epilepsy and AEDs on the pregnancy,

Women with epilepsy should be informed that they are likely to have a healthy outcome.

For women who have been seizure free for 9 months to a year prior to pregnancy, over 75% will remain seizure free throughout their pregnancy.

All women on AEDs should be offered 5mg of folic acid. This should be commenced at least 3 months prior to pregnancy.

Aim to be seizure free prior to pregnancy. This is especially important for women with generalised tonic-clonic epilepsy. Consider advising the continuation of contraception whilst stabilising epileptic control.

Consider the potential adverse effect of AEDs and aim to use the lowest effective dose possible, avoiding the use of polytherapy where possible.

Consider a baseline AED level for those planning pregnancy who are taking any of the following: Carbamazepine, Lamotrigine, Levetiracetam, Oxcarbazepine, Phenobarbital, Phenytoin.

Ask women about their adherence to medication.

Appendix 1

Management of seizures in pregnancy and birth

- Termination of seizures is important for maternal wellbeing and reduction or fetal hypoxia
- Most self-arrest in less than 2 minutes. Manage conservatively in left lateral tilt and create safe environment. Do not restrain the woman. Remove hazards as much as possible.

Status epilepticus

This is where seizure activity is ongoing for >5 minutes or where one seizure is followed by another without regaining consciousness. This is a life threatening emergency.

Remember to consider eclampsia in all women with seizures >20/40.

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- Call for help and put out crash call 2222
- Position patient to avoid injury, ideally in left lateral.
- Apply high flow oxygen and maintain airway

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- Seizures are best managed with IV benzodiazepines
    - **IV Lorazepam 4 milligrams (Diazepam 10 milligrams IV if no lorazepam)**
- In the absence of IV access:
    - Diazepam 10-20milligrams Rectal (PR)
    - Midazolam 10milligrams Buccal
    - Lorazepam 4milligrams intramuscular (IM)

If no response REPEAT DOSE within 5-10 mins

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- Continuous or recurrent seizures without recovering consciousness 20 minutes after seizure onset IV LEVETIRACETAM 60milligrams/kg (max 4500mg) over 5 to 15 minutes or IV Lacosamide 400milligrams if allergic to Levetiracetam with support from neurology and critical care.

- If uterus is persistently hypertonic, consider tocolysis.
- Once mother stabilised, commence CTG and if fetal heart does not recover in 5 minutes, expedite delivery.
- Inform neonatal team if benzodiazepines/phenytoin given.

Appendix 2

Contraception and AEDs

Enzyme inducing drugs:	**Non-enzyme inducing drugs:**
• Carbamazepine • Phenytoin • Phenobarbital • Primidone • Oxcarbazepine • Topiramate • Eslicarbazepine **Safe to use:** • Copper IUD • Levonorgestrel-releasing intrauterine device (Mirena) • Medroxyprogesterone acetate (DEPO injection) **Avoid:** • Implants • COC • POP	• Sodium valproate • Levetiracetam • Gabapentin • Vigabatrin • Tiagabine • Pregabalin • Lamotrigine **Safe to use all methods** ***Exception*** ***If on lamotrigine (LTG) do not use combined hormonal contraception as reduces LTG levels leading to loss of seizure control.***

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