TYGERBERG HOSPITAL

Department of Obstetrics and Gynaecology: General Specialist Services

PROTOCOL FOR THE MANAGEMENT OF EPILEPSY IN PREGNANCY AT TYGERBERG HOSPITAL

Epilepsy affects about 0.5% of women of child-bearing age and is the commonest chronic neurological disorder to complicate pregnancy. It carries significant risk of morbidity for both mother and fetus. Up to a third of pregnant women may have loss of seizure control. Women with epilepsy are also at increased risk for caesarean section and abruptio placenta. On the fetal side there is the risk of teratogenicity of Anti-epileptic drugs to consider, a 4% lifetime risk of epilepsy and a risk for the development of neonatal coagulopathy.

Contents

1. List of abbreviations

AEDs	Anti-epileptic drugs	IOL	Intelligence quotient	UGD	Urogenital defects
CAB	Circulation-Airway-Breathing	IQ	Intelligence quotient	TB	Tuberculosis
CTG	Cardiotocograph	MEC	Medical eligibility criteria	TBH	Tygerberg Hospital
CVS	Cardiovascular	MSE	Mental state examination	TTP	Thrombotic thrombocytopenic purpura
ETOH	Ethanol	NTD	Neural tube defects	WHO	World Health Organisation
HRC	High risk clinic	PR	Per rectum	WWE	Women with epilepsy
IVI	Intra-venous injection	SFH	Symphysis fundal height		

2. Pre-conception counselling

- Ensure therapy with lowest teratogenicity used
    - First line: Lamotrigine; Levetiracetam (expensive, must be prescribed by Neurologist)
    - Carbamazepine or Phenytoin should be continued if well controlled
    - Sodium Valproate should be avoided, and patient counselled to change to Lamotrigine, as valproate
        - poses a significant risk to the fetus/offspring
        - 10% risk of congenital abnormality (NTD, UGD, CVS and limb malformations)
        - Up to 40% risk of neurodevelopmental problems (lower IQ, autism)
- Optimise seizure control on lowest effective dose of treatment
- More than one seizure per year (poor control) is a risk factor for seizures during pregnancy
- Initiate folate 5mg/d at least 6 weeks preconception and use for the duration of the pregnancy
- Link with Epilepsy South Africa
    - Education, counselling and support groups for WWE and her family
    - Help to get a MedicAlert® bracelet
    - Tel: 0860374537 (office hours)

3. Antenatal care

- Women with good seizure control (≤ 1 seizure during the past year) can follow-up at a district hospital
- Women with ≥2 seizures the past year must be seen at TBH HRC
- Discuss patients with uncontrolled seizures at their first TBH HRC visit with neurology to optimise their AEDs and refer to the Neurology clinic
- Any change in AEDs must be discussed with a consultant obstetrician

First visit

- Full clinical history
    - Type of seizures, date of diagnosis, causative factors (head trauma or surgery, intra-cranial masses, meningitis), medication history, seizure control
- Do dating ultrasound, encourage adherence to AED
- Book detailed fetal anomaly ultrasound at 18-22 weeks' gestation at TBH US unit (ext 5572) on a Monday for all patients on teratogenic drugs (Sodium Valproate, Carbamazepine or Phenytoin)
- High dose folate supplementation (5mg daily per os)

Every visit

- Plot SFH with every visit: growth scan if poor SF growth
- Each follow up visit, assess
    - Seizure control
    - Adherence to medication
    - Risk factors for seizures: sleep deprivation, stress, or substance abuse
    - MSE in each trimester, safety-net regarding depression symptoms and where to access mental health help if needed
- Routine serum drug level screening is not indicated. Women with epilepsy in pregnancy are managed according to clinical seizure control.
- Routine Vit K administration at 36w for mother **not** supported by evidence

4. Women with epilepsy presenting with a seizure during pregnancy

- Resuscitate mother as needed (CAB)
- Turn into recovery position
- Check glucose: if <3 mmol/L give dextrose 10% 5ml/kg IVI and continue glucose management
- Once seizure has terminated, perform full maternal vitals
- If typical seizure for this woman, rapid termination of seizure and short post-ictal period with normal vital signs, appropriate management would include
    - Discuss compliance of AEDs
    - Load with anti-epileptic therapy if sub-therapeutic doses suspected
    - Very important to note that this loading with AEDs can be done **orally,** preferably with the AED that the patient is already using
    - IVI loading is inherently dangerous and needs monitoring, only for patients that need emergency treatment as in the case of status epilepticus
    - Phenytoin is loaded as follows: loading dose of 20 mg/kilogram. Half of the load is given stat and the remaining half 30 minutes or 60 minutes later. Prescribing doctor must remember to always institute daily therapy at the same time.
    - **Consider** taking blood for serum drug levels if compliant on therapy, do not do levels routinely in this scenario or as a method to assess compliance
- Only initiate CTG monitoring once mother is deemed stable (discuss with consultant first)
- If atypical or prolonged seizure with abnormal post-ictal period or vital signs, consider full work-up to exclude other pathology
- **Eclampsia should be excluded in all WWE presenting with a seizure after 20 weeks' gestation**

5. Differential diagnosis for women presenting with a seizure during pregnancy

Vascular	**Eclampsia** Intra-cranial haemorrhage (subarachnoid) Hypertensive encephalopathy Cerebral vein thrombosis TTP
Infection	Meningitis (+/- TB), Encephalitis, Toxoplasmosis
Metabolic	Hyponatremia Hypoglycemia Hypercalcaemia Renal/Hepatic failure
Cardiovascular	Cerebral venous thrombosis Vasovagal syncope Cardiac arrythmia
Neurological	Epilepsy (usually has history) Tumours Traumatic brain injury Previous surgery Stroke
Other	Pseudo seizure Drug/ETOH withdrawal Lithium toxicity Tricyclic antidepressants Gestational epilepsy Postdural puncture

6. Intra-partum management

- The risk of seizures are highest peripartum
- Allow for spontaneous labour at term
- IOL/assisted delivery/caesarean only as per obstetric indication
- Ensure optimal analgesia during labour, offer epidural if available
- Avoid risk factors for seizures: dehydration, insomnia
- Continue AEDs as usual
- Continuous fetal monitoring with CTG during labour
- Pethidine could be epileptogenic if administered repeatedly. Follow standard protocol when prescribing.
- If seizures occur during labour
    - Manage as above
    - **Keep the differential of eclampsia in mind**: consider loading with MgSO4
    - Terminate seizure with short-acting benzodiazepine
        - Lorazepam 2mg IVI (first choice)
        - Clonazepam 0.5-1mg IVI
        - Diazepam 5mg IVI

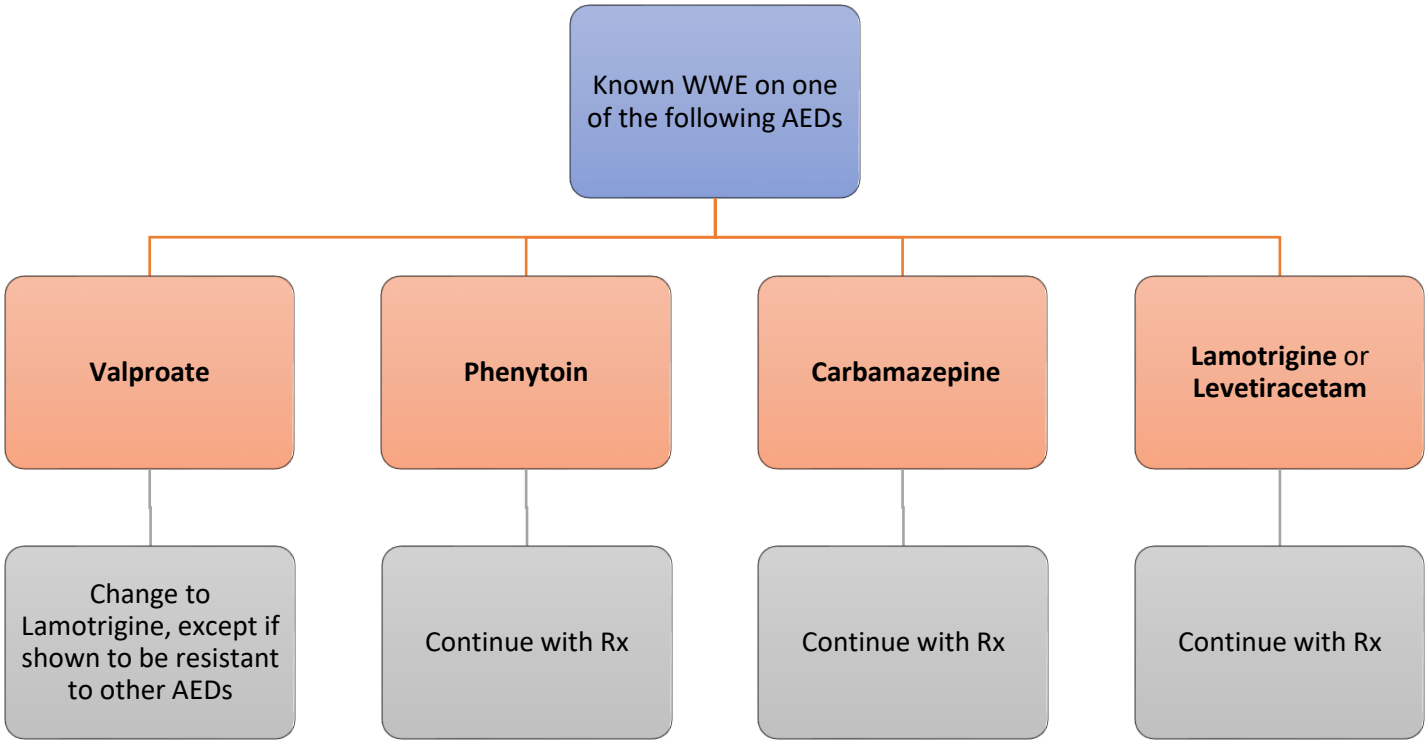
        - If seizure persists load with Phenytoin 20mg/kg IVI over 60 minutes (give phenytoin through different line than benzodiazepine)
        - Phenytoin is loaded as follows: loading dose of 20 mg/kilogram. Half of the load is given stat and the remaining half 30 minutes or 60 minutes later. Prescribing doctor must remember to always institute daily therapy at the same time.
    - Seizures may result in uterine hypertonus-if clinically suspected, add tocolytic (especially if not using MgSO4)
    - Do not perform CTG during seizure or directly post-ictal as CTG will be difficult to interpret
    - Recommence CTG monitoring once mother is stable

7. Post-partum care

- Careful observations for seizure for at least 24 hours as seizure risk is increased
- Preferable to nurse WWE in a room with other mothers, not a single room
- If patient is well controlled, do not change AEDs. If seizures occur, discuss with neurology.
- Screen for post-partum depression (MSE screening)
- Ensure good support and counsel regarding safe practices
    - Adequate sleep, nurse baby on the floor, assistance during bath time, avoid co-sleeping
- Baby
    - to receive routine Vitamin K to prevent neonatal coagulopathy
    - review by paediatric colleagues
    - advise mom and nursing staff to alert doctors if baby suffers lethargy, feeding difficulties, excessive sleepiness, or inconsolable crying
- Breastfeeding is recommended for WWE as it is safe for mother and babies
- Contraception
    - Check WHO MEC if on enzyme-inducing medication
    - 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.
- Give all patients with WWE with poor control during pregnancy a date at Neurology clinic TBH 4 weeks post delivery or alternatively at their closest physician clinic.

8 Guidance on the use of AEDs

8.1 Approach to drug regimens in WWE (pre-conception and pregnant)



8.2 Specific AEDs

8.2.1 Lamotrigine

- First line for use in pregnancy as limited effect on fetus
- Side-effects
    - 10% of patients may experience a rash, 0.1% severe rash that may lead to Stevens-Johnsons syndrome or toxic epidermal necrolysis
    - Thus, it may not be suitable for patients who are not adherent to treatment
- Initiation or change-over from another AED during pregnancy, needs to be done slowly to reduce the risk of triggering a potentially fatal skin reaction.
- If changing from Valproate, this needs to happen even slower, as valproate causes a rise in blood level of Lamotrigine.
- Usual maintenance dose is 100-200mg per day, in divided doses.

8.2.2 Levetiracetam

- Also considered to have limited fetal effect, but also limited data.
- Can be used as second line after Lamotrigine
- Needs to be prescribed/motivated by neurology at TBH
- Avoid in women with history of depression or aggressive behavior.
- Dosage: Initially 500mg twice a day. If further increase needed, increase in increments of 500mg twice daily every 2-4 weeks. Maximum dose is 1500mg twice a day.

8.2.3 Carbamazepine

- Keep on current treatment if well controlled.
- Usual dose is 200mg twice a day

8.2.4 Phenytoin

- Keep on Phenytoin if well controlled, unless she is planning to fall pregnant, then change to Lamotrigine pre-conception

8.2.5 Valproate

- Avoid Valproate, as not only does it have the highest risk of teratogenesis, but also increased risk for neurodevelopmental delay of the fetus (low IQ, autism)
- In rare cases, where Valproate is the only effective therapeutic option, try to limit dose to less than 600mg per day.

8.3 Changing or starting Lamotrigine

- Only specialists and designated prescribers may initiate lamotrigine, thus discuss with neurology and/or obstetrics consultant
- Lamotrigine requires slow upward dose titration
- Patients should specifically be advised to return to a healthcare facility within 24hours should a rash or fever develop. No additional dose of lamotrigine should be taken until a doctor is consulted. The rash may present with fever, flulike symptoms, red or burning eyes, blistering of the skin, or sores on mouth / eyes / vagina

- **Switching valproate to lamotrigine: always discuss with neurology consultant**
    - STEP 1: Lamotrigine started and increase slowly as per table 8.3.1
    - STEP 2: Stop Valproate the same day as initiating Lamotrigine
    - STEP 3: **Add Clobazam** as bridging therapy: duration to be discussed with neurology
        - Start 10mg twice daily
    - STEP 4: Lamotrigine to be adjusted by 50mg every 1-2 weeks according to response.

Table 8.3.1 Lamotrigine initiation: recommended dose schedule	
Weeks	**Dose**
1,2	25mg daily
3,4	25mg twice a day
5	25mg morning, 50mg at night
6	50mg twice a day
Further increase by 50mg every 1-2 weeks, according to response Usual maintenance dose: 100-200mg/day in divided doses	

9. Liaison with Neurology department

- **Same-day** discussion with the **consultant on call for neurology is advised.**
- If urgent assessment by neurology is not indicated, a two-week combined review at both the HRC and the TBH Epilepsy clinic (**only on Tuesdays**) should be booked after discussion with neurology consultant.
    - Make note in patient's folder that they must be seen **early** at HRC as the patient needs to present to the Epilepsy clinic by 12h30 (ext 5541, 7th floor)
- Neurology consultant may give telephonic advice on the same day if the case is complicated by:
    - high frequency of seizures, change in type of seizures, possible non-epileptic seizures

10. References

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