Management of HELLP/AFLP/Eclampsia

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Key Amendments

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Introduction

This guideline aims to offer a clear and comprehensive plan for the management of:

- Severe pre-eclampsia and Eclampsia
- HELLP syndrome
- Acute Fatty Liver of pregnancy

Severe Pre-Eclampsia: Multi-organ disease and clinical features depend upon end organ involvement. It commonly present as proteinuric hypertension.

Eclampsia: Tonic clonic seizures commonly occurring in association with features of pre-eclampsia. More than one third of women experience their first convulsion before the development of hypertension and proteinuria. Convulsions may occur antepartum (38%), intrapartum (18%) and postpartum (44%).

HELLP: Haemolysis Elevated Liver enzymes Low Platelet count (HELLP) is one of the several possible crises that may develop as a variant of severe pre-eclampsia. The incidence of HELLP in pre-eclamptic pregnancies is around 5 – 20%.

Acute Fatty Liver of Pregnancy (AFLP): AFLP is rare occurring in 1:7000 to 1:15000 pregnancies and it is potentially lethal for both the mother and the baby. This condition is more common in primigravidas and it usually presents after 30 weeks often near term.

Diagnosis

Signs of severe pre-eclampsia:

- Severe hypertension (>/= 160/110mmHg) and proteinuria with or without any of the following signs.
- Mild to moderate hypertension (140-150/ 99-109mmHg) and proteinuria with at least one of the following:
  - Severe headache
  - Problems with vision such as - Blurred vision/ flashing ,
  - Altered consciousness
  - Clonus>/= 3beats
  - Epigastric or right hypochondrial pain / Liver tenderness
  - Vomiting
  - Papilloedema
  - Thrombocytopenia <100x10^9/litre
  - Abnormal LFT (ALT/ AST>70in/litre)

- HELLP Syndrome
- Pulmonary Oedema
- Oliguria <500mls in 24 hours

HELLP & AFLP: Pre-eclampsia could be associated with HELLP and some of the presenting symptoms may overlap with symptoms of AFLP. The key features of HELLP are:

- Haemolysis, elevated bilirubin reflecting the extent of haemolysis, elevated transaminases, low or falling platelet count (<100x10^9/L). Elevated LDH > 600u/L.
- HELLP & AFLP can present with vague symptoms and there is often a delay in diagnosis. Therefore a high index of suspicion is required.

Differential diagnosis of HELLP syndrome and AFLP

SYMPTOMS	**HELLP**	**AFLP**
Epigastric pain	++	+
Vomiting	+/-	++
Hypertension	++	+
Proteinuria	++	+
Elevated liver enzymes	+	++
Hypoglycaemia	+/-	++
Hyperuricaemia	+	++
Thrombocytopenia	++	+/-
↑WCC	+	++
USS	Normal/hepatic haematoma	Normal/hepatic steatosis

ECLAMPSIA: Tonic clonic seizures commonly occurring in association with features of pre-eclampsia. More than one third of women experience their first convulsion before the development of hypertension and proteinuria. Exclude other causes of seizures.

Management of Severe Pre-Eclampsia

Transfer the patient to Delivery Suite and commence:

- BP monitoring : Frequency of monitoring as per individual management plan
- If BP >160mmHg systolic and or diastolic >110mmHg treat hypertension as per guideline (WAHT-OBS-028)
- Insert a urinary catheter and maintain hourly Intake & output record / fluid balance.
- Check (haematology)
  - FBC
  - Coagulation screen including fibrinogen levels
  - Group and save serum
- Check (biochemistry)
  - Urea & Electrolytes
  - Liver function tests Requested as PET profile
  - Uric acid
  - Serum creatinine
  - LDH (If there is suspicion of HELLP syndrome)
- Continuous fetal monitoring (CTG)
- Discuss further management with Consultant on call both obstetric and anaesthetist.

- **Prophylactic magnesium sulphate**: Some women with severe hypertension or severe pre-eclampsia (see above for the signs of severe pre-eclampsia) may require prophylactic magnesium sulphate infusion. Prophylactic magnesium sulphate should be considered for women with:
  - Severe hypertension or severe pre-eclampsia who previously had an eclamptic fit.
  - Severe hypertension or severe pre-eclampsia when birth is planned within 24 hour
  - Severe hypertension or severe pre-eclampsia in the immediate postpartum period.

  The MAGPIE study has demonstrated that administration of magnesium sulphate to women with pre-eclampsia reduces the risk of an eclamptic seizure. (See below for regime.)
- Decision regarding timing and mode of delivery should be made by on-call consultant.
- Inform Neonatal Intensive Care Unit if gestation <36 weeks.

Management of Eclampsia
***Remember early involvement of the consultant obstetrician and anaesthetist is of utmost importance.**

Inform the consultant obstetrician, consultant anaesthetist, paediatrician and labour ward co-ordinator.

Aims:
- Resuscitation
- Control and prevent fitting
- Control of hypertension and management of fluid balance
- Safe delivery of the fetus

A - Resuscitation
- Do not leave the patient alone
- Call for help & Inform senior staff and on-call anaesthetist
- Establish airway (± oxygen if 0_2 saturation < 94%)
- Secure I/V access
- Take bloods to check FBC/ urea &electrolytes, serum creatinine& uric acid / LFT/ blood glucose/ clotting profile/ Group & save serum.
- Check initial observations
  - temperature
  - pulse
  - blood pressure
  - plus check fetal heart continuous where possible (CTG)
- Attach pulse oximeter, ECG and BP monitor.
- Consider blood gases
- Catheterise – and record hourly urine output

B - Control and Prevent Fits
Intravenous Magnesium sulphate (MgSO4) is the therapy of choice to control seizures.

Recurrent seizures should be treated with further bolus of magnesium sulphate.

Magnesium toxicity is unlikely with these regimens and levels do not need to be routinely measured. Magnesium sulphate is mostly excreted in the urine. Urine output should be closely observed and if it becomes reduced below 20 ml/hour the magnesium infusion should be halted. Magnesium toxicity can be assessed by clinical assessment as it causes a loss of deep tendon reflexes and respiratory depression.

(See appendix 1 for $MgSO_4$ regime and $MgSO_4$ toxicity)

C - Control the Blood Pressure & Management of fluid Balance
(See the guideline for management of management of severe hypertension and pre-eclampsia)
If the patient is on magnesium Sulphate nifedipine should be avoided.

D - How should the fetus be assessed?

- In the acute setting, an initial assessment with cardiotocography should be undertaken.
- Women in labour with severe pre-eclampsia should have continuous electronic fetal monitoring.
- If conservative management is planned then further assessment of the fetus with ultrasound measurements of fetal size, umbilical artery Doppler and liquor volume should be undertaken. Serial assessment will allow timing of delivery to be optimised.

E - Delivery
Depends on:

- severity of illness
- condition of fetus
- state of cervix

The decision to deliver should be made once the woman is stable and with appropriate senior personnel present.

After 24 hours the benefits of conservative management should be reassessed. If the gestation is greater than 34 weeks, delivery after stabilisation is recommended.

- Prolonging the pregnancy at very early gestations may improve the outcome for the premature infant but can only be considered if the mother remains stable.
- The mode of delivery should be determined after considering the presentation of the fetus and the fetal condition, together with the likelihood of success of induction of labour after assessment of the cervix.
- **Before 34 weeks** caesarean section is more likely as the success of induction is reduced.
- **After 34 weeks** with a cephalic presentation, vaginal delivery may be considered if cervix is favourable. The consultant obstetrician should discuss the mode of delivery with the mother. If the woman is labouring then the second stage should be short with consideration given to an elective operative vaginal delivery
- The third stage should be managed with 10 units intramuscular oxytocin)or 5 units intravenous oxytocin given slowly.
- **Ergometrine or Syntometrine should be avoided** in these women for the management of third stage as this can further increase the blood pressure in women with hypertension or if her blood pressure has not been checked in labour.

F - Care after delivery

- If there has been recurrent episode of eclamptic fit, consider CT scan after delivery.
- Maintain vigilance as the majority of the eclamptic fits occur after delivery.
- Enhanced care should be provided as long, as clinically indicated. Some patients may need to be managed in ITU initially.
- Monitoring should be by experienced staff.
- Close attention should be given to fluid balance.
- Reduce antihypertensives as indicated.
- Women should be advised to stay in hospital for at least 4 days after delivery and PET blood screen should be performed before discharge.
- Women with history of severe PET / Eclampsia should be reviewed and discharged by the registrar or consultant.
- Women whose pregnancies have been complicated by eclampsia/HELLP/AFLP should be offered a formal postnatal review to discuss the events of the pregnancy and recurrence risk with their named obstetrician.

Management of HELLP/ AFLP

- The optimal treatment of both HELLP and AFLP is delivery.
- Hypertension if present should be managed as per Management of Significant Hypertension guideline
- The consultant obstetrician and on-call anaesthetist should always be involved in management of the patients with HELLP / AFLP.
- Consultant physician may need to be involved in cases of AFLP / HELLP.
- If platelet count is less than $100x10^9$/L the consultant anaesthetist should be involved.
- If platelet count is less than $80x10^9$/L the consultant haematologist should be involved.
- Platelet transfusion is reserved for active bleeding or prior to surgery if the platelet count is less than $50x10^9$/L.
- Fresh Frozen Plasma (FFP) should be considered to correct any coagulopathy.

Follow up after Eclampsia/ AFLP/ HELLP

The woman must be discharged by either the consultant obstetrician or registrar and the following should be done and documented in the notes

- Discuss with the woman +/- partner what has happened to her and its significance for future pregnancies and the recurrence risk.
- Discuss contraception
- Inform GP and CMW in form of a letter.
- Arrange follow up in 8-12 weeks to discuss recurrence risk and implications for future pregnancy. Specific investigations may need to be carried out at this visit e.g. APA, LA, Thrombophilia screen.

In rare cases only inherited fatty acid oxidation defects may be the cause of severe PET / AFLP.

Some babies born to pregnancies complicated by HELLP (haemolysis, elevated liver enzymes, low platelets) syndrome or acute fatty liver of pregnancy (AFLP) are affected by inherited fatty acid oxidation defects. It is important to diagnose these disorders long-chain 3-hydroxyacylCoA dehydrogenase deficiency **(LCHADD)** and medium-chain acylCoA dehydrogenase deficiency **(MCADD)** because of genetic and treatment issues.

LIVE BORN If a fatty-acid oxidation disorder is diagnosed in a live-born baby it should be treated early; the mother should be advised about the risks of recurrence and offered antenatal diagnosis in future pregnancies.

STILL BORN If the child is stillborn, skin biopsy, fibroblast culture and DNA studies for the common fatty-acid oxidation mutations should be considered following discussion with the parents

MOTHER (during acute illness)

- Urine organic acids - 10 ml random in plain bottle - store and transport deep frozen
- Blood spot and plasma carnitine and acyl carnitines - 1 ml lithium heparin + 1 newborn screening bloodspot card (4 spots)

BABY (when born)

- Acyl carnitine profile: 1ml blood into lithium heparin

Worcestershire Acute Hospitals NHS Trust

APPENDIX 1

MAGNESIUM SULPHATE ($MgSO_4$) REGIME

Management:

Initial eclamptic fit:
Remember ABC with tilt

Summon help via 2222,
Place woman in left lateral position and protect her from injury

↓

Commence $MgSO_4$ loading dose: 8ml of $MgSO_4$ 50% (4gm) made up to 50mls with 42 ml sodium chloride 0.9% for injection given via Graseby 3500 syringe driver (WRH) or Alaris Pump (Alx) at 300mls/hour (4g/10 mins).

↓

Maintenance dose : 1 gm $MgSO_4$ hourly.
Using 50ml syringe draw up 5g (10ml) of $MgSO_4$ (50%) and mix with 40ml sodium chloride 0.9% and run at 10ml/hr for 5 hours given via Graseby 3100 syringe driver (WRH) or Alaris Pump (Alx)

↓

If fits recur give a second bolus of 2g (4ml of 50% $MgS0_4$) made up to at least 20ml with sodium chloride 0.9% and given over 5-10mins) or the rate of the maintenance infusion is increased to 1.5 – 2g/hr (i.e. 15-20ml/hr).

↓

Continue for 24 hrs after the last fit
or 24 hrs after starting, if commenced prophylactically.
Prophylactic after delivery only.

↓

Magnesium toxicity is unlikely with these regimens and levels do not need to be routinely measured. Magnesium sulphate is mostly excreted in the urine. Urine output should be closely observed and if it becomes reduced below 20 ml/hour the magnesium infusion should be halted. Magnesium toxicity can be assessed by clinical assessment as it causes a loss of deep tendon reflexes and respiratory depression.

↓

DO NOT INCREASE $MgSO_4$ above maximum of 2g/hr.

Take bloods for

FBC, U&E, uric acid, LFT, LDH, Group & save, clotting+fibrinogen

↓

Repeat FBC, U&ELFTs including LDH after62 and 24 hrs

↓

*MAGNESIUM LEVELS **NOT ROUTINELY TAKEN** **See Appendix 3**

When using $MgSO_4$ monitor: (Frequency of monitoring as per individual care plan)
Respiratory rate

- O2 Saturation
- Patellar reflexes or biceps reflex if has epidural
- Hourly urine output

Stop MgSO4 if toxicity is suspected on clinical grounds (see below) and discuss with the consultant obstetrician

- Loss of patellar reflexes. Always get suppression of reflexes before respiratory depression.
- RR<16/min
- Urine output <20mls/hr

- Further seizure occur

APPENDIX 2

MAGNESIUM TOXICITY

Loss of biceps / Patellar reflex →	Stop maintenance infusion May start Mg infusion after review by senior obstetrician when reflexes return and urine output improves
O^2 saturation <90% →	Commence oxygen Stop Mg infusion Inform anaesthetist Check for Pulmonary Oedema
Cardiorespiratory Arrest →	ABC Stop Mg infusion Call crash team Give Ca gluconate Intubate Assisted ventilation until spontaneous respiration

Mg Toxicity & Blood level of Mg

Therapeutic blood magnesium levels 2.0 – 3.5 mmol/l

Magnesium level	**Effect**
3.5 – 5.0 mmol/l	Deep tendon reflexes abolished Respiratory depression occurs
> 5 mmol/l	Serious risk of respiratory arrest
12 – 15 mmol/l	Cardiac arrest occurs

MAGNESIUM LEVELS ABOVE THERAPEUTIC RANGE (i.e 3.5)

>3.5 but < 4.0 Reduce infusion rate to 0.5g/hr and check Mg level 4 hrs later (5ml/hr)

>4.0 Stop the infusion / check for signs of toxicity and check Mg level 2 hrs later.

If on rechecking – Mg level fallen to <3.5 mmol/l restart infusion at 0.5g/hr (5ml/hr) and repeat Mg level in 4 hrs.

APPENDIX 3

MAGNESIUM SULPHATE IN THE PRESENCE OF POOR RENAL FUNCTION

* In cases of poor renal functions in addition to the following management discuss with renal physician.

A satisfactory urine output is regarded as >20mls/hr – averaged over a 2 hour period.

OLIGURIA	Give the 4 gram (8mls) loading dose only. If no signs of toxicity reduce maintenance infusion rate to 0.5 grams/hr (5ml/hr) and review fluid balance.
CREATININE (100-150 µmol/L)	Continue with maintenance dose at 1gram/hr Check Mg level every 2 hours.
CREATININE (>150 µmol/L)	If no signs of toxicity reduce infusion rate to 0.5 grams/hr (5ml/hr) and review fluid balance. Check Mg level every 1 hour. Check renal function every 4 hours.
ANURIA	Stop Magnesium Check catheter not blocked Check Mg level / Potassium and renal function Transfer to ITU/HDU

Antidote to Magnesium Toxicity

Calcium gluconate
Dose: 1gram (10ml of 10%) I/V over - 5 mins