

MANAGEMENT OF PRE-ECLAMPSIA / ECLAMPSIA**DEFINITION**

A diagnosis of pre-eclampsia can be made when hypertension arises after 20 weeks of gestation and is accompanied by one or more of the following: ¹

- Renal involvement
 - Significant proteinuria-dipstick subsequently confirmed by spot urine protein/creatinine ratio $\geq 30\text{mg}/\text{mmol}$. In view of the close correlation between spot urine protein/creatinine ratio and 24hour urine excretion, the later is rarely required
 - Serum or plasma creatinine $> 90\mu\text{mol}/\text{L}$
 - Oliguria
- Haematological involvement
 - Thrombocytopenia
 - Haemolysis
 - Disseminated intravascular coagulation
- Liver involvement
 - Raised serum transaminases
 - Severe epigastric or right upper quadrant pain
- Neurological involvement
 - Convulsions (eclampsia)
 - Hyper-reflexia with sustained clonus
 - Severe headache
 - Persistent visual disturbances(photopsia, scotoma, cortical blindness, retinal vasospasm)
 - Stroke
- Pulmonary oedema
- Placental abruption
- Fetal growth restriction

Severe pre-eclampsia is variously defined but involves systolic blood pressure ≥ 160 mmHg or diastolic blood pressure ≥ 110 mmHg on two occasions and significant proteinuria (protein /creatinine ratio $30\text{mg}/\text{mmol}$ or $>300\text{mg}$ in 24 hours)². It may also involve HELLP syndrome (haemolysis, elevated liver enzymes, and low platelet count).

Severe pre-eclampsia - clinical features may include:

- Symptoms of severe headache
- Visual disturbance
- Epigastric pain and/or vomiting
- Severe hypertension ($\geq 160 / 110\text{mmHg}$)
- Hyper-reflexia with clonus (> 3 beats)
- Papilloedema
- Liver tenderness
- Falling platelet count raised liver function, abnormal renal function

INITIAL ASSESSMENT AND DIAGNOSIS

- Assessment of symptoms – headache, visual disturbance, epigastric pain, general malaise, decreased fetal movements
- Blood pressure, oxygen saturation and proteinuria measurement
- MSU to exclude UTI
- General examination, epigastric tenderness, hyper-reflexia with clonus (> 3 beats)
- Uterine size, fetal heart rate and CTG (gestation more than 28 completed weeks)

Blood pressure measurement¹

- Rested and sitting 45 degree angle (chair or bed)
- Appropriate sized cuff at level of heart
- Phase 5 Korotkoff (disappearance of pulsation sound) appropriate measure for diastolic BP
- BP should be measured manually as automated devices may markedly underestimate systolic BP in pre-eclampsia.

Proteinuria measurement

- Dipstick 1+ or greater (use automated dipstick reader if possible)
- Must be confirmed by protein / creatinine ratio on a spot urine sample (> 30mg/mmol)

Investigations

- Full blood count
- Coagulation profile only in severe pre-eclampsia and women with low platelet count.
- Liver function tests
- Renal function
- Urate
- Group and Hold
- CTG (continuous if unstable or in labour)
- Ultrasound scan if appropriate to assess fetal growth, liquor and doppler

ONGOING MONITORING

**Acute Observation monitoring chart should be used for all measurement and results.
This should be reviewed at every handover**

Blood Pressure

- BP measured every 15 minutes initially
- Reduce to 30 minutes once stable
- Checked 4 hourly if conservative management is planned and the woman is stable with no symptoms

→ If stable, admit to ward (See Appendix A)

Fluid Balance

- Maintain fluid balance chart
- Urinary catheter is used in severely ill women to allow hourly urine measurements.

Deep Tendon Reflexes including assessment for clonus

- Every 60 minutes while on magnesium sulphate infusion
- If absent, suspect magnesium toxicity

If patient remains hyper-reflexic with >3 beats clonus present after 2 hours of being on a magnesium sulphate infusion she requires another loading dose of magnesium - senior doctor to review and confirm prior to repeat loading dose⁴.

Note: Check reflexes in the upper limb when epidural/spinal anaesthesia is in situ.

Respiratory Rate

- Every 60 minutes while on magnesium sulphate infusion.

Temperature

- Every 4 hours.

MANAGEMENT

Ongoing management should be multidisciplinary, involving the obstetric, anaesthetic and physician services.

Control of Blood Pressure

- Antihypertensive treatment should be commenced if Systolic BP ≥ 160 mmHg, or diastolic BP ≥ 105 mmHg, or MAP ≥ 125 mmHg.

Acute treatment

Consider placement of an arterial line before instituting acute control of blood pressure

Whenever acute treatment is required background antihypertensive treatment should also be initiated.

- Labetalol oral or IV (*avoid if history of asthma*)
- Nifedipine
- Hydralazine IV

→ See Appendix B for recommended dosage

Non-acute (background) treatment for hypertension

- Methyldopa
- Labetalol
- Nifedipine slow release

Avoid Atenolol, ACE inhibitors or Angiotensin Receptor blocking drugs, and Diuretics

→ See Appendix C for recommended dosage

Fluid Balance

- Most women who are already oedematous from fluid retention do not need IV fluids and once able to drink are best left to take fluids according to thirst.
- If IV fluids are required, use very cautiously and limit to a maximum of **80 ml/hour unless ongoing fluid losses². In addition to IV fluids, the woman can drink fluids according to thirst.**
- IV fluid restriction is advised to reduce overload in the intrapartum and postpartum periods, which may result in pulmonary oedema.
- Oliguria is common in pre-eclampsia, and there is no evidence that fluid expansion or maintenance of a specific urine output prevents renal failure (which is rare) or improves preeclampsia outcome.

PPH

- In the event of postpartum haemorrhage, the lost volume requires replacement, close fluid balance monitoring is essential. However CVP lines are rarely necessary.
- Oxytocin is the drug of choice for PPH. Oxytocin infusion should run at an increased concentration to avoid fluid overload (40 units of oxytocin in 100ml 0.9% sodium chloride run at 25 ml /hour over 4 hours).
- Misoprostol and carboprost can be safely used as per PPH guideline (GL/M/0021).
- Avoid routine use of Syntometrine[®] and ergometrine, which can lead to fatal cerebral haemorrhage in the context of hypertension

Prevention of Seizures (Eclampsia)³

- Magnesium sulphate is advised when severe preeclampsia is diagnosed.
- Magnesium sulphate should be continued for 24 hours following birth or 24 hours after the last seizure, whichever is the later, unless there is a clinical reason to continue.

→ See Appendix D for recommended dosage regimen and monitoring

Management of Seizures³

- Assess and maintain Airway, Breathing, Circulation
- Obtain help by pressing the red emergency bell in the room.
- Press green clinical emergency button and leave the red bell on.
- Inform senior obstetric anaesthetist and senior obstetrician
- Position the woman in left lateral and administer oxygen.
- Prevent maternal injury wherever possible.
- Magnesium sulphate is the treatment of choice to **prevent** further seizures.
- Most eclamptic seizures self terminate within 2 to 3 minutes.
- Stabilise the woman prior to considering birth, even if there is fetal distress.

Timing of birth

- Decision regarding birth should be made once the woman is stable and appropriate senior personnel are present. A carefully planned birth with all professionals available is appropriate. Vaginal birth is generally preferable but caesarean section is more likely in case of extreme prematurity.
- If gestation less than 36 weeks gestation corticosteroids should be offered.
- Conservative management at very early gestations may improve perinatal outcome but must be carefully balanced against risk of maternal morbidity
- If required, regional analgesia / anaesthesia is preferable to general anaesthesia. In the event of thrombocytopenia (platelets less than $50-100 \times 10^9 /l$) general anaesthesia should be considered
- Active management of 3rd stage is advised with oxytocin.

Avoid routine use of Syntometrine[®] and ergometrine, which can lead to fatal cerebral haemorrhage in the context of hypertension

Postpartum Management

- Intensive observation should continue on Birthing Suite (AOU) for at least 24 hours with severe pre-eclampsia. Intravenous fluid restriction should continue until spontaneous diuresis occurs.
- Monitor bloods (FBC, renal and liver function) the day after birth, and twice weekly until stabilised (may need more frequent monitoring if very unstable)
- 44% of eclamptic seizures occur postpartum. Late seizures do occur and clinicians should review carefully before discharge (although majority of these seizures occur during the first 48hours).
- Anti-hypertensive treatment should be continued after birth as dictated by blood pressure.
- Formal medical discharge summary to the GP and LMC must be provided and should include a plan for postnatal management of blood pressure.
- Women should be offered a follow-up appointment at 6weeks postpartum in CWH gynaecology outpatients department.
- Early-onset pre-eclampsia (< 32 weeks gestation), particularly if associated with IUGR, requires further investigation at 6-8 weeks (inherited and acquired thrombophilia, antiphospholipid syndrome), and renal ultrasound if proteinuria persists. In the event of extreme and fluctuating levels of hypertension pheochromocytoma needs to be considered and appropriately investigated.

REFERENCES

1. SOMANZ. Guidelines for the management of hypertensive disorders of pregnancy. 2008
2. NICE guidelines. Hypertension in pregnancy. August 2010.
3. Duley L et al. The Collaborative Eclampsia Trial. Lancet 1995; 345:1455-63.
4. Evan J Begg. Textbook of 'Instant Clinical Pharmacology'. 2nd Edition 2007

APPENDIX A**Maternity ward observation of stable pre-eclampsia****Maternal**

- **BP** - 6 hourly or 4 hourly if significantly elevated
- **Blood tests** – FBC, LFTs, U&Es and creatinine and uric acid on the day of admission and repeat twice weekly (Monday and Thursday).
- **Urine protein / creatinine ratio** - day of admission.
- **Observations to be documented on MEOWS chart and score calculated.**

Fetal

- **CTG** daily or twice daily if concerned
- **Ultrasound scan**
 - Growth every 2 weeks
 - Amniotic fluid index (AFI) and UA Doppler weekly if concerns with growth.

Management

- Steroids if less than 36 weeks gestation
- Anti-hypertensive treatment, as outlined in this guideline.

Timing of Birth

- Gestation greater than 36weeks
- Uncontrolled hypertension despite treatment
- Deterioration in LFT, renal function, or fall in platelet count
- Maternal symptoms
- Concern regarding fetal wellbeing

APPENDIX B**Acute Management of Severe Hypertension**

Systolic blood pressure \geq 160 mmHg and /or diastolic blood pressure \geq 110 mmHg

On at least 2 separate measurements 10 minutes apart

Aim to reduce BP to systolic 140-160 mmHg and diastolic 90-100 mmHg

First-line therapy

NB: Commence background therapy at the same time

Labetalol (*exclude asthma*)**Oral**

200mg stat dose. BP should fall within 30 minutes

Repeat oral 200mg dose if BP not controlled at 30 minutes

IV therapy**Bolus****Preparation:**

Use undiluted labetalol from vial (100mg/20mL)

Administration:

Give 50mg (10mL) bolus over at least 1 minute.

There should be a fall in BP within 5 minutes.

Repeat at 5 minute intervals to a maximum dose 200mg (40mL).

Infusion**Preparation:**

1) Discard 40mL from a 100mL bag of 0.9% Sodium Chloride

2) Add 40mL labetalol (200mg) to bag.

This makes a 2mg/mL solution for infusion.

Administration:

Commence labetalol infusion at rate 10mL/hr (20mg/hr) via IV infusion pump.

Increase infusion rate by 10mL/hr every 30 minutes until BP controlled, up to maximum 50mL/hr (100mg/hr).

If BP not controlled on 100mg/hr seek medical review.

Second-line therapy**Nifedipine**

Oral 10mg stat dose (not slow release) Repeat every 30 minutes until BP controlled.

At the same time commence slow release preparation twice daily

Third-line therapy

Hydralazine (exclude cardiac / renal disease)

IV therapy

Bolus

Preparation:

Hydralazine comes in a vial containing 20mg of lyophilised powder for reconstitution.

- 1) Add 1mL of 0.9% sodium chloride to reconstitute the vial.
- 2) Add the contents of reconstituted vial of hydralazine to a further 19 mL of 0.9% sodium chloride (total volume = 20mL).

This makes a 1mg/mL solution of hydralazine for bolus injection.

Administration:

Give a 5mg (5mL) bolus injection over 5 minutes.

Repeat every 20 minutes until BP is controlled, i.e. systolic 140-160 mmHg and diastolic 90-100 mmHg.

Then run maintenance infusion as follows.

Infusion

Preparation:

Hydralazine comes in a vial containing 20mg of lyophilised powder for reconstitution.

- 1) Reconstitute 2 vials of hydralazine by adding 1mL 0.9% sodium chloride to each vial.
- 2) Remove 30mL from a 100mL* bag of 0.9% sodium chloride.
- 3) Add the contents of 2 vials of reconstituted hydralazine to the remaining 0.9% sodium chloride in the bag .

This makes 40mg in 80ml = 1mg/2ml solution of hydralazine for infusion.

(* Each 100mL bag contains 8mL overage i.e. total volume = 108mL hence the need to remove 30mL from the bag in step 2)

Administration:

Run maintenance infusion at 5mg (10mL) per hour.

APPENDIX C

Non-acute (background) antenatal management of hypertension**First-line therapy****Methyldopa**

Oral 500mg stat dose, then regular dose of 250mg three times a day.
Can increase up to 500mg four times a day
Warn woman that she may feel "dopey"
After birth consider using an alternative antihypertensive if required
Monitor LFT's monthly

Second-line therapy**Labetalol** (exclude asthma)

Oral 100mg stat dose, then regular dose of 100mg three times a day
Can increase up to 200mg four times a day

Third-line therapy**Nifedipine**

Oral 10mg slow release twice daily, and can increase up to 30mg slow release twice daily

Postnatal BP Management:

Labetalol, Nifedipine or Enalapril are all appropriate antihypertensives to use in the postpartum period. Can breast feed with all these medications:

- Labetalol - **avoid if asthmatic** Usually first-line choice, starting at 100mg three times a day and can increase to 200 mg three times a day
- Nifedipine - Useful additional therapy after Labetalol, as get less side-effects from the vasodilatory aspect of the drug. Start at 10mg SR bd, and can increase to 20mg SR twice daily
- Enalapril – Start at 5-10 mg daily. Usually used in those with likely chronic hypertension Ensure normal renal function (in both mother and neonate) before commencing and measure serum creatinine 3-5 days after commencing therapy.

APPENDIX D

Magnesium Sulphate

Supplied as

- **Premixed Bags** of Magnesium Sulphate 40mmol in 128mL 0.9% sodium chloride (=10g magnesium sulphate per 128mL) from Baxter Healthcare
- **If premixed bags are not available then** prepared by adding the contents of 4 vials of 10mmol/5mL magnesium sulphate to a 100mL* bag of 0.9% sodium chloride)
- Magnesium Sulphate 10mmol/5mL vials ($\approx 2.5\text{g}/5\text{mL}$)
(If premixed magnesium sulphate bags are unavailable a solution for infusion of magnesium sulphate 40mmol in 128mL 0.9% sodium chloride can be
*Note all 100mL bags of 0.9% sodium chloride contain 8mL overage hence the final volume is 128mL

Indications

- Prophylaxis of convulsions in the presence of severe pre-eclampsia
- Treatment of eclamptic convulsions

Contraindications

- Cardiac disease or acute renal failure

Loading Dose 4g magnesium sulphate over 20 minutes

Run magnesium sulphate 40mmol/128mL (= 10g/128mL) at 153mL per hour for **20 minutes ONLY**

Volume to be infused (VTBI) **must** be set at 51mL

Maintenance Dose 1g magnesium sulphate per hr

Run magnesium sulphate 40mmol/128mL (=10g/128mL) at 13 mL per hour

Monitor

- Cardiac monitoring during and for 1 hour post loading dose
- Hourly check that deep tendon reflexes are present
- Continue baseline recordings – BP, pulse
- Hourly Respiratory rate (should be > 12 rpm)
- Continuous pulse oximetry
- Magnesium levels not required
- Hourly urine output

If >3 beats clonus present after 2 hours, senior doctor to review and confirm and repeat loading dose⁴

Magnesium Toxicity

Disappearance of deep tendon reflexes is an early sign of magnesium toxicity and occurs before respiratory muscle weakness occurs.

If concern about toxicity, stop magnesium sulphate.

If major concern over respiratory depression, consider **calcium gluconate** (1g/10mL) over 10 minutes)