

PHARMACOLOGICAL MANAGEMENT OF ECLAMPSIA AND PRE-ECLAMPSIA

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MANAGEMENT OF PRE-ECLAMPSIA (PET)

Definition

Pre-eclampsia is a complex multi-system disorder that may sometimes precede eclampsia. There are several definitions of pre-eclampsia, which generally involve hypertension occurring after 20 weeks gestation (blood pressure above 140/90 or a rise of 30 systolic or 15 diastolic above baseline BP), with the involvement of at least one other organ system, for example headache or epigastric pain. The classical diagnostic triad for pre-eclampsia of hypertension, proteinuria and oedema is no longer considered useful.

Features of severe pre-eclampsia (in addition to hypertension and proteinuria) include:

- sustained severe hypertension ($\geq 160/110$)
- severe proteinuria, oliguria (urine output $< 500\text{ml}/24$ hours), raised creatinine
- neurological symptoms and signs including headache, visual disturbance, confusion, papilloedema and clonus
- platelet count falling to below $100 \times 10^9/\text{l}$
- epigastric pain and/or right upper quadrant (liver) tenderness
- abnormal liver enzymes (ALT or AST rising to above 70 IU/l)
- HELLP syndrome (haemolysis, elevated liver enzymes and low platelet count)

Goals of management

- Prevent convulsions (progression to eclampsia).
- Control blood pressure (BP). The goal is to stabilise the diastolic BP between 90 and 100mmHg.
- Anticipate and prevent complications.
- Prevent damage to the foetus.

Initial assessment and management

Use 'ABC'

A – Airway:

- Usually no problems.

B – Breathing:

- Increased respiratory rate can be an early sign of pulmonary oedema.
- Auscultate chest to exclude pulmonary oedema.

C – Circulation:

- Measure BP, pulse, oxygen saturation.
- Left lateral tilt.
- Insert IV cannula - at least 18G (green).
- Take blood for Hb, platelets, clotting, blood group.
- If platelets low ($< 100 \times 10^9/\text{l}$) check liver function tests.
- Insert urinary catheter, dip for protein, monitor urine output hourly.
- Record strict fluid balance and administer maintenance fluids (Hartmann's or 0.9% saline), initially at 1000ml per 12 hours. There is a delicate balance between two potential complications; renal failure exacerbated by hypovolaemia and fluid overload causing cerebral and/or pulmonary oedema. Awareness of this balance is crucial to successful treatment of patients with pre-eclampsia and eclampsia.
- If oliguric (urine output $< 30\text{ml}/\text{h}$ average over 4 hours) consider a modest fluid challenge (250ml 0.9% saline).
- Look for oedema.

D – Disability:

- ask specifically about headache, blurring of vision or fits
- assess reflexes, looking for clonus and perform fundoscopy

Record vital signs on a flow sheet or critical care chart.

Further management of pre-eclampsia

The main aims are:

1. To prevent convulsions:

- If severe PET (BP $\geq 160/110$) and/or symptoms of CNS irritability, suggesting risk of progression to eclampsia (headache, blurred vision), start magnesium sulphate (MgSO_4). Administer as described below.

2. To control BP

- Re-assess BP after loading dose of MgSO_4 as it will reduce BP.
- Institute further treatment if BP $\geq 160/110\text{mmHg}$.
- Aim to slowly reduce BP to 130-140/90-100mmHg.

Prevention of convulsions - administration of MgSO₄

The Magnesium Sulphate for Prevention of Eclampsia (MAGPIE) Trial found that women with pre-eclampsia taking magnesium sulphate had a 58% lower risk of eclampsia and a lower mortality rate compared to women in the placebo group. The magnesium sulphate group had a 27% lower relative risk of placental abruption. The trial did not detect a difference in neonatal mortality between the two groups.

Indications

Severe PET with signs of increased irritability of central nervous system:

- headache
- visual disturbances
- hyperreflexia

Administration

MgSO₄ can be diluted in 5% glucose or 0.9% saline.

Two regimens are described.

A. Combined intramuscular/intravenous administration of MgSO₄

Loading dose:

Add 8ml 50% MgSO₄ (**4g**) in 100ml 0.9% saline or 5% glucose: administer IV over 20 min.

(Alternatively, if you have a syringe-driver pump: add 8ml 50% MgSO₄ (**4g**) to 12ml 0.9% saline or 5% glucose and infuse over 20 min - 60ml/hour).

and

Give **2.5g** MgSO₄ IM into each buttock.
(Total initial dose 4g IV + 2x 2.5g IM = 9g).

If the convulsions do not stop:

Administer a further 2g MgSO₄: draw 4ml (2g) of 50% MgSO₄ into a 10ml syringe and add 6ml of 0.9% saline or 5% glucose; inject over 2 min (5ml/min).

Do not exceed 8g total IV dose of MgSO₄ during the first hour

If convulsions still continue consult medical staff and consider diazepam 5mg or 1mg lorazepam. Be aware of risk of respiratory depression.

Maintenance:

2.5g MgSO₄ IM 4 hourly using alternate buttocks if there are no signs of MgSO₄ overdose.

Check reflexes before giving MgSO₄.

Continue for 24 hours after the last convulsion or delivery.

B. Intravenous administration of MgSO₄

Loading dose:

Fill a paediatric infusion burette set with 22ml 5% glucose.

Add 8ml 50% MgSO₄ (4g).

Infuse at 60 drops/min (60 ml/hr); the total of 30ml will run over 30 min.

If the convulsions do not stop:

As above.

Maintenance:

Fill a paediatric infusion burette with 112ml 5% glucose.

Add 8ml 50% MgSO₄ (4g).

Infuse at 30 drops/min (30 ml/hr); the total of 120ml will run over 4 hours = 1g/hour.

Repeat the same management every 4 hours for at least 24 hours after the last convulsion or delivery.

For recurrent seizures:

Administer a second loading dose or increase the infusion to 1.5 or 2g/hour (45 or 60 drops per minute)

Adverse effects of MgSO₄

- hypotension, arrhythmias.
- respiratory depression.
- flushing, nausea/vomiting.
- drowsiness, slurred speech, double vision.

Monitoring

Measure hourly:

- Urine output: aim for urine output > 120ml over 4 hours (average 30ml/hour). If low, assess for symptoms or signs of MgSO₄ toxicity.
- Respiratory system: stop infusion if RR less than 10/min and/or general condition deteriorates (drowsiness, difficulty speaking).
- Check patellar reflex (knee-jerk) every 2-4 hours. If knee-jerk depressed, stop infusion.
- Blood pressure: if diastolic blood pressure (DBP) is more than 110mmHg start antihypertensive therapy (see below).
- Continuous CTG (cardiotocograph) monitoring of foetus if available.
- If available, monitor serum Mg²⁺ levels 4-6 hourly.
- After delivery: check uterus is contracted and whether there is any vaginal bleeding.

If any sign of overdose:

- Stop MgSO₄ infusion.
- Call for help.
- Assess and resuscitate guided by 'ABC'.
- Calcium gluconate should be available to treat

magnesium toxicity: administer 10ml 10% calcium gluconate (1g) IV over 2-3 minutes.

Duration of treatment

- If magnesium sulphate is given, it should be continued for 24 hours following delivery or 24 hours after the last seizure, whichever is the later, unless there is a clinical reason to continue longer.

Blood pressure control in pre-eclampsia

Indications

- Diastolic BP over 110mmHg or systolic BP over 160 mmHg. For women with other markers of potentially severe disease, treatment can be considered at lower degrees of hypertension.

When measuring the blood pressure, the woman should be rested and sitting at a 45-degree angle. The blood pressure cuff should be of the appropriate size and should be placed at the level of the heart. Multiple readings should be used to confirm the diagnosis. Korotkoff phase 5 (the last sound heard) is the appropriate measurement of diastolic blood pressure. The method used should be consistent and documented.

Automated methods need to be used with caution, as they may give inaccurate blood pressure readings.

Agents to consider are: nifedipine (oral or sublingual), labetalol (oral or IV), and IV hydralazine.

Atenolol, angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor-blocking drugs and diuretics should be avoided.

Nifedipine

Mode of action

- Peripherally acting calcium antagonist.

Administration

- Use orally or sublingually.
- Give 10mg nifedipine, repeating dose after 30 minutes if required.
- Maintenance dose is given 8 hourly, with a maximum dose of 20mg.

Adverse effects

- Sublingual use may cause a rapid profound BP drop and impair uteroplacental perfusion if other agents are also in use.
- Use cautiously with MgSO₄ (both antagonise calcium).

Labetalol

Mode of action

Combined α - and β -adrenergic blocker.

Administration

- Give 5-20mg boluses slowly IV at 10 minute intervals to a maximum of 50mg.
- Alternatively, start IV infusion at 20 mg/hour. Double infusion rate every 30 minutes as needed to a maximum of 160 mg/hour.
- May be given orally (dose: 100-200mg PO hourly, until BP controlled - maintenance dose is given 12 hourly). Absorption may be reduced in labour.

Contraindications

- Asthma and cardiac failure.

Intravenous hydralazine infusion

Mode of action

Direct acting arterial vasodilator.

Administration

- Never infuse hydralazine via the same cannula as magnesium sulphate – preferably avoid using the same arm.
- Dilute 80mg (4 vials) of hydralazine in 500ml of 0.9% saline or Hartmann's solution (not in 5% glucose).

Infuse hydralazine at 2mg/hour (= 12.5ml/hour). The correct number of drops per minute can be calculated from information on the packets of the IV giving set.

- If you have a syringe-driver pump, use 40mg hydralazine in 40ml and start at 2 ml/hour (= 2mg/hour)
- If diastolic blood pressure (DBP) is still over 100, increase rate by 1mg/hour and check BP in next 30 min (maximum of 5 mg/hour).
- If DBP is between 90-100 keep same rate and continue to monitor BP every 30 min.
- If DBP is less than 90, reduce hydralazine infusion by 1mg/hour.

Monitoring

- Record BP results and rate of infusion on a monitoring sheet.

Adverse effects

- Hypotension. If DBP decreases suddenly below 90mmHg stop the infusion and administer a 250ml fluid bolus over 1 hour.
- Maternal tachycardia is often a limiting side effect of hydralazine.

MANAGEMENT OF ECLAMPSIA

Definition

The occurrence of seizures in a parturient who may have no underlying pathology.

Goals of management

- Cessation of seizures.
- Stabilisation of airway, breathing and circulation.

- Prevention of further seizures.
- Prevention of damage to and safe delivery of the foetus.

Initial assessment and management

Use ABC as for any life threatening emergency.

A – Airway:

- Maintain the airway, using airway adjuncts (e.g. Guedel airway) as necessary, position patient on the left side, give oxygen via face mask (15 l/min).

B – Breathing:

- Ensure patient is breathing. Be aware of influence of administered drugs on respiration (e.g. diazepam).

C – Circulation:

- Insert 2 IV cannulas (18G at least), take blood investigations as for PET.
- Look for pulmonary oedema - a major cause of maternal mortality in eclampsia.
- Restrict fluids unless indicated by blood loss.

D – Disability:

- Assess consciousness level using Glasgow Coma Score chart.
- Protect from injuries (falling from bed).

Further management of eclampsia

The main aims are:

1. To terminate convulsions:

- Start magnesium sulphate ($MgSO_4$) (see above) and continue for 24 hours after delivery or last fit.

2. To control BP

- As described for PET, above.

3. To deliver the baby

- Start steroids if gestation <36 weeks.
- Plan delivery when patient is stable.
- Regional anaesthesia is preferred if coagulation and platelet count is adequate.
- Avoid ketamine and ergometrine.

Don't forget that:

- The ultimate treatment of pre-eclampsia or eclampsia is delivery of the baby.
- Eclampsia can happen 48 hours or longer after delivery.

Further reading

1. Guidelines of the Royal College of Obstetricians and Gynaecologists (UK), available at: www.rcog.org.uk/resources/Public/pdf/management_pre_eclampsia_mar06.pdf

2. The Magpie Trial Collaborative Group. Do women with preeclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomized, placebo-controlled trial. *Lancet* (2002); 359: 1877-90

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