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CONSENSUS STATEMENT ON THE MANAGEMENT OF PRE-ECLAMPSIA

Introduction

Pre-eclampsia is associated with significant morbidity and mortality for mother and baby, with post partum resolution. The disorder is triggered by a placental pathology followed by a wide spectrum of maternal systemic response. However, controversy remains in many aspects of the condition.

This Consensus Statement is drawn up to improve the consistency of management of women with pre-eclampsia. As different members of the team of doctors and midwives are involved in the provision of care, standardisation should improve the efficiency of the management. They are not intended to replace the process of critical evaluation of every case and individualised decision making, but merely to serve as a guide and framework for consideration.

Definition

Pre-eclampsia (PE)

BP>/= 140/90mmHg with proteinuria >/= 0.3g/24hr or 1+ on labstix, after 20 weeks amenorrhoea. The definition of gestational proteinuria is derived from studies calculating the 95th centile for an uncomplicated population. A protein loss of over 300 mg in 24 hours is associated with an increased morbidity to the mother and her baby [1]

Severe Pre-eclampsia (SPE)

PE with BP>/= 160/110mmHg OR
proteinuria >/= 3g/24hr OR
symptoms impending eclampsia (eg epigastric pain, headache, visual symptoms) OR
biochemical derangements - hepatic, hematological or renal dysfunction

Eclampsia

tonic-clonic seizures in a woman with PE, in the absence of other causes

Management of Mild to Moderate PE

No evidence of anti-hypertensive therapy improving outcome in cases with mildly elevated BP, although it may prevent occurrence of severe hypertension. On those occasions when an antihypertensive agent is indicated for mild gestational hypertension the choice of drug should be governed by the clinician s experience and the woman s tolerance. Appropriate first-line choices include the methyldopa, labetalol or nifedipine. There is little good evidence that one antihypertensive is better than another. [2, 3]

Antihypertensive drug treatment is not usually indicated for women with non-proteinuric gestational hypertension. However, a diastolic BP >105mmHg represents an appropriate level at which to initiate anti-hypertensive therapy as protection against intracerebral haemorrhage. A lower threshold may be considered where the disease has arisen before 28 weeks gestation. [3]

1. All women with blood pressure greater than 140/90 mmHg with or without proteinuria* should be evaluated and investigated further for maternal end organ disease and fetal well being. (*women with 3+ to 4+ proteinuria on labstix should have a quantification of 24 hour urinary protein excretion)

2. All women with persistent proteinuria, even in the absence of hypertension, should be evaluated and investigated further for maternal end organ disease and fetal well being.

3. All women with blood pressure greater than 140/90 mmHg with or without proteinuria should be either referred to a day assessment unit, or be monitored very closely for development of severe hypertension, hematological / biochemical abnormalities or proteinuria.

Admission for inpatient monitoring should be considered if:

- there is severe pre-eclampsia
- there is persistent hypertension or proteinuria

Management of Severe PE and Eclampsia

The management of these cases relies upon:

- control of blood pressure through the use of anti-hypertensive drugs
- effective management of the fluid and hemodynamic status
- monitoring for biochemical or hematological derangements
- seizure control or prophylaxis
- timely delivery such that maternal interests are balanced against fetal maturity

Corticosteroids to enhance fetal lung maturity are not contraindicated in severe pre-eclampsia [4]

In patients with mild to moderate hypertension, both chronic and pregnancy induced, antihypertensive treatment improves the maternal outcome, whereas no clear-cut evidence of benefit have been reported at the fetal level. Among the different antihypertensive drugs that have been reported to be effective, safe and well tolerated

during pregnancy, methyldopa and calcium channel blockers (nifedipine) represent the more suitable solution. The use of some beta blockers (such as atenolol and propanolol) has been associated intra-uterine growth restriction.

Severe hypertension during pregnancy (blood pressure > 170/110 mmHg) should be immediately treated with drugs that have been proven to prolong pregnancy and to improve both maternal and fetal outcome (see Annex 1)[5].

Optimal management of the fluid balance requires close monitoring for (see Annex 2):

- oliguria (to clinically assess renal function and/or volume loading)
- pulmonary edema (which would confirm fluid overloading)
- serum creatinine (for biochemical assessment of renal function)
- invasive monitoring via CVP or Swan Ganz catheter where necessary

Serial biochemical and hematological parameters should be monitored to detect end-organ compromise early[6]. These parameters include:

- full blood count and platelets
- urea and electrolytes
- uric acid
- transaminases
- 24 hour urinary total protein

Magnesium sulphate is the anticonvulsant of choice for both prevention and treatment of eclampsia (including treatment of acute seizure)[7, 8]. Magnesium sulphate is recommended for women with pre-eclampsia deemed at risk of seizure and for whom there is a plan for delivery[1]. (see Annex 3)

Women with severe pre-eclampsia should have early referral to a specialist centre. A woman should not be transferred unless it is considered safe to do so and she has been stabilised[1].

Close fetal monitoring is essential, in view of the adverse perinatal outcome associated with severe pre-eclampsia. Fetal monitoring, including umbilical artery Doppler studies, should be considered to detect early evidence of fetal compromise in pre-eclampsia [9, 10]

Delivery should be considered when:

- there is evidence of fetal compromise
- blood pressure is labile and poorly controlled despite pharmacological therapy
- there is impending eclampsia or eclampsia
- there is biochemical evidence of severe organ dysfunction or muti-organ dysfunction
- the clinician is confident of fetal maturity

Women with pre-eclampsia, admitted for inpatient care are at increased risk of thromboembolic disease. The use of TED stockings and encouragement of passive leg exercises is recommended. Should such women require delivery by emergency Caesarean section, the use of low molecular weight heparin for thromboprophylaxis should be considered in the absence of contraindication.

Screening and Prophylaxis

Although pregnancies associated with an abnormal uterine artery Doppler waveform are at significant risk of adverse outcome (particularly severe pre-eclampsia requiring early delivery)[11, 12] its introduction as a screening test for all women cannot currently be recommended other than in clinical trials[1].

Low dose aspirin appears to reduce the risks of hypertension in pregnancy and of preeclampsia, especially in women at high risk. Aspirin may be offered for prophylaxis for women considered to be at high risk of hypertensive disorders. (75mg aspirin daily, commenced after the first trimester appear to be appropriate doses)[1, 3]

Antiplatelet therapy, in particular, low dose (≤ 75 mg) aspirin, reduces the risk of pre-eclampsia by around 15% for women at both low and high risk. There appears to be a similar reduction in the risk of perinatal death. Aspirin should be considered, particularly for women at high risk (e.g. pre-existing hypertension, history of pre-eclampsia in previous pregnancy, abnormal uterine artery doppler studies etc)[13, 14]

Data from small trials suggest that supplementation with vitamins C and E and calcium may reduce the risk of pre-eclampsia[15, 16]. Large trials are now underway. In the meantime, supplementation with vitamins C and E cannot be recommended for routine clinical care[1].

Women with a history of severe early onset pre-eclampsia (before 32 weeks), especially if associated with growth restriction or late fetal loss, should be screened for antiphospholipid syndrome and the implications for future pregnancies should be discussed[1].

This consensus statement is produced on behalf of the College of Obstetricians and Gynaecologists, Singapore by:

Dr Kenneth Kwek
Dr Chang Tou Choong

Valid until 2008
unless otherwise indicated

Annex 1

Anti-hypertensive Therapy in Severe Pre-eclampsia

Aim to reduce blood pressure to around 130-140 mmHg systolic and between 90-100mmHg diastolic.
Precipitous falls in blood pressure may:

- result in fetal hypoxia in a compromised fetus. It is important to monitor fetal heart rate with CTG prior to commencement of therapy
- be minimized by judicious volume loading with iv fluids prior to therapy

Hydralazine: 10 mg IV slowly over 10-15 minutes Repeat doses: 5 mg IV at 20 minute intervals may be given if necessary (the effect of a single dose can last up to 6 hours) If no lasting effect with boluses (assess over 20 minutes), consider an infusion at 2.0 mg/hour increasing by 0.5 mg/hour as required (2-20 mg/hour usually required)

Close liaison with anaesthetists: may require plasma expansion

Labetalol: If BP still uncontrolled, Labetalol 50 mg IV slowly; if necessary repeat after 20 minutes or commence IV infusion of 200 mg in 200 ml N Saline, starting at 40 mg/hour, increasing dose at 1/2 hourly intervals as required to a maximum of 160 mg/hour If blood pressure does not respond to the above, discuss with renal physicians and anaesthetists

Nifedipine

Oral route is safer and as effective as sublingual route
Dose: 10 mg orally
This dose may be repeated in 45 minutes if no clinical effect is observed. If the blood pressure remains above 160/110 90 minutes after commencing therapy, parenteral therapy should be considered.[17, 18]

Annex 2

Principles of Fluid Balance

Iatrogenic fluid overload is the main cause of maternal death in Pre-eclampsia / Eclampsia

Maintenance fluids should be given as crystalloid but additional fluid (colloid) may be necessary prior to vasodilatation to prevent maternal hypotension and fetal compromise. Consideration should also be given to correcting hypovolaemia in women with oliguria.

1. **Accurate recording of fluid balance** (including blood loss, input/output deficit)
2. **Maintenance crystalloid infusion** - 85 ml/hour, or urinary output in preceding hour plus 30 ml, with selective colloid expansion prior to pharmacological vasodilatation, or in instances with oliguria secondary to volume depletion.
3. **Diuretics** - only for women with confirmed pulmonary oedema
4. **Early involvement of anesthetists** in cases with oliguria, pulmonary edema, with very selective use of invasive monitoring

Annex 3

Magnesium Sulphate Seizure Prophylaxis

The vast majority of the initial seizures are self-limiting

MAGNESIUM SULPHATE is the anticonvulsant drug of choice[14]
Avoid polypharmacy to treat seizures - increases risk of respiratory arrest
After **ABC**:
Loading Dose: 4 g IV over 10-15 minutes
Add 8 ml of 50% $MgSO_4$ solution to 12 ml of N Saline
= 4 g in 20 ml = 20% solution

Maintenance 1 g per hour

Dose: Add 25 g $MgSO_4$ (50 ml) to 250 ml N Saline
1 g mgso4 = 12 ml per hour IV
1 g/hour is infused for 24 hours after last fit provided that:

- respiratory rate > 16 breaths/minute
- urine output > 25 ml/hour, and
- patellar reflexes are present

Administer via infusion pump

Remember to subtract volume infused from total maintenance infusion volume (85 ml/hour)

If seizure continues, or if seizures recur, give a second bolus of magnesium sulphate:
2-4 g depending on weight of patient, over 5-10 minutes
(2 g if < 70 kg and 4 g if > 70 kg)
One stat dose only

If seizures continue despite a further bolus of magnesium sulphate, diazepam (10 mg) can be considered. Intubation may become necessary in such women to protect the airway and ensure adequate oxygenation.

Further seizures should be managed by intermittent positive pressure ventilation with muscle relaxation in collaboration with the anesthetist.

When using Magnesium Sulphate:

Monitor:
Hourly urine output Respiratory rate, oxygen saturation patellar reflexes - every 10 minutes for first two hours and then every 30 minutes Check serum magnesium levels every day if infusion is continued for > 24 hours
Request $MgSO_4$ Respiratory rate < 16 breaths/minute Urine output < 25 ml/hour for 4 hours Serum Creatinine above 90mmol/L Loss of patellar reflexes Further seizures occur

Magnesium Therapeutic Levels 2.0-4.0 mmol/l
With increasing magnesium levels, the following may occur:

Feeling of warmth, flushing, double vision, slurred speech.....3.8-5.0 mmol/l
Loss of tendon reflexes.....>5.0 mmol/l
Respiratory depression.....>6.0 mmol/l
Respiratory arrest.....6.3-7.1 mmol/l
Cardiac arrest.....>12.0 mmol/l

Magnesium Toxicity
• **Urine output < 100 ml in 4 hours:** If no clinical signs of **Toxicity:** magnesium toxicity, decrease rate to 0.5 g/hour
Review overall management with attention to fluid balance and blood loss
• **Absent patellar reflexes:** Stop $MgSO_4$ infusion until reflexes return
• **Respiratory depression:** Stop $MgSO_4$ infusion
Give oxygen via facemask and place in recovery position because of impaired level of consciousness
Monitor closely
• **Respiratory arrest:** Stop $MgSO_4$ infusion
Give IV Calcium gluconate
Intubate and ventilate immediately
• **Cardiac arrest:** Commence CPR

Stop $MgSO_4$ infusion
Give IV Calcium gluconate
Intubate and ventilate immediately
If antenatal, immediate delivery
Antidote: 10% Calcium gluconate 10 ml IV over 10 minutes

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Clinical practice guideline is not intended to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances and patterns of care evolve.

These parameters of practice should be considered guidelines, based on the best available evidence at the time of development. Adherence to them will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement regarding a particular clinical procedure or treatment plan, must be made by the doctor in the light of the clinical data presented by the patient and the diagnostic and treatment options available.