COMPLICATIONS OF PREGNANCY

HYPERTENSION IN PREGNANCY

MEDICAL MANAGEMENT

TABLE OF CONTENTS

AIM

The aim of this guideline is to standardise the approach to the management of severe pre-eclampsia and eclampsia in the immediate pre- and post- delivery interval in order to improve the outcome for the mother and child[1].

BACKGROUND

Hypertensive disorders during pregnancy occur in women with pre-existing primary or secondary chronic hypertension, and in women who develop new-onset hypertension in the second half of pregnancy. Hypertensive disorders during pregnancy carry risks for the woman and the baby. Although the rate of eclampsia in the United Kingdom (UK) appears to have fallen, hypertension in pregnancy remains one of the leading causes of maternal death in the UK[2].

In Western Australia alone, Hypertension occurs in 4.0% of all pregnancies, 2.7 % due to Pre-Eclampsia and 13.6% due to Essential Hypertension. 2.4 % of Perinatal Deaths are due to Hypertension in pregnancy[3, 4].

KEY POINT

TRANSFER TO A TERTIARY SETTING IS INDICATED FOR:

All pre term pregnancies with severe pre eclampsia, eclampsia or HELLP syndrome

All term pregnancies complicated by eclampsia or HELLP syndrome

Any pregnancy in which the health care provider believes his/her health care facility would be unable to manage the complications of hypertension in pregnancy.

Note: Magnesium sulphate therapy should be considered prior to transfer in women with severe pre eclampsia, eclampsia or HELLP syndrome[5], **provided that the women will be accompanied in transfer by a medical practitioner (in case of respiratory arrest).**

DEFINITIONS

HYPERTENSION IN PREGNANCY[6]

1. Systolic blood pressure greater than or equal to 140 mmHg and/or
2. Diastolic blood pressure greater than or equal to 90 mmHg (Korotkoff 5)

These measurements should be confirmed by repeated readings over several hours[6].

Normal pregnancy is characterized by a fall in blood pressure, detectable in the first trimester and usually reaching a nadir in the second trimester. Blood pressure rises towards pre-conception levels towards the end of the third trimester.

Detecting a rise in blood pressure from 'booking' or preconception blood pressure (> 30/15 mmHg), rather than relying on an absolute value, has in the past been considered useful in diagnosing pre-eclampsia in women who do not reach systolic blood pressures of 140 mmHg or diastolic blood pressures of 90 mmHg[6]. Available evidence however, does not support the notion that these women have an increased risk of adverse outcomes. [7, 8] Nevertheless such a rise may be significant in some women, particularly in the presence of hyperuricemia and proteinuria. Further data are required and in the meantime, closer monitoring of pregnant women with an increment in blood pressure of ≥30 mmHg systolic and/or 15 mmHg diastolic is appropriate.

SEVERE HYPERTENSION IN PREGNANCY

Systolic blood pressure greater than or equal to 170 mmHg and/or diastolic blood pressure greater than or equal to 110 mmHg.

This represents a level of blood pressure above which the risk of maternal morbidity and mortality is increased. It is generally acknowledged that severe hypertension should be lowered promptly, albeit carefully, to prevent cerebral haemorrhage and hypertensive encephalopathy[6, 9]. This degree of hypertension requires urgent assessment and management. It is important to acknowledge that systolic as well as diastolic hypertension increases the risk of cerebral haemorrhage.

WHITE COAT HYPERTENSION

Is defined as hypertension in a clinical setting with normal blood pressure away from this setting when assessed by 24 hour ambulatory blood pressure monitoring or home blood pressure monitoring using an appropriately validated device. Women with this condition present early in pregnancy with apparent chronic hypertension, but their outcomes are better than those of women with true chronic hypertension. They may generally be managed without medication by using repeated ambulatory or home blood pressure monitoring. A small proportion will go on to develop preeclampsia [10].

PROTEINURIA

Is defined as the urinary excretion of ≥0.3 g protein in a 24-hour specimen. This will usually correlate with ≥30 mg/dL (≥1+ reading on dipstick) in a random urine determination with no evidence of urinary tract infection[9, 11].

OEDEMA

Oedema is no longer included in the definition of pre eclampsia as it occurs equally in women with and without this condition. Nevertheless rapid development of generalised oedema should alert the clinician to screen for preeclampsia[6].

RECORDING BLOOD PRESSURE IN PREGNANCY

The woman should be seated comfortably with her legs resting on a flat surface. In labour, the blood pressure may be measured in the left arm in lateral recumbency. The supine posture should be avoided because of the supine hypotension syndrome. Measurement of blood pressure should be undertaken in both arms at the initial visit to exclude rare vascular abnormalities such as aortic coarctation, subclavian stenosis and aortic dissection. Generally the variation in blood pressure between the upper limbs should be less than 10 mmHg.
The systolic blood pressure is accepted as the first sound heard (K1) and the diastolic blood pressure the disappearance of sounds completely (K5)(8-10). Where K5 is absent, K4 (muffling) should be accepted. Correct cuff size is important for accurate blood pressure recording. A large cuff with an inflatable bladder covering 80% of the arm circumference should be used if the upper arm circumference is greater than 33 cm. This helps to minimise over-diagnosis of hypertension during pregnancy [6, 12, 13].

CLASSIFICATION OF HYPERTENSION IN PREGNANCY

This classification of the hypertensive disorders in pregnancy reflects the pathophysiology of the constituent conditions as well as the risks and potential outcomes for both mother and baby. The following clinical classification has been adopted by numerous International and National bodies, differing predominantly in whether they require proteinuria or not for the diagnosis of pre eclampsia.T The International Society for the Study of Hypertension in Pregnancy (ISSHP) guideline no longer requires proteinuria for the diagnosis of pre eclampsia, leaving on the British NICE guideline with this requirement[17].

The classification is as follows:

- **Preeclampsia – eclampsia**
- **Gestational hypertension**
- **Chronic hypertension**
  - **-essential**
  - **-secondary**
  - **-white coat**
- **Preeclampsia superimposed on chronic hypertension**[6, 14]

PRE ECLAMPSIA

This is a multi-system disorder characterised by hypertension and involvement of one or more other organ systems and/or the fetus. Raised BP is commonly but not always the first manifestation. Proteinuria is also common but should not be considered mandatory to make the clinical diagnosis[6]

Diagnosis can be made when:
• hypertension arises after 20 weeks gestation

• accompanied by one or more of the following signs of organ involvement

Renal involvement

- Significant proteinuria – a spot urine protein / creatinine ration ≥ 30mg / mmol
- Serum or plasma creatinine greater than or equal to 90 micromol/L or
- Oliguria < 80mL / 4 hours

Haematological involvement

- Thrombocytopenia < 100,000 /µL
- Haemolysis :schistocytes or red cell fragments on blood film, raised bilirubin, raised lactate dehydrogenase > 600mIU/L, decreased haptoblobin
- DIC

Liver involvement

- Raised transaminases
- Severe epigastric or right upper quadrant pain

Neurological involvement

- Convulsions (Eclampsia)
- Persistent visual disturbances (photopsia, scotomata, cortical blindness, posterior reversible encephalopathy syndrome, retinal vasospasm)
- Persistent, new headache
- Stroke

Pulmonary oedema
Fetal growth restriction (FGR)

GESTATIONAL HYPERTENSION

- New onset of hypertension arising after 20 weeks gestation
- No additional maternal or fetal features of preeclampsia
- Resolves within 3 months postpartum

The earlier the gestation at presentation and the more severe the hypertension, the higher the likelihood of developing preeclampsia or an adverse pregnancy outcome[6, 14].

CHRONIC HYPERTENSION

Pre-existing hypertension is a strong risk factor for the development of preeclampsia and requires close clinical surveillance.

1 Essential

BP greater than 140/90 mmHg preconception or prior to 20 weeks without an underlying cause[16]

or

BP less than 140/90 entering pregnancy on antihypertensives

2 Secondary

Hypertension due to:

- chronic kidney disease (e.g. glomerulonephritis, reflux nephropathy and adult polycystic kidney disease)
- renal artery stenosis
- systemic disease with renal involvement (e.g. diabetes mellitus, systemic lupus erythematosus)
- endocrine disorders (e.g. phaeochromocytoma, Cushing's syndrome and primary hyperaldosteronism)
- coarctation of the aorta

PREECLAMPSIA SUPERIMPOSED ON CHRONIC HYPERTENSION

This is diagnosed when a woman with pre-existing hypertension develops systemic features of preeclampsia, after 20 weeks gestation. Worsening or accelerated hypertension should increase surveillance for preeclampsia but is not diagnostic.

RISK FACTORS FOR PRE ECLAMPSIA[1, 17]

Moderate risk

- Age 40 years or more
- First pregnancy
- Multiple pregnancy
- Interval since last pregnancy of more than 10 years
- Body mass index of 35 or more at presentation
- Family history of pre-eclampsia

High risk

- Chronic hypertension
- Chronic kidney disease
- Hypertensive disease during a previous pregnancy
- Diabetes
- Autoimmune disease

INVESTIGATION OF NEW ONSET HYPERTENSION AFTER 20 WEEKS GESTATION

Any woman presenting with new hypertension after 20 weeks gestation should be assessed for signs and symptoms of preeclampsia. Initially assessment and management in a day assessment unit may be appropriate. If features of preeclampsia are detected, admission to hospital is indicated. The presence of severe hypertension, headache, epigastric pain, oliguria or nausea and vomiting are

ominous signs which should lead to urgent admission and management, as should any concerns about fetal wellbeing.

MATERNAL

The following investigations should be performed in all women with new onset hypertension after 20 weeks gestation.

- Spot urine PCR
- FBP
- Urea, creatinine, electrolytes
- Liver function tests
- Ultrasound assessment of fetal growth, amniotic fluid volume and umbilical artery Doppler assessment

If features of preeclampsia are present, additional investigations should include:

- Urinalysis for protein and urine microscopy on a carefully collected mid-stream urine sample.
- If there is thrombocytopenia or a falling haemoglobin, investigations for disseminated intravascular coagulation and / or haemolysis are indicated

Table 1

Test	Age Group	Levels deemed to be elevated (KEMH Lab)
LDH	>16 years	> 618u/L
ALT	>15 years	> 35 u/L
AST	>15 years	> 32 u/L
Uric Acid	>15 years	> 0.36 mmol/L

Notes:

- Patients with severe early onset preeclampsia warrant investigation for associated conditions e.g. systemic lupus erythematosus, underlying renal disease, antiphospholipid syndrome or thrombophilias. The timing of these investigations will be guided by the clinical features.
- Acute Fatty Liver can also present itself as HELLP syndrome.
- Although a very rare disorder, undiagnosed phaeochromocytoma in pregnancy is potentially fatal and may present as preeclampsia[21, 22] . Measurement of fasting plasma free metanephrines/normetanephrines or 24 hour urinary catecholamines should be undertaken in the presence of very labile or severe hypertension.

- Subsequent management will be based on the results of ongoing blood pressure measurement and these investigations – see table 2 below[6]

- Amongst women referred for assessment of new onset hypertension, a number will have normal blood pressure and investigations. These women are considered to have transient or labile hypertension. Repeat assessment should be arranged within 3-7 days as many will subsequently develop pre-eclampsia

Table 2 Ongoing Investigation of women with hypertension in pregnancy

Classification	Modality	Frequency
Chronic Hypertension	Urinalysis for protein* Pre Eclampsia bloods	Each visit If sudden increase in BP or new proteinuria
Gestational Hypertension	Urinalysis for protein Pre Eclampsia bloods	1-2 x per week Weekly
Pre Eclampsia	Urinalysis for protein Pre Eclampsia bloods	At time of diagnosis: if non-proteinuric, repeat daily Twice weekly or more frequent if unstable

ASSESSMENT OF SEVERITY IN PRE ECLAMPSIA

All patients with pre eclampsia must be regarded as being at risk of major maternal and fetal complications. However, there are certain indicators of particular concern when they occur in a woman with definite pre eclampsia:

HELLP syndrome – any component (see section on HELLP Syndrome Page 14)

Severe hypertension refractory to usual treatment

Renal impairment – creatinine greater than 106µmol/L

Pulmonary oedema

Persistent neurological symptoms – headache / altered mental state / clonus

“Pre eclamptic angina” – severe epigastric pain and/or vomiting with abnormal liver enzymes

Fetal growth restriction

- Pre eclampsia usually pursues a course of deterioration, sometimes slowly and sometimes quickly. It may evolve from mild to moderate to severe over a period of hours or days, and requires frequent reassessment by medical staff.

MANAGEMENT OF PRE ECLAMPSIA AND GESTATIONAL HYPERTENSION

Preeclampsia is a progressive disorder that will inevitably worsen if pregnancy continues. Current therapy does not ameliorate the placental pathology nor alter the pathophysiology or natural history of preeclampsia. Delivery is the definitive management and is followed by resolution, generally over a few days but sometimes much longer. Obstetric consultation is mandatory in all women with severe pre eclampsia. In those women with preeclampsia presenting at extreme preterm gestations consultation with KEMH should be arranged.At mature gestational age, delivery should not be delayed. Even so, it is important to control severe hypertension and other maternal derangements before subjecting the woman to the stresses of delivery[6].
Prolongation of pregnancy in the presence of preeclampsia carries no benefit for the mother but is desirable at early gestations to improve the fetal prognosis as in general, fetal outcome is proportional to gestational age at delivery[22]. In cases of preterm preeclampsia before 34 weeks, delivery should be delayed for at least 24-48 hours if maternal and fetal status permit, to allow fetal benefit from antenatal corticosteroids administered for lung maturation[23]. Continuation of pregnancy carries fetal risk and some stillbirths will occur despite careful monitoring.
The management of women with preeclampsia between gestational ages of 24-32 weeks should be restricted to those centres with appropriate experience and expertise. Clear “endpoints” for delivery should be defined for each patient (Table 3), such that the decision to terminate the pregnancy is based on agreed criteria. In many cases, the timing of delivery will be based upon a number of factors, maternal and/or fetal rather than a single absolute indication for delivery.

In the presence of HELLP syndrome, expectant management is harmful with a 6.3% incidence of maternal death and an increased risk or placental abruption. In such cases delivery should be planned as soon as feasible.

Table 3 Indications for delivery in women with preeclampsia or gestational hypertension[6]

Maternal	**Fetal**
Gestational Age >37weeks	Severe fetal growth restriction
Inability to control hypertension	Non-reassuring fetal status
Deteriorating platelet count	
Deteriorating liver function	
Deteriorating renal function	
Placental abruption	
Persistent neurological symptoms Eclampsia	
Persistent epigastric pain, nausea or	

vomiting with abnormal liver function tests	
Acute pulmonary oedema	

Table 4 Timing of Delivery and gestation of Presentation of Preeclampsia

Gestation at onset	**Previable < 23 weeks**	**23 - 31[6]**	**32 - 36[6]**	**37+ 0 onwards**
Delivery Plan	Consult with KEMH: likely to need termination of pregnancy or extreme preterm delivery. High risk patient	Consult and transfer to KEMH: likely to need preterm delivery. Aim to prolong pregnancy where possible.	Aim to prolong pregnancy where possible, deliver in an institution with appropriate paediatric care.	Plan delivery on best day in best way

Except in the situation of acute fetal compromise, urgent delivery is not helpful in pre eclampsia and the mother must be resuscitated before being subjected to the delivery process. Therefore, in severe pre eclampsia, delivery must always be preceded by:

- control of severe hypertension
- attention to fluid status
- correction of coagulopathy (usually thrombocytopenia)
- control of eclampsia, or prophylaxis against eclampsia if indicated (see below)

A team approach, involving obstetrician, midwife, neonatologist, anaesthetist and physician provides the best chance of achieving a successful outcome for mother and baby. Regular and ongoing reassessment of both the maternal and fetal condition is required. Careful daily assessment for clinical symptoms and signs should be complemented by regular blood and urine tests as indicated (Table 1 and 3).

The only controlled studies of bed rest for preeclampsia have shown no significant maternal or fetal benefit[24] . However, admission to hospital allows close supervision of both mother and fetus as progress of the disorder is unpredictable. Outpatient monitoring may be appropriate in milder cases after a period of initial observation.

OUTPATIENT MANAGEMENT

Women with mild gestational hypertension can be cared for at home, in as long as:

- there are no obstetric contraindications
- there are no geographic contraindications
- there is no evidence of fetal compromise
- the patient has her blood pressure monitored regularly either at home by a visiting midwife with obstetrician back up or in MFAU [25]
- the patient visits the clinic 1-2 times per week

Note: Any evidence of maternal and or fetal compromise or failure to respond to outpatient treatment requires hospitalisation.

INPATIENT MANAGEMENT

Maternal

Evaluate patient to determine if the admission should be to Labour and Birth Suite or to the ward.

Perform baseline laboratory evaluations (FBP, Serum creatinine, LDH, ALT, AST, Uric Acid and PCR)

Review by obstetric registrar/ Consultant, at least daily (including weekends and public holidays) to evaluate the patient for evidence of maternal deterioration (headaches, visual changes, or epigastric distress)

Fetal

Fetal surveillance by biophysical Profile, Doppler studies and cardiotocography as appropriate.

Administer betamethasone 11.4 mg IM x 2 doses, 24 hours apart, if appropriate. Corticosteroid therapy in pregnancies between 23 and 36+6 weeks accelerates fetal lung maturity, decreases Respiratory Distress Syndrome (RDS), intraventricular haemorrhage (IVH) and the risk of fetal death in these pregnancies.

SPECIAL MANAGEMENT ISSUES FOR PATIENTS WITH HYPERTENSIVE CRISES (BP OF ≥ 170/110).

Admit to the Adult Special Care Unit/Labour and Birth Suite for close observation and antepartum care. Manage in the Adult Special Care Unit postpartum until the crisis has resolved.

Evaluate and stabilize with frequent maternal and continuous fetal surveillance.

Consider $MgSO_4$ therapy for seizure prophylaxis.

Magnesium sulphate should be considered for women with pre-eclampsia for whom there is concern about the risk of eclampsia. This is usually in the context of severe pre-eclampsia once a delivery decision has been made and in the immediate postpartum period. In women with less severe disease the decision is less clear and will depend on individual case assessment[1].

Anaesthesia: May consider epidural/spinal anaesthesia if maternal platelet count is > 100,000 and platelet function is normal.

DRUG THERAPY

ANTIHYPERTENSIVE THERAPY

Evidence suggests that antihypertensive drug therapy confers no clear benefit to women with mild pre eclampsia[26-28]. Randomized control trials of women with mild pre eclampsia remote from term, which compared antihypertensive drug therapy with no medication or a placebo, have been reported. In some of these trials, the frequency of proteinuria, progression to severe disease, and neonatal respiratory distress syndrome were higher in the women not treated.[29-32] These observations however have not been confirmed in other trials.[33-35]

In the absence of compelling evidence, treatment of mild to moderate hypertension in the range 140-160/90-100 mm Hg should be considered an option and will reflect local practice. Above these levels, treatment should be considered mandatory[6].

In women with severe pre eclampsia, or those who have received treatment for hypertensive crisis, maintenance control of BP is essential to reduce the risk of cerebral events and to prolong the pregnancy for fetal benefit where possible. However, the maternal blood pressure must not be lowered too drastically because inadequate placental perfusion may occur where placental circulation has adapted to a higher blood pressure.

ACUTE TREATMENT OF SEVERE HYPERTENSION

Antihypertensive treatment should be commenced in all women with a systolic blood pressure ≥170 mm Hg or a diastolic blood pressure ≥110 mm Hg because of the risk of intracerebral haemorrhage and eclampsia [26]. Whilst there is no controlled trial to determine how long severe hypertension may be left untreated, it is recommended that treatment be administered promptly aiming for a gradual and sustained lowering of blood pressure.
A recent systemic review of the literature regarding antihypertensive agents used for the management of severe hypertension acknowledged that each medication had benefits and risks.[56] Both intravenous and oral agents may be used depending on the clinical situation.

The agent of choice for the acute treatment of hypertension is oral nifedipine. This is administered as a 10mg oral dose initially, with a repeat dose of 10mg if there is inadequate response after 30 minutes. Headache is frequently a side effect.

Intravenous labetolol is the agent of choice for intravenous administration. This is administered as a 20-80mg bolus dose over 2 minutes. Associated side effects may be bradycardia, bronchospasm and headache.

The third agent of choice is hydralazine. This is administered as an intravenous or intramuscular dose of 5-10mg every 20-30 minutes to control hypertension of ≥170 systolic and / or 110 diastolic.

Table 4 - Acute blood pressure lowering for severe hypertension[36-38]

Medication	Dose	Route	Onset of action
Nifedipine	10mg IR tablet Maximum 40mg	Oral	30-45 minutes. Repeat after 45 minutes if response is inadequate
Labetolol	20-80mg Maximum 80mg	IV bolus over 2 minutes. Repeat every 10 minutes prn	Maximal effect usually occurs within 5 minutes of each dose.
Hydralazine	5-10mg (First dose 5mg if fetal compromise)	IV bolus over 2 minutes IM injection	20 minutes. May be repeated after 20 minutes.
Diazoxide	15-45mg Max 300mg	Rapid IV bolus	3-5 minutes , repeat after 5 minutes

Note: Blood pressure should not be allowed to fall below a level of 140/80**.**

ONGOING TREATMENT FOR HYPERTENSION

In terms of lowering blood pressure in preeclampsia, a number of drugs have demonstrated safety and efficacy (Table 4). First line drugs include methyldopa, and labetolol [39-41]. Second line agents are hydralazine, nifedipine and prazosin[42-45]. Angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers are contraindicated in pregnancy. Their use in the third trimester has been associated with fetal death and neonatal renal failure. All of the drugs in Table 4 along with enalapril, captopril and quinapril are considered compatible with breastfeeding [46].

Antihypertensive therapy should be considered:

- When the SBP ≥ 150 mm Hg at least twice in a 24 hour period separated by four hours.
- When DBP ≥ 95 mm Hg at least twice in a 24 hour period separated by four hours.
- Following the acute treatment of severe hypertension (170/110) [26]

Table 5. Guidelines for selecting antihypertensive drug treatment in pregnancy[6]

Drug	Dose	Action	Contraindications	Practice points
Methyldopa	250-750 mg tds	Central	Depression	Slow onset of action over 24 hrs. Dry mouth, sedation, depression, blurred vision. Withdrawal effects:rebound hypertension
Labetolol	100-400 mg tds	B blocker with mild alpha vasodilator effect	Asthma, Chronic airways limitation	Bradycardia, bronchospasm, headache, nausea, scalp tingling which usually resolves within 24-48 hrs (labetolol only)
Nifedipine	20 mg SR once a day to a maximum of 60mg SR once a day	Calcium channel antagonist	Aortic Stenosis	Severe Headache associated with flushing and tachycardia. Peripheral oedema, constipation
Prazosin	0.5-5mg tds	Alpha blocker		First dose effect-orthostatic hypotension
Hydralazine	25-50 mg tds	Vasodilator		Flushing, headache, nausea, lupus-like syndrome

It is important to control severe hypertension at any gestation and post partum. Induction of labour or Caesarean section does not control hypertension even though

delivery begins the process of resolution of preeclampsia. Thus, antihypertensive medication will usually be required even when delivery has been arranged[6].
When either of these has been unsuccessful, consider consultation with Obstetric Physician. In some cases of severe hypertension, it is necessary to add a second or even third agent.

FETAL SURVEILLANCE IN WOMEN WITH HYPERTENSION IN PREGNANCY

HYPERTENSION	MODALITY	FREQUENCY
Chronic Hypertension	Early dating ultrasound U/S for fetal growth /AFV/Doppler	First trimester 3rd trimester:repeat as indicated
Gestational hypertension	U/S for fetal growth / AFV/Doppler	At time of diagnosis and 3 – 4 weekly
Preeclampsia + / - Fetal growth restriction	U/S for fetal growth/AFV/Doppler Cardiotocography	At time of diagnosis. Subsequent frequency is dependent on the clinical progression of the disease.

AFV = Assessment of amniotic fluid volume

ECLAMPSIA

Eclampsia remains rare in Australia. There are no reliable clinical markers to predict eclampsia and conversely, the presence of neurological symptoms and/or signs is rarely associated with seizures[6, 47]. Seizures may occur antenatally, intra-partum or postnatally, usually within 24 hours of delivery but occasionally later. Hypertension and proteinuria may be absent prior to the seizure and not all women will have warning symptoms such as headache, visual disturbances or epigastric pain[48].
The further from delivery that the seizure occurs, the more carefully should other diagnoses be considered. Cerebral venous thrombosis in particular may occur in the first few days of the puerperium. It should be remembered that eclampsia is not the commonest cause of seizures in pregnancy and the differential diagnosis includes epilepsy and other medical problems that must be considered carefully, particularly when typical features of severe preeclampsia are lacking.

MANAGEMENT OF ECLAMPSIA

There are four main aspects to care of the woman who sustains eclampsia[6].

1. Resuscitation

Resuscitation requires institution of intravenous access, oxygen by mask, assuring a patent airway and institution of intravenous access[6] Intravenous diazepam (2mg/min to maximum of 10mg) or Midazolam (0.1 – 0.2mg /kg IV or IM) may be given if the seizure is long.

Intravenous Magnesium Sulphate is the agent of choice.
See Loading dose- 4gm over 20 mins (rate 150 mL/hr for 20 mins only = 50mL).

2. Prevention of further seizures

Following appropriate resuscitation, treatment should be continued with Magnesium Sulphate.

Ref. Administration of Magnesium sulphate clinical guideline Magnesium Sulphate Anticonvulsant Therapy

3. Control of hypertension

Control of severe hypertension to levels below 160/100 mmHg by parenteral therapy is essential as the threshold for further seizures is lowered after eclampsia, likely in association with vasogenic brain oedema. In addition, the danger of cerebral haemorrhage is real.

4. Delivery

Arrangements for delivery should be decided once the woman's condition is stable. In the meantime, close fetal monitoring (continuous CTG) should be maintained. There is no role, with currently available treatment, for continuation of pregnancy once eclampsia has occurred, even though many women may appear to be stable after control of the situation has been achieved.

Prevention of eclampsia in the woman with preeclampsia

The drug of choice for the prevention of eclampsia is magnesium sulphate[49]. Although there is good evidence for the efficacy of this therapy, the case for its routine administration in women with preeclampsia in countries with low maternal and perinatal mortality rates is less than compelling[50].

Evidence indicates that magnesium sulphate is the superior drug to use in the prevention and the treatment of eclamptic seizures.[18,19]
In the patient with known renal disease or myasthenia gravis however, phenytoin sodium is the anti-seizure medication of choice. Phenytoin sodium is administered in a total dose of 15mg/kg at an infusion rate of 40mg/min with continuous cardiac and blood pressure monitoring.

ADMINISTRATION OF MAGNESIUM SULPHATE

See clinical guideline Magnesium Sulphate Anticonvulsant Therapy

Magnesium Sulphate should not be prescribed for the prevention of eclampsia without discussion with the Consultant Obstetrician on call.

Magnesium sulphate therapy is recommended for use antepartum, intrapartum and within the first 24 hours postpartum for severe pre eclampsia (as defined on page 2) when the following factors are present:

- persistently elevated blood pressure despite adequate hypotensive therapy and appropriate fluid management,
- evidence of CNS dysfunction, thrombocytopenia or liver disease[2, 5, 16].

Before discontinuation of $MgSO_4$ therapy:

the blood pressure should be stable (consistently below 150/100)

the patient should have adequate diuresis

the patient should be clinically improved (absence of headache, epigastric pain).

Postpartum Management

Monitor the patient in the Adult Special Care Unit[52] or Labour and Birth Suite until she begins to recover.

Continue magnesium sulphate until stabilisation and adequate diuresis is achieved.

Antihypertensive therapy should be commenced if the BP is >150 mmHg systolic or >100 mmHg diastolic in the first four postpartum days. Options for antihypertensive therapy include:

- Labetolol 100mg TDS to start
- Atenolol 50mg daily. On rare occasions, may need increasing to 100mg/day.
- Nifedipine SR 20mg BD to start.
- Enalapril 5-10mg daily.

Resolution of preeclampsia

After delivery, all clinical and laboratory derangements of preeclampsia recover, but there is often a delay of several days, and sometimes longer, in return to normality. On the first day or two after delivery, liver enzyme elevations and thrombocytopenia will often worsen before they reverse. Hypertension may persist for days, weeks or even up to three months and will require monitoring and slow withdrawal of antihypertensive therapy. Resolution is still assured if the diagnosis was pre-eclampsia and there is no other underlying medical disorder. The woman and her family are often overwhelmed and distressed from their experience and appropriate counselling post partum should include psychological and family support.
All women who develop preeclampsia and gestational hypertension are at risk of these disorders in future pregnancies and should receive appropriate counselling before embarking upon another pregnancy[6].

NOTE: Magnesium Sulphate may also be used antenatally prior to preterm birth for Neuro Protection of the fetus post birth- to reduce the incidence of cerebral palsy.

HELLP SYNDROME

HELLP Syndrome is a variant of severe preeclampsia (**H**aemolysis, **E**levated **L**iver enzymes and **L**ow **P**latelet) count. Maternal mortality is reported to be as high as 1-2%

The elements of this variety of severe pre eclampsia are:

- thrombocytopenia (common)
- haemolysis (rare) and
- elevated liver enzymes (ALT, LDH - common).

Epigastric or right upper quadrant pain in a woman with preeclampsia often represents hepatic involvement. This is called 'Pre eclamptic Angina' [45]. The pain responds poorly to analgesia but both the pain and associated increases in liver enzymes (AST, ALT) may subside (albeit temporarily) after blood pressure lowering, particularly with vasodilators. If the cause of epigastric or right upper quadrant pain is not clear, close ongoing assessment is required, with careful review of all indicators of maternal and fetal wellbeing and appropriate imaging of the liver and gallbladder[6]. Thrombocytopenia is the commonest hematologic abnormality seen in preeclampsia; the lower limit of the normal platelet count in pregnancy is approximately $140x10^9$/L but the risk of spontaneous bleeding is not significantly increased until the count falls below 50×10^9/L. Even so, there are concerns with central neuraxial anaesthesia and analgesic techniques at higher levels ($50\text{-}75 \times 10^9$ /L), and surgical bleeding may be increased even with moderate thrombocytopenia[6].

In a woman with pre eclampsia, the presence of any one of the following is an indicator of severe disease, even if not suggested on other criteria such as severity of hypertension.

- a maternal platelet count of $<100{,}000 \times 10^9$/L
- a transaminase level or LDH more than double the normal upper limit
- haemolysis of any quantity

MANAGEMENT OF HELLP SYNDROME

Antenatal management

If the platelet count is sufficiently low to present a hazard for operative delivery, a platelet transfusion should be considered[6] (consult with Consultant Haematologist or Obstetric Physician).

Postpartum management

If there is significant bleeding attributed to pre-eclamptic thrombocytopenia at any time in the puerperium a platelet transfusion should be given[6] (consult with Consultant Haematologist or Obstetric Physician).

In the absence of bleeding, consider a platelet transfusion in the first 72 hours only if the count falls below 40,000 and there is concern of possible bleeding (e.g. after Caesarean Section).
If the count remains below 40,000 after 72 hours from delivery without significant bleeding and without sign of impending recovery, consultation with the Consultant Haematologist or Obstetric Physician is indicated.

CHRONIC HYPERTENSION

Hypertension affects up to 13.6% of the West Australian adult population[4], the prevalence increasing with age. The diagnosis can be difficult in women whose blood pressure before pregnancy or early in the first trimester is unknown. Very rarely preeclampsia can present before 20 weeks' gestation and the physiological fall in blood pressure in the second trimester can obscure pre-existing chronic hypertension[6].
Women with chronic hypertension have an increased risk of accelerated hypertension in the third trimester, superimposed preeclampsia, fetal growth restriction, placental abruption, premature delivery and stillbirth. These events are seen more often in women who develop preeclampsia and are not correlated with actual blood pressure levels[39, 47]. The exception to this appears to be uncontrolled hypertension in the first trimester when later fetal and maternal morbidity and mortality are markedly increased [9]. Other indicators of poor prognosis include a failure of blood pressure to normalize in the second trimester, the presence of secondary hypertension, a history of longstanding severe hypertension, and concurrent cardiovascular and/or renal disease.
The woman with chronic hypertension, whether essential or secondary, should be observed frequently during pregnancy by an obstetrician and by a physician familiar with the management of hypertension in pregnancy[6].
Benefits of therapy for the treatment of mild chronic hypertension in pregnancy have not been proven. In general, treatment is considered when systolic blood pressure exceeds 150 mm Hg and/or diastolic pressure exceeds 95 mm Hg on several occasions. Possible benefits include reduction in hospital admission (when the hypertension is not due to pre-eclampsia) and prolongation of gestation when uncontrolled hypertension would result in delivery. For agents used, see below.

BASELINE ASSESSMENTS

Maternal

Ophthalmic examination.

Spot urine protein: creatinine ratio where there is doubt about proteinuria on dipstick, i.e., +1 or +2 proteinuria.

Serum electrolytes.

ECG (if not done recently).

24 hour urine catecholamines if there is severe hypertension.

Fetal

Baseline ultrasound for the assessment of fetal anatomy.

Follow-up ultrasound at 26-28 weeks.

From 28 weeks, ultrasound every 2-3 weeks to evaluate fetal growth.

Weekly non-stress tests from 30 weeks.

ORAL DRUG THERAPY

Methyldopa: a centrally acting adrenergic agonist is the most commonly prescribed medication for the treatment of hypertension in pregnancy. Start at a dose of 250mg TDS, increasing to a maximum of 750mg TDS as required.

Labetolol: is an alpha and beta-blocking agent. Commence at a dose of 100mg TDS, increasing up to 400 mg TDS as required

Nifedipine: a calcium channel blocker that can be used in acute hypertensive situations. Nifedipine may be added as a second line agent to either labetolol or methyldopa. Commence at 20mg SR once a day increasing to a maximum dose of 60mg SR once a day as required.

Atenolol and other highly selective beta blocker drugs are not recommended for prolonged use in pregnancy as they have been associated with fetal growth restriction[41, 53, 54]. The use of ACE-inhibitors and angiotensin receptor blockers is contraindicated in pregnancy. They have been associated with an increased risk of fetal, particularly cardiovascular, malformations in early pregnancy in one study and are known to cause adverse sequelae for the fetus in late pregnancy[55] . Diuretics, although not teratogenic, may restrict the natural plasma volume expansion of pregnancy and are not recommended for the treatment of hypertension.

POST PARTUM MANAGEMENT OF WOMEN WITH CHRONIC HYPERTENSION

In many women with chronic hypertension or superimposed pre-eclampsia, blood pressure is unstable for 1-2 weeks after delivery and may be difficult to control. It may be particularly high on the third to the sixth day after delivery and it is often necessary to increase or commence antihypertensive medication at that time. All of the agents mentioned earlier are compatible with breast feeding, as are the ACE inhibitors enalapril, captopril and quinapril[6].

CHRONIC HYPERTENSION WITH SUPERIMPOSED PREECLAMPSIA

As already mentioned, the main risk of chronic hypertension in pregnancy is the development of superimposed preeclampsia in the second half of pregnancy which occurs in about 20% of women. This is of considerable concern as the risks to both mother and fetus are greater than those of chronic hypertension alone. Management of superimposed preeclampsia should be as outlined above for pre-eclampsia unless specific diagnostic issues, such as some secondary causes of hypertension, are present[6]. It is recommended that all women with a hypertensive complication of pregnancy have a postpartum hypertension follow-up. Depending on the severity of the hypertension this follow-up should be 2-6 weeks after discharge from hospital.

REFERENCES / STANDARDS	
National Standards – 1 Clinical Care is Guided by Current Best Practice 4 Medication Safety Legislation - Nil Related Guidelines / Policies – Hypertension in Pregnancy Other related documents – **Nil**	
RESPONSIBILITY	
Policy Sponsor	Medical Director OGCCU
Initial Endorsement	November 2003
Last Reviewed	January 2015
Last Amended	April 2016
Review date	January 2018

1. Royal College of Obstetricians and Gynaecologists. Management of Pre Eclampsia/ Eclampsia,. **Greentop guidelines No 10(A),**. 2010;London.
2. Empson M, Lassere M, Craig J, Scott J. Prevention of recurrent miscarriage for women with antiphospholipid antibody or lupus anticoagulant. **The Cochrane Database of Systematic Reviews** 2005(8).
3. Le M, Tran BN. Perinatal Statistics in Western Australia, 2008: Twenty-sixth Annual Report of the Western Australian Midwives' Notification System,. **Department of Health- Government of Western Australia,**. 2008.
4. Coghill A E, Hansen S, Littman A J. Risk factors for eclampsia: a population-based study in Washington State, 1987-2007. **American Journal of Obstetrics and Gynecology**. 2011;In Press, Corrected Proof.
5. Duley L, and the The Magpie Trial Collaborative Group. Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial. **The Lancet**. 2002;359(9321):1877-90.
6. Lowe SA, Bowyer L,, Lust K, McMahon LP, Morton M, et al. Guidelines for the management of hypertensive disorders of pregnancy. **Society of Obstetric Medicine of Australia and New Zealand**. 2014.
7. North RA., Taylor RS., Schellenberg JC. Evaluation of a definition of pre-eclampsia. **American Journal of Obstetrics and Gynaecology**. 1999;106:767-73.
8. Levine RJ. Should the definition of preeclampsia include a rise in diastolic blood pressure ≥15 mm Hg? **American Journal of Obstetrics and Gynaecology**. 2000;182:225.
9. National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy. Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy. **American Journal of Obstetrics and Gynecology**. 2000;183(1):S1-S22.
10. Brown MA, Mangos G, Davis G, Homer C. The natural history of white coat hypertension during pregnancy. **British Journal of Obstetrics and Gynaecology**. 2005;112(5):601-6.
11. Côté A-M, Brown MA, Lam E, Dadelszen Pv, Firoz T, Liston RM, et al. Diagnostic accuracy of urinary spot protein:creatinine ratio for proteinuria in hypertensive pregnant women: systematic review. **BMJ**. 2008 May 3, 2008;336(7651):1003-6.
12. Duckitt K, Harrington D. Risk factors for pre-eclampsia at antenatal booking: systematic review of controlled studies. **British Medical Journal**. 2005;330(7491):565.
13. Mostello D, Kallogjeri D, Tungsiripat R, Leet T. Recurrence of preeclampsia: effects of gestational age at delivery of the first pregnancy, body mass index, paternity, and interval between births. **American Journal of Obstetrics and Gynecology**. 2008;199(1):55.e1-.e7.
14. Fagermo N., et al. Hypertensive disorders of pregnancy. **Statewide Maternity and Neonatal Clinical Guidelines- Government of Queensland,**. 2010.
15. Askie LM, Duley L, Henderson-Smart DJ, Stewart LA. Antiplatelet agents for prevention of pre-eclampsia: a meta-analysis of individual patient data. **The Lancet**. 2007;369(9575):1791-8.

16. Lelia Duley, Shireen Meher, Edgardo Abalos. Management of pre-eclampsia. **British Medical Journal**. 2006;332:463-8.
17. NICE. Hypertension in pregnancy: the management of hypertensive disorders during pregnancy.National Institute for Health and Clincial Excellence.2012
18. Royal College of Obstetricians and Gynaecologists. Pre-elampsia- study group statement. **RCOG**. 2011;http://www.rcog.org.uk/womens-health/clinical-guidance/pre-eclampsia-study-group-consensus-statement.
19. Edlow AG, Srinivas SK, Elovitz MA. Investigating the risk of hypertension shortly after pregnancies complicated by preeclampsia. **American Journal of Obstetrics and Gynecology**. 2009;200(5):e60-e2.
20. Mostello D, Catlin TK, Roman L, Holcomb WL, Leet T. Preeclampsia in the parous woman: Who is at risk? **American Journal of Obstetrics and Gynecology**. 2002;187(2):425-9.
21. Sibai B.M. Diagnosis, Prevention, and Management of Eclampsia. **Obstetic and gy**. 2005;105:402-10.
22. Duley. L., Meher. S., Abalos. E. Management of pre-eclampsia. **British Medical Journal**. 2006;332:463-8.
23. Matchaba PT, Moodley J. Corticosteroids for HELLP syndrome in pregnancy (Review). **The Cochrane Database of Systematic Reviews,**. 2009;doi/10.1002/14651858.CD002076.pub3.
24. Meher S, Abalos E, Carroli G. Bed rest with or without hospitalisation for hypertension during pregnancy (Review). **The Cochrane Database of Systematic Reviews,**. 2010.
25. Meher S, Duley L. Rest during pregnancy for preventing pre-eclampsia and its complications in women with normal blood pressure (Review),. **The Cochrane Database of Systematic Reviews,**. 2010;doi/10.1002/14651858.CD005939.
26. Duley. L., Henderson-Smart., D.J., Meher. S. Drugs for treatment of very high blood pressure during pregnancy (Review). **The Cochrane Database of Systematic Reviews,**. 2009;doi/10.1002/14651858.CD001449.pub2/pdf.
27. Lubarsky SL, Barton JR, Friedman SA, Nasreddine S, Ramadan MK, Sibai BM. Late postpartum eclampsia revisited. **Obstetic and gy**. 1994;83:502-5.
28. Leslie K, Thilaganathan B, Papageorghiou A. Early prediction and prevention of pre-eclampsia. **Best Practice & Research Clinical Obstetrics & Gynaecology**. 2011;25(3):343-54.
29. Pickles CJ. Pipkin FB. Symonds EM. A randomized placebo controlled trial of labetalol in the treatment of mild to moderate pregnancy induced hypertension. **Br J Obstet Gynecol**. 1992;99::964-8 (Level II).
30. Rubin PC. Butters L. Clark DM. Placebo-controlled trial of atenolol in treatment of pregnancy associated hypertension. **Lancet**. 1983;1(8322):431-4 (Level II).
31. Pickles CJ. Symonds EM. Pipkin FB. The fetal outcome in a randomized double blind controlled trial of labetalol versus placebo in pregnancy induced hypertension. **Br J Obstet Gynecol**. 1989;96::38-43 (Level II).
32. Phippard AF. Fischer WE. Horvath JS. Early blood pressure control improves pregnancy outcome in primigravid women with mild hypertension. **Med J Aust**. 1991;154::378-82 (Level II).
33. Sibai BM. Gonzalez AR. Mabie WC. Moretti M. A comparison of labetalol plus hospitalization versus hospitalization alone in the management of pre eclampsia remote from term. **Obstet Gynecol**. 1987;70::323-7 (Level II).
34. Sibai BM. Barton JR. Aki S. Sarinoglu C. Mercer BM. A randomized prospective comparison of nifedipine and bed rest versus bedrest alone in the management of preeclampsia remote from term. **Am J Obstet Gynecol**. 1992;167::879-84. (Level II).
35. Wide-Swensson DH. Ingemarrsson I. Lunnell NO. Forman A. Skajaa K. Lindeberg B. Marsal K. Andersson KE. Calcium channel blockade (isradipine) in treatment of hypertension in pregnancy: a randomized placebo-controlled study. **Am J Obstet Gynecol**. 1995;173::872-8 (Level II).
36. Sibai B M, Makie W C, Harvey C J, Gonzalez A R. Pulmonary oedema in severe preeclampsia-eclampsia: analysis of 37 consecutive cases,. **American College of Obstetrics and Gynaecology**. 1987;156:1174-9.
37. Walters BNJ, Redman CWG. Treatment of severe pregnancy-associated hypertension with the calcium antagonist nifedipine. **British Journal of Obstetrics and Gynaecology**. 1984;91:330-6.

38. Douglas N, Robinson N, Fahy K. Inquiry into Obstetric and Gynaecological Services at King Edward Memorial Hospital 1990–2000- R5.20.26. **Government of Western Australia,**. 2001;State Law Publishers, (Perth).
39. Lloyd C. Hypertensive disorders in pregnancy,. In: Fraser D M, Cooper M A, editors. **Myles textbook for midwives,**. 15th ed. Edinburgh: Churchill Livingston; 2009. p. 397-413.
40. Roberts D, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth,. **Cochrane Database of Systematic Reviews,**. 2006(Issue 3- Art. No.: CD004454,).
41. Olds SB, London M L, Ladewig P A. Maternal Newborn Nursing: a Family and Community Based Approach. New Jersey: Prentice Hall Health; 2000.
42. Enkin M, Keirse MJ, Neilson J, et al, editors. **A guide to Effective Care in Pregnancy and Childbirth,**. 3rd ed. Oxford: Oxford University Press; 2000.
43. Morley A. Pre-eclampsia: pathophysiologyand its management,. **British Journal of midwifery**. 2004;12(1):30-7.
44. Meads C A, Cnossen J S, Meher S, Juarez-Garcia A, ter Riet G, Duley L, et al. Methods of prediction and prevention of pre-eclampsia: systematic reviews of accuracy and effectiveness literature with economic modelling. **Health Technology Assessment**. 2008;12(6).
45. Walters B. N. J. Preeclamptic Angina – A Pathognomonic Symptom of Preeclampsia. **Hypertension in Pregnancy, Informa Healthcare USA, Inc,**. 2010;Early Online:1–8,.
46. Hutcheon J A , Lisonkova S, Joseph K.S. Epidemiology of pre-eclampsia and the other hypertensive disorders of pregnancy. **Best Practice & Research Clinical Obstetrics and Gynaecology**. 2011;25(4):391-403.
47. Thangaratinam S, Langenveld J, Khan K S. Prediction and primary prevention of pre-eclampsia. **Best Practice & Research Clinical Obstetrics and Gynaecology**. 2011;25(419-433).
48. Payne B, Magee L A, von Dadelszen Assessment, surveillance and prognosis in pre-eclampsia. **Best Practice & Research Clinical Obstetrics and Gynaecology**. 2011;25(4).
49. Thornton C, Hennessy A, Grobman W A. Benchmarking and patient safety in hypertensive disorders of pregnancy. **Best Practice & Research Clinical Obstetrics and Gynaecology**. 2011;25(4).
50. Poston L, Briley AL, Seed PT, Kelly FJ, Shennan AH. Vitamin C and vitamin E in pregnant women at risk for pre-eclampsia (VIP trial): randomised placebo-controlled trial. **The Lancet**. 2006;367(9517):1145-54.
51. The Magpie Collaborative Group. Do women with pr-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial. **The Lancet**. 2002;359(June 1):1877-89.
52. Martin SR, Foley MR. Intensive care in obstetrics: An evidence-based review. **American Journal of Obstetrics and Gynecology**. 2006;195(3):673-89.
53. Firoz T , Melnik T. Postpartum evaluation and long term implications. **Best Practice & Research Clinical Obstetrics and Gynaecology 25**. 2011;24(4).
54. Douglas N, Robinson N, Fahy K. Inquiry into Obstetric and Gynaecological Services at King Edward Memorial Hospital 1990-2000- R5.20.18,. **Government of Western Australia,**. 2001;State Law Publishers(Perth).
55. Seligman S. Which blood pressure? **British Journal of Obstetrics and Gynaecology**. 1983;94:497-8.
56. Duley L MS, Jones L. 2013, Issue 7. Art. No.: CD001449. DOI: 10.1002/14651858.CD001449.pub3. . Drugs for treatment of very high blood pressure during pregnancy. . Cochrane Database of Systematic Reviews. 2013(7).