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TRAINING MANUAL ON HDP

Tutorial for practical lessons of obstetrics for students of 5^{th}-6^{th} courses of medical faculty

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Abbreviations

HDP-hypertensive disorders of pregnancy
MAP- mean arterial blood
SVR- systemic vascular resistance
PIH- pregnancy induced hypertension
GH- gestational hypertension
PE- pre-eclampsia
BP-blood pressure
SBP-systolic blood pressure
DBP-diastolic blood pressure
IUGR- intrauterine growth retardation
APS -anti-phaspholipid syndrome
RCOG- royal college of obstetricians and gynaecologists
FGR-foetal growth retardation
CTG- cardiotocography
PR- pulse rate
IV-intravenous
IM-intramuscular
O&G-obstetrician and gynaecologist
CS-caesarean section
ICU - Intensive Care Unit
HDU- high dependency area
DIVC- disseminated intravascular coagulation
NICU - neonatal intensive care unit
LDH- lactate dehydrogenase
SGOT- serum glutamic-oxaloacetic transaminase
PCV- peripheral venous catheter
BUSE- blood urea and serum electrolyte
PPH-postpartum hemorrhage
CVP- central venous pressure

Contents

PREFACE

Hypertensive disorders of pregnancy are one of the most common obstetric medical problems and are associated with a high maternal and fetal morbidity. Maternal deaths from preeclampsia and eclampsia are on the rise and according to the UK Confidential Enquiry into Maternal Deaths, the mortality rate for 2006 - 2008 triennium was 0.83 per 100 000 maternities (22 deaths) compared with 0.66 (15 deaths) in the triennium 2003 - 2005.[1] Cerebral haemorrhage remains the commonest cause of death in this group and hence rapid and effective treatment of hypertension to prevent haemorrhagic stroke is highlighted in this report.

Ancient Greeks believed that preeclampsia was caused by the imbalance of the body fluids (blood, phlegm, yellow and black bile). Symptoms of the disease were later thought to be due to woman's extremely porous skin and also the 'wandering womb', where the uterus wandered in the body and caused havoc upon the liver, spleen, brain and lungs. Early treatment was aimed at blood-letting and treating the woman to a warm bath in a calm and dark environment. However, from an early time the importance of hastening delivery was recognised.

1. Centre for Maternal and Child Enquiries (CMACE). Saving Mother's Lives: reviewing maternal deaths to make motherhood safer: 2006-2008. The Eighth Report on Confidential Enquiries into Maternal Deaths in the United Kingdom. *BJOG* 2011; 118: (Suppl.1): 1-203

PATHOPHYSIOLOGY

HDP (HYPERTENSIVE DISORDERS IN PREGNANCY)constitutes a group of diseases of distinct etiology of which hypertension is the chief clinical manifestation. Pregnant women who are hypertensive will generally fall into two groups: normotensive women who develop the pre-eclampsia syndrome (PE), characterised by hypertension and proteinuria with or without oedema and women with chronic hypertension who are at a higher risk for superimposed PE.

Much progress was made in understanding the pathophysiology of hypertensive disorders of pregnancy in the 20th century when poor invasion of the placental trophoblast cells of the maternal spiral arteries was identified as a major component of the disorder. This results in small muscular high resistance vessels instead of large low resistance vessels, leading to limited distensibility of spiral arteries restricting blood flow to the placenta and fetus. **(Figure 1**)

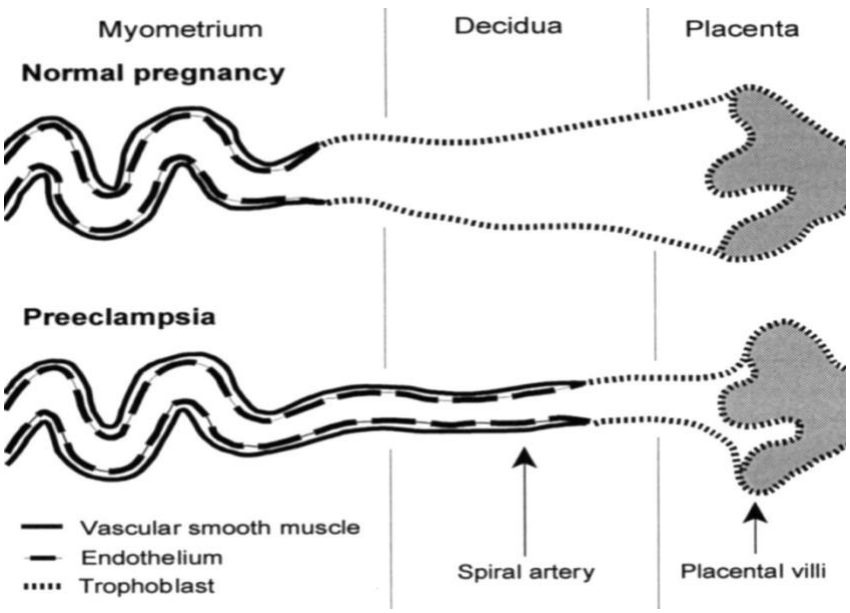


Figure 1. Spiral artery invasion by trophoblasts in normal and pre-eclamptic placenta. Reproduced with permission from Oxford University Press

A two-stage process of pathogenesis has been described. Abnormal placentation along with endothelial dysfunction gives rise to the spectrum of the disease.

STAGE I

Abnormal placentation & vascular remodeling
decreased placental perfusion

Maternal factors:

- *Genetic*
- *Behavioral*
- *Environmental*

STAGE II

Maternal Syndrome of pre-eclampsia with endothelial dysfunction

The maternal syndrome of preeclampsia is characterised by decreased perfusion due to vasospasm and activation of coagulation cascade with microthrombi formation and end organ damage.

Resulting endothelial dysfunction produces an imbalance of pro and anti-angiogenic factors, with an increase in anti-angiogenic factors. It should be noted that these biomarkers do not have sufficiently high positive predictive value when used alone.

Pro angiogenic factors	**Anti angiogenic factor**
Vascular Endothelial Growth factor (VEGF) Placental GrowthFactor (PlGF) Placental protein 13(PP-13) Pregnancy associated plasma protein A (PAPP-A)	Soluble fms-like tyrosine kinase 1 receptor (sFlt1) Soluble Endoglin (sEng) Asymmetric Dimethyl Arginine (ADMA)

Normally pregnancy causes a fall in mean arterial blood pressure (MAP) and systemic vascular resistance (SVR) in the first half of pregnancy as a result of vascular smooth muscle relaxation secondary to progesterone. There is a gradual increase of MAP from 24 weeks until term when pre- pregnancy levels are reached.

The cardiovascular changes during pregnancy with relation to heart rate, cardiac output and stroke volume are shown in**(Figure 2.)**

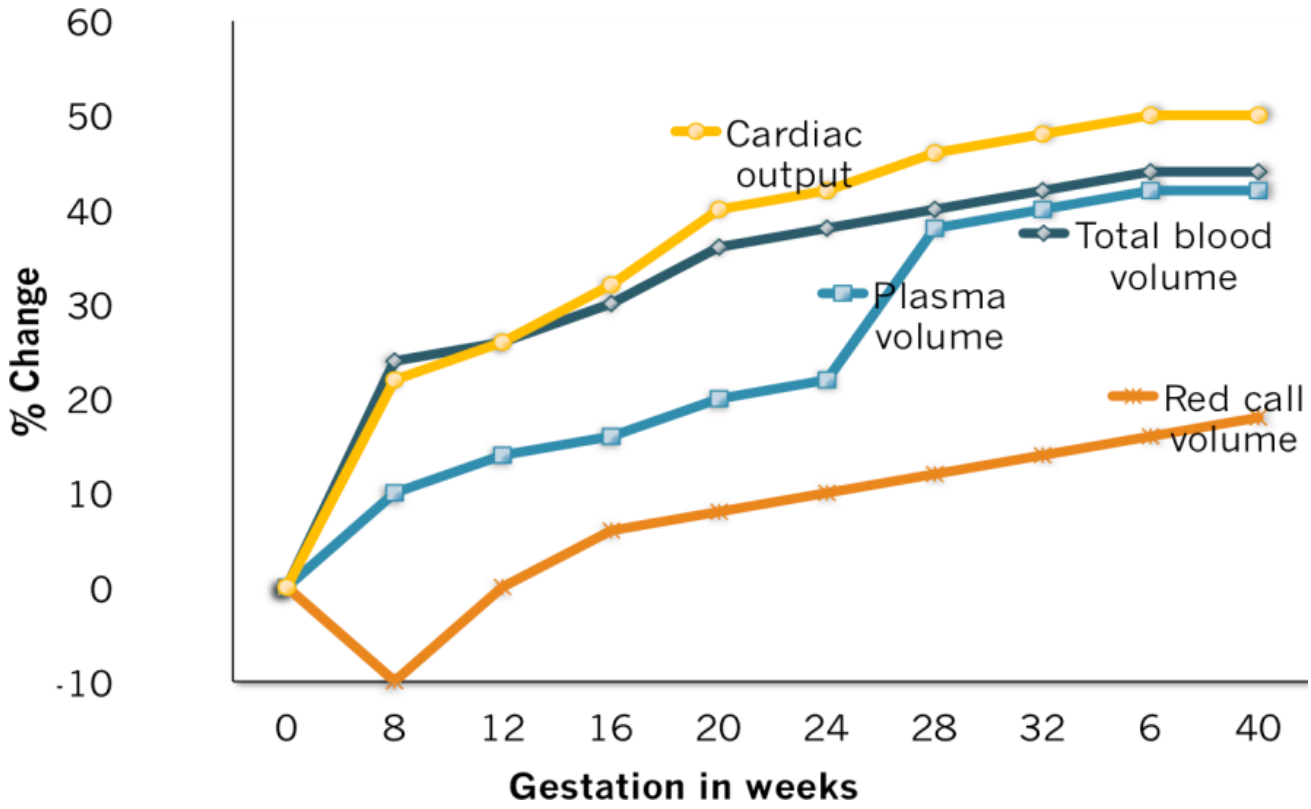


Figure 2. A graphical representation of normal cardiovascular changes in pregnancy

Definition of Hypertension:

Hypertension in pregnancy is defined as:
BP of 140/90 mm Hg taken after a period of rest on two occasions.

OR
Rise of systolic blood pressure (SBP) of 30 mmHg and /or a rise in diastolic blood pressure (DBP) of 15 mmHg[3] compared to pre pregnancy levels.

Classification of Hypertension in Pregnancy:

1) Pregnancy Induced Hypertension (PIH)

Hypertension after the 20th week of pregnancy in a previously normotensive woman. It may be associated with proteinuria. The condition is expected to return to normal after pueperium.

(a) Gestational Hypertension (GH)-PIH without proteinuria

(b) Pre-eclampsia (PE)-PIH with proteinuria(mild,severe)

(c) Eclampsia-PIH with convulsions

HELLP syndrome is a severe form of PE manifested by Haemolysis, Elevated Liver Enzymes and Low Platelets.

2) Chronic Hypertension (includes essential and secondary hypertension)

3) Chronic Hypertension with superimposed Pre-eclampsia

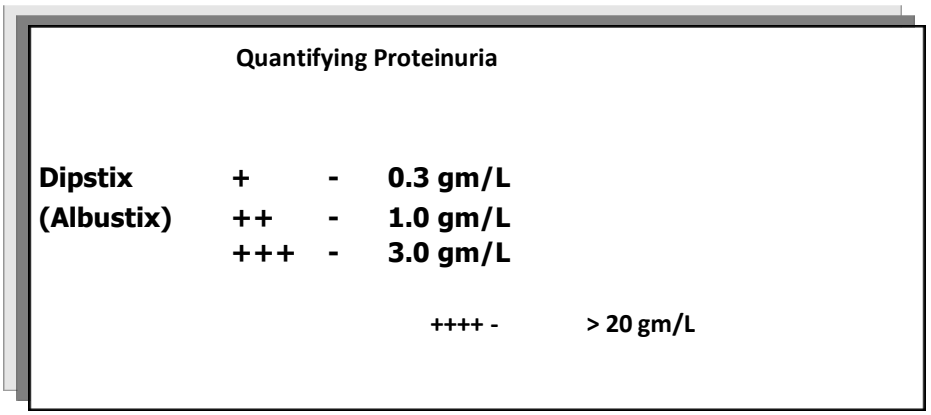
- **Chronic Hypertension** is defined as the presence of hypertension of at least 140/90 before 20 weeks of pregnancy OR beyond 6 weeks postpartum.
- **Chronic Hypertension with superimposed PE** refers to the development of PE in women who have pre-

existing hypertension. Criteria used should include worsening hypertension, proteinuria and non-dependent oedema.

- **Essential Hypertension and Secondary Hypertension** are best categorised under chronic hypertension as pregnancy outcomes in all these categories are similar.

- **Proteuniria**

Urinary tract infection must be excluded. **Proteinuria** is defined as 300 mg/24 hours urine collection or 1 gm/L or more in two randomly collected urine samples 6 hours apart. Semiqualitative assessment of proteinuria using dipstix is convenient and has collaborated well with maternal outcome.



(+) proteinuria carries a high false positive rate. Therefore the presence of proteinuria should be confirmed by measuring 24 hour protein excretion or a protein:creatinine ratio.

- **Oedema**

Oedema is commonly seen in pregnancy and may not be a usual sign for early detection of PIH. In **severe PIH**, there is generalised accumulation of fluid largely due to endothelial damage resulting in accumulation of fluid evidenced by pitting oedema following 12 hours of recumbant bedrest. A weight gain of 1 kg within a week may point to increasing severity of PIH especially in the presence of proteinuria.

- **Severity of PE:**

(a) Mild

Characterised by BP >140/90 mmHg ,proteinuria 0,3-3,0gm/L, OR a rise in SBP 30 mmHg or a DBP 15 mmHg

(b) Severe

Severe HDP is characterised by progressive deterioration in both maternal and foetal condition. It is characaterised by:

- ✓ SBP >160 mmHg or DBP >110 mmHg on two occasions 6 hours apart
- ✓ Proteinuria of (3+) or > 3 gm/L
- ✓ Oliguria (< 400 ml/24 hours)
- ✓ Headache

- ✓ Cerebral or visual disturbances
- ✓ Epigatric pain
- ✓ Hyper-reflexia
- ✓ Pulmonary Oedema
- ✓ Impaired liver function tests
- ✓ Increased serum creatinine (> 1.2 mg/dl)
- ✓ Retinal haemorrhage, exudates or papilloedema
- ✓ Thrombocytopenia
- ✓ IUGR(intrauterine growth retardation)

IDENTIFYING THE MOTHER AT RISK:

HDP cannot be prevented. However, a certain subset of pregnant women are at risk of developing HDP. Identifying this group early, prenatally and during early booking will assist health providers to keep these patients under surveillance. The risk factors include:

- Maternal age <20 years and >35 years
- Nulliparity
- Previous history of HDP
- Multiple gestation
- Polyhydramnios
- Non-immune foetal hydrops
- Underlying renal disease
- Chronic hypertension
- Diabetes mellitus
- Gestational Trophoblastic Disease (Molar pregnancy)
- Low socio-economic group
- Pregnancies with different partners
- Excessive weight gain
- Rh incompatibility.

Identification of high risk patient at community level

History and complaints

- Family history of hypertension
- History of pregnancy induced hypertension
- Primigravida
- Associated conditions

    - multiple pregnancy
    - diabetes mellitus
    - renal disease
    - SLE/APS (Anti-Phaspholipid Syndrome)
    - obesity (>80 kg. BMI >27)
    - maternal age

    -pre existing chronic hypertension

- Symptoms:

    - headache
    - visual disturbance
    - nausea and vomiting

    - epigastric pain

Physical examination

- Excessive weight gain (> 1 kg per week)
- Oedema in the face and abdomen and/or non-dependant oedema
- Proteinuria
- Obesity (Body Mass Index >27 or 80 kg.)
- Abdominal examination

  -polyhydramnios
  -multiple pregnancy

Blood pressure:

- BP of 140/90 mmHg taken on 2 occasions 6 hours apart
- If baseline BP is known :

  - increase in systolic BP by 30 mmHg
  - increase in diastolic BP by 15 mmHg

Checklist for Identifying Severity of HDP

1. **Blood Pressure:**

- Initial reading after a period of rest
- Ideally at 6 hours later
- Increase in previous or pre-pregnancy BP (mmHg):

  - systolic
  - diastolic

2. **Weight Gain (kg**.)

- 1 week
- 2 weeks
- 3 weeks
- 1 month

3. **Oedema**:

- Legs

  -ankle
  -pretibial

  -abdomen

- Hands
- Generalised

4. **Proteinuria (dipstick)**

- Trace
  +

  + +

  + + +

- Solid (++++)

5. **Patient's complaints**:

- epigastric pain
- nausea
- vomiting
- headache
- blurring of vision

1. Interpretation

1 …….

2 ……

3 ……..

Name of Health Provider : _____ _____

(Date/time)

MANAGEMENT OF HYPERTENSIVE DISORDERS IN PREGNANCY

Management of Mild HDP

1. INTRODUCTION

Being a multi-organ disease, the progress of HDP is often unpredictable and could lead to rapid deterioration in maternal and fetal condition. In view of this, the management of mild HDP requires continuous and close surveillance.

A decision must be made at the time of diagnosis whether to manage mild HDP as an out- patient or as an in-patient. The RCOG Consensus is of the opinion that mild HDP in the absence of proteinuria may be managed on an outpatient basis. It has been shown that this could reduce 60-80% of hospital stay, with no detrimental effects on maternal or fetal care. However, in our context we have to look at the cases on an individual basis, in terms of logistics, socio-economic factors and patient's educational level.

2. GOAL OF MANAGEMENT OF MILD HDP

In mild HDP, the aim is to prolong the pregnancy to near term as possible provided there are no evidence of maternal complications or fetal compromised (fetal distress, FGR,oligohydramnios)

3. AMBULATORY CARE (OUT-PATIENT MANAGEMENT)

a) Criteria for selection of patient for ambulatory care:

- B/P ≥ 140/90 mmHg but less than 160/100mmHg
- NO proteinuria
- NO signs/symptoms of impending eclampsia
- NO excessive weight gain
- No signs of intrauterine growth retardation
- Normal biochemical investigation

b) Antenatal Care

- Mild HDP can be managed in health clinics.
- Every patient should be monitored to detect any deterioration in maternal and fetal condition
- The frequency of each visit should be individualized depending whether patient requires medication or in the presence of other complication
- In patient who do not require medication and absence of maternal or fetal complications, the patient should be attending the normal antenatal follow up
- Patient should be counsel with regards her condition, management option and need for regular antenatal care.
- Maternal and fetal monitoring and surveillance is the mainstay of management of *HDP*.

During visit to the doctor, the following should be monitored;

All decisions must be documented in the patient's antenatal card.

Maternal Surveillance

- Blood Pressure,
- Urine for protein,
- Weight gain
- Signs/symptoms of impending eclampsia should be elicited.
- Biochemical Investigation:
  - Platelet count
  - Heamatocrit
  - Serum Uric Acid
  - Serum Creatinine
  - 24 Urine Protein (if necessary)

Fetal Surveillance

- Fundal Height
- Fetal Heart
- Fetal Movement (Fetal Kick Chart)
- Serial Ultrasound - (if available)
  - growth parameters (BPD/FL/AC/HC)
  - Amniotic Fluid Index. (AFI)

c) Antihypertensive Therapy

Not all mild HDP require antihypertensive treatment. A majority of them may benefit from adequate rest. Patients with BP of 140/90mmHg, **without any complications** may not require antihypertensive treatment. Antihypertensive treatment may be considered when BP is persistently above DBP 100 mmHg.

4. IN-PATIENT MANAGEMENT

(a) Indications for hospitalization

Generally the indication for in-patient management is for those who fail ambulatory care (out-patient) management. The reasons for admission are:-

- symptomatic patients
- maternal or fetal complications
- persistent diastolic blood pressure > 100 mmHg or systolic > 160 mm Hg for stabilization
- abnormal biochemical PE profile
- presence of severe proteinuria > 2+

b) Management in the ward

All observations should be documented in HDP (PE) chart, which consist of the following:-

- Four hourly Blood Pressure and Pulse Rate monitoring
- Daily urine for protein
- Weekly weight
- Sign and symptoms of impending eclampsia.
- Investigations eg: RBC, Renal Profile, serum uric acid
- Fetal monitoring eg: fundal height, fetal movement, CTG

c) Antihypertensive therapy

A decision to start antihypertensive therapy and the selection of the agent should be individualized. It should be based on an assessment of the relative risks and benefits for the mother and her fetus.

Antihypertensive therapy should start when the DBP is ≥ 100mmHg, and or systolic BP is ≥ 160 mmHg

d) Medication used

In mild HDP, the following antihypertensive drugs may be considered:

- Alpha-Methyl dopa or
- Labetolol (appendices)
- Calcium Channel Blockers(nifedipine)

Start with monotherapy and increase gradually till maximum dose. Consult the specialist if there is a need to add the 2^{nd} drug medication.

e) Aim of treatment

The aim of treatment is to maintain a DBP around 90 -100 mmHg to:

- minimize the risk to the mother from events such as cerebral vasculo- accident , cardiac failure and placental abruption etc.
- avoid placental hypoperfusion which may lead to IUGR, fetal hypoxia and Intrauterine Death.

e) Disharge and follow-up

Discharge may be considered when BP is stabilized (diastolic pressure between 90-100 mmHg) with no complications. A clear plan of management should be documented in the patient's antenatal card. The patient should be counselled on the importance of compliance to medication, adequate rest, frequent follow-up and to observe for warning signs of PE. The patient should be advised for hospital delivery. The nearest health facility should be notified for continued care by way of telephone .

g)Timing of delivery

In the absence of maternal and fetal complication, pregnancy should not be allowed beyond dates i.e before 40 weeks. If at anytime the maternal and fetal condition is compromised, early delivery is mandatory and appropriate corticosteroid usage is necessary.

INTRA-PARTUM MANAGEMENT

Mild HDP may become severe during labour, hence close vigilance monitoring is essential.

Maternal surveillance:

- Labour should be monitored using Partogram.
- Antihypertensives should be continued if patient is on such treatment.
- Intravenous line should be set-up.
- I.V. Hydrallazine should be considered if DBP is more than 110mmHg
- Adequate analgesia is essential
- USE only Syntocinon during third stage of labour
- Fluid regime therapy (appendices)
- Assist second stage if indicated.

Fetal surveillance:

- Auscultation of fetal heart rate every 15 minutes
- Institute electronic monitoring (cardiotocography) continuously or intermittently as indicated.

IMMEDIATE POST-PARTUM PERIOD

The blood pressure may settle after delivery, however the patient is still at risk to develop complications. Therefore, continuation of maternal monitoring is essential.

First 24 hours after delivery

- Monitor BP, PR every 4 hours.
- Antihypertensive drugs should be continued after delivery as dictated by blood pressure.
- If the diastolic BP < 90 mmHg, the medication can be withhold.
- While rest is encouraged, patient should be assisted for early mobilization.
- Encourage and assist patient to breast-feed her baby.

After 24 hours post-partum

- Continue antihypertensive agent aiming for DBP between 90-100 mmHg.
- Counsel patient on the importance of:
    - Compliance to medication and follow up.
    - Symptom or signs of impending eclampsia
    - Effective contraception.
- Upon discharge, a clear summary and plan of management should be written in the patient's antenatal card.
- The nearest health clinic should be notified either by phone, verbally, written letter, fax or through family members.

Management of Severe HDP

1. INTRODUCTION

Severe hypertension in pregnancy is an obstetric emergency state and generally acknowledged that it should be lowered promptly, albeit carefully, to prevent cerebral hemorrhage and hypertensive encephalopathy. This degree of hypertension therefore requires urgent assessment and management. It is important to acknowledge that systolic as well as diastolic hypertension increases the risk of cerebral hemorrhage.

2. DEFINITION

Severe HDP is characterized by progressive deterioration in both maternal and fetal conditions. The characteristics are:

- SBP ≥ 170 mmHg or DBP ≥ 110 mmHg on two occasions 6 hours apart
- Proteinuria of 3+ or > 3 gm/L
- Oliguria (< 400 ml/24 hours)
- Headache
- Cerebral or visual disturbances
- Epigastric pain
- Hyper-reflexia
- Pulmonary oedema
- Impaired liver function tests
- Increased serum creatinine (> 1.2 mg/dl)
- Retinal haemorrhage, exudates or papilloedema
- Thrombocytopenia
- Impairment of fetal growth (IUGR)

3. MANAGEMENT

The aim of the management of severe HDP is to prevent a cerebro-vascular accident to the mother whilst trying to achieve a clinically useful prolongation of the pregnancy This is because it is also aimed at delivering a live baby as mature as possible. Pre-eclampsia when diagnosed at term, mandates delivery as there is no advantage to either the fetus or mother in prolonging the pregnancy. Magnesium sulphate should be considered to prevent seizure in 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.

4. MANAGEMENT AT HOME AND HEALTH CLINIC

- The patient should be referred to the hospital immediately.
- Arrange for transport and accompany the patient to hospital . To inform the receiving hospital (labour room) prior to referral.
- Set up an IV drip with normal saline for emergency administration of drugs for resuscitation if the need arises. To give deep IM MgSO4 10g bolus (5g each buttock) to prevent eclampsia.
- To lower blood pressure give oral nifedipine (10mg stat) or IM hydralazine 6.25 mg. (preparation: 1 ampule contain 20mg hydralazine + 9ml distill water = 2mg/ml. Give 3.1 ml (equivalent to 6.2mg)

During Transfer

- Monitor and record the maternal BP, pulse rate and fetal heart rate every 15 minutes.
- If an acute situation arises, stop the vehicle to carry out resuscitative measures or divert to the nearest health facility.

5. MANAGEMENT AT HOSPITAL WITHOUT O&G SPECIALIST

- The patient should be admitted, managed and monitored in a high dependency area while awaiting transfer to a hospital with specialist.
- Maintain an IV drip of normal saline. To give IV MgSO4 4g slow bolus over 10 minutes if not given earlier. This is followed by maintenance IV infusion of MgSO4 1g per hour

to prevent eclampsia . If bolus MgSO4 has been given earlier to continue with the maintenance dose only.

- Monitor the maternal BP, pulse rate, respiratory rate and the fetal heart rate every 15 minutes.

- If DBP ≥ 110 mmHg, set up an IV infusion of Hydralazine 20 mg in either 500 ml of Hartman's solution or normal saline. Starting at 5-10 drops per minute (dpm), increase by 5 dpm every 15 minutes until the DBP is around 90 mmHg.

- Continue oral antihypertensive medication.

- Insert a Foley's catheter and record urine output.

- Test for proteinuria.

- Consult the O&G Specialist in the nearest hospital and alert the hospital staff of the receiving hospital about transfer.

- Arrange for an ambulance and ensure that basic resuscitative equipments are available.

- The husband or next of kin should be informed. They should accompany the patient to the hospital.

- If the fetus is preterm, dexamethasone should be administered to improve lung maturity.

6. MANAGEMENT IN HOSPITAL WITH O&G SPECIALIST

- The patient should be admitted and managed in a high dependency area.

- Alert the O&G consultant immediately, so as to be involved in the patient management.

- Monitor the maternal BP, pulse rate, respiratory rate and fetal heart rate every 15 minutes until stabilized.

- Set up an IV drip of Hartman's solution or normal saline for emergency resuscitative therapy. To give IV MgSO4 4g slow bolus over 10 minutes if not given earlier. This is followed by maintenance IV infusion of MgSO4 1g per hour to prevent eclampsia. If bolus MgSO4 has been given earlier to continue with the maintenance dose only.

- Close monitoring of fluid balance(appendices) is essential to prevent pulmonary oedema.

- If DBP is ≥ 110 mmHg, set up another IV infusion of Hartman's or normal saline with Hydralazine 20 mg. Titrate at 5 dpm against the BP, increasing 5 dpm every 15 minutes until DBP is around 90 mmHg.

- Continue any oral antihypertensive previously started and consider increasing the dosage.
- Insert Foley's catheter and record urine output hourly
- Test for proteinuria
- If the fetus is preterm, administer Dexamethasone
- The fetus should be monitored.

Obstetric management

- If the gestation is below 34 weeks, there is a place to try to prolong the pregnancy to as near 36 weeks as possible provided there is no danger to the mother or the fetus. This is to reduce the problems of immaturity
- If the gestation is 34 weeks or more, consider delivery if crisis recur.
- In the presence of maternal or fetal complication, then delivery is indicated after stabilization.
- In the absence of obstetric contraindication, aim for vaginal delivery. Otherwise Caesarean section (CS) is recommended.
- The paediatrician should be informed and be present at delivery.

Maternal surveillance:

- ✓ Labour should be monitored using Partogram.
- ✓ Antihypertensives should be continued if patient is on such treatment.
- ✓ Intravenous line should be set-up.
- ✓ Adequate analgesia is essential
- ✓ USE Syntocinon in place of ergometrine and syntometrine during third stage of labour
- ✓ Fluid regime therapy
- ✓ Paediatrician to be present during delivery.

- ✓ **Fetal surveillance**:

- ✓ Auscultation of fetal heart rate every 15 minutes
- ✓Institute electronic monitoring (cardiotocography) as indicated.

Role of Steroid

Antenatal administration of corticosteroids like Dexamethasone prior to preterm delivery reduces neonatal morbidity and mortality. Thus every effort should be made to initiate antenatal corticosteroid therapy in women between 24 – 36 weeks gestation provided there is no evidence of tuberculosis or intrauterine infection

Dosage: 12 mg 12 hourly x 24 hours

Intrapartum Management

- Adequate analgesia preferably epidural
- To complete Magnesium sulphate infusion to at least 12 hours postpartum
- Strict input/output chart
- Monitor magnesium toxicity
- Paediatrician to standby at delivery

Maternal surveillance:

- ✓ Labour should be monitored using Partogram.
- ✓ Antihypertensives should be continued if patient is on such treatment.
- ✓ Intravenous line should be set-up.
- ✓ I.V. Hydrallazine should be considered if DBP is more than 110mmHg
- ✓ Adequate analgesia is essential
- ✓ USE only Syntocinon during third stage of labour
- ✓ Fluid regime therapy .
- ✓ Assist second stage if indicated.

Fetal surveillance:

- ✓ Auscultation of fetal heart rate every 15 minutes
- ✓ Institute electronic monitoring (cardiotocography) continuously or intermittently as indicated.

Postpartum Care

- Patient should be observed at OHDU
- Continue her oral antihypertensive agent
- BP control should be between diastolic 90-100 mmHg
- Magnesium infusion should be continue at least 12 hours after delivery
- Monitor input/output

7. CONCLUSION

The principle of management of severe HDP is to stabilise the BP, to prevent complication and eclampsia. Pregnancy can be prolonged to as near term as possible in the absence of maternal and fetal complication. Prophylaxis Magnesium Sulphate should be considered in severe HDP.

Management of Eclampsia

1. INTRODUCTION

Eclampsia is the occurrence of convulsions in a patient with HDP. A clear cut syndrome of pre-eclampsia (PE) nearly always precedes the convulsions, but it may occur even in a modest hypertension without proteinuria. It is thus crucial to recognize that any case of HDP is a potential prelude to eclampsia. In Malaysia, two third of deaths due to eclampsia occurred in antenatal mothers.

The pathophysiology of eclampsia is thought to involve cerebral vasospasm leading to ischaemia, disruption of the blood brain barrier and cerebral oedema. Neurological complications may include coma, focal motor deficits and cortical blindness. Cerebrovascular haemorrhage may complicate about 2% of cases.

2. PREVENTION

Being of unclear aetiology, it is not easy to prevent pre-eclampsia. Currently, a simple and effective way of reducing the dangers of pre-eclampsia is to screen pregnant women for proteinuria and hypertension during antenatal care. Otherwise the following steps may be considered:

- The early recognition and treatment of mild HDP
- The early recognition and treatment of severe HDP

The signs of HDP usually appear over a period of several days in the following order:

- fluid retention (or excessive weight gain e.g. >1 kg per week)
- hypertension of 140/90 mmHg or more

- proteinuria

However, they can appear in any order or all together in less than 24 hours. The symptoms and signs of impending eclampsia should always be looked for in patients with HDP:

Severe frontal headache

Vomiting

Blurring of vision

Epigastric pain Hyper-reflexia

Severe hypertension

Eclampsia is the occurrence of epileptiform convulsions. Four stages are described:

- Premonitory stage: This lasts 10 – 20 seconds during which:
  - the eyes roll or stare
  - the face and hand muscles may twitch
  - there is loss of consciousness
- Tonic stage: This lasts 10 – 20 seconds during which:
  - the muscles go stiff or rigid
  - the diaphragm is in spasm so that breathing stops and colour of skin becomes cyanosed
  - the back may be arched
  - the teeth are clenched
  - the eyes bulge
- Clonic stage : This lasts 1 – 2 minutes and is marked by:
  - violent contraction and relaxation of muscles
  - increased saliva causes “foaming” at mouth
  - deep noisy breathing
  - inhalation of mucous or saliva
  - face looks congested and swollen
  - tongue is bitten by violent action of jaws
- Coma stage: This may last minutes or hours during which:
  - there is a deep state of unconsciousness
  - breathing is noisy and rapid
  - cyanosis fades but face remains congested
  - further fits may occur

3. TREATMENT

The goals of treatment are:

- To treat convulsions
- To control the blood pressure
- To stabilise the mother
- To deliver the fetus

4. MANAGEMENT OF ECLAMPSIA AT HOME & HEALTH CLINICS

Immediate measures

- Call for medical assistance.
- The patient should be placed in the lateral position. Maintain airway, O2 given through nasal prong/ ventimask.
- 10 gm 50% solution (20 mls) is injected intramuscularly. One half is injected into upper outer quadrant of each buttock in zigzag manner *(proceeded by local anaesthesia if necessary)* using a 21 gauge needle.
- Antihypertensive therapy eg. Hydralazine or Labetalol if available or Nifedipine, may be needed to be administered to control hypertension.
- Set up an IV drip with normal saline for emergency administration of drugs for further resuscitation.
- Suck out secretions/saliva
- Insert a Foley's catheter to record and monitor urine output
- Monitor and record the maternal BP, pulse rate, respiration rate and the fetal heart beat every 15 minutes using a Labour Progress Chart.
- Arrange for transport and accompany the patient to hospital . To inform the labour room personnel of the receiving hospital prior referral.

During Transfer

- Continue the monitoring of the mother and fetus as above.
- Maintain patient in lateral position.
- Maintain airway with oxygen
- Continue IV drip: normal saline .
- To prepare IV MgSO4 2g or 5g/IM in a syringe in case patient threw recurrent seizure during transfer.

5. MANAGEMENT OF ECLAMPSIA AT THE HOSPITAL WITHOUT O&G SPECIALIST

Eclampsia is an obstetric emergency, and although there is no O&G Specialist, the management of the ill patient has to be carried out appropriately:

Immediate measures

- calling other doctors to help.
- Put the patient in the lateral position.
- Suck out secretions/saliva
- Insert an airway and give oxygen 6-8L/ min
- Give IV MgSO4 4g slow bolus over 10 minutes if not given earlier. This is followed by maintenance IV infusion of MgSO4 1g per hour to prevent eclampsia.
- If **IV line is not secure**, 10 gm 50% solution (20 mls) is injected intramuscularly. One half is injected into upper outer quadrant of each buttock in zigzag manner *(proceeded by local anaesthesia if necessary)* using a 21 gauge needle.

- To run normal saline (NS) infusion for further resuscitative measures.
- Insert a Foley's catheter and record urine output. Test for proteinuria.
- Monitor and record the maternal BP, pulse rate, respiratory rate and also fetal heartbeat every 15 minutes.
- If the DBP ≥ 110 mmHg, Hydralazine infusion should be started : 20 mg in 500 ml of NS or Hartman's solution , starting at 5 dpm and increasing by 5 dpm every 15 minutes until the DBP is about 90 mmHg.
- Consult the O&G Specialist at the nearest hospital to transfer the patient and alert the hospital staff. The patient should be transferred **only after the initial stabilisation.**

During Transfer

- **The patient should be accompanied by a doctor**.
- An ambulance with basic resuscitative equipment is required for the transfer to the referral hospital.
- The husband or next of kin should be informed and they should accompany the patient too.
- Continue the monitoring of the vital signs as above during the transfer and document the readings.
- Continue normal saline infusion
- To be ready with IV $MgSO_4$ 2g or 5g/IM in a syringe in case patient develop recurrent convulsion during transfer.

6. MANAGEMENT OF ECLAMPSIA AT THE HOSPITAL WITH O&G SPECIALIST

Eclampsia is an obstetric emergency which should be managed by a team of doctors and nurses.

- O&G consultant, specialist and Registrar
- Anaesthetic consultant, specialist and Registrar
- Matron/Sister on-call
- Blood bank specialist/technician

During convulsions

- The patient is managed in the lateral position.
- Suck out secretions/saliva. Maintain airway and O2.
- Give MgSO4:

  10 gm 50% solution (20 mls) is injected intramuscularly. One half is injected into upper outer quadrant of each buttock in zigzag manner *(proceeded by local anaesthesia if necessary)* using a 21 gauge needle **OR** intravenously.

***NB**: Clinical monitoring for magnesium toxicity is an acceptable, reliable and safe technique. Hourly assessment of patellar reflex and respiratory rate should be carried out. If the reflexes are absent or respiratory rate less than 16 per minute, 1 gm IV calcium gluconate (over 10 minutes) should be given.*

After convulsions

- Continue maintain airway and oxygen administered at 6-8 L/min.
- Set up an IV line with Normal Saline.
- Insert Foley's catheter to check urine output.

- Monitor maternal vital signs: BP, pulse rate, respiration rate and also tendon reflexes.

- Continue MgSO4 infusion 1 gm/hour and to be continue till 24 hours after delivery or convulsion whichever is later

- If DBP is more than 110mmHg, treat with Hydralazine infusion titrate to BP using syringe pump 20mg in 50 mls normal saline Start at 5 mls/hr and titrate every 15 minutes and aim blood pressure diastolic about 90 mmHg.

  Or

- Using syringe pump, IV labetalol 50mg in 50 ml NS, start with 5 mls/hour after excluding heart failure and bronchial asthma. (refer protocol in the procedure)

- Alert the Anaethesiologist for possible operative procedure, and the need for ICU or HDU care.

- Reassess the pregnancy to decide the timing and mode of delivery

Investigations

Eclampsia is a multisystem disorder and the following complications may occur: Haemolysis, elevated liver enzymes, low platelets (HELLP), DIVC, renal failure, acute pulmonary oedema, intracranial haemorrhage, adult respiratory distress syndrome. Thus the following investigations should be sent for:

- Haemoglobin
- Platelet count
- Coagulation profile
- Transaminases (Liver function test)
- Renal profile, Uric acid
- CT scan in the presence of neurological deficits or recurrent fits

Obstetric Management

- The mainstay of treatment of eclampsia is delivery after stabilisation of the patient irrespective of gestational age. Delivery should be conducted in fully equipped hospital with ICU, HDU and NICU facilities.

- If patient is in advance stage of labour (cephalic and dilation of cervix 8cm and above) vaginal delivery is possible in the absence of fetal or maternal complication. Otherwise Caesarean section is advisable.

- The husband or next of kin should be informed on the progress and plan of management.

- The paediatrician should be informed and be present at the delivery

- After delivery, high dependency care should be continued **for at least 24 hours**.

Choice of anaesthesia/analgesia

If there are no contraindications, epidural analgesia is the preferred mode of providing pain relief during labour as this can be extended for any operative delivery/ procedure.

Immediate postpartum care

After delivery, eclamptic patients should continue to be nursed and monitored in the high dependency area (HDU) for at least 24 hours since the risk of recurrence of convulsions is still very high. Once the condition is stabilised/optimised, the patient can be transferred to the general ward to be nursed according to the postnatal care of patients with HDP .

On discharge, it is preferred that the follow-up postnatal visit to be at the referral hospital.

7. CONCLUSION

Eclampsia is an obstetric emergency and requires multidisciplinary approach. Delivery is the mainstay of treatment after the maternal condition has been optimized. With the availability of Magnesium sulphate and training of its use at the peripheral clinic, a reduction and better management of eclampsia is anticipated in near future.

Management of HELLP Syndrome

1. INTRODUCTION

The acronym HELLP Syndrome is a variant of severe preeclampsia and is characterised by:

- Haemolysis (H)
- Elevated Liver enzymes (EL)
- Low Platelets (thrombocytopenia) (LP)

The syndrome has been described in various gestational ages, ranging from mid-second trimester of pregnancy until several days postpartum. It rarely occurs before 25 weeks pregnancy. Its clinical significance is it's association with increased maternal and perinatal complications. The maternal mortality is high (24% in one series) and perinatal mortality ranges from 30-40%.

3. CLINICAL RECOGNITION

The signs and symptoms of PE-Eclampsia must be present. In addition, the following derrangements must be confirmed by laboratory tests.

- Microangiopathic haemolytic anemia
- Thrombocytopenia
- Hepatic Dysfunction

The exact levels of biochemical and haematological values and criteria that are used to make the diagnosis are debated in the literature

4. INVESTIGATIONS

- ✓ Full blood count including peripheral blood smear for evidence of haemolysis
- ✓ Liver function tests (SGOT, LDH)
- ✓ Renal function test (Creatinine Clearance, uric acid)
- ✓ Coagulation Profile (Prothrombin time, Partial Thromboplastin Time, INR, Fibrinogen)

5.DIFFERENTIAL DIAGNOSIS

- ✓ Thrombotic thrombocytopenic purpura
- ✓ Haemolytic-uremic syndrome
- ✓ Acute fatty liver of pregnancy
- ✓ Connective tissue disorders (SLE)
- ✓ Dengue Fever

6.COMPLICATIONS OF HELLP SYNDROME

- ✓ Disseminated intravascular coagulation
- ✓ Abruptio placenta
- ✓ Acute pulmonary oedema
- ✓ Acute renal failure
- ✓ Intracerebral haemorrhage/stroke
- ✓ Subcapsular liver haematoma
- ✓ Retinal detachment
- ✓ Death

7.TREATMENT

- ✓ Early recognition and institution of appropriate therapy in HDU or ICU
- ✓ Additional investigations may be necessary, depending on severity of condition *eg.* arterial blood gas, chest x-ray
- ✓ LDH, SGOT, platelets, PCV, BUSE every 12-24 hours and a further 48 hours after delivery
- ✓ Control Hypertension

  80% have elevated BP necessitating antihypertensive treatment. Aim to reduce BP without compromising placenta perfusion *(if undelivered).*

> Although hydralazine or labetalol may be prescribed, calcium channel antagonists have potent peripheral arterial vasodilation properties with renal and cardiac sparing effect. Urine output is improved and rapid normalisation of postpartum platelet count has been reported.

- ✓ If spontaneous haemorrhage from injection sites are noticed (or platelet count is <50,000/ul) platelets should be transfused
- ✓ Role of corticosteroid in improving platelet count in the treatment of HELLP syndrome is rather limited. Although in some observational studies did show dexamethasone significantly increase the platelet count but this however did not translate to improvement in outcomes and the clinical relevance of this is unclear.
- ✓ Assess coagulation profile, determine if DIVC is present and treat for this disorder
- ✓ Manage fluid and electrolytes
- ✓ If epigastric pain is present, treat as for eclampsia.
- ✓ Assess fetal condition
  - Corticosteroids if fetus is 24-36 weeks gestation with caution
  - Deliver in 24-48 hours after steroids are administered and maternal condition is stable
- ✓ Correct thrombocytopenia

- Transfuse platelets regardless of platelet count if there is bleeding from intravenous site
- PPH is seen in vaginal delivery if platelets count is <40000/cm^3
- Platelet transfusion indicated after delivery for first 24 hours to maintain counts >50000/ cm^3 in Caesarean section and >20000/ cm^3 in vaginal delivery.

✓ Labour and Delivery

- Aim for vaginal delivery and avoid episiotomy if possible
- Caesarean section done only for obstetric indication and vertical skin incision preferred to pfannensteil incision
- Allow for spontaneous expulsion of placenta rather than manual extraction at caesarean section
- Uterine repair is done in-situ, rather than exteriorisation to minimize uterine and adnexal trauma
- Mass closure should be done for abdominal incision
- Antibiotics should be prescribed for 3 days.
- In the non-obstetric population a level of <$50x10^9$/L is considered significant in the context of surgery or major haemorrhage

Aim for carefully controlled, skillfully executed non-operative vaginal delivery

✓ Postpartum Care

- Care as for severe PE-Eclampsia in HDU/ICU
- Watch for hepatic rupture/haemorrhage (PE-Eclampsia + HELLP + Right Hypochondrial pain + Hypotension)
- Watch for upward trend in platelets, downward trend of LDH, SGOT
- Dexamethasone 12 mg 12 hrly till platelets >100,000/ul, than Dexamethasone 5 mg 12 hrly for further 2 doses.

APPENDICES

Basic Facts on Common Drugs Used in the Management of Hypertension

1. **Methyldopa** is a centrally acting antihypertensive drug that is altered in the CNS to alpha-methylnorepinephrine, which stimulates inhibitory alpha-2 adrenergic receptors in the hypothalamus (inhibits sympathetic nervous system outflow from the vasomotor centre to the periphery). Available in tablets, suspension and injection.

   Cardiovascular effects are a decrease in systemic vascular resistance and blood pressure, whereas cardiac output (renal, cerebral and myocardial blood flow) is maintained.

   Contraindications are acute hepatic disease, history of depression, and phaeochromocytoma

   Side-effects are sedation, depression nightmares, nasal congestion, hemolytic anemia and liver disorders.

2. **Hydralazine** decreases blood pressure by exerting a direct relaxant effect on vascular smooth muscle (arterioles greater than veins). Available in tablets and injections.

   Cardiovascular effects include the preferential dilation of arterioles compared with veins minimizes orthostatic hypotension and promotes an increase in cardiac output (stroke volume and heart rate increases).

   Contraindication is tachycardia.

   Side-effects are reflex tachycardia, sodium and water retention, vertigo, myocardial stimulation, SLE-like syndrome.

3. **Labetolol** exhibits selective alpha-1 antagonist and nonselective beta-2 antagonisteffects following oral or intravenous administration. Available in tablets and injections.

CVS effects : it acutely lowers BP by decreasing systemic vascular resistance and reflex tachycardia triggered by vasodilation is attenuated by simultaneous beta blockade

Contraindication is partial heart block, CCF.

Side-effects are fluid retention, orthostatic hypotension, bronchospasm, cardiac failure.

4. Calcium Channel Blockers

Two common drugs used in pregnancy:

i) Nicardipine

ii) Nifedipine

Mechanism of action

Calcium channel blocker inhibits the passage of calcium through the voltage gate L typeof membrane channels of smooth and cardiac muscle, reduces available intracellular calcium and causes muscles to relax and hence vasodilation occurs.

Some of the group have weakly negative cardiac inotropic action and negative chronotropic effect via pacemaker cells and depress conducting tissue.

Pharmacokinetics

Generally all Calcium channel blockers are well absorbed from the gut and are metabolised by the liver.

Adverse Effects

Headache

Flushing

Dizziness

Palpitation

s Lethargy

Hypotension – may occur during 1st few hours after dosing

Ankle oedema

Bradycardia

GIT effects
- constipation
- nausea
- vomitin

Gum hypertrophy (Nifedipine)

Individual Calcium blockers:

Nifedipine has greater coronary and peripheral arterial vasodilator properties than verapramil.

There is minimal effect on venous capacitance vessels. Has little or no depressant activity on sinoatrial or artrioventricular nodal activity.

Peripheral vasodilation and resultant decrease in blood pressure produced by nifedipine activate baroreceptors leading to increased peripheral sympathetic nervous system activity, most often manifesting as tachycardia.

Side effects are headaches and flushing. Abrupt discontinuation of nifedipine has been associated with coronary artery spasm.

(Half-life) T1/2 : 2 hours

Selectively dilates arteries with little effect on veins

Can be given sublingually or orally

Dosage 30 – 60 mg daily

5. Parenteral Antihypertensives

Aim to keep diastolic blood pressure between 90-95 mmHg

Labetolol is contraindicated in Bronchial Asthma, CCF and Atrio-Ventricular Heart Blocks.

i) Labetolol Infusion

a) For rapid control

- I/V Labetolol 10 mg (2 mls) over 1 minute and repeat at 5 minute intervals (Maximum dose : 200 mg (40 mls)
- Effective dose : 20-150 mg/hr (4-30 mls/hr)
- Infusion syringe pump (put 200 mg or 40 mls Labetolol in 50 mls syringe and start at 20 mg/hr ie. 20 mg or 4 mls/hr and increase at 30 minutes. Stop infusion if rate exceeds 150 mg/hr (30 mls/hr) and inform specialist.

ii) Hydralazine Infusion

a) For rapid control

- I/V bolus 6.25 mg over 20 minutes and repeat every 20 minutes only if DBP >90 mmHg (1-10 mg/hr infusion is preferred)

b) Maintenance Dose

- Effective dose : 1-10 mg/hr
- Infusion Pump
- Dilute 50 mg Hydralazine in 50 mls Normal saline ie. 1 mg/ml and start at 5 mls/hr

  Increase every 20 minutes by 1 ml/hr until maximum dose of 10 mls/hr or 10 mg/hr
- Infusion Drip Set

- Dilute 20 mg Hydralazine in 500 mls Normal Saline and start at 10 dpm.
  Increase every 20 minutes at 10 dpm to titrate against blood pressure so as to maintain at 140/90 mmHg.

- Prevent fluid over load.

Antihypertensive Drugs Commonly Used In Pregnancy

Drug	Mode of action	Start. Dosage (mg/day)	Max. dosage (mg/day)	Half-life T1/2 (hours)	Adverse effects
Methyldopa	Centrally-acting (false transmitter precursor)	250	3000	1.8	Depression, drowsiness, lupus-like syndrome, blood dyscrasias, liver dysfunction
Labetolol	beta - Blockers	100	2000	4	Complete heart. block, pulmonary odema, bronchoconstriction
Nifedipine	Ca-channel blocker	15	60	3.4	Headaches, flushing
Hydralazine	Vasodilator	25	300	2.2-2.6	Tachycardia, hypotension, headache tachyphlyaxis

Drugs and Fetal Risks

Drug	Fetal risk
Methyldopa	Positive Coomb's test in fetus, doses > 2g/day meconium ileus
Hydralazine	Fetal heart rate changes when given acutely at term
Magnesium sulphate	Bladder atony & myotonia but these are rare
Beta-Blockers	IUGR, hypotonia at birth, neonatal bradycardia, hypoglycaemia

Drugs Used In Eclampsia

Drug	Mode of action	Dosage	Adverse effects
Diazepam	GABA receptors, choloride gates	bolus 10mg, infusion 40mg & titrate	Respiratory. depression, tolerance, drowsiness
Magnesium sulphate	Cerebral depressant, reverses cerebral vasoconstriction	See text	Respiratory arrest, arrythmias, oliguria

6. Anticonvulsant Therapy in HDP

MAGNESIUM SULPHATE

This drug has gained prominence in the management of convulsions in HDP.

It is available as $MgSO_4 H_2O$ – 50% solution. This contains 50 gm in 100ml solution i.e.: 5ml ampule contains 2.5 gm $MgSO_4$; 20% solutions are also available.

The drug can be administered intravenously or intramuscularly.

- 50% solution is suitable for intramuscular use
- 20% solution is suitable for intravenous route

Administration

- Intravenous
- Intramuscular

Intravenous route is preferred to intramuscular route which is painful and is complicated by local abscess formation.

a) **Loading dose**: I/V 4 gm $MgSO_4$ slow bolus

- An initial dose of 4 gm $MgSO_4$ is given over 10-15 mins (rapid injection causes cardiac arrest)
- 4 gms (8 mls) $MgSO_4$ is diluted in 12 mls Normal Saline or sterile water to a total volume of 20 mls
- If further convulsions persists after 15 minutes, a further 2 gms $MgSO_4$ is diluted and given over 15 minutes

b) **Maintenance Treatment** IV 1 gm/hour $MgSO_4$

- Syringe Pump
  Ideally $MgSO_4$ is given by a syringe infusion pump

  1 mls $MgSO_4$ is diluted in 48 mls of 5% Dextrose and infused at 50 ml/per hour

  Drip Infusion Set

  5 mg $MgSO_4$ (10 mls) in 500 mls 5% Dextrose is run at 33 drops per minute

This infusion is only continued if the following criteria are satisfied

- Patellar (knee jerk) reflex is present
- Respiratory rate > 16/min
- Urine Output >100 mls over 4 hours
- Serum Magnesium level are within therapeutic range of 1.7 – 3.5 mmol/L

- **Intramuscular Loading Dose**

10 gm 50% solution (20 mls) is injected intramuscularly. One half is injected into upper outer quadrant of each buttock in zigzag manner (proceeded by local anaesthesia if necessary) using a 21 gauge needle and this is followed by a maintenance dose every 4 hours.

Caution: The loading dose of $MgSO_4$ must be reduced in oliguria.

- **Maintenance Dose for Intramuscular Route**

5 gm 50% solution is injected deep intramuscular in alternate buttocks every 4 hours after ascertaining that:

a) Knee (patellar) jerk is present
b) Respiratory rate is > 16/min
c) Urine output >100 ml/4 hours

Caution

1. Patients who have received diazepam should not be administered intravenous loading dose. Only intra-muscular loading dose should be given.

2. If convulsions recur, after loading 2 gm 20% solution (10 ml) intravenous can be repeated slowly over 3 minutes

The therapeutic plasma concentration is 4-7 mmol/l

Magnesium sulphate is eliminated by **the kidneys**.

c) Mechanism of Action

Magnesium sulphate is not an anticonvulsant but it does **relax vascular smooth muscle**, therefore it is likely that magnesium sulphate acts by **reversing cerebral vasoconstriction**.

Magnesium sulphate is an effective **cerebral depressant** and hence reduces neuromuscular irritability.

d) Recurrent convulsions

Both intramuscular and intravenous regimens:

Further 2-4 grams (depends on weight, 2 gram if <70 kg) to be given

Intravenously over 5 min.

MAGNESIUM SULPHATE REGIMENS FOR WOMEN WITH ECLAMPSIA

INTRAMUSCULAR MAINTENANCE REGIMEN

LOADING DOSE	MAGNESIUM SULPHATE INTRAMUSCULAR	Deep intramuscular injection 5 gm in each buttock
MAINTENANCE THERAPY	MAGNESIUM SULPHATE INTRAMUSCULAR	Deep intramuscular injection 2.5 gm in each buttock every 4 hours. Continue for 24 hours after last convulsion, or delivery

INTRAVENOUS MAINTENANCE REGIMEN

LOADING DOSE	MAGNESIUM SULPHATE INTRAVENOUS	Slow intravenous injection over a period not less than 5 minutes preferably 10-15 minutes
	MAGNESIUM SULPHATE INTRAVENOUS	Rate of infusion 1 gm/hour
MAINTENANCE THERAPY	MAGNESIUM SULPHATE INTRAVENOUS	Rate of infusion 1 gm/hour. Continue for 24 hours after last convulsion, or delivery

e) Monitoring During Magnesium Sulphate Therapy

The next intra-muscular dose can only be given or the intravenous infusion can only be continued if:

Respiratory rate > 16/min - check every 15 min

Urine output > 25 ml/hr - check every hour

Patellar reflexes are present -check every 15 min

Intravenous regime needs more frequent monitoring. In the first 2 hours monitoring should be every 10 min.

f) Side-effects and Toxicity of Magnesium Sulphate

Effects associated with various serum magnesium levels

Effects	Serum level mmol/l
Anticonvulsant prophylaxis	4 - 6
ECG changes	5 – 10
Loss of deep tendon reflexes	10
Respiratory paralysis	15
General anaesthesia	15
Cardiac arrest	>25

Other side effect : May enhance the action of curare-like drugs and Ca channel blocker

Effects on newborn: Magnesium sulphate crosses the placenta freely, however there is little evidence of toxicity eg. hypermagnesaemia associated with hyperreflexia and respiratory depress-ion, provided maternal serum limits are observed.

g) Steps to be taken in Magnesium Toxicity

The following guidelines are provided for management of the potential complications of magnesium sulphate.

Respiratory arrest

- Intubate and ventilate immediately
- Stop magnesium therapy
- Give 1 g IV of calcium gluconate

Repiratory depression

- Give oxygen by mask
- Stop magnesium therapy
- Give 1g IV of calcium gluconate
- Maintain the airway
- Nurse in the recovery position

Absent patellar reflexes

- If respiration normal - withold further doses of magnesium sulphate until the reflexes return
- If respiration depressed - manage as above

Urine output <100ml in 4 h

If no other signs of magnesium toxicity, reduce the next dose

IM dose to 2.5g OR

IV dose to 0.5g/h

If there are other signs of magnesium toxicity, manage as for the appropriate section above.

h) Magnesium Sulphate Pack

The entire components are kept in a readily available portable carrier container.

- **Intravenous Infusion**

  i) 500 ml Normal Saline
  ii) Intravenous cannula
  iii) Infusion giving set
  iv) Tape to secure cannula
  v) Swab to clean skin

- **Magnesium Sulphate Pack**

  i) 4 g loading dose
  ii) 5 x 5 gm maintenance dose
  iii) 5 gm (for recurrent convulsions)
  iv) Pharmacology of MgSO4

- Available as $MgSO_4 H_2O$ – 50% solution. This contains 50 mg 100 ml solutionie.
  : 5ml ampoule contains 2.5 gm $MgSO_4$

- Drug can be administered **intravenously** or intramuscularly. 50% solution is suitable for intramuscular use, 20% solution is suitable for intravenous route.

- Magnesium sulphate is cleared by the kidney, hence the dose must be reduced if there is impairment of renal function. In the presence of oliguria, cumulative toxicity can result with repeated doses; thus dose must be reduced or omitted in such situations.

- Serum levels of $MgSO_4$ correlate with clinical signs. $MgSO_4$ depresses neuromuscular transmission and can cause muscular paralysis. Loss of patellar (knee) reflex is usually the first clinical manifestation of toxicity. Respiratory depression follows if levels go higher. Thus laboratory testing of serum $MgSO_4$ may be unnecessary.

- **Syringes and needles**

- **Calcium Gluconate**

    i) 1 gm (intravenous) for toxicity

- **Observation Chart**

    i) Fluid Chart
    ii) BP/Pulse/Respiratory rate/knee jerk reflexes

- **Protocol**

    i) Summary Flow Chart
    ii) Detailed Regime
    iii) Guidelines for other aspects of care

i) Route of administration of $MgSO_4$

- There is no evidence of any difference between intramuscular and intravenous regimes in their effects on recurrent convulsion except that intramuscular injections are painful and have a 0.5% risk of abscess formation

- All staff must be familiar with both routes of administration. Repeat doses are only given when the respiratory rate is >16/minute and the knee reflexes are present

- The intramuscular route is especially convenient where infusion sets are not available.

DIAZEPAM

Diazepam is a minor tranquilliser that has been used as an anti-convulsant

Advantages:

a) readily available
b) cheap
c) easy to administer

Disadvantages:

a) Profound maternal sedation
b) Respiratory depression
c) Loss of fetal heart variability
d) Neonatal hypotonia and poor sucking
e) Tachyphylaxis

Dosage and Administration

- The recommended regime is

  - 40 mg Diazepam in 500 ml of 5% Dextrose/Normal saline (preferably glass container)

  - Infusion rate is titrated against patient's level of consciousness ie to keep her drowsy but arousable

  - Regime to continue for 24 hours after the last convulsion and to half the concentration for the next 24 hours

  - Recurrent convulsions can be managed with an additional IV injection of 5-10 mg over 1-2 min

  - Patient should be nursed in the HDU/ICU

Fluid Regimen for Patients with HDP

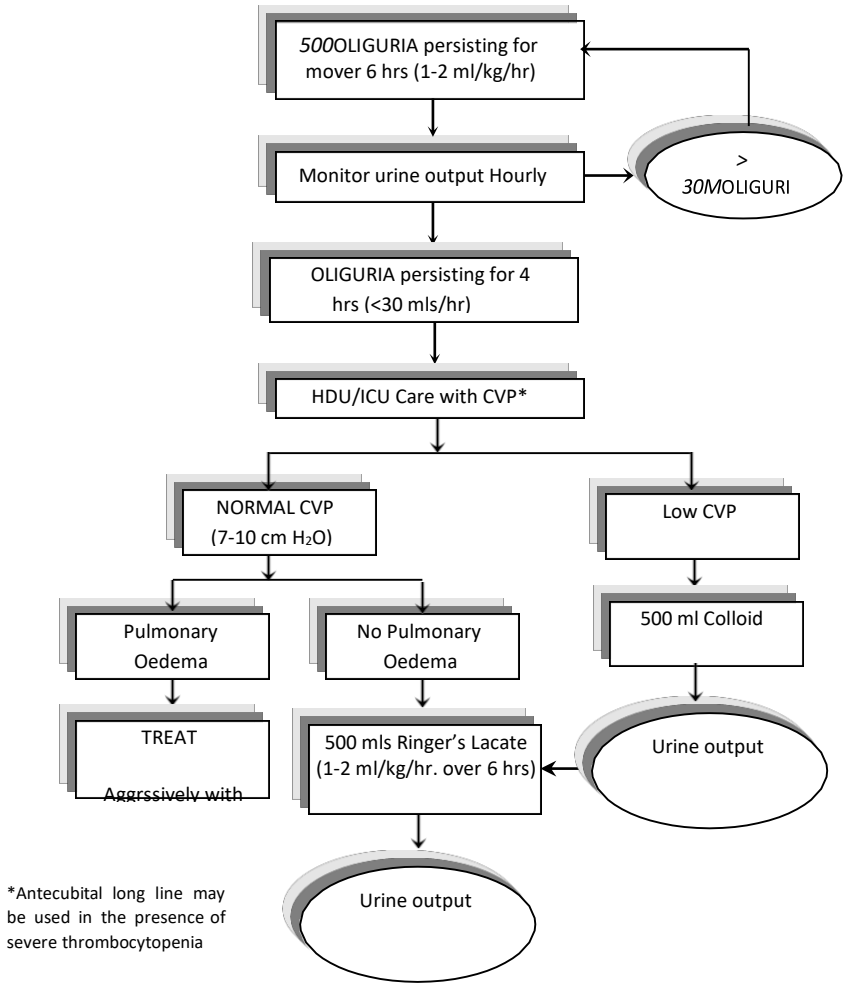
In pre eclampsia/eclampsia there is diminished intravascular volume, high systemic vascular resistance and low colloid osmotic pressure. In view of this, infusion of fluids must be cautiously undertaken. The appropriate use of intravenous fluids in terms of both fluid type and quantity may influence morbidity and mortality. In the extreme, acute pulmonary oedema is a leading cause of death in women with pre-eclampsia and a frequent cause for admission to intensive care

For practical purposes close monitoring of fluid intake and urine output is mandatory.
The presence or absence of pulmonary oedema can be assessed clinically by auscultation for basal crepitation, tachypnoea and continuous measurement of oxygen saturation using a pulse oximeter.

Suggested total fluid replacement: (See Fig. 1)

- Should not exceed 1-2 ml/kg/h[1] or 85 ml/hr whichever is lower.
- Urine output of more than 30 ml/h (0.5 ml – 1 ml/kg/h) should be maintained
- If CVP line is present, then the CVP level should not be higher than 7 cm of H_2O
- If the patient has started taking oral fluids, then this amount should be taken away from the intravenous fluid regimen of 1-2 ml/kg/h
- If pulmonary oedema develops i/v Frusemide 40 mg should be given, oxygen administered and patient managed in ICU
- If oliguria develops and urine output is less than 30 ml/h for 4 hours, then a fluid challenge with 200 ml of crystalloid solution over 5 minutes should be tried. Evaluation should be done at 4 hours period because in most cases the kidneys will recover. If oliguria persists and CVP is above 7-10 cm H_2O, then referral should be made to the Physician for further management.

Attention to fluid management is vital in view of the contracted plasma volume in PIH/Eclampsia.



Central venous pressure measurements in an HDU/ICU setting may be warranted to assist fluid management.

Types of Intravenous Fluids

The types of intravenous fluids that can be used in the management of patients with HDP are:

(i) crystalloids
(ii) colloids

Composition of common intravenous fluids:

(i) Crystalloids:

Name	**pH**	**Osmolality Mosmol /litre**	**Na+ mmol/litre**	**K+ mmol/litre**	**Cl-mmol/litre**	**HCO3 mmol/litre**	**Misc. mmol/litre**	**Carbohydrate /litre**	**Protein g/litre**
Sodium Chloride 0.9%	5.0	308	154	0	154	0	0	0	0
Ringer's Lactate	6.5	280	131	5	112	29	Ca 1 Mg 1	0	0
Gluose 5% + NaCl 0.9%	4.5	585	154	0	154	0	0	50	0
Glucose 5%	4.0	280	0	0	0	0	0	50	0
Glucose 4% + NaCl 0.18%	4.5	286	31	0	31	0	0	40	0

Normal Saline:

Is essentially isotonic with human plasma and contains sodium as the primary osmotically active particle. It distributes evenly throughout the extracellular space. About ¼ of the infused volume remains in the intravascular space after one hour. After infusion equilibration with the extracellular space occurs within 20 to 30 minutes. Normal Saline is used as a replacement fluid.

Ringer's Lactate:

This is a balanced salt solution and it equilibrates with the extracellular space within 20 to 30 minutes and is mainly used as a replacement fluid. The lactate is metabolised in the liver to form bicarbonate, to counteract acidosis. If normal saline or Ringer's lactate solution is used to replace lost blood volume at least 3 times the volume of blood lost, must be infused.

Dextrose/Saline solutions:

These are usually maintenance fluids. Five percent dextrose solution is isotonic and may be used for fluid maintenance and to keep an intravenous route open for medication. When stored blood is followed by glucose solution, rouleaux formation takes place. This causes clumping in the drip set. Dextrose 5% is distributed throughout all body fluids and is ineffective as a volume expander.

(ii) Colloids:

Name	pH	Oncotic Pressure (cm H2O)	Na+ mmol/litre	K+ mmol/litre	Cl-mmol/litre	Misc. mmol/litre	Carbo Hydrateg/litre	Protien g/litre	Half-life in Plasma (hours)
Gelatin (succinylated urea. Haemaccel)	7.4	37	145	5.1	145	Ca 6.25 PO4 trace SO4 trace	0	35	5 h
Gelatin (polygeline. Gelofusin)	7.4	46.5	154	0.4	125	Ca 0.4 Mg 0.4	0	40	4 h
Hetastarch (Hespan)	5.5	31	154	0	154	0	0	0	17 days

Colloids:

Colloids maintain or increase plasma oncotic pressure and so help to draw fluid into the intravascular space. Examples of colloids in clinical use are gelatins, starches and albumin.

- Gelatins :
  These are produced by the hydrolysis of collagens. Gelatins have an incidence of adverse reactions (1 in 2,000 to 13,000 have been reported).

  They have a long shelf- life and are of reasonable cost. Risk of transmissible diseases is not there.

  (i) **Haemaccel**: is a 3.5% urea linked gelatin with a molecular weight of 35,000 in electrolyte solution. As Haemaccel contains calcium, it should not be given in the same infusion set as citrated blood and fresh frozen plasma.

  (ii) **Gelofusine** : is a 4% succinylated modified fluid gelatin in normal saline. It has a molecular weight of 30,000 and pH of 7.4. It has a biological half-life of about 4 hours. The duration of useful plasma expansion is about 2 hours and 85% is excreted by the kidneys.

- **Starch:**

  Hetastarch: is a synthetic colloid derived from corn starch. Its molecular weight ranges from 10,000 to over one million. Intravascular volume is expanded to the same volume as that infused, and this state may last for about 3 hours. Smaller molecules, with molecular weight less than 50,000 will be excreted in urine, and the larger molecules will undergo hydroxyethylation before being eliminated. Its biological half-life is about 17 days.[3] The recommended volume is 500ml to 1000ml per day for a 70 kg adult. Over- infusion can lead to pulmonary oedema. The incidence of anaphylatic reaction to hetastarch is less than 0.085%.[3,4]

Albumin: has a molecular weight of 66,300 to 69,000 and exerts 80% of the plasma colloid oncotic pressure. Its half-life is 16 hours. Albumin is used in the resuscitation of patients with an acutely diminished intravascular volume to draw in fluid from the extravascular space into the intravascular space. When 100ml of 25% albumin isinfused, intravascular volume increases to 450ml in 30 to 60 minutes. Caution has to be exercised as over-infusion can easily lead to pulmonary oedema. Anaphylatic reaction to albumin is between 0.47% and 1.53%.

The list of recommended literature:

1. **Наказ МОЗ України від 24.05.2012 № 384 "Про затвердження та впровадження медико-технологічних документів зі стандартизації медичної допомоги при артеріальній гіпертензії"**

2. **Royal College of Obstetrics and Gynaecology guidelines**

3. **Cochrane Library**

4. **www.medscape.com**

5. **Carmen Dolea, Carla AboZahr : Global burden of HDP in the year 2000 :Evidence and Policy WHO Geneva 2003**

6. **Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy. Am J Obstet Gynecol 2000; 183:1-22.**

7. **Tuffnell DJ, Shennan AH, Waugh JJ, Walker JJ. The management of severe pre-eclampsia/eclampsia. London (UK): Royal College of Obstetricians and Gynaecologists; 2006 Mar. 11 p. (Guideline; no. 10(A)). [52 references]**

8. **Australian and New Zealand College of Anaesthetists 2008**

9. **Katz LM, de Amorim, MM, Figueiroa JN & Silva JL 2008, 'Postpartum dexamethasone for women with hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome: a double-blind, placebo-controlled, randomized clinical trial', Am J Obstet Gynecol, vol. 198. pp. 283 e1-8.**

10. **A.T Dennis. Management of pre-eclampsia: issues for anaesthetits. Anaesthesia 2012, 67, 1009-1020**

11. **Sujata C, Rashmi S, Subarachnoid block for caesarean section in severe preeclampsia. Journal of Anaesthesiology and Clinical Pharmacology,2011:27,2,169-173**