Pre eclampsia

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Pre eclampsia

- What is it?
- Why are we worried?
- What can we do ?
- How do we prevent it?
- What do we tell the women?
- Newer developments

What is it?

- Multi-system disorder/ disease of theories
- New onset hypertension > 20 weeks
- Sustained DBP≥90mmHg, SBP≥140 mmHg
- Proteinuria: ≥0.3 gram per 24hrs
  urinary PCR>30mg/mmol
  urine dipstick +1 or more

- NICE: Mild, moderate, severe

Classification of hypertensive disorders

- **Pre existing hypertension**
  - Before 20 weeks of pregnancy
  - Not d/t GTD
  - Diagnosis can be difficult
  - May be diagnosed in postnatal period

Classification

- **Gestational hypertension**:
  - No proteinuria
  - ↑BP after 20 weeks
  - Resolves by 12 weeks
  - No symptoms of pre eclampsia

Classification

- **Chronic hypertension with superimposed pre eclampsia**

  New onset proteinuria (>300 mg/24 hr)

  No proteinuria before 20 weeks

  OR

  A sudden increase

  in proteinuria or blood pressure > 20 weeks
- **Pre eclampsia**
- **Eclampsia**

Demographics

- Incidence 10-20% globally
- More common in developed countries (28/1000 live births)
- 50,000 deaths globally due to PE related complications
- Incidence of pre eclampsia is reduced in developed countries (4/1000 live births)

MBRACE

- Maternal deaths from PET lowest rate recorded (since 1952)
- 19/261 2006-2008
- 10/253 2009-2011
- 9/243 2010-2012
- 6/214 2011-2013 (0.25 per 100,000 maternities)

Possible reasons for improvement

- Low dose aspirin
- Magnesium sulphate for severe PE/Eclampsia
- NICE guidelines

Why are we worried then?

- Remains an important cause of maternal and perinatal mortality and morbidity
- 19 deaths occurred d/t pre eclampsia in 2006-8 enquiry
- 91% of deaths were because of substandard care

Why are we worried then?

Maternal

- Cerebral haemorrhage
- Cardiac arrest
- Liver necrosis/haemorrhage
- Multi-organ failure
- Pulmonary oedema
- Coagulopathies
- Renal failure

Foetal

- Still birth 5%
- SGA
- Preterm delivery (8-10%)

consequences

Why are we worried then?

- Implications for future pregnancies

- Long term cardiovascular risks (8 times ↑risk with PE < 34 weeks)
- (Meta-analysis BMJ 2007)

  doubles the risk of stroke

  quadruples the risk of hypertension in later life

  doubles the risk of fatal/nonfatal IHD

  quadruples the risk of ESRD

What can we do?

- Not entirely preventable
- Risk can be reduced
- Morbidity and mortality can be reduced

Pathophysiology

Susceptibility to PE

↓

Failure of remodelling of spiral arterioles

↓

Defective placentation

↓

↓ Angiogenic factors

(PGLF, EGF)

↑ Antiangiogenic factors

FGR ← Placental hypoxia

↓

release of antiangiogenic factors

Thrombocytopenia

seizures ↖

↓ ↓ ↑

BP↑ ← vasospasm ← endothelial damage→ coagulation cascade activated

oliguria ↙ ↓

liver ischaemia

↓

capillary leak → proteinuria

↓ ↘ oedema

Haemoconcentration

Prediction of preeclampsia

- Clinical history and risks
- But majority occur in healthy nulliparous women

- One test may not fit all

  high risk (different groups)

  healthy nulliparous
- Best screening test will be combination of biomarkers and clinical risks

Identify risk factors

Maternal

- Nulliparity
- Previous history 7.19
- Age>40 <18
- Chronic hypertension
- Chronic renal disease
- APLS 9.72
- Diabetes
- Afro-Caribbean race
- BMI> 35
- New partner

Foetal

- Multiple pregnancy 2.93
- Hydrops
- Molar pregnancy

Primary prevention

- **Avoid risk factors:**

not always possible

1/3rd of pregnancies are unplanned

age>40, <20 years

multiple pregnancy ↑ with IVF

long birth interval

optimal control of chronic HT, DM,CKD

connective tissue disease in remission

Prevention

- **Lifestyle interventions**:

  optimal BMI

  healthy diet

  exercise

  stop smoking

  no need for salt reduction except if chronic HT

- **Calcium intake:**

  up to 50%↓ in PET in high risk women with low intake ***/*** no effect on neonatal outcome

Pre pregnancy counselling

- Chronic hypertension
- Previous severe/early onset PET
- SLE
- Type 1 and type 2 diabetes

Pre pregnancy counselling

- Review of anti hypertensive drugs
- Stop ACE inhibitors/ ARB/Chlorthiazide/consider safer drugs
- Aim for a pre pregnancy BP of 140/90mmHg or less
- Can be re-started in post natal period

Anti hypertensive to avoid

- **ACE inhibitors:**

  teratogenic in 1st trimester

  renal dysfunction/skull hypoplasia/

  oligohydramnios in 2nd & 3rd trimester

- **Angiotensin receptor blockers**:

  teratogenic in 1st trimester

  renal dysfunction/ oligohydramnios

Anti hypertensive to avoid

- **Diuretics:**

  reduction in maternal blood volume

  foetal electrolyte disturbances

- **B blockers** (except labetalol)

  foetal bradycardia/ IUGR with atenolol

- **Calcium channel blockers:** except nifedipine

  maternal hypotension/ foetal hypoxia

Anti hypertensives to be used

- Methyldopa — Avoid in post natal period (depression)
  headache, nasal congestion, lethargy
- Labetalol — bradycardia, bronchospasm
  Avoid in asthma
- Nifedipine — severe headache, peripheral oedema
  Avoid before 20 weeks

- Hydralazine — flushing, headache, lupus like symptoms

Safety of drugs in breast feeding

No known adverse effect

- Labetalol
- Captopril
- Nifedipine
- Atenolol
- Enalpril
- Metoprolol

Insufficient evidence

- Angiotensin receptor blockers
- Amlodopine
- Other ACE inhibitors

Aspirin prophylaxis

High risks:

previous pre eclampsia

hypertension

type 1 and 2 diabetes

SLE and antiphospholipid syndrome

renal disease

One high risk recommend Aspirin 75 mg

NICE

Aspirin prophylaxis

Moderate risk factors:

first pregnancy

age> 40 years

BMI >35

multiple pregnancy

pregnancy interval> 10 tears

F/H of pre eclampsia

If 2 or more moderate risk factors consider Aspirin

NICE

Prophylaxis with Aspirin

- In PE: imbalance of prostacyclin and thromboxane

  net result is vasoconstriction

- Inhibition of cyclo-oxygenase in platelets

- increases prostacyclin to thromboxane ratio

  net result is vasodilatation

Aspirin prophylaxis
Is it effective?

- Over all 19% reduction in PET in high risk patients
  (CLASP Trial)
- 14% reduction in preterm delivery/10% reduction in IUGR
- No adverse foetal or maternal effects
- Ideally around 12 weeks
- May start earlier if severe or early onset PET
- Avoid if allergy, platelet disorders, established PET
- Caution in asthmatics

Useless interventions

- No evidence for:
  - nitric oxide donors
  - progesterone
  - diuretics
  - LMWH
- No evidence for nutritional supplements:
  - magnesium
  - folic acid
  - fish oil
  - garlic
  - vitamin C and E

Indications for early referral

- Underlying medical condition

  CKD

  DM

  APLS
- previous PET
- Multiple pregnancy
- If 2 of the moderate risk factors

  (PRECOG 2004)

Early detection

- **Substandard care in 91% of cases** (2006-8 enquiry)
  - Failure to identify risks and referral to secondary care
  - Failure to recognise and act on signs and symptoms
  - Not treating systolic hypertension

Early detection

- **What are the signs and symptoms?**

  severe headache

  blurred vision/ flashing lights/ blindness

  vomiting

  severe RUQ pain

  sudden swelling of face, hands, feet

  h/o not feeling well

- Educate women to report these symptoms urgently
- Ask about foetal movements

Early detection

- Take BP after 10 minutes of rest:
  - use calibrated device
  - use correct size cuff
  - automated device undermeasure
  - take BP manually as well
- Check proteinuria
- P/A : FH measurement/tenderness
  - foetal heart
- Reflexes/clonus
- Fundoscopy if possible

Same day referral to hospital

- If DBP≥ 90mmHg < 100mmHg and symptomatic
- DBP > 100mmHg SBP>160mmHg
- DBP≥ 90 mmHg with at least 1+ proteinuria
- Maternal symptoms with DBP< 90mmhg with no proteinuria

PRECOG 2004

Assessment within 48 hours

- New hypertension without proteinuria >20 weeks

  DBP ≥ 90mmHg but under100mmHg

- If h/o reduced FM/ clinically SGA: follow local protocol

- If proteinuria < 20 weeks with normal BP: repeat assessment in 1 week

- If ≥2+ proteinuria: routine referral to hospital

Routine Antenatal care

- **No risk factor** :

  Follow local/NICE antenatal guidelines for multiparous women

- **One risk factor which does not meet the criteria for early referral:**

  24-32 weeks no more than 3 weeks

  32 weeks-delivery no more than 2 weeks

  individualise the care

  NICE antenatal guidelines for primiparous women

When to deliver?

Preeclampsia:

- Hospital admission does not improve outcome for mother or the baby in mild PE
- Mild PE without significant proteinuria can be treated as O/P
- **Before 34 weeks** deliver if severe refractory BP/foetal or maternal concerns
- **34- 34+6/7** if severe hypertension or mild to moderate hypertension with foetal or maternal concerns
- **After 37 /40** deliver within 24-48 hours if mild/ moderate hypertension

When to deliver?

- Balance of prematurity and maternal and foetal wellbeing
- Maternal condition always comes first
- **Chronic hypertension and gestational hypertension**

  deliver after 37/40 if BP < 160/110

  deliver before 37/40 if refractory severe hypertension

Chronic hypertension

- Pre-pregnancy care/Lower dietary salt
- Optimise BP on safe medications
- Low dose aspirin from 12 weeks
- Early referral
- Aim for BP < 150/100 mmHg, 140/90 mmHg if end organ damage
- Care in the community/ hospital based on individual needs
- Detect signs and symptoms of PE
- If secondary hypertension refer to nephrology/endocrinology

Postnatal management:

- Check BP daily for first 2 days
- At least once between D3 and D5
- As clinically indicated if medication is changed
- Stop methyldopa after birth and change to pre pregnancy medication
- Aim is to keep BP< 140/90mmHg
- Review long term treatment in 2 weeks
- Ideally 8 weeks postnatal review/ plan for next pregnancy/ long term complications

Gestational hypertension

- Associated with adverse outcome if

  early onset/severe/PE
- Refer as per PRECOG guidelines
- 25 % will progress to pre eclampsia
- Treat if BP≥150/100 mmHg
- If develops< 32 weeks and mild/ check BP/urine once weekly
- If severe ≥170/110 mmHg, admit and stabilise in hospital
- Once stable, community monitoring biweekly/ bloods weekly
- Bed rest in hospital is ineffective

Postnatal management

- Continue medication
- If BP ≥ 150/100 mmHg, start labetalol
- Daily BP for first 2 days or as indicated
- At least once between D3 and D5
- Reduce treatment if BP< 140/90, stop if, 130/80
- If on treatment at discharge, GP review in 2 weeks
- Postnatal review by GP in 8 weeks
- If treatment still needed at 12 weeks, refer to specialist

Preeclampsia

- Present diagnostic criteria are not ideal
- Parameters used are end points in disease and don't predict adverse outcome accurately
- Proteinuria is not necessary to diagnose PET
- If proteinuria is absent diagnose preeclampsia:

platelets<100

serum creatinine >1.1mg/dl

elevated liver transaminases twice the normal

pulmonary oedema

cerebral or visual symptoms

(ACOG)

Predictors of adverse outcome

Piers trial

- Multicentre trial to look into adverse outcome
  - gestational age
  - platelet count
  - raised serum transaminases
  - dyspnoea or chest pain
  - oxygen saturation in air

(Lancet 2011)

Postnatal management

Not on medications:

- Measure BP at least 4 times a day/enquire about symptoms
- Measure PET bloods 48-72 hours post delivery
- Fluid balance not required if creatinine normal
- Transfer to community

  BP< 150/100 mmHg/no symptoms/bloods normal
- Check once at least between D3 and D5

  if abnormal measure on A/D till normal

  if > 150/100 start medication

Post natal management

On medication:

- Continue medication
- BP check at least 4 times a day
- Transfer to community if BP≤ 149/99/ no symptoms/ bloods normal/stable
- Measure BP every1-2 days for 2 weeks

  ↓ medication if BP < 140/90

  stop if BP < 130/80
- Review if still on medication at 2 weeks after birth

Postnatal management

- At 6-8 weeks
- Contraception, avoid OCP
- Offer specialist referral if still on medication
- Repeat bloods if indicated
- Check urine if ≥ 1+

  see in 3/12 to assess kidney function

  refer to specialist if proteinuria persists

Future pregnancy risks

- Gestational hypertension 13-53%
- Overall future risk of PE up to 16%
- About 25% risk if severe, HELLP, eclampsia, delivered < 34 /40
- About 55% risk if delivered< 28/40

- Discuss lifetime cardiovascular risks
- Lifestyle modification, optimising BMI, LDA in next pregnancy

Future developments

Can we predict PE in first trimester?

- Maternal risk factors: **50%**
- Maternal risk factors + UAD + MAP : **85%**
- Maternal risk factors + UAD + MAP + PLGF + PAPP-A : **95%**

  (Nicolaides et al)
- PLGF can detect PE < 35 weeks

  normal PGLF rules out PE **(98% NPV)**

  low PGLF **96% sensitivity** in detecting PE

  (PELICAN Study)

Thank you