Updates in Hypertension & Preeclampsia

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Do you give MgSO4 for eclampsia prophylaxis to patients with:
1. Mild PreE
2. Severe PreE
3. All of the above

Patients with a history of early onset PreE should be counseled regarding:
1. Recurrent PreE
2. Risk of cardiovascular disease later in life
3. Thrombophilia evaluation
4. 1 & 2
5. All of the above

Postpartum HELLP syndrome is improved with the use of corticosteroids.
1. True
2. False
Objectives

- Review latest definitions
- New ideas regarding pathophysiology
- Discuss new diagnostic techniques
- Discuss new management styles
  - MAGPIE
  - BP control
  - Steroids for HELLP
  - Outpatient Management of Mild PreE
  - Chronic hypertension
  - Preconception counseling

Incidence

- Preeclampsia: 2-8% of pregnancies
  - 40% increase over last decade
    - Multiple gestations/IVF
    - Obesity epidemic
    - Older gravidas
  - Remains a leading cause of maternal morbidity & mortality in US & worldwide

Review Terminology

- PIH—term not recommended because it means different things to different people
- Gestational Hypertension
- Chronic Hypertension
- Preeclampsia

Gestational Hypertension

Definition:

- De novo appearance of hypertension in pregnancy (after 20wks)
  - Without proteinuria
  - Includes pts who later develop preeclampsia
  - Includes undiagnosed chronic hypertensives*

Chronic Hypertension

Definition:
• Elevated BP that predates the pregnancy
  - Can be assumed with elevated BPs < 20wks
  - Can be diagnosed if BPs don’t normalize 12wks postpartum

Working Group on Research in Hypertension in Pregnancy, 2003

Preeclampsia

Definition:
De novo appearance in pregnancy (after midgestation) of:
• Hypertension
  systolic BP ≥140 mmHg OR diastolic BP ≥90 mmHg
  And
• Proteinuria
  >300 mg/24 hrs or ≥+1
  Urine Protein to Cr Ratio
  Thresholds 0.14 to 0.19 proposed

Working Group on Research in Hypertension in Pregnancy, 2003

Proteinuria: Spot Protein/Creatinine

• Nephrologists have adopted spots
• Easier than 24 hour urine
  • Can be run on spot sample
  • Quick turn-around
  • Spot Pr/Cr 0.19 ~ = 24 hr urine 190 mg
• Spot 0.19 → PPV 75%, NPV 87% for dx of preE (>300mg/24 hrs)
  • Therefore, cutoff 0.14 for threshold for sending confirmatory 24 hr collection
  • Clinical implications

Magali ObGyn 1997, Durnwald AJOG 2003

Pathogenesis

• Five broad hypotheses have been proposed
  - Genetic imprinting
  - Placental ischemia
  - Generalized endothelial dysfunction
  - Immune maladaptation
  - Defective FFA, lipid peroxidase metabolism
• There is no unifying hypothesis
• However, there is a pathologic hallmark ...

Working Group on Research in Hypertension in Pregnancy, 2003
Pathogenesis

- Shallow endovascular invasion of the placenta
  - ischemia → release of soluble factors
  - systemic endothelial dysfunction

NICHD - Funded Project - J Clin Investigation May, 1997

Soluble Factors

- Interaction between vascular endothelial growth factor (VEGF) & soluble fms-like tyrosine kinase (sFlt-1)
  - VEGF & PI GF are angiogenic growth factors
  - Oxidative stress in placenta → release sFlt-1
  - sFlt-1 binds/inactivates VEGF & PI GF → antagonizes vascular growth factors; increases pro-inflammatory cytokines

- Serum & urinary sFlt-1 levels increased in women destined to develop severe preE
- PPV and NPV low: not yet clinically helpful


Discuss Current Management Styles

- Deciding to deliver
- MAGPIE
- BP control
- Steroids for HELLP
- Outpatient management of mild PreE
- Preeclampsia prevention
- Preconception

Deliver at What GA?

- Mild PreE: 37 – 38 weeks
- Severe PreE preivable: immediately
- Severe PreE 23-34 wks:
  - Admit L&D, maternal/fetal evaluation
  - MgSO4, steroids, antihypertensives prn
  - Delivery by 34 weeks
**Eclampsia Prevention**

- MgSO$_4$ therapy
  - Consensus re: prevention of recurrent sz
  - Consensus re: Mg better than diazepam or phenytoin
  - Controversy re: prophylaxis in mild vs. severe preeclampsia

*Br J ObGyn 1996;103:1085*

**MagPie Trial: MAGnesium Sulfate for Prevention of Eclampsia**

- RCT: 10,141 women in 33 countries
- MgSO$_4$:
  - 4g IV load, followed by 1g/hr IV
  - or 10g IM followed by 5g IM q 4hrs
- vs. Placebo (identical packaging)

*Lancet 2002*

**MagPie Patient Population**

- Any GA
- BP $\geq 140$mmHg systolic or $90$mmHg diastolic on at least 2 occasions
- Proteinuria $\geq 1+$
- ~ 26% of pts had severe preE
  - Of these, > 50% had “imminent eclampsia”

*Lancet 2002*

**MAGPIE Outcomes**

- Eclamptic sz—decreased
- Maternal deaths—decreased
- Perinatal deaths—unchanged
- Side effects—increased
- No difference in PPH, length of labor, mode of delivery

*Lancet 2002*
MagPie Take Home

- NNT 91 (all pts); NNT 63 (severe preE); NNT 110 (mild preE)  
  [Ehrenberg ObGyn 2006]
- MgSO₄: 4gm IV load, 1gm IV/hr maintenance routine at UCSF  
  All severe preeclamptics  
  If mild: patient/provider dependent (eg sz d/o)  
- Mg levels not checked unless renal dysfunction  
  [Lancet 2002]

Postpartum Magnesium

- Mild preeclamptics: 12 hrs Mg long enough post-delivery  
- CHTN, IDDM: at risk for progression postpartum  
- Severe disease: 24 hrs  
  [Ehrenberg ObGyn 2006]

BP Control

- Treat SBP > 150 mm Hg—SBP better indication of stroke risk  
- Treat DBP > 100 mm Hg  
- Don’t drop DBP below 80-90 mm Hg  
- No consensus on which drug—Cochrane recommends using most familiar agent  
- No evidence that use of anti-HTN medications alters course of preE, but decreases CNS, cardiovascular complications  
  [Martin ObGyn 2005]

BP Control

- Favor Labetalol in labor  
  - Fewer incidence of fetal distress than hydralazine  
  - More rapid onset of action  
  - Reduces maternal oxygen requirements  
  - Doesn’t promote cardiac arrhythmias  
BP Control

- Labetolol
  - Dose: begin w/ 20 mg IV – repeat 20 mg, 40 mg, 80 mg q10 min until maximal dose 300 mg given
  - Constant infusion of 1-2 mg/min
- Hydralazine
  - Dose: begin w/ 5 mg IV over 1-2 mins, repeat 5-10 mg IV at 20 min, max bolus dose is 20 mg
- Ca-channel blockers
  - Sublingual use dangerous, can precipitate profound hypotension

Controversy: Steroids for HELLP

- Most data retrospective
- Small sample sizes
- Some antepartum, some postpartum
- Some dexamethasone, some betamethasone, some IV, some IM
- No placebo controls

Controversy: Steroids for HELLP

- Corticosteroids shown to improve platelet counts and decrease LFTs
- Urine output improved
- Shorter length of stay

Dose: begin w/ 5 mg IV over 1-2 mins, repeat 5-10 mg IV at 20 min, max bolus dose is 20 mg

Controversy: Steroids for HELLP

- Wait for more evidence for antepartum use, max for 48 hours
- Postpartum use more data, but NNT to improve clinical outcome likely high
- Dose: Dexamethasone 10 mg q 12 hrs followed by 5 mg at 24 and 36 hrs
Preeclampsia: Outpatient Expectant Management

- Can women with mild preeclampsia be managed as outpatients?
- Benefits vs. Risks
  - Eclampsia at home
  - Iatrogenesis at hospital
  - Better bedrest at hospital
  - Patient satisfaction at home
- Societal perspective – inpatient quite expensive

Management
- Careful, thorough counseling re: R/B/A
- Stable in house for minimum 48 hours (BMZ)
- F/U 2x per wk for ANTC / labs
- Delivery at 37 weeks

Preeclampsia Prevention: ASA

<table>
<thead>
<tr>
<th>Study</th>
<th>Aspirin (mg/d)</th>
<th>Control (mg/d)</th>
<th>Relative Risk (95% CI)</th>
<th>Weight (kg)</th>
<th>Relative Risk (95% CI)</th>
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<tbody>
<tr>
<td>Study 1 (0.25G)</td>
<td>1000</td>
<td>125</td>
<td>0.75 (0.56-0.98)</td>
<td>60</td>
<td>0.75 (0.56-0.98)</td>
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<td>Study 2 (0.50G)</td>
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<td>0.65 (0.55-0.75)</td>
<td>70</td>
<td>0.75 (0.56-0.98)</td>
</tr>
</tbody>
</table>

- Studies heterogenous: generally LDA, <20wks
- 17% reduction in risk of preeclampsia
- NNT 19 for high risk women
- NNT 119 for moderate risk women

Cochrane 2008

Prevention: Not efficacious

- Calcium
- Anti-oxidant vitamins (C,E)
- Fish oil
Management of CHTN

- Baseline 24 hour urine for total protein, creat clearance
  - Could skip if pro/cr ratio low
- Baseline LFTs, creatinine, platelets
- Consider ASA if other risk factors
- BP control: aim to decrease vascular complications, doesn’t alter risk of preeclampsia
- Serial ultrasounds for growth
- Antenatal testing at 32 weeks
- No indication for preterm IOL unless superimposed preeclampsia or IUGR

Preconception counseling

- Blood pressure control prior to pregnancy
  - Labetolol good choice
  - Ca-channel blocker if significant asthma
  - Avoid ACE inhibitors
- Evaluate for end organ damage
- Weight loss
- Screen for diabetes
- Early dating ultrasound

Summary

- Latest definitions
- New pathophysiology/diagnostic techniques
- Current management
  - When to deliver?
  - Magnesium
  - BP control
  - Steroids for HELLP
  - Outpatient management of mild preE
  - Prevention