Preeclampsia: What’s old is new again

Gene Chang, MD
Maternal Fetal Medicine
Objectives

- Define Preeclampsia
- Review current guidelines
  - Role of proteinuria
  - Timing of delivery
- Seizure prevention
- Severe Hypertension
Real Disclosure

• Love-Hate Relationship with the new guidelines
  • Preeclampsia as dichotomous disorder
  • Gestational HTN doesn’t get respect
  • Change for sake of change

• Absence of “real world” providers
Honors       A
High Pass    B
Pass         C
Marginal     D
Fail         F
Preeclampsia

- 60 Different names in English/40 in German

- Preeclampsia (Mild vs Severe)
  - Pregnancy induced hypertension

- Preclampsia (Mild vs Severe)
  - Gestational Hypertension

- Preeclampsia (without severe features vs severe)
  - Gestational Hypertension
Pre-eclampsia
Rationale

- Incidence increasing
- 50-60,000 deaths worldwide annually
  - In US for every death, 50-100 “near-misses”
- Less than optimal care in up to 80%
  - Severe maternal complications
- Identification of severe preeclampsia
  - Remains difficult

Kukliina et al. Obstet Gynecol 2009
Van Dillen et al. BJOG 2010
What is preeclampsia?

“In pregnancy, the onset of drowsy headaches with heaviness is bad”

Coacae Praenontiones, XXXI, No 523
Preeclampsia Defined

- Pregnancy Specific Hypertensive disorder
  - Multisystem involvement
  - Variable expression
- New onset HTN + Proteinuria
  - Proteinuria is/was the critical finding
    - Management based on this finding
Pre-eclampsia

- HTN
- +/- Proteinuria
- Everything Else

- HTN
- Proteinuria
- Edema

- HTN
- Proteinuria

Everything Else
Classification

- Mild Preeclampsia
- “Never Mild”
- Increased mortality
- Increased morbidity
- Rapid progression
Classification

- Mild preeclampsia false sense of security
- Preeclampsia without severe features
- Preeclampsia with severe features
# Classification

<table>
<thead>
<tr>
<th>Mild</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Acute Maternal/Fetal Complications</td>
<td>Severe Maternal/Fetal Outcomes</td>
</tr>
<tr>
<td>Term Delivery</td>
<td>Eclampsia</td>
</tr>
<tr>
<td>Baby fine</td>
<td>Maternal Death</td>
</tr>
<tr>
<td>Near term Delivery</td>
<td>Preivable delivery</td>
</tr>
<tr>
<td>Prolonged stay</td>
<td>Perinatal death</td>
</tr>
<tr>
<td>Cesarean Section</td>
<td></td>
</tr>
<tr>
<td>Term SVD</td>
<td></td>
</tr>
<tr>
<td>Mom fine</td>
<td></td>
</tr>
</tbody>
</table>
Hypertension

- New-onset HTN in 2\textsuperscript{nd} trimester
- BP measurement
  - Seated
    - Arm supported at level of right atrium
- Left lateral falsely lowers BP
In view of recent studies that indicate a minimal relationship between the quantity of urinary protein and pregnancy outcome in preeclampsia, massive proteinuria (greater than 5 g) has been eliminated from the consideration of preeclampsia as severe. Also, because
Proteinuria

- International guidelines typically support 300mg
  - Origin of this number is unclear
  - Upper 95% Confidence limit: 260mg/24h\(^1\)
- Threshold of 500mg/24hr or PCR 0.5
  - Possibly better predictor of outcome
  - Relevant for outcome and/or hospitalization

Systematic Review

- Thangaratinam et al BMC 2009
- Systematic Review
- Proteinuria as predictor for maternal/fetal complications
- Proteinuria poor predictor
Systematic Review

• Proteinuria poor predictor of complications

• Maternal outcomes studied
  • HELLP Syndrome
  • Abruption
  • Eclampsia

• Small but significant increase in IUFD, SGA, NICU
PIERS

PIERS Proteinuria: Relationship With Adverse Maternal and Perinatal Outcome

Beth Payne, BSc,1,2 Laura A. Magee, MD, FRCPC, MSc,1,2,3,4 Anne-Marie Côté, MD, FRCPC,5 Jennifer A. Hutcheon, PhD,1,2,3 Jing Li, MCSc,1,2 Phillipa M. Kyle, MBChB, FRANZCOG,6 Jennifer M. Menzies, MSc,1,2 M. Peter Moore, MBChB, FRACP,7 Claire Parker, BSc,8 Barbra Pullar, RN, RM, M Midwifery (Appl),6 Peter von Dadelszen, MBChB, DPhil, FRCSC,1,2,3 Barry N. Walters, MBChB, FRACP, FRANZCOG8,9; for the PIERS Study Group (Appendix)

1Department of Obstetrics and Gynaecology, University of British Columbia, Vancouver BC

Predetermined guidelines for assessment and management
Continuous Quality Improvement Project
Proteinuria doesn’t singly predict adverse outcome
Association of Proteinuria Threshold in Pre-Eclampsia with Maternal and Perinatal Outcomes: A Nested Case Control Cohort of High Risk Women

Kate Bramham¹*, Carlos E. Poli-de-Figueiredo¹,²*, Paul T. Seed¹, Annette L. Briley¹, Lucilla Poston¹, Andrew H. Shennan¹, Lucy C. Chappell”

1 Division of Women’s Health, Women’s Health Academic Centre, King’s College London and King’s Health Partners, London, United Kingdom, 2 School of Medicine, Pontificia Universidade Catolica do Rio Grande do Sul, Rio de Janeiro, Brazil

- 946 women studied at risk for Preeclampsia
- Nested case-control study VIP
- Four groups compared
  P300 (300-499 mg/24hr)
  P500 (>500 mg/24h)
  GHTN
  CHTN
Preeclampsia vs GHTN

- GHTN ≠ Preeclampsia
  - Decision to use MgSO$_4$
  - Timing of delivery
- Gestational HTN may give false sense of security

Outcomes in women with gestational hypertension usually are quite successful, although some of these women experience BP elevations to the severe level with outcomes similar to women with preeclampsia.
Mild gestational hypertension remote from term: Progression and outcome

John R. Barton, MD,a John M. O’Brien, MD,a Niki K. Bergauer, RN,b Debbie L. Jacques, MPH,b and Baha M. Sibai, MDc

Lexington, Kentucky, Marietta, Georgia, and Cincinnati, Ohio

748 pts with GHTN 24-35 w
46% Progressed to Preeclampsia
9.6% Severe Preeclampsia
Proteinuria

- Important but not that important
- Should not be sole trigger for delivery < 34w
  - Reflects what many already do
- ? in patients 34-37w
  - Pt w/controlled BP on Labetalol and 5gm/24hr
  - Pt w/nonsevere HTN and 5gm/24hr
Timing of Delivery
FIGURE 5-1. Management of mild gestational hypertension or preeclampsia without severe features.  

- Maternal and Fetal Findings
  - 37 0/7 weeks or more of gestation
  - 34 0/7 weeks or more of gestation with:
    - Labor or rupture of membranes
    - Abnormal maternal-fetal test results
    - Ultrasonographic estimate of fetal weight less than fifth percentile
    - Suspected abruptio placenta

  [Yes]  
  - Delivery
  - Prostaglandins if needed for induction

  [No]
  - Less than 37 0/7 weeks of gestation
  - Inpatient or outpatient management
  - Maternal evaluation: twice weekly
  - Fetal evaluation
    - With preeclampsia: twice weekly nonstress test
    - With gestational hypertension: weekly nonstress test

  [Yes]
  - 37 0/7 weeks or more of gestation
  - Worsening maternal or fetal condition*
  - Labor or premature rupture of membranes
Induction of labour versus expectant monitoring for gestational hypertension or mild pre-eclampsia after 36 weeks' gestation (HYPITAT): a multicentre, open-label randomised controlled trial

Corine M Koopmans, Denise Bijlenga, Henk Groen, Sylvia M Cwijgen, Jan GAamoudse, Dick JBeekhuizen, Paul Pvan den Berg, Karin de Boer, Jan M Burggraaf, Kitty WM Boemenkamp, Addy PDrogter, Arie Franx, Christopher JM de Groot, Anjole JM Huisjes, Anneke Kwee, Aren J van Loon, Annemiek Lub, Dimitri NM Rapossonis, Joris AM van der Post, Frans JM EReuten, Hubertina CJScheppers, Christine Willekes, Ben WJMol, Maria Gvan Pampus, for the HYPITAT study group
HYPITAT

- 36-41 weeks gestation
- Gestational HTN or Mild Preeclampsia
- Immediate delivery
- Expectant management
  - Inpt or outpt
HYPITAT

- Expectant group delivered for:
  - HELLP
  - >5g proteinuria
  - Eclampsia
  - NRFS
  - PROM, MSAF
  - >41w
Primary outcome: composite morbidity
- Eclampsia
- HELLP
- VTE
- Pulmonary edema
- Abruption
- Progression to severe disease
<table>
<thead>
<tr>
<th>Event</th>
<th>Induction of labour (n=377)</th>
<th>Expectant monitoring (n=379)</th>
<th>Relative risk (95% CI; p value)</th>
<th>Absolute risk reduction (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite adverse maternal outcome</td>
<td>117 (31%)</td>
<td>166 (44%)</td>
<td>0.71 (0.59–0.86; &lt;0.0001)</td>
<td>12.76% (5.87–19.49)</td>
</tr>
<tr>
<td>Maternal death</td>
<td>0</td>
<td>0</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Severe hypertension (mm Hg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic BP</td>
<td>55 (15%)</td>
<td>88 (23%)</td>
<td>0.63 (0.46–0.86; 0.003)</td>
<td>8.63% (3.05–14.16)</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>62 (16%)</td>
<td>103 (27%)</td>
<td>0.61 (0.46–0.80; &lt;0.0001)</td>
<td>10.73% (4.85–16.52)</td>
</tr>
<tr>
<td>Severe proteinuria*</td>
<td>3 (2%)</td>
<td>4 (2%)</td>
<td>0.91 (0.21–4.02; 0.90)</td>
<td>NS</td>
</tr>
<tr>
<td>HELLP syndrome</td>
<td>4 (1%)</td>
<td>11 (3%)</td>
<td>0.37 (0.12–1.14; 0.07)</td>
<td>NS</td>
</tr>
<tr>
<td>Eclampsia</td>
<td>0</td>
<td>0</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Lung oedema</td>
<td>0</td>
<td>2 (1%)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Postpartum haemorrhage</td>
<td>35 (9%)</td>
<td>40 (11%)</td>
<td>0.88 (0.57–1.35; 0.55)</td>
<td>NS</td>
</tr>
<tr>
<td>Thromboembolic disease</td>
<td>1 (&lt;1%)</td>
<td>0</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Placental abruption</td>
<td>0</td>
<td>0</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Severe hypertension measured twice (mm Hg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic BP</td>
<td>26 (7%)</td>
<td>44 (12%)</td>
<td>0.60 (0.38–0.95; 0.03)</td>
<td>4.71% (0.57–8.92)</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>28 (7%)</td>
<td>50 (13%)</td>
<td>0.56 (0.36–0.87; 0.01)</td>
<td>5.77% (1.42–10.16)</td>
</tr>
<tr>
<td>Drugs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral antihypertensive</td>
<td>67 (18%)</td>
<td>111 (29%)</td>
<td>0.61 (0.47–0.80; &lt;0.0001)</td>
<td>11.52% (5.48–17.45)</td>
</tr>
<tr>
<td>Intravenous antihypertensive</td>
<td>13 (3%)</td>
<td>39 (10%)</td>
<td>0.34 (0.18–0.62; &lt;0.0001)</td>
<td>6.84% (3.28–10.59)</td>
</tr>
<tr>
<td>Intravenous anticonvulsive</td>
<td>24 (6%)</td>
<td>46 (12%)</td>
<td>0.53 (0.33–0.84; 0.01)</td>
<td>5.77% (1.64–9.98)</td>
</tr>
<tr>
<td>Maternal hospital care</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intensive care</td>
<td>6 (2%)</td>
<td>14 (4%)</td>
<td>0.41 (0.16–1.07; 0.059)</td>
<td>NS</td>
</tr>
<tr>
<td>Medium care</td>
<td>14 (4%)</td>
<td>15 (4%)</td>
<td>0.90 (0.44–1.84; 0.777)</td>
<td>NS</td>
</tr>
<tr>
<td>Maternal ward</td>
<td>340 (90%)</td>
<td>319 (84%)</td>
<td>1.03 (0.99–1.07; 0.145)</td>
<td>NS</td>
</tr>
<tr>
<td>Unknown</td>
<td>17 (5%)</td>
<td>31 (8%)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Duration of hospital stay (days)</td>
<td>2.0 (1.0–3.0)</td>
<td>2.0 (1.0–4.0)</td>
<td>0.12†</td>
<td>NA</td>
</tr>
</tbody>
</table>

Data are number of patients (%) or median (IQR), unless otherwise indicated. NA = not applicable. BP = blood pressure. NS = not stated because indicator was not significantly associated. HELLP = haemolysis, elevated liver enzymes, and low platelet count. *Data are missing for some participants: n=157 for induction of labour, and n=191 for expectant monitoring. †Relative risk and absolute risk reduction not stated because not clinically relevant.

Table 3: Maternal outcome
<table>
<thead>
<tr>
<th>Clinical features indicating that caesarean section was needed</th>
<th>Induction of labour (n=377)</th>
<th>Expectant monitoring (n=379)</th>
<th>Relative risk (95% CI; p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arrest of first stage of labour</td>
<td>15 (28%)</td>
<td>24 (33%)</td>
<td>NA</td>
</tr>
<tr>
<td>Arrest of second stage of labour</td>
<td>3 (6%)</td>
<td>7 (10%)</td>
<td>NA</td>
</tr>
<tr>
<td>Failed instrumental delivery</td>
<td>4 (7%)</td>
<td>2 (3%)</td>
<td>NA</td>
</tr>
<tr>
<td>Fetal distress</td>
<td>17 (31%)</td>
<td>20 (27%)</td>
<td>NA</td>
</tr>
<tr>
<td>Failure to progress and fetal distress</td>
<td>12 (22%)</td>
<td>8 (11%)</td>
<td>NA</td>
</tr>
<tr>
<td>Maternal complication</td>
<td>2 (4%)</td>
<td>2 (3%)</td>
<td>NA</td>
</tr>
<tr>
<td>Elective</td>
<td>1 (2%)</td>
<td>2 (3%)</td>
<td>NA</td>
</tr>
</tbody>
</table>

Data are number of patients (%), unless otherwise indicated. (95% CI 0.65 to 9.98).

Table 4: Method of delivery

<table>
<thead>
<tr>
<th>Birthweight (g)</th>
<th>Induction of labour (n=377)</th>
<th>Expectant monitoring (n=379)</th>
<th>Relative risk (95% CI; p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3220 (2890–3565)</td>
<td>3490 (3080–3810)</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Composite adverse neonatal outcome</td>
<td>24 (6%)</td>
<td>32 (8%)</td>
<td>0.75 (0.45–1.26; 0.276)†</td>
</tr>
<tr>
<td>Fetal deaths</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Apgar score of &lt;7 after 5 min</td>
<td>7 (2%)</td>
<td>9 (2%)</td>
<td>0.79 (0.30–2.09; 0.632)</td>
</tr>
<tr>
<td>Arterial pH &lt;7.05‡</td>
<td>9 (3%)</td>
<td>19 (6%)</td>
<td>0.46 (0.21–1.00; 0.043)§</td>
</tr>
<tr>
<td>Admission to intensive care</td>
<td>10 (3%)</td>
<td>8 (2%)</td>
<td>1.26 (0.50–3.15; 0.625)</td>
</tr>
</tbody>
</table>

Neonatal hospital care

| Medium care | 68 (18%) | 69 (18%) | 0.99 (0.73–1.34; 0.952) |
| High care   | 12 (3%)  | 10 (3%)  | 1.21 (0.53–2.76; 0.656) |
| Intensive care | 10 (3%) | 8 (2%)   | 1.26 (0.50–3.15; 0.625) |

Duration of stay in a neonatal medium, high, or intensive care unit (days)

<table>
<thead>
<tr>
<th>Induction of labour (n=377)</th>
<th>Expectant monitoring (n=379)</th>
<th>Relative risk (95% CI; p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3·0 (2·0–6·0)</td>
<td>4·0 (2·8–7·0)</td>
<td>0·077*</td>
</tr>
</tbody>
</table>
To Mg or not to Mg?

**Magnesium Sulfate Prophylaxis**

There are only two double-blind, placebo controlled trials that have evaluated the use of magnesium sulfate in women with preeclampsia without severe features (17, 18). No instances of eclampsia occurred among 181 women assigned to placebo, and no differences occurred in the percentage of women who progressed to severe preeclampsia (12.5% in magnesium group versus 13.8% in the placebo group; RR, 0.90; 95% CI, 0.52–1.54). However, the number of
MAGPIE Trial

Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial

The Magpie Trial Collaborative Group*

Multicenter international trial
10,141 randomized
HTN and 1+ protein
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Magnesium sulphate (n=5068)*</th>
<th>Placebo (n=5068)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weekend ha</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epigastric pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blurred vision</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyper-reflexia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Irrespective of BP or proteinuria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (mean, SD) (years)</td>
<td>27.1 (6.7)</td>
<td>27.2 (6.7)</td>
</tr>
<tr>
<td>Primiparous‡</td>
<td>2604 (52%)</td>
<td>2591 (51%)</td>
</tr>
<tr>
<td>Multiple pregnancy</td>
<td>217 (4%)</td>
<td>203 (4%)</td>
</tr>
<tr>
<td>History of epilepsy</td>
<td>56 (1%)</td>
<td>56 (1%)</td>
</tr>
<tr>
<td>Systolic BP at entry</td>
<td>801 (16%)</td>
<td>808 (16%)</td>
</tr>
<tr>
<td>≥170 mm Hg</td>
<td>1119 (22%)</td>
<td>1146 (23%)</td>
</tr>
<tr>
<td>Diastolic BP at entry</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥110 mm Hg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proteinuria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trace/none</td>
<td>2 (0.04%)</td>
<td>5 (0.1%)</td>
</tr>
<tr>
<td>1+</td>
<td>1571 (31%)</td>
<td>1568 (31%)</td>
</tr>
<tr>
<td>2+</td>
<td>1704 (34%)</td>
<td>1721 (34%)</td>
</tr>
<tr>
<td>3+</td>
<td>1310 (26%)</td>
<td>1270 (25%)</td>
</tr>
<tr>
<td>4+</td>
<td>481 (9%)</td>
<td>504 (10%)</td>
</tr>
<tr>
<td>Severe pre-eclampsia</td>
<td>1303 (26%)</td>
<td>1349 (27%)</td>
</tr>
<tr>
<td>Imminent eclampsia§</td>
<td>816 (16%)</td>
<td>833 (16%)</td>
</tr>
<tr>
<td>Oliguria</td>
<td>131 (3%)</td>
<td>129 (3%)</td>
</tr>
<tr>
<td>Previous treatment with anticonvulsant</td>
<td>440 (9%)</td>
<td>435 (9%)</td>
</tr>
<tr>
<td>Magnesium sulphate</td>
<td>242 (5%)</td>
<td>241 (5%)</td>
</tr>
<tr>
<td>Other anticonvulsant</td>
<td>196 (4%)</td>
<td>192 (4%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>2 (0.04%)</td>
<td>2 (0.04%)</td>
</tr>
<tr>
<td>Previous treatment with antihypertensive</td>
<td>2508 (49%)</td>
<td>2502 (49%)</td>
</tr>
<tr>
<td>If treated with antihypertensive, highest BP before entry</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic BP ≥170 mm Hg</td>
<td>1149 (23%)</td>
<td>1172 (23%)</td>
</tr>
<tr>
<td>Diastolic BP ≥110 mm Hg</td>
<td>1540 (30%)</td>
<td>1554 (31%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>8 (0.2%)</td>
<td>4 (0.1%)</td>
</tr>
<tr>
<td>Postpartum at randomisation</td>
<td>640 (13%)</td>
<td>697 (14%)</td>
</tr>
<tr>
<td></td>
<td>Magnesium sulphate (n=5055)</td>
<td>Placebo (n=5055)</td>
</tr>
<tr>
<td>----------------------</td>
<td>-----------------------------</td>
<td>------------------</td>
</tr>
<tr>
<td><strong>Eclampsia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>4 (0.08%)</td>
<td>3 (0.06%)</td>
</tr>
<tr>
<td>Number of fits</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>27</td>
<td>63</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>24</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>≥4</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Unknown</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td><strong>Maternal death</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>2 (0.04%)</td>
<td>2 (0.04%)</td>
</tr>
<tr>
<td>Main cause of death</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac arrest or failure</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Stroke</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Eclampsia or pre-eclampsia</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Anaemia or postpartum haemorrhage</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Anaesthetic death</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Respiratory failure or pneumonia</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Renal failure</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Infection</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

Risk difference (95% CI) is *−1.1 (−1.6 to −0.7), †−0.2 (−0.4 to 0.04).

**Table 6: Eclampsia and maternal death**
<table>
<thead>
<tr>
<th>Condition</th>
<th>Relative risk (95% CI)</th>
<th>Number of events</th>
<th>Magnesium sulphate</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe pre-eclampsia</td>
<td>0.42 (0.23–0.76)</td>
<td>15/1297</td>
<td>37/1345</td>
<td></td>
</tr>
<tr>
<td>Not severe pre-eclampsia</td>
<td>0.42 (0.26–0.67)</td>
<td>25/3758</td>
<td>59/3710</td>
<td></td>
</tr>
<tr>
<td>Randomised before delivery</td>
<td>0.40 (0.27–0.59)</td>
<td>36/4416</td>
<td>88/4359</td>
<td></td>
</tr>
<tr>
<td>&lt;34 weeks</td>
<td>0.54 (0.28–1.06)</td>
<td>13/1206</td>
<td>24/1206</td>
<td></td>
</tr>
<tr>
<td>≥34 weeks</td>
<td>0.35 (0.22–0.57)</td>
<td>23/3210</td>
<td>64/3153</td>
<td></td>
</tr>
<tr>
<td>Randomised after delivery</td>
<td>0.54 (0.16–1.80)</td>
<td>4/639</td>
<td>8/696</td>
<td></td>
</tr>
<tr>
<td>Anticonvulsant before trial*</td>
<td>1.24 (0.49–3.11)</td>
<td>10/439</td>
<td>8/435</td>
<td></td>
</tr>
<tr>
<td>No anticonvulsant before trial*</td>
<td>0.34 (0.23–0.51)</td>
<td>30/4590</td>
<td>88/4583</td>
<td></td>
</tr>
<tr>
<td>Imminent eclampsia</td>
<td>0.26 (0.12–0.57)</td>
<td>8/810</td>
<td>31/829</td>
<td></td>
</tr>
<tr>
<td>No imminent eclampsia</td>
<td>0.49 (0.32–0.75)</td>
<td>32/4245</td>
<td>65/4226</td>
<td></td>
</tr>
<tr>
<td>High PMR country</td>
<td>0.34 (0.21–0.56)</td>
<td>22/2814</td>
<td>64/2812</td>
<td></td>
</tr>
<tr>
<td>Middle PMR country</td>
<td>0.54 (0.28–1.03)</td>
<td>14/1463</td>
<td>26/1461</td>
<td></td>
</tr>
<tr>
<td>Low PMR country</td>
<td>0.67 (0.19–2.37)</td>
<td>4/778</td>
<td>6/782</td>
<td></td>
</tr>
<tr>
<td>All women</td>
<td>0.42 (0.29–0.60)</td>
<td>40/5055</td>
<td>96/5055</td>
<td></td>
</tr>
</tbody>
</table>

Figure 2: Effects of treatment on eclampsia
PMR=Perinatal mortality rate. *Not known whether previous anticonvulsant was given to 26 women allocated magnesium sulphate and to 37 allocated placebo.
MAGPIE

- NNT for Severe Preeclampsia: 63
- NNT for Non-severe preeclampsia: 91
Management of Severe Hypertension
Severe Hypertension

Hydralazine: drug of choice >45 years

- Onset slow (10-20 minutes)
- Dose: 5-10 mg q20 mins (max 30 mg)
- Mom: Tachycardia, Hypotension, HA
- Neonate: thrombocytopenia, low platelets
Hydralazine: Metanalysis

- Metanalysis of RCT’s 1966-2002
- Short acting antihypertensives
- 21 trials (893 women)
  - 8 with Hydralazine v. Nifedipine
  - 5 with Hydralazine v. Labetalol
Hydralazine: Metanalysis

Hydralazine:

- Hypotension (13 trials): 3.29 [1.50-7.23]
- C/S (14 trials): 1.30 [1.08-1.59]
- Abruption (5 trials): 4.17 [1.19-14.28]
- Oliguria (3 trials): 2.04 [1.32-3.16]
- Adverse effect on FHR (12 trials): 2.04 [1.32-3.16]

BMJ 2003
Severe Hypertension

- Labetalol
  - Continuous infusion (1 mg/kg)
  - More commonly IV Bolus
  - Initial bolus not > 20 mg
  - Dose (40, 80, 80, 80) every 15 minutes
  - Max dose 300 mg
  - Onset: 5 min, Peak: 10-20 min, Duration 6 hrs.
Severe Hypertension

Nifedipine

- Oral Ca channel blocker
- Used for HTN and for tocolysis
- 10 mg PO q15-30 minutes (max 30 mg)

Long Acting Nifedipine?

- Absorption 70-90 minutes
- Onset of action 45-90 minutes
- Consensus: lower BP w/in 30-60 minutes
Labetalol vs. Nifedipine

Labetalol

- **Advantages**
  - Significant hypotension uncommon
  - No decrease in CO vs. B-blockers

- **Disadvantages**
  - Many pts already taking labetalol
  - 1% risk of arrhythmia
    - 10 mg/min don’t need telemetry

Frontiers in Bioscience 2007
Labetalol vs. Nifedipine

Nifedipine

- **Advantages**
  - Increases cardiac index\(^1\)
  - Minimal impact on uteroplacental blood flow
  - Higher BP = Higher decrease\(^2\)
  - Selective renal arteriolar dilator\(^3\)

- **Disadvantages**
  - Concern over short-acting Nifedipine
  - Risk of Interaction with MgSO4

Labetalol vs. Nifedipine

Therapy with both magnesium sulfate and nifedipine does not increase the risk of serious magnesium-related maternal side effects in women with preeclampsia

Laura A. Magee, MD, a,b,c,* Saman Miremadi, MD, d Jing Li, MSS, a Carol Cheng, BSc, d Mary H. H. Ensom, PharmD, e Bruce Carleton, PharmD, a,e Anne-Marie Côté, MD, b Peter von Dadelszen, MBChB, DPhil a,d

Centre for Healthcare Innovation and Improvement, British Columbia Research Institute for Children’s and Women’s Health, a Department of Specialized Women’s Health, BC Women’s Hospital and Health Centre, b and

Mg Toxicity requiring Calcium Gluconate 0.5% (n = 162)
Labetalol vs. Nifedipine

- Randomized Double Blind trial (50 pts)
- Nifedipine vs. Labetalol

### Table II. Cumulative urine outputs

<table>
<thead>
<tr>
<th>Duration (h)</th>
<th>Nifedipine (mL)</th>
<th>Labetalol (mL)</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>99 ± 99</td>
<td>44 ± 19</td>
<td>P &lt; .001</td>
</tr>
<tr>
<td>2</td>
<td>226 ± 154</td>
<td>100 ± 53</td>
<td>P &lt; .001</td>
</tr>
<tr>
<td>6</td>
<td>707 ± 336</td>
<td>404 ± 162</td>
<td>P &lt; .001</td>
</tr>
<tr>
<td>12</td>
<td>1335 ± 569</td>
<td>794 ± 227</td>
<td>P &lt; .001</td>
</tr>
<tr>
<td>18</td>
<td>2024 ± 831</td>
<td>1135 ± 382</td>
<td>P &lt; .001</td>
</tr>
<tr>
<td>24</td>
<td>2709 ± 1184</td>
<td>1534 ± 509</td>
<td>P &lt; .001</td>
</tr>
</tbody>
</table>

Data shown are mean ± SD.
Severe Hypertension

- 1\textsuperscript{st} line agents
  - Labetalol
  - Nifedipine
    - Avoid when: Known CV disease
    - Age > 45 or IDDM > 15 years
  - Hydralazine still a consideration
Severe Hypertension

Use what you are comfortable with

Use what is available
PP Management
stop these medications (61, 67, 68). Health care providers should be reminded of the contribution of non-steroidal antiinflammatory agents to increased BP. It is suggested that these commonly used postpartum pain relief agents be replaced by other analgesics in women with hypertension that persists for more than 1 day postpartum. Experts recommend antihyperten-
NSAID’s and HTN

- Pope et al
  - Meta-analysis of 54 trials with 123 trial arms
  - 1324 pts mean age 46 (29-62)
  - Mean duration of therapy 15d (1-42)
  - Mean increase in MAP 3.74 mmHg
NSAID’s and HTN

- Johnson et al
- 50 RCT’s
- 771 subjects
- Mean age 47.6
- Duration of treatment at least 1w
- Map increased 5mmHg

NSAID’s and HTN

- Sheridan et al 2005
- Controlled observational study
- HTN on NSAID’s vs. unexposed
- 184 users vs. 762 nonusers
- No significant difference in SBP or DBP
ORIGINAL ARTICLE

Ibuprofen versus acetaminophen as a post-partum analgesic for women with severe pre-eclampsia: randomized clinical study

Paulino Vigil-De Gracia, Valentín Solís, and Nelson Ortega

Departamento de Ginecología y Obstetricia, Complejo hospitalario de la caja de seguro social, Unidad de CEGO, Panamá, Panamá
Original Research

Association of Nonsteroidal Antiinflammatory Drugs and Postpartum Hypertension in Women With Preeclampsia With Severe Features

Oscar A. Viteri, MD, Joey A. England, MD, Mesk A. Alrais, MD, Kayla A. Lash, MD, Maria I. Villegas, MD, Olaide A. Ashimi Balogun, MD, Suneet P. Chauhan, MD, and Baha M. Sibai, MD
For women in whom gestational hypertension, pre-eclampsia, or superimposed preeclampsia is diagnosed, it is suggested that BP be monitored in the hospital or that equivalent outpatient surveillance be performed for at least 72 hours postpartum and again 7–10 days after delivery or earlier in women with symptoms.

Quality of evidence: Moderate
Strength of recommendation: Qualified
PP: Followup

- 0.3% PP visits to ER related to HTN disorders
- Symptoms precede stroke and preeclampsia
  - Hours to days
- No knowledge regarding benefit of Rx
Conclusions

- Pre-eclampsia
  - Multisystem disorder
  - Variable presentation
- Trust your clinical assessment of patients
Conclusions

• Proteinuria- important but not important
• Seizure prevention- clinical decision
• Timing of delivery- HYPITAT
• Hypertension- Severe and PP