Update on Hypertension in Pregnancy

Marijo Aguilera
Minnesota Perinatal Physicians
May 6, 2016

CME Presentation Objectives

+ Review the definitions of hypertensive disorders of pregnancy
+ Understand the management of hypertension in pregnancy

Disclosures

I have nothing to disclose

Hypertensive disorders of pregnancy

+ Complicate up to 10% of pregnancies
+ One of the greatest causes of maternal and perinatal morbidity and mortality
+ ~50,000-60,000 preeclampsia deaths/year worldwide
+ In the U.S., ~50-100 “near miss” morbidity events for every death
+ Incidence has increased ~25% in the U.S. in the past couple of decades
  + Obesity, advancing age, underlying comorbidities
+ Major contributor to prematurity
+ Risk factor for future cardiovascular disease

Hypertension in pregnancy

+ Preeclampsia-eclampsia
+ Chronic hypertension (of any cause)
+ Chronic hypertension with superimposed preeclampsia
+ Gestational hypertension

BP measurement in pregnancy

+ Patient sitting
  + Legs uncrossed
  + Back and arm supported
+ Middle of cuff of upper arm at level of right atrium
+ Patient should be relaxed and no talking
+ Allow 5 minutes to elapse
+ Left lateral position will falsely lower BP

© AllinaHealthSystems
Preeclampsia

+5-8% of all pregnancies
+Pregnancy specific disorder with multisystem involvement, usually occurs after 20 weeks gestation
+Syndrome of hypertension ± proteinuria ± severe features
+Proteinuria NOT required -- WithOUT proteinuria, diagnosis = HTN + one of severe features

ACOG Task Force Bulletin 2013
National High Blood Pressure Education Program Working Group ACOG 2000

Preeclampsia definition changes

+No longer "mild"
+Morbidity and mortality increased despite absence of "severe" disease
+Proteinuria >5g NO LONGER criteria for severe disease/feature
+UGR (EFW<10th %ile) NO LONGER criteria (but if <5%ile, see delivery criteria)

ACOG Task Force Bulletin 2013
National High Blood Pressure Education Program Working Group ACOG 2000

Preeclampsia without severe features

+SBP≥140 or DBP≥90 on 2 occasions 4 hours apart >20 wks
+Previously normotensive patient <20 weeks
+Proteinuria ≥300mg on 24 hour collection OR urine protein:creatinine ratio (UPC) ≥0.3 mg/dL
+Dipstick 1+ only if other quantitative methods not available

ACOG Task Force Bulletin 2013
National High Blood Pressure Education Program Working Group ACOG 2000

Preeclampsia with severe features

+SBP ≥160 or DBP ≥110 on 2 occasions 4 hours apart
+Proteinuria ≥300mg on 24 hour collection OR UPC ≥0.3 mg/dL
+Plt <100K
+LFTs=twice normal or severe RUQ/epigastric pain
+Cr>1.1 (or doubled)
+Pulmonary edema
+New-onset cerebral or visual sx's

ACOG Task Force Bulletin 2013
National High Blood Pressure Education Program Working Group ACOG 2000

Eclampsia

+Convulsive phase
+New onset grand mal seizures
+Often preceded by premonitory events
+Severe headache, hyperreflexia
+Can occur in the absence of warning signs or symptoms
+Can occur before, during, or after labor

ACOG Task Force Bulletin 2013
National High Blood Pressure Education Program Working Group ACOG 2000

HELLP syndrome – preeclamptic subtype

+Laboratory abnormalities to include hemolysis, elevated liver enzymes and low platelets
+Hemolysis on peripheral smear, LDH >600 U/L or total bilirubin >1.2 mg/dL
+AST> twice normal
+Platelet count <100,000 cell/mm³
Preconception recommendations

- Counseling on risks and education – consultation with MFM
  - Superimposed preeclampsia 13-40%
  - Fetal growth restriction
  - Accelerated HTN with resultant end organ damage
    - Renal compromise
    - Placental abruption
    - Fetal demise
    - Iatrogenic preterm delivery
    - Gestational diabetes
  - Evaluation of any underlying end organ damage
  - Preexisting renal disease significantly increases risk!
  - Screen for left ventricular function if longstanding HTN (ie. more than 4 years)
  - Review of medication use
    - ACE inhibitors, ARBs, mineralocorticoid antagonists contraindicated

Early pregnancy management

- Review risks
- Baseline HELLP laboratory assessment
- Home BP monitoring suggested if poorly controlled BP
- Discuss pregnancy management
  - Increased visits
  - Educate on signs superimposed preeclampsia
  - Growth ultrasounds
  - Antenatal testing
  - Delivery timing
- Review of medication use
  - ACE inhibitors, ARBs, mineralocorticoid antagonists contraindicated
- Discuss if treatment necessary
  - "White coat HTN"
Aggressive treatment can lower maternal cardiac output or decrease systemic vascular resistance. Decreased uterine perfusion can lead to fetal compromise.

In response to the CHIPS trial (Control of hypertension in pregnancy study), CHIPS assessed “less tight control” to “tight control.” Given the available data, SMFM recommends that clinicians follow existing guidelines:

- Mild to moderate hypertension in pregnancy (without end organ damage) should NOT be treated with pharmacologic antihypertensive therapy.
- Long term risks and benefits unknown.
- Increased SGA infants with treatment.
- No reduction in adverse pregnancy outcome.

The SMFM Statement on the benefit of antihypertensive therapy for mild-to-moderate chronic hypertension during pregnancy remains uncertain (AJOG, 2015).

For pregnant women with persistent chronic hypertension with systolic BP of 160 mm Hg or higher or diastolic BP of 105 mm Hg or higher, antihypertensive therapy is recommended. Treatment of mild hypertension has not been shown to decrease the incidence of preeclampsia or improve pregnancy outcomes. No direct fetal benefit. Conflicting evidence of SGA infant and minimal increased risk of cardiac abnormalities. Lower BP goals if evidence of end organ damage.

For pregnant women with persistent chronic hypertension with systolic BP of 160 mm Hg or higher or diastolic BP of 105 mm Hg or higher, antihypertensive therapy is recommended. Antihypertensive therapy prior to pregnancy?

- Review of women who decreased the dosage or stopped medication in the 1st trimester reported no increase in preeclampsia, abruption, or perinatal death.
- Discontinuing medications during the 1st trimester and restarting them if BP approaches severe range is reasonable.
- Individualized.
- End organ damage: BP goals <140 SBP and <90 DBP.

Antihypertensives for women with CHRONIC hypertension:

- For pregnant women with persistent chronic hypertension with systolic BP of 160 mm Hg or higher or diastolic BP of 105 mm Hg or higher, antihypertensive therapy is recommended.
- Treatment of mild hypertension has not been shown to decrease the incidence of preeclampsia or improve pregnancy outcomes.
- No direct fetal benefit.
- Conflicting evidence of SGA infant and minimal increased risk of cardiac abnormalities.
- Lower BP goals if evidence of end organ damage.

Antihypertensives:

- Goal = prevention of intracranial bleeding and stroke.
- Goal not to reach normotensive range.
- Compromises uterine perfusion.
- Recommended agents:
  - Nifedipine ER/XL 30-120 mg/day.
  - Labetalol 200-2400 mg/day divided.
  - Methyldopa 500-3000 mg/day divided.
  - Diuretics as 2nd line.

Nonpharmacologic treatment:

- Exercise.
- Assess patient for any contraindications.
- If poorly controlled HTN, exercise not generally recommended.
- Maintaining ideal weight.
- Weight loss not recommended.
- Dietary changes.
- Low sodium diets have not been extensively studied for management of HTN in pregnancy.
Prevention of superimposed preeclampsia

- Alterations in prostacyclin-thromboxane contributory?
  - Thromboxane promotes vasoconstriction
- Increased inflammation

Prevention of superimposed preeclampsia

- Alterations in prostacyclin-thromboxane contributory?
  - Thromboxane promotes vasoconstriction
  - Increased inflammation
- ASA low dose (81mg or less)
  - Blocks thromboxanes
  - Anti-inflammatory

Prevention of preeclampsia – ASA 81mg or less

- Small trials suggested protective effect
- 3 large RCTs did not find significant difference
  - Nonsignificant trend
  - No major adverse effects
- Meta-analysis found RR 0.90 (0.84-0.97)
- Cochrane meta-analysis: 17% reduction in women at high risk for disease

Prevention of preeclampsia – ASA 81mg or less

<table>
<thead>
<tr>
<th></th>
<th>Baseline event rate</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preeclampsia</td>
<td>2%</td>
<td>500</td>
</tr>
<tr>
<td>Preterm &lt;34 weeks</td>
<td>2%</td>
<td>500</td>
</tr>
<tr>
<td>Perinatal death</td>
<td>1%</td>
<td>1111</td>
</tr>
<tr>
<td>SGA infant</td>
<td>1%</td>
<td>1000</td>
</tr>
<tr>
<td>Serious adverse outcome</td>
<td>7%</td>
<td>143</td>
</tr>
</tbody>
</table>

Prevention of preeclampsia

- For women with medical history of early onset preeclampsia and preterm delivery <34w0d, OR preeclampsia in >1 prior pregnancy → ASA 60-80mg suggested beginning late 1st trimester
- Other dietary supplements and restriction (including salt) not recommended
- Activity restriction/bedrest not recommended

Baseline event rate NNT

<table>
<thead>
<tr>
<th></th>
<th>Baseline event rate</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preeclampsia</td>
<td>18%</td>
<td>56</td>
</tr>
<tr>
<td>Preterm &lt;34 weeks</td>
<td>20%</td>
<td>50</td>
</tr>
<tr>
<td>Perinatal death</td>
<td>7%</td>
<td>159</td>
</tr>
<tr>
<td>SGA infant</td>
<td>15%</td>
<td>67</td>
</tr>
<tr>
<td>Serious adverse outcome</td>
<td>25%</td>
<td>40</td>
</tr>
</tbody>
</table>
**Broader aspirin use favored by the U.S. Preventive Services Task Force**

- Women with:
  - History of preeclampsia
  - Multiple gestation
  - Chronic HTN
  - DM
  - Renal disease
  - Autoimmune disease
  - 2 or more moderate risk factors (AMA, FH preeclampsia, personal history of pregnancy complications)
  - Preeclampsia rate in the above population 4.18%
  - ACOG recommendations: 4.17%
  - USPSTF recommendations: 3.83%

**Continued pregnancy management**

- Laboratory assessment if increase in BP or symptoms
- Inpatient monitoring if concern for accelerated HTN or superimposed preeclampsia
- Home BP monitoring if poorly controlled BP or increase in BP
- Increased visits - individualized based on severity, treatment, end organ damage, history
- Educate on s/sxs superimposed preeclampsia
- Growth ultrasounds every 4-6 weeks (at least at ~28 and 34 weeks depending on control)
- Antenatal testing starting weekly at 32 weeks if uncomplicated and well controlled
- Antenatal testing twice weekly if superimposed preeclampsia or growth concerns

**Timing of delivery for chronic hypertension**

- If no additional maternal or fetal complications:
  - If controlled without medication, delivery 39 0/7-39 6/7
  - If controlled with medication, delivery 38 0/7-39 6/7
  - If not well controlled, delivery 34+ weeks
  - If superimposed preeclampsia
    - Without severe features: 37 0/7
    - With severe features: 34 0/7 or similar indications <34 0/7 weeks

**Chronic HTN with superimposed preeclampsia**

- Develops in 13-40%
- New onset or sudden, substantial, and sustained increase in proteinuria
- Sudden increase in blood pressure
- Other severe features
- Risk increased over preeclampsia without preexisting HTN
  - Decidual vessels with preexisting HTN demonstrate vascular changes. Decrease in uteroplacental perfusion may be additive (decidual vascular changes of preeclampsia)

**Initial evaluation for superimposed preeclampsia**

- CBC, Cr, LFTs, uric acid, UPC or 24 hour urine (+/- LD, coags)
- Assess maternal symptoms
- Close BP monitoring, I/Os
- Growth ultrasound, NST/BPP
- Inpatient management if severe features
  - Magnesium during initial evaluation
**Expectant management of superimposed preeclampsia with severe features**

- Inpatient management
- Magnesium and BMZ initially
- Vital signs, I/Os, maternal symptoms every 8 hours
- CBC, LFTs, Cr daily
- Every other day if labs remain stable and patient asymptomatic
- Daily NST
- Twice weekly BPP
- Serial growth every 2-3 weeks and Dopplers if concern for fetal growth restriction

ACOG Task Force Bulletin 2013

**Emergent Therapy for Acute-Onset, Severe Hypertension During Pregnancy and the Postpartum Period**

ABSTRACT: Acute-onset, severe systolic hypertension; severe diastolic hypertension; or both can occur in pregnant women or women in the postpartum period. Introducing standardized, evidence-based clinical guidelines for the management of patients with preeclampsia and eclampsia has been demonstrated to reduce the incidence of adverse maternal outcomes. Individuals and institutions should have mechanisms in place to initiate the prompt administration of medication when a patient presents with a hypertensive emergency. Once the hypertensive emergency is treated, a complete and detailed evaluation of maternal and fetal well-being is needed with consideration of, among many issues, the need for subsequent pharmacotherapy and the appropriate timing of delivery.

**Systolic BP >160 mm Hg or diastolic BP >110 mm Hg persisting for ≥15 minutes is a hypertensive emergency**

2/3 of maternal deaths in the UK from 2003-2005 resulted from cerebral hemorrhage of infarction

Systolic hypertension may be the most important predictor of cerebral injury and infarction

+ Case series 28 women who experienced stroke
  + 12 antepartum, 10 postpartum
  + 24 women treated by a provider prior to the stroke
  + 23/24 had severe systolic HTN preceding the stroke
  + 3/24 had severe diastolic HTN preceding the stroke

**Acute-onset severe hypertension**

- Systolic BP >160 mm Hg or diastolic BP >110 mm Hg persisting for ≥15 minutes is a hypertensive emergency
- 2/3 of maternal deaths in the UK from 2003-2005 resulted from cerebral hemorrhage of infarction
- Systolic hypertension may be the most important predictor of cerebral injury and infarction
- Case series 28 women who experienced stroke
  - 12 antepartum, 10 postpartum
  - 24 women treated by a provider prior to the stroke
  - 23/24 had severe systolic HTN preceding the stroke
  - 3/24 had severe diastolic HTN preceding the stroke

ACOG Committee Opinion 2015

**Labetalol 20 mg IV over 2 minutes**

- Repeat BP in 10 min
- If still >160/110, give Labetalol 40mg IV
- Repeat BP in 10 min
- If still >160/110, give Labetalol 80mg IV
- Repeat BP in 10 min
- If still >160/110, give Hydralazine 10 mg IV
- Repeat BP in 20 min
- If still >160/110, get help

- Max labetalol 300mg

ACOG Committee Opinion 2015
Acute treatment of severe hypertension – 1st line Hydralazine

- Hydralazine 5-10 mg IV over 2 minutes
- Repeat BP in 20 min
- If still >160/110, give Hydralazine 10mg IV
- Repeat BP in 20 min
- If still >160/110, give Labetalol 20mg IV
- Repeat BP in 10 min
- If still >160/110, give Labetalol 40mg IV and get help
  - Max hydralazine 30mg

Acute treatment of severe hypertension – 1st line Nifedipine

- Nifedipine 10mg PO
- Repeat BP in 20 min
- If still >160/110, give nifedipine 20mg PO
- Repeat BP in 20 min
- If still >160/110, give nifedipine 20mg PO
- Repeat BP in 20 min
- If still >160/110, give Labetalol 40mg IV and get help

Acute treatment of severe hypertension – side effects

- Hydralazine IV
  - Increased risk of maternal hypotension
- Labetalol IV
  - Neonatal bradycardia
  - Avoid with asthma, heart disease, or CHF
- Nifedipine
  - Increase in maternal heart rate
  - Overshoot hypotension
- No significant changes in umbilical blood flow
- Maternal and perinatal outcomes similar

Acute treatment of severe hypertension – No IV

- Labetalol 200mg PO, repeat in 30 min
  - Once stable – monitor BP
  - Q10 min x 1 hr
  - Q15 min x 1 hr
  - Q30 min x 1 hr
  - Qhr x 4 hrs
**Acute treatment of severe hypertension – 2nd line therapy**
- Labetalol or nicardipine infusion
- Sodium nitroprusside only if extreme emergency
- Cyanide toxicity
- Increased intracranial pressure

**Indications for Delivery - Maternal**
- Recurrent severe hypertension
- Recurrent maternal symptoms
- Persistent Pt <100K
- LFTs > twice normal or severe RUQ/epigastric pain
- Cr > 1.1 (or doubled)
- Pulmonary edema
- Eclampsia
- Suspected abruptio placenta
- Progressive labor or SROM

**Indications for Delivery - Fetal**
- Gestational age 34 0/7 weeks
- Severe FGR (EFW <5%tile)
- Persistent oligohydramnios (MVP <2cm)
- BPP of 4/10 or less on 2 occasions 6 hours apart
- REDF on umbilical artery Doppler studies
- Recurrent decelerations
- Fetal demise

**Delay delivery for corticosteroids (48 hours) ≤ 33 6/7 weeks**
- PPROM or labor
- Pt < 100,000
- Persistently elevated LFTs (>2x normal)
- FGR (<5%tile)
- Severe oligohydramnios (AFI <5cm)
- REDF on Doppler studies
- New onset or increasing renal dysfunction

**Do NOT delay delivery for corticosteroids**
- Uncontrollable severe hypertension
- Eclampsia
- Pulmonary edema
- Abruptio placenta
- DIC
- Evidence of nonreassuring fetal status
- Demise
Mode of delivery

- Determined by fetal gestational age, fetal presentation, cervical status, and maternal-fetal condition

ACOG Task Force Bulletin 2013

Postpartum hypertension and preeclampsia

- NSAIDS may contribute to increased BP
  - Replace with other analgesics if hypertension persists more than 1 day postpartum
  - Avoid in women with chronic HTN
  - Antihypertensives if SBP≥150 or DBP≥100 on at least 2 occasions 4-6 hours apart
  - Persistent SBP≥160 or DBP≥100 treat within 1 hour

ACOG Task Force Bulletin 2013

Postpartum hypertension and preeclampsia

- For women in whom gestational hypertension, preeclampsia, or superimposed preeclampsia is diagnosed, it is suggested that BP be monitored in the hospital or that equivalent outpatient surveillance for at least 72 hours postpartum and again 7-10 days after delivery or earlier if symptoms persist.

ACOG Task Force Bulletin 2013

Minnesota Perinatal Physicians

- Contact Information: 612-863-4502
- Midwest Fetal Care Center: 855-693-3825
- MEFetalCare@allina.com
- Children’s Physician Access: 612-343-2121

Minnesota Perinatal Physicians

- Marijo Aguilera, MD
- Suresh Ahanya, MD
- Elizabeth Balsen, MD
- Marina Bissett-Barnes, MD
- Nancy Fairstein, MD
- David Feaster, MD
- Patricia Mills, MD
- Lisa Sosa, MD
- Heidi Thorsen, MD
- William Wagner, MD
- Donald Wothe, MD
- Meiling Parker, MD
- Matthew Loichinger, MD

Thank you!