**HYPERTENSION IN PREGNANCY**

**TIME TO GET "HIP"**

October 27, 2016
Obstetrics & Gynecology Update:
What Does The Evidence Tell Us?

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**DISCLOSURES**

• None

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**LEARNING OBJECTIVES**

• Define hypertensive disorders of pregnancy
• Identify associated morbidity and mortality
• Review current guidelines for management
• Discuss specific patient cases

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**HYPERTENSIVE DISORDERS OF PREGNANCY**

• Preeclampsia
• Gestational HTN
• Chronic (preexisting) HTN
• Superimposed preeclampsia
PREECLAMPSIA
- BP ≥ 140/90 x 2
  - > 4 hours apart
- If BP ≥ 160/110
  - Minutes apart
- GA > 20 wks
- No preexisting cHTN
  and any 1 of these →
  - Proteinuria
    - ≥ 300 mg in 24 hours
    - Protein:creatinine ≥ 0.3
    - Dipstick 1+
  - PLT < 100,000
  - CR > 1.1 or doubling
  - AST or ALT > 2X normal
  - Pulmonary edema
  - HA or visual symptoms

GESTATIONAL HTN
- HTN > 20 weeks GA
  but
- No proteinuria
- No other features of preeclampsia

CHRONIC HTN
- BP ≥ 140/90 at one of the following times
  - pre-pregnancy
  - GA < 20 weeks
  - > 12 weeks postpartum

SUPERIMPOSED PREECLAMPSIA
- History of cHTN
  and
- Worsening HTN in pregnancy > 20 weeks GA
  with
- New onset proteinuria
  or
- Other features of preeclampsia
HIP: MORBIDITY

- IUGR
- Placental abruption
- Preterm birth
- Maternal seizure (eclampsia)
- CVA

CDC: CAUSES OF MATERNAL MORTALITY

PREGNANCY RELATED MORTALITY

- Death during pregnancy/100,000 live births
  - Or within 1 year of delivery if related to pregnancy
  - Not accidents or incidental causes
- Rising maternal mortality
  - Doubled from 1987 to 2012
    - 1987 7.2/100,000
    - 2012 15.9/100,000
- 2006 CDC vital statistics
  - Black population maternal mortality 3.4Xs > white

CDC: MATERNAL MORTALITY TRENDS
GLOBAL MATERNAL MORTALITY DATA

- 1990 → 2015
  - Global maternal mortality ↓44%
  - But still ~830 pregnancy related deaths/day in 2015
- 2015 Maternal mortality data
  - Developed countries 12/100,000 live births
  - Developing countries 239/100,000 live births
  - Causes: PPH, infection, preeclampsia, unsafe abortions, delivery complications
- 2030 Sustainable Development Agenda Goal
  - Global maternal mortality <70/100,000 live births

COUNTRY SPECIFIC MATERNAL MORTALITY DATA 2015

<table>
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<th>Country</th>
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HIP GUIDELINES

- Obstetrics & Gynecology
  - November 2013; 122(5):1122-1131
- ACOG task force on HTN in pregnancy
  - “HTN in pregnancy” 99 page document
  - ACOG HIP Executive Summary 10 pages
- Maurice Druzin, MD, Stanford
- Catherine Spong, MD, NICHD
- Baha Sibai, MD, UT Houston

HIGHLIGHTS OF THE HIP GUIDELINES

- Magnesium sulfate seizure prophylaxis
  - NOT for preeclampsia without severe features
  - Do not turn off magnesium during cesarean
- Proteinuria >5grams/24hrs
  - Not diagnostic of severe
- IUGR
  - Not diagnostic of severe

Obstet & Gynecol 2013; 122(5):1122-1131
**DIAGNOSIS OF SEVERE PREECLAMPSIA**

- INDEPENDENT of proteinuria if ≥ 1 of:
  - PLT < 100,000
  - LFTs > 2x NL
  - CR > 1.1
  - Pulmonary edema
  - HA/visual disturbances
  - Abdominal pain

**HIP: INDICATED IMMEDIATE DELIVERY**

- Do NOT delay delivery regardless of BMZ if:
  - Uncontrollable severe BP
  - Eclampsia
  - Pulmonary edema
  - Placental abruption
  - DIC
  - NRFHT

**HIP: EXPECTANT MANAGEMENT**

- You can expectantly manage until after BMZ if:
  - PLT < 100,000
  - LFTs > 2x NL
  - IUGR
  - Oligohydramnios
  - UA AEDF/REDF
  - Renal dysfunction

**HIP: GESTATIONAL HTN**

- Management is the SAME as preeclampsia without severe features
  - Deliver at 37 weeks
**HYPITAT**

- Hypertension and preeclampsia intervention trial at term
  - Dutch multicenter trial, 2005-8
  - Singletons 36-41 wks
  - N=377 IOL v. 379 expectant management
  - 31% v 44% poor maternal outcome
    - RR 0.71 (95% CI 0.59-0.86)
  - IOL ≥ 37 weeks GA if gHTN or preeclampsia without severe features had better maternal outcomes compared to expectant management


**HIP: CHRONIC HTN**

- Antihypertensive medication if BP >160/105
- Goal BP when on medication 120-160/80-105
- Delivery at 38 weeks

**TREATMENT: METHYLDPAPA**

- Central α-adrenergic stimulator
  - ↓Sympathetic outflow to heart, kidneys, vessels
- Pros
  - Long term safety data
- Cons
  - Slow onset of action (3-6 hrs)
  - Many failures
  - Sedative at high doses

**TREATMENT: LABETALOL**

- β but also α-blockade
  - α1 vascular receptors → vasoconstriction
  - β1 renal receptors → RAA system activation
  - β1 cardiac receptors → inotrope
- Pros
  - More uteroplacental blood flow preservation than atenolol
  - Faster onset of action than methyl dopa (2 hrs)
  - Can be given IV for acute severe HTN
- Cons
  - Hepatotoxicity
  - TID dosing
TREATMENT: OTHER COMMON MEDS

- Nifedipine XL
  - Pros: long acting for QD or BID dosing
  - Cons: less long term data
- Hydralazine
  - Pros: rapid IV action for acute HTN treatment
  - Cons: unpredictable hypotension, oral side effects
    - Reflex tachycardia and fluid retention

TREATMENT: MORE RARE MEDS

- Thiazide diuretics
  - Not first line
  - OK to continue in cHTN patients
    - Fluid loss occurs in 1st 2 weeks of treatment
- Clonidine
  - Similar mechanism as methyldopa
  - Pros: transdermal patch if cannot take PO
  - Cons: rebound HTN if stopped

CONTRAINDICATED TREATMENTS

- ACE inhibitors
- Angiotensin II receptor blockers (ARBs)
- Direct renin inhibitors
- Fetal cardiac anomalies 1st trimester
- Fetal renal toxicity 2nd and 3rd trimester

TREATMENT: BREASTFEEDING

- Beta blockers
  - Propranolol, metoprolol, labetalol
    - Low transfer to breast milk (<2%)
  - Atenolol
    - High transfer to breast milk with infant β-blockade
- Calcium channel blockers
  - Low transfer to breast milk (<2%)
- ACEI likely safe but risk of newborn hypotension
- Diuretics likely safe but risk of milk volume ↓
ALGORITHM: ACUTE SEVERE HTN Rx

- Labetalol IV push over 2min, q10 min  
  - 20 mg $\rightarrow$ 40 $\rightarrow$ 80 $\rightarrow$ 80 (max 300 mg)
- Lasts 3-6hrs

- Hydralazine IV push over 1-2min, q20 min  
  - 5-10 mg $\rightarrow$ 20 (max 30 mg)
- Lasts 2-4hrs

OTHER ACUTE TREATMENTS

- Nifedipine 10mg PO q20min
- NTG IV 5mcg/min $\rightarrow$ q3-5 min  
  - Max 100 mcg/min

HIP: POSTPARTUM CARE

- Serial outpatient BP follow-up checks  
  - 72 hours
  - 7-10 days
  - L&D triage v. OB clinic workflows needed
- Indications for PP anti-HTN medication  
  - BP > 150/100 2x > 4-6 hrs apart
  - Treat BP > 160/110 within one hour
- Readmit if BP > 160/110 and/or neuro symptoms  
  - Magnesium x 24 hrs

Obstet & Gynecol 2013; 122(5):1122-1131

HIP: POSTPARTUM CARE

- Counseling  
  - Increased risk of CV disease 2x - 9x
- If PTD or recurrent preE regardless of GA:  
  - Annual BP, lipids, fasting glucose, BMI
  - Baby ASA in next pregnancy 12 to 36 weeks GA

Obstet & Gynecol 2013; 122(5):1122-1131
USPSTF 2014 Ann Intern Med

- Grade B: For women at high-risk of preeclampsia
  - Aspirin 81mg after 12 weeks GA
- "High-risk" if 1 or more risk factors
  - History of preeclampsia, especially if adverse outcome
  - Multifetal gestation
  - Chronic HTN
  - Type 1 or 2 DM
  - Renal disease
  - Autoimmune disease (SLE, APS)

ASPIRIN FOR PREVENTION

- Who?
  - HIP guidelines v. USPSTF
- Dosing?
  - Low dose better than regular dose
  - Prostacyclin (vasodilator) > thromboxane A2 (vasoconstrictor)
  - But which low dose? 81mg v. 150mg
- Timing?
  - qHS timing thought to be more effective than AM
- Preventing what?
  - Preeclampsia
  - Other adverse outcomes such as IUGR

USPSTF

- Aspirin if 2 or more moderate risk factors
  - Nulliparity
  - Obesity (BMI >30)
  - Family history of 1st degree relative
  - Low SES
  - African-American
  - Age ≥ 35yo
  - >10yr pregnancy interval
  - Personal history IUGR or adverse pregnancy outcome

ACOG ENDORSES USPSTF

- New ACOG practice advisory July 11, 2016
- Aspirin and prevention of preeclampsia
  - Updated recommendations
- ACOG endorsed the USPSTF “high-risk” list
  - Baby aspirin 81 mg daily initiated 12-28 weeks
  - “Moderate-risk” list
    - Not enough data to recommend
USPSTF 2014 Ann Int Med

- 15 RCTs assessing benefits of aspirin
  - 8 good quality
- 13 RCTs assessing preeclampsia incidence
  - 8 good quality
- Largest RCTs included were the MFMU & CLASP trials
- 24% decrease in preeclampsia
  - NNT 42
- 14% decrease in PTB
  - NNT 65
- 20% decrease in IUGR
  - NNT 71

MFMU 1998 NEJM

- 13 U.S. sites
- N=2503 high risk women
- 60 mg daily starting 13-26 weeks
- No difference between ASA and placebo
  - Overall incidence of preE 18 v 20%
  - Pregestational DM 18 v 22%
  - cHTN 26 v 25%
  - Multifetal gestation 12 v 16%
  - History of preE 17 v 19%

CLASP 1994 Lancet

- 16 International sites
  - U.K., U.S., Canada, Germany, Spain & Hong Kong
- N=9364, 60 mg daily, 2/3rd < 20wks GA start
  - 74% of participants enrolled for prophylaxis
    - 12% specifically for IUGR
    - 12% for treatment of preE
    - 3% for treatment of IUGR
- 12% decreased incidence of preeclampsia
- No effect on IUGR, IUF, neonatal death
- Yes safe
- Yes – aspirin if very high-risk for preterm preE

CASE #1

42yo G1P0 Asian woman
- 33 weeks GA
- cHTN on max labetalol
- Now has severe range BPs
- No other signs/symptoms of severe preeclampsia

TIMING OF DELIVERY?

A. Now
B. 34 weeks
C. 37 weeks
D. 38 weeks

27% 19% 35% 18%
CASE #2
40yo G1P0 Caucasian woman
- 38 weeks GA
- cHTN well controlled on low dose labetalol

TIMING OF DELIVERY?
A. Now 66%
B. 39 weeks 28%
C. 40 weeks 5%
D. 41 weeks 1%

CASE #3
35yo G1P0 African-American woman
- 12 weeks GA
- BMI 30

Aspirin or no aspirin?
A. Yes 62%
B. No 38%

THANK YOU Dr. Bill Parer