HYPERTENSION in PREGNANCY

GREGORY L. GOYERT, MD
Division Head, Maternal-Fetal Medicine
Women's Health Services
Henry Ford Health System

Hypertension in Pregnancy

- Second leading cause maternal mortality in US
  - VTE most common cause
- Accounts for 15% of maternal deaths
- Complicates 6% - 8% of all pregnancies
- Significant risk for intrauterine fetal death and neonatal morbidity/mortality
- Maternal risk of abruption, DIC, intracranial hemorrhage, hepatic failure, and renal failure

"Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy"

Management guidelines for 2 distinct groups

- Chronic hypertension predating pregnancy
- Hypertension first appearing during pregnancy
Hypertension in Pregnancy
ACOG Task Force 2013

- 17 expert clinician-scientists met 2012
  - Reviewed data last 10 years
  - Published evidence based recommendations

Highlights regarding preeclampsia
- Association with later life CV disease
- Failure to note multisystemic nature of disease
- Emphasized dynamic nature of disease
  - 'Mild' Dx applies only at time of diagnosis
  - Disease is progressive, although at variable rates
  - Frequent postpartum appearance of preeclampsia

Classification of Hypertension in Pregnancy

- Chronic hypertension
- Preeclampsia-eclampsia
  - Significant modifications made
- Superimposed preeclampsia
- Gestational hypertension
  - Transient hypertension of pregnancy
  - Persistent chronic hypertension
  - Preeclampsia

Chronic Hypertension

- Present and observable prior to pregnancy or diagnosed prior to 20 weeks’ gestation; use of anti-hypertensive medication prior to pregnancy
- BP > 140 mm Hg systolic or >90 mm Hg diastolic
  - Mild: systolic 140-159 or diastolic 90-109
  - Severe: systolic >160 or diastolic >110
- Hypertension diagnosed initially during pregnancy that does not normalize by 12 weeks post partum
Chronic Hypertension

- Increased risk adverse outcomes
  - Maternal mortality 4.8 x; CVA 5.3 x
  - Pulmonary edema 5.2 x; renal failure 6.0 x
  - Placental abruption 2-3 x
  - Cesarean section 2.7 x
  - SGA infants 2-5 x
  - IUFD 2 x; NND 2.5 x;
  - Superimposed preeclampsia 20%-75%

Preeclampsia-Eclampsia

- Pregnancy-specific syndrome of reduced organ perfusion tied to vasospasm and activation of coagulation cascade
- Presents after 20 weeks’ gestation
  - Earlier with trophoblastic disease
  - BP >140 mm Hg systolic or >90 mm Hg diastolic in patients previously normotensive
  - Accompanied by proteinuria

Preeclampsia-Eclampsia

- Proteinuria removed as requirement
  - If absent, severe preeclampsia diagnosed with
    - Thrombocytopenia (< 100,000)
    - Impaired LFTs (> twice normal)
    - New-onset renal dysfunction (creatinine > 1.1)
    - Pulmonary edema
    - New-onset cerebral or visual disturbances
  - Bottom line: may diagnose severe preeclampsia without proteinuria
Preeclampsia-Eclampsia

- Proteinuria defined as > 300 mg/24 Hrs
  - Protein/creatinine ratio > 0.3
  - Dipstick 1+ or greater (discouraged)
- Massive proteinuria (> 5 g)
  - Eliminated as diagnostic of severe disease
- IUGR
  - Eliminated as diagnostic of severe disease
- Eclampsia is above syndrome with seizures

Preeclampsia

‘Severe Features’

- Systolic BP > 160 or diastolic BP >110
  - Two occasions; 4 hours apart
- Thrombocytopenia (< 100,000)
- Impaired liver function
  - LFT’s > twice normal levels
  - Severe, persistent RUQ/epigastric pain
- Progressive renal dysfunction
  - Creatinine > 1.1 or doubling from baseline
- Pulmonary edema
- New-onset, severe cerebral or visual disturbances

Preeclampsia-Eclampsia

- Spectrum of syndrome: mild to severe
- Progression typically slow, if at all
- Beware: fulminant disease may evolve within days, or even hours
  - Syndrome is unpredictable
  - "wears many faces"
- Maintain high index of suspicion
  - Remember: even if disease appears mild, it has been present for weeks, if not months
Preeclampsia superimposed on chronic hypertension

- Maternal/fetal prognoses worse versus either condition alone
- Diagnosis of superimposed disease likely:
  - New-onset proteinuria after 20 weeks’
  - Sudden increase in proteinuria
  - Sudden increase in blood pressure
    - If previously well controlled
  - Thrombocytopenia/increased LFT’s

Gestational hypertension

- HTN w/o proteinuria > 20 weeks’
  - Absent ‘features of severe preeclampsia’
- Designation during pregnancy only until more specific diagnosis can be assigned
  - Preeclampsia develops
  - Transient HTN: preeclampsia does not develop and patient normotensive 12 weeks’ pp
  - Chronic HTN: persistent HTN 12 weeks’ pp

Pathophysiology

- Critical to emphasize: preeclampsia is not simply HTN
  - Systemic syndrome
  - Potentially lethal complications in setting of only modest blood pressure elevations
- ‘Cause’ of preeclampsia remains unknown
Pathophysiology

- Syndrome characterized by
  - Vasospasm
  - Coagulation cascade activation
  - Ischemic insult to placenta, liver, kidney, CNS
- Abnormal trophoblastic invasion (or "remodeling process") of spiral arteries may represent morphologic basis for syndrome

Pathophysiology

- Blood pressure
  - Altered vascular reactivity
  - Increased peripheral resistance
  - Decreased prostacyclin/increased thromboxane
  - Decreased nitric oxide synthase activity
- The heart

Pathophysiology

- The kidney
  - Glomerular endotheliosis
    - Pathognomonic lesion
  - GFR/RBF decreased
  - ATN/cortical necrosis rare
  - Fractional urate clearance decreased
  - Hemoconcentration/CVP-PCWP low normal
Pathophysiology

- Coagulation system
  - Thrombocytopenia most common abnormality
  - Platelet deposition at endothelial damage
- The liver
  - Peri-portal hemorrhage/ischemic lesions
  - Wide spectrum of damage: mild necrosis to HELLP syndrome to subcapsular hemorrhage to hepatic rupture
- The CNS
  - Eclampsia: precipitating cause unknown
  - Headaches/visual symptoms

Diagnostic Evaluation

- Attempt to differentiate
  - Preeclampsia vs chronic vs transient HTN
  - Also, assess severity of process
- Screening/predictive tests not effective
- Baseline testing (high-risk pts w/normal BP)
  - CBC w/platelets
  - Serum creatinine/uric acid
  - 24 hr urine protein/creatinine clearance
  - Early dating US/follow-up US for growth

Diagnostic Evaluation

- Patients w/HTN before 20 weeks’
  - Consider screening for secondary HTN
    - Renal, renovascular, aldosteronism, Cushing syndrome, pheochromocytoma
    - Judgment required
  - Other baseline tests as above
- Patients w/HTN presenting after 20 weeks’
  - Add LFT’s/coagulation profile to baseline tests
Chronic Hypertension

- Preconceptional counseling
  - Evaluate for potentially reversible causes
  - Discontinue ACE inhibitors and angiotensin II receptor antagonists
  - Cranial abnormalities, renal dysgenesis, pulmonary hypoplasia, IUGR, IUFD, oligohydramnios, NND
  - Thiazide diuretic therapy does not require discontinuation
- Screen for end-organ damage
  - LVH, retinopathy, renal disease
- Address activities, exercise, weight management

Treatment indications
- Value of treating mild CHTN unclear
  - Reduces risk severe HTN crisis
  - Does not improve perinatal outcome
- Many authorities treat BP > 150-160/100-110
  - 'reasonable' to treat if BP in 150/100
  - Particularly in patients with end-organ damage

Drug selection
- Labetalol ‘good option’ first-line treatment
  - 200-2400 mg/day in 2-3 divided doses
  - Nifedipine also widely studied; safe and effective
  - 30-120 mg/day slow-release
  - Potential negative effect with magnesium not observed in large trial
- Methyldopa used for decades; appears safe
  - 0.5-3.0 gm/day in 2-3 divided doses

Emergency Therapy

Acute-Onset, Severe HTN: > 160 or > 110

- Labetalol 20 mg IV over 2 minutes
  - Repeat BP in 10 minutes
    - If still elevated, labetalol 40 mg IV over 2'
    - Repeat BP in 10 minutes
    - If still elevated, labetalol 80 mg IV over 2'
    - Repeat BP in 10 minutes
    - If still elevated, hydralazine 10 mg IV over 2'
    - If still elevated, consult MFM, IM, Anesth, etc.
Emergency Therapy
Acute-Onset, Severe HTN: > 160 or > 110

- **Hydralazine** 5-10 mg IV over 2 minutes
  - Repeat BP in 20 minutes
  - If still elevated, hydralazine 10 mg IV over 2'
  - Repeat BP in 20 minutes
  - If still elevated, hydralazine 20 mg IV over 2'
  - Repeat BP in 10 minutes
  - If still elevated, labetalol 40 mg IV over 2'
  - Consult MFM, IM, Anesthesia, Critical Care, etc.

- **Nifedipine** 10 mg orally
  - Repeat BP in 20 minutes
  - If still elevated, Nifedipine 20 mg orally
  - Repeat BP in 20 minutes
  - If still elevated, Nifedipine 20 mg orally
  - Repeat BP in 10 minutes
  - If still elevated, labetalol 40 mg IV over 2'
  - Consult MFM, IM, Anesthesia, Critical Care, etc.

Chronic Hypertension

- With mild renal disease
  - Creatinine < 1.4 mg/dL
  - Good fetal survival/limited disease progression

- With moderate/severe renal disease
  - Fetal survival jeopardized/disease may accelerate
  - Dialysis/renal transplant: guarded prognoses
  - Modify magnesium sulfate maintenance dosage
Chronic Hypertension

- Fetal assessment
  - Monitor for superimposed preeclampsia/IUGR
  - Abruption remains constant risk
  - Serial ultrasound for fetal growth
  - Assess acute utero-placental function
    - NST, BPP, CST

Chronic Hypertension

- Timing of delivery
  - No medication: 38-39 weeks
  - Controlled on medication: 37-39 weeks
  - Difficult to control on medication: 36-37 weeks
  - Superimposed preeclampsia
    - Consider delivery at 34 weeks
    - Judgment required
    - 2013 Task Force recommendations:
      - If MF status stable/no severe features; deliver at 37 wks

Preeclampsia Prevention

- Baby ASA data
  - Evolving recommendations: 2013
    - Meta-analyses 30,000 patients
    - History of early-onset preeclampsia and PTD at < 34 weeks in > 1 prior pregnancy
    - Initiation of baby asa late first trimester suggested
  - USPSTF: December 2014
    - Much more aggressive prophylaxis
      - History of preeclampsia, particularly with adverse outcome
      - Chronic hypertension
      - Renal disease, SLE, APS, pregestational DM
    - Not recommended as effective prevention strategies
      - Vitamin C or Vitamin E
      - Restriction of dietary salt
      - Calcium supplementation
      - May be useful in low calcium intake populations; not U.S.
      - Bed rest or physical activity restriction
Preeclampsia Management Rationale

- Delivery is always appropriate for mother—may not be so for fetus
  - Any management, other than delivery, must reduce perinatal morbidity and mortality
  - Management based upon determination of whether fetal prognosis is better in utero or in nursery

Preeclampsia Management Rationale

- Basic pathophysiology of severe preeclampsia is ischemia
  - Treating only Sx/Sx may worsen status
- Pathologic features of syndrome present long before clinical Sx/Sx appear
  - “Evidence” of syndrome typically appears late in natural history of disease

Preeclampsia Management

- Preeclampsia/GHTN w/o severe features
  - Serial assessment maternal symptoms
  - Fetal kick counts
  - BP checks twice weekly
  - Check LFT’s and platelets weekly
  - If BP < 160/110, no antihypertensive Rx
  - Strict bedrest not recommended
  - EFW’s and NST’s recommended
    - If IUGR diagnosed, assess umbilical artery dopplers
  - Deliver at 37 weeks
  - Universal magnesium sulfate prophylaxis not suggested
Preeclampsia Management

- Ultimately, only delivery is curative
- Delivery timing
  - Limited role for FLM amniocentesis
  - Gestational hypertension: 37–38 wk
  - Preeclampsia—mild: 37 wk
  - Preeclampsia—severe: at diagnosis if > 32-34 wks
- Severe disease remote from term
  - Deliver if after 32-34 wks
  - Selective expectant management at 23-32 wks
    - Tertiary centers only
    - Steroids to enhance FLM

Preeclampsia Management

- Vaginal delivery preferable
  - “Aggressive” labor induction
- Epidural analgesia preferred intrapartum
- Parenteral magnesium sulfate prophylaxis
- Invasive hemodynamic monitoring
  - Rarely indicated
  - Pulmonary edema, oliguria, intractable HTN

Postpartum Counseling

- HTN and organ dysfunction resolve rapidly
- Postpartum follow up important:
  - Within 3-7 days if medication was used L/D or postpartum
  - within 7-14 days if no medication was used
- Recurrence risks vary
  - Early/severe disease: 25-40%
  - Late/mild disease: < 10%
  - HELLP SYNDROME: 5-10%
- Screen for Antiphospholipid Syndrome (APS) with early and/or severe disease
  - Lupus Anticoagulant
  - Anticardiolipin antibodies
  - Anti-β2 Glycoprotein I antibodies

ACOG Practice Bulletin #118 January 2011
Questions