

# HYPERTENSIVE DISORDERS OF PREGNANCY

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# Hypertensive disorders in pregnancy

- One of the leading causes of maternal morbidity and mortality
  - Renal damage
  - Liver damage
  - Seizure/ Stroke
  - DIC
- Fetal complications
  - Preterm birth
  - Growth restriction
  - Placental abruption
  - Stillbirth



# Classification

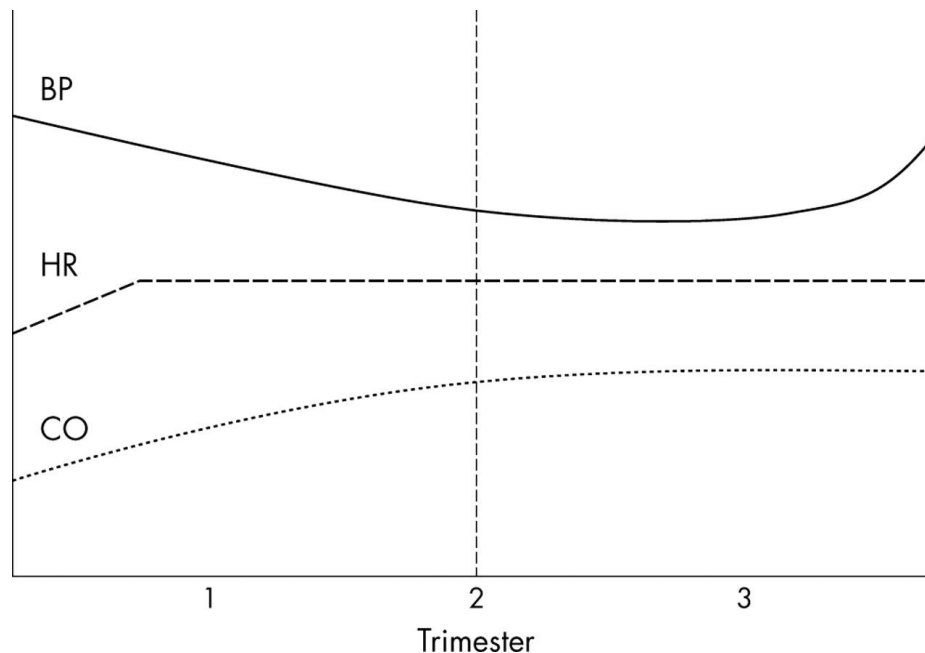
- Chronic hypertension
- Gestational hypertension
- Preeclampsia
- Eclampsia
- Chronic hypertension with superimposed preeclampsia



Occur only in pregnancy and postpartum period

# Chronic hypertension

- Hypertension that predates pregnancy or detected before 20 weeks
  - Can be confusing when women present in 2<sup>nd</sup> trimester and have normal BP due to the physiologic decrease in pregnancy
  - Stop ACE In., ARBs, and statins



# Chronic hypertension

- Increased risk of preeclampsia
  - Baseline labs: CBC, Cr, AST/ALT, 24h urine
  - EKG or echocardiogram in women with severe hypertension for >4yrs
- Increased risk of fetal growth restriction
  - Due to preeclampsia and antihypertensive medications
  - May be as high as 40% in women with severe hypertension
  - Growth ultrasounds and antenatal testing
- Studies suggest delivery b/w **38-39 weeks** is optimal in women with uncomplicated CHTN

# Chronic hypertension

- Home BP monitoring is suggested
- For women with persistent SBP  $\geq 160$  or DBP  $\geq 105$ , antihypertensive therapy is recommended
  - Treatment goal SBP 120-160  
DBP 80-105
- If a woman starts pregnancy on an antihypertensive discontinuation in the 1<sup>st</sup> trimester and restarting them if BP becomes severe is reasonable
- In women with end-organ damage such as CKD and cardiac disease (CHF, prior MI) BP should be kept  $< 140/90$

# Antihypertensive therapy

- Treatment has been shown to:
  - Decrease risk of severe hypertension
  - Increase the rate of SGA infants
  - No effect on development of preeclampsia, fetal or neonatal death, preterm birth
  - Conflicting data as to increased cardiac malformations
- Reviews have concluded that there is insufficient evidence that treatment of nonsevere hypertension improves maternal or neonatal outcomes

# Antihypertensives in pregnancy

- Labetalol ( $\beta$  blocker with vascular  $\alpha$  blocking ability)
  - 200-2,400mg daily divided in 2-3 doses
  - Fatigue, sleep disturbances, bronchoconstriction
  - Avoid in asthma and CHF
  - May increase risk of SGA
- Methyldopa ( $\alpha$ -2 adrenergic agonist)
  - 0.5-3gm daily divided in 2-3 doses
  - Childhood safety data up to 7yo
  - May not be affective for control of severe hypertension
- Nifedipine (Ca channel blocker)
  - 30-120mg daily extended release
  - Does not appear to adversely affect uterine blood flow



# Antihypertensives in pregnancy

- Diuretics (HCTZ)
  - Considered a 2<sup>nd</sup> line agent
  - Theoretical concerns about intravascular volume restriction and FGR have not been shown in meta-analysis
- ACE In/ ARB
  - 2<sup>nd</sup> and 3<sup>rd</sup> trimester use associated with fetal renal failure, oligohydramnios, pulmonary hypoplasia, and FGR
  - 1<sup>st</sup> trimester use associated with an increase in cardiac and CNS malformations

# Gestational hypertension

- Blood pressure elevation  $\geq 140/90$  in a previously normotensive woman
- Absence of proteinuria
- Development of hypertension after 20 weeks and resolves  $< 12$  weeks postpartum

# Gestational hypertension

- Can progress to preeclampsia
- 10% of eclamptic seizures occurred before proteinuria
- Assessment of BP and proteinuria weekly in office with additional weekly measurement of BP at home
- Timing of delivery: **37 0/7 weeks**

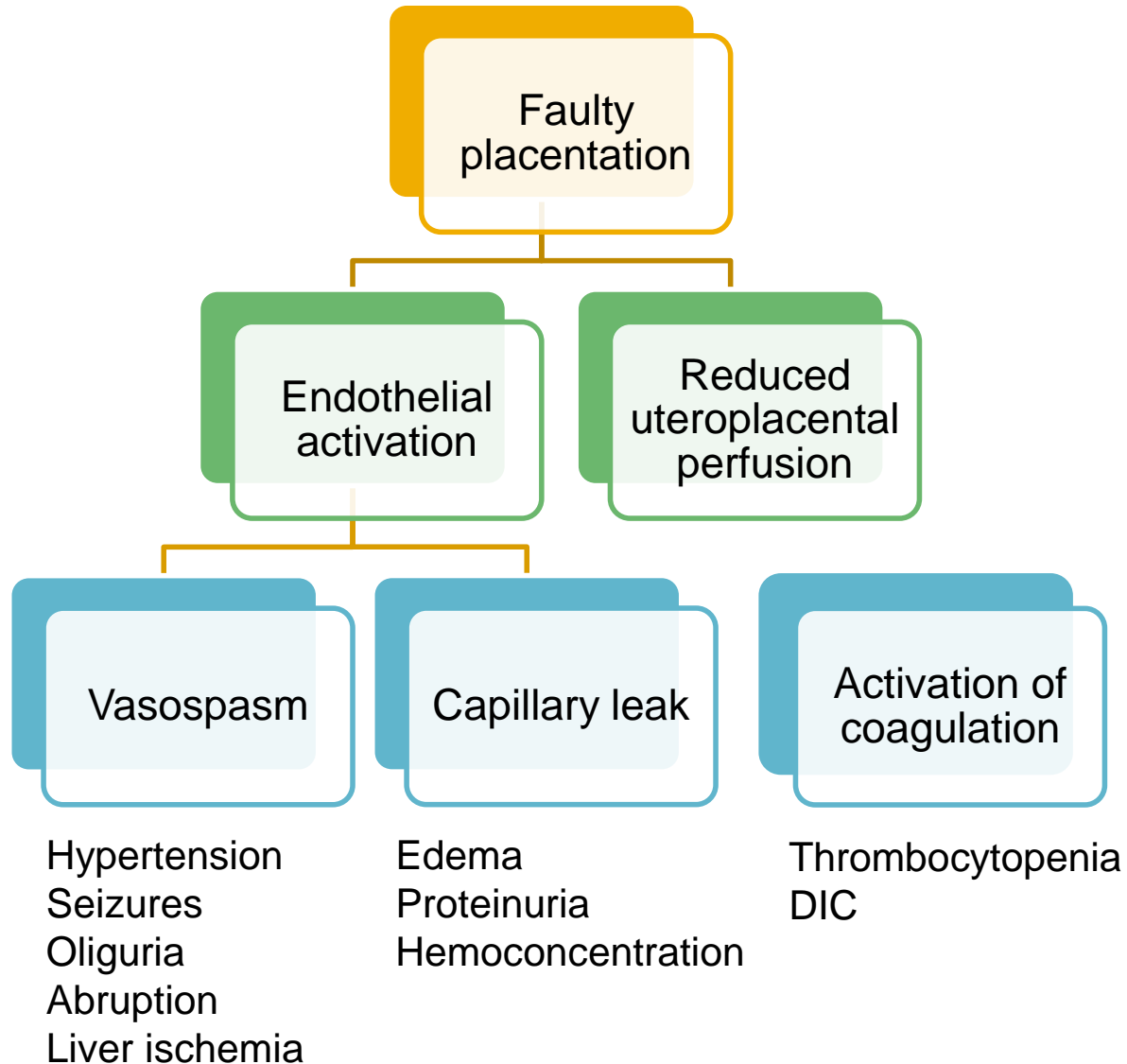
# Risk factors for preeclampsia

- Nulliparity
- Age > 35 years
- Connective tissue disorders
- CHTN
- Diabetes
- Renal disease
- Obesity
- Multiple gestations



**Occurs in 3-8%  
of pregnancies**

# Cause of preeclampsia



# Diagnosis of Preeclampsia

- SBP  $\geq 140$  or DBP  $\geq 90$  on 2 occasions at least 4 hours apart after 20 weeks
- Proteinuria:
  - $\geq 300$ mg protein in a 24h urine collection
  - $\geq 0.3$ mg/dL on protein/creatinine ratio
  - $\geq +1$  on dipstick (high FP and FN rate)
- Amount of proteinuria does not predict maternal or fetal outcomes

# Diagnosis of Preeclampsia

- In the absence of proteinuria, new onset hypertension and any of the following:
  - Platelet  $< 100,000$
  - Creatinine  $> 1.1\text{mg/dL}$  or doubling of creatinine
  - AST/ALT  $>2\text{x ULN}$
  - Pulmonary edema
  - New-onset cerebral or visual disturbances

# Additional signs/symptoms of preeclampsia

- Epigastric or RUQ pain
- Headache or visual disturbances
- Thrombocytopenia
- Hemolysis
- Elevated creatinine
- Elevated AST/ALT
- Seizures
- Pulmonary edema
- Fetal growth restriction





# Initial evaluation for preeclampsia

- Initial evaluation:
  - Ask about symptoms
  - Vitals and physical exam
  - CBC, Cr, AST/ALT, 24h urine for protein
  - Fetal EFW and AFI, NST

# Management of preeclampsia without severe features

- “Mild preeclampsia” should be replaced with “Preeclampsia without severe features”
- Can rapidly progress to severe preeclampsia
- Daily assessment of symptoms and fetal movement (by the woman)
- Twice weekly measurement of BP
- Weekly assessment of CBC, Cr, and AST/ALT
- Ultrasound to assess fetal growth (every 3-4 weeks) and antenatal testing to assess fetal status
- Timing of delivery: 37 0/7 weeks

# Diagnosis of severe preeclampsia

- SBP  $\geq 160$  or DBP  $\geq 110$  on 2 occasions a least 4 hours apart while on bed rest (unless antihypertensives started before this time)
- Platelet count  $< 100,000$
- AST/ALT  $> 2x$  ULN or severe, persistent RUQ/epigastric pain
- Creatinine  $> 1.1$ mg/dL or doubling of creatinine
- Pulmonary edema
- New-onset cerebral or visual disturbances

# Maternal complications of severe preeclampsia

- Pulmonary edema
- MI
- Stroke
- ARDS
- Coagulopathy
- Renal failure
- Retinal injury

# Initial evaluation < 34 weeks

- Observe in L&D for first 24-48 hours
- Administer antenatal corticosteroids
- Magnesium sulfate for seizure prophylaxis
- Antihypertensives for BP > 160/110

# Immediate delivery after stabilization

- Eclampsia
- Pulmonary edema
- DIC
- Uncontrollable severe hypertension
- Abnormal fetal test results
- Placental abruption
- Fetal demise
- Previabile

# Delivery after corticosteroids

- Corticosteroids administered and delivery deferred for 48 hours if maternal and fetal conditions remain stable at or less than 33 6/7 weeks with any of the following
- Persistent symptoms
- HELLP or partial HELLP
  - Platelet  $<100,000$ , AST/ALT  $> 2xULN$
- EFW  $< 5\%$
- AFI  $< 5cm$
- REDF on umbilical artery Doppler
- Labor or PPRROM
- Renal dysfunction

# Expectant management till 34 0/7wks

- Inpatient only (facilities with adequate maternal and NICU resources)
- Stop magnesium sulfate
- NST daily, growth ultrasound every 3-4 weeks
- Symptoms should be assessed at least every 8h
- Vital signs and I/O at least every 8h
- CBC, AST/ALT, Cr should be done daily and may be spaced out to every other day if the patient remains asymptomatic
- Oral antihypertensive therapy for BP > 160/110



# Management of severe preeclampsia

- For women with diagnosis after 34 0/7 weeks, delivery soon after maternal stabilization is recommended
- The mode of delivery need not be CD, but should be determined by fetal gestational age, presentation, cervical status, and maternal and fetal conditions
  - CD rate with IOL
    - 93-97% at less than 28 weeks
    - 53-65% at 28 – 32 weeks
    - 31-38% at 32 – 34 weeks

# Treatment of severe hypertension

- For women with severe hypertension (sustained SBP  $\geq 160$  or DBP  $\geq 110$ ) the uses of antihypertensive therapy is recommended
- Target BP is 130-150/80-90
- Over treatment of initial BP can cause fetal distress
- Persistent severe hypertension is associated with
  - Maternal stroke
  - Eclampsia
  - Myocardial ischemia
  - Liver complications

# Drugs for urgent lowering of BP

- Labetalol: 10-20mg IV, then 20-80mg q20-30min (max 300mg)
  - Onset: 1-2 min lasts for 6-16hrs
  - Considered first line
  - Tachycardia less common
  - Contraindicated in asthma and heart disease
- Hydralazine: 5mg IV, then 5-10mg q20-40min
  - Onset: 10-20min lasts for 3-8hrs
  - Frequent dosing associated with hypotension, HA, and fetal distress
- Nifedipine 10-20mg PO, repeat in 30min then 10-20mg q2-6h
  - Onset: 5-10 min lasts for 4-8hrs
  - May cause reflex tachycardia and headaches

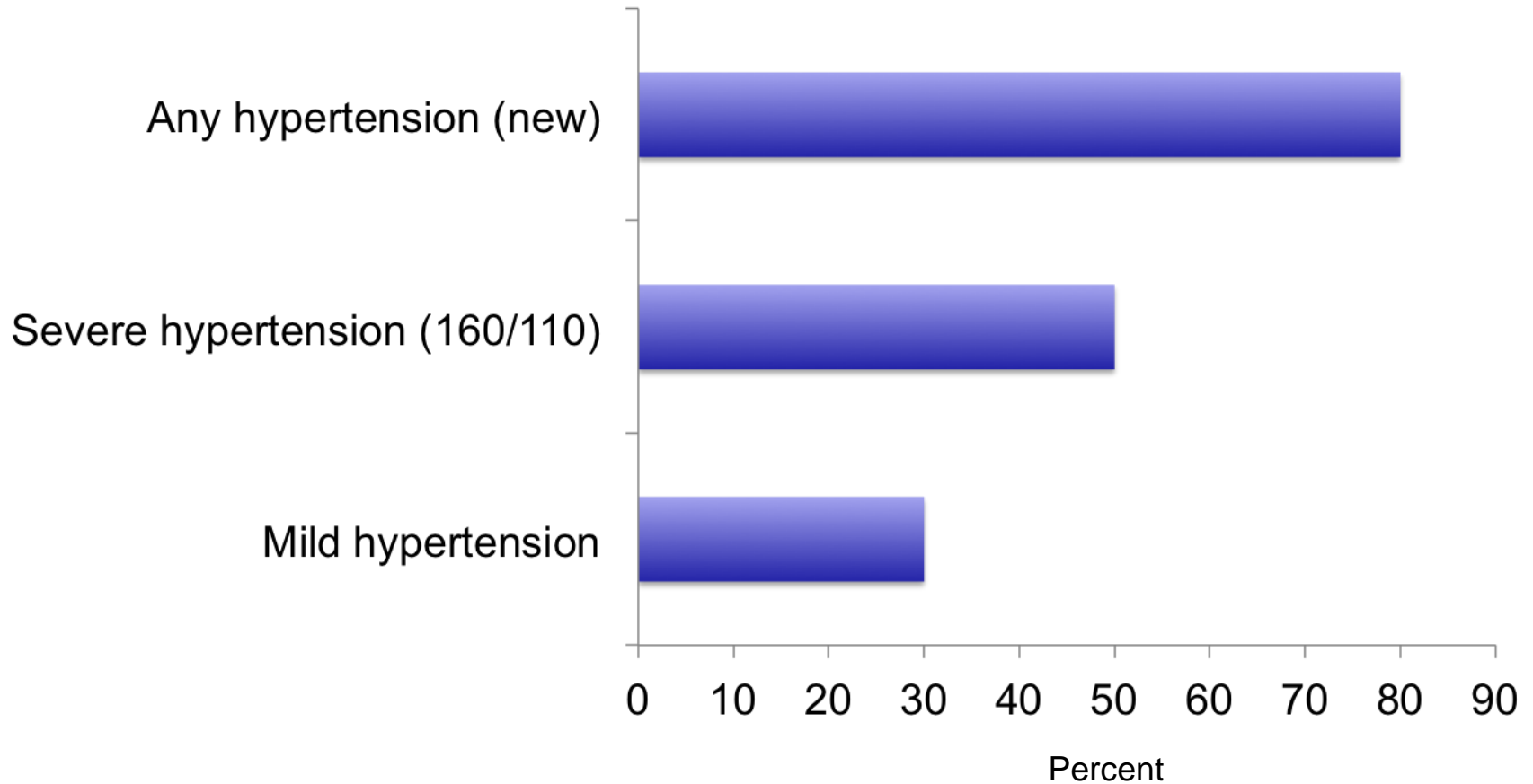
# Eclampsia

- New onset grand mal seizure in a woman with preeclampsia
- Elevated BP and proteinuria not always present
- Symptoms can be helpful
  - Persistent occipital or frontal headache
  - Blurred vision, photophobia
  - Epigastric or RUQ pain
  - Altered mental status

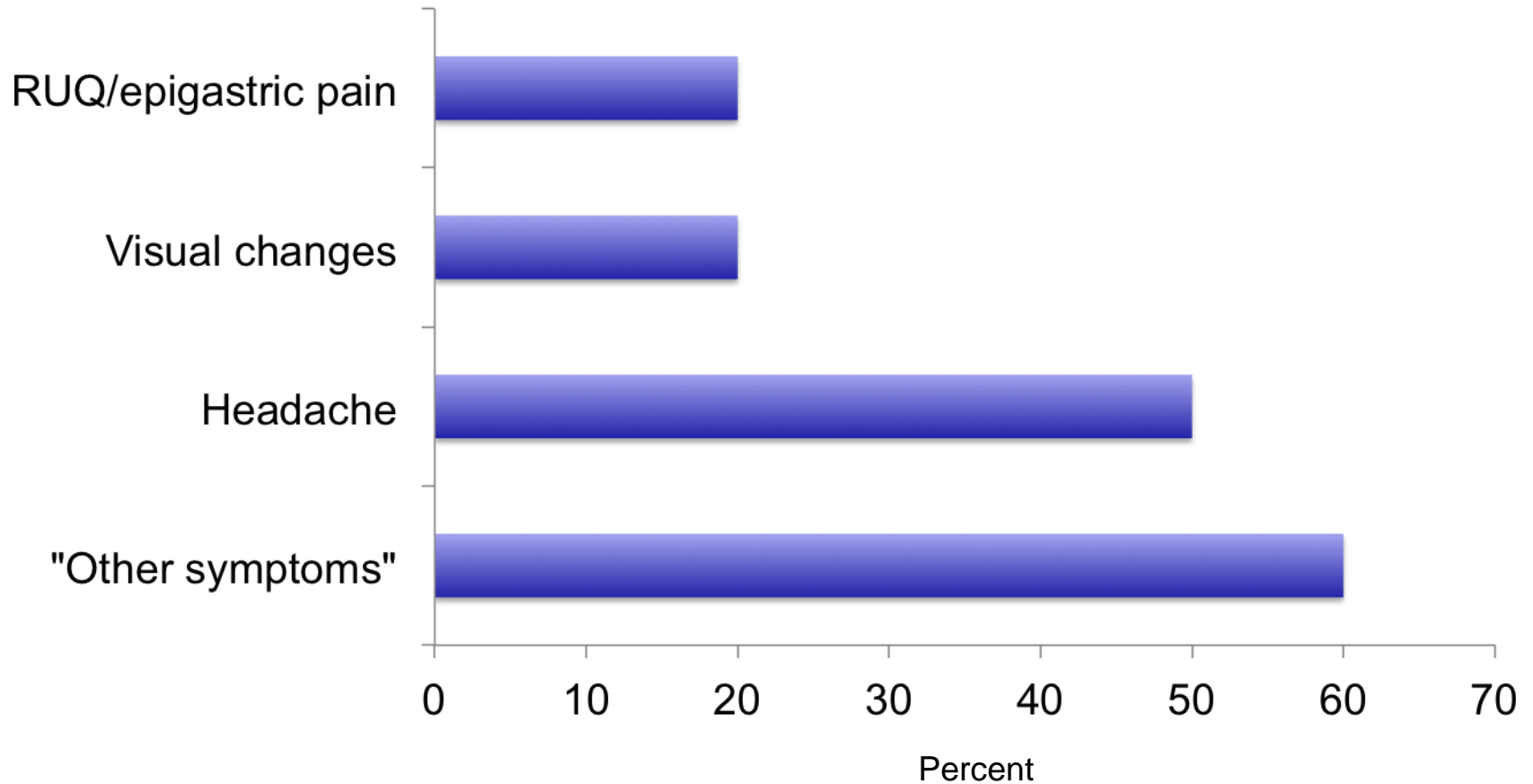
# Eclamptic seizures

- Brief (10-60 seconds) in duration
- Variable neurologic changes (transient)
  - Focal deficits
  - Cortical blindness (10%, usual resolves)
  - Coma (very rare)
- Temporary cessation of breathing followed by tachypnea
- Fetal bradycardia (3-5 minutes)

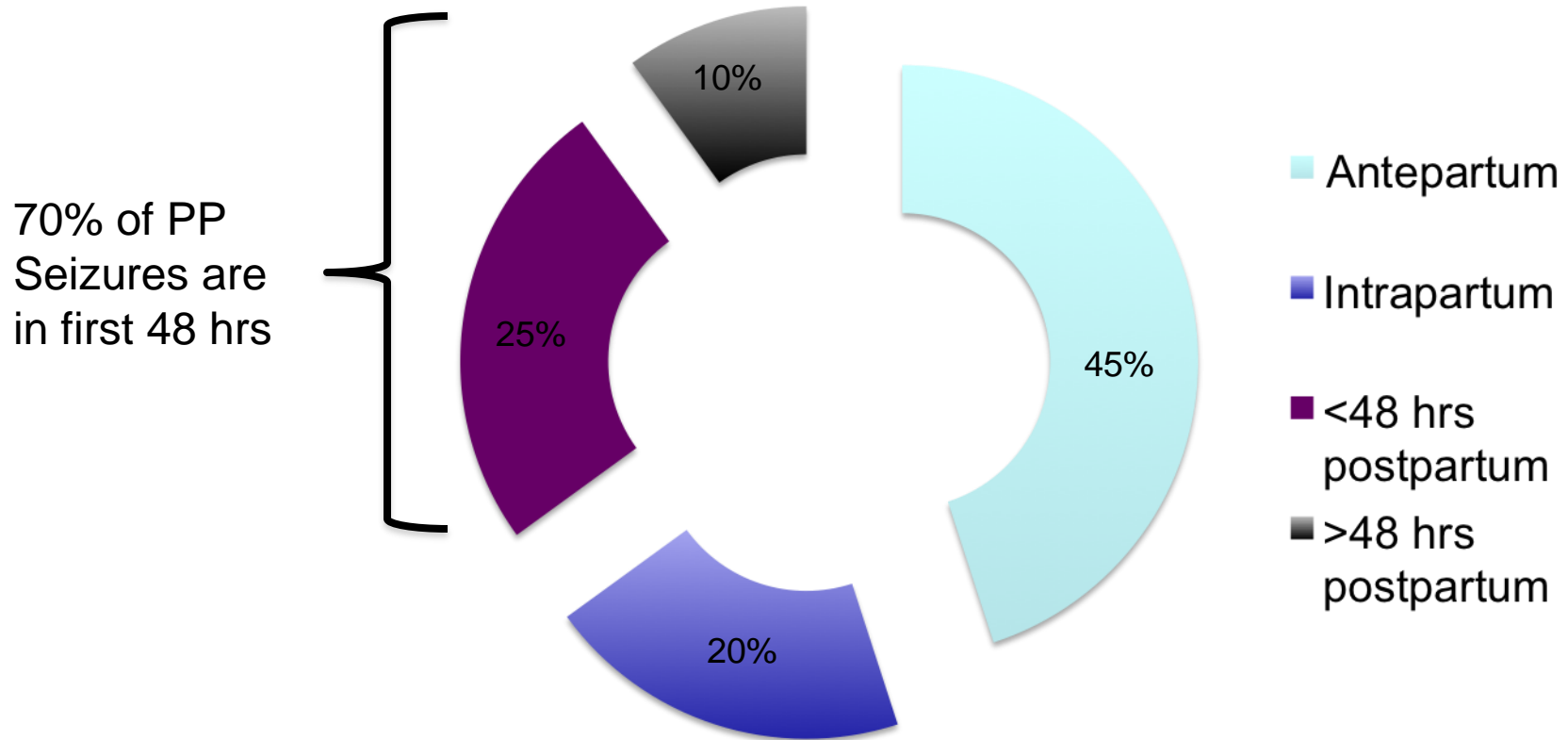
# Eclampsia and BP



# Associated symptoms



# Timing of seizure



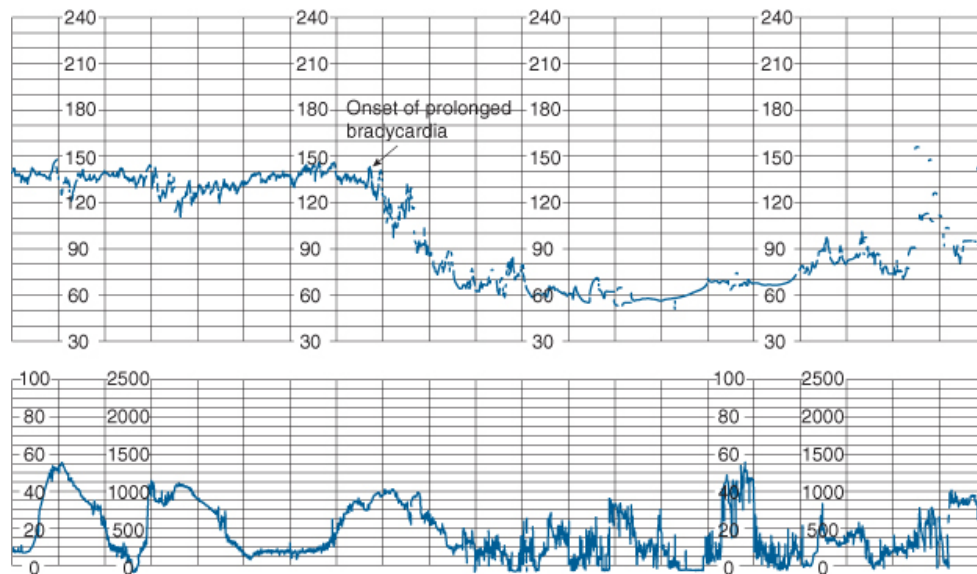


# Management of eclampsia

- General approach to seizing obstetric patient
  - Maintain airway
  - Prevent next seizure
  - Control blood pressure (Goal < 160/105)
- Assume diagnosis of eclampsia until proven otherwise
- Optimize patient (LL displacement, IV access)
- Secondary assessment including laboratory data
- Delivery planning

# Fetus

- During acute event fetal monitoring is not helpful
  - **Fetal bradycardia is common**
- Before assessing and considering intervention for the fetal status it is imperative to assess, stabilize and optimize the maternal condition

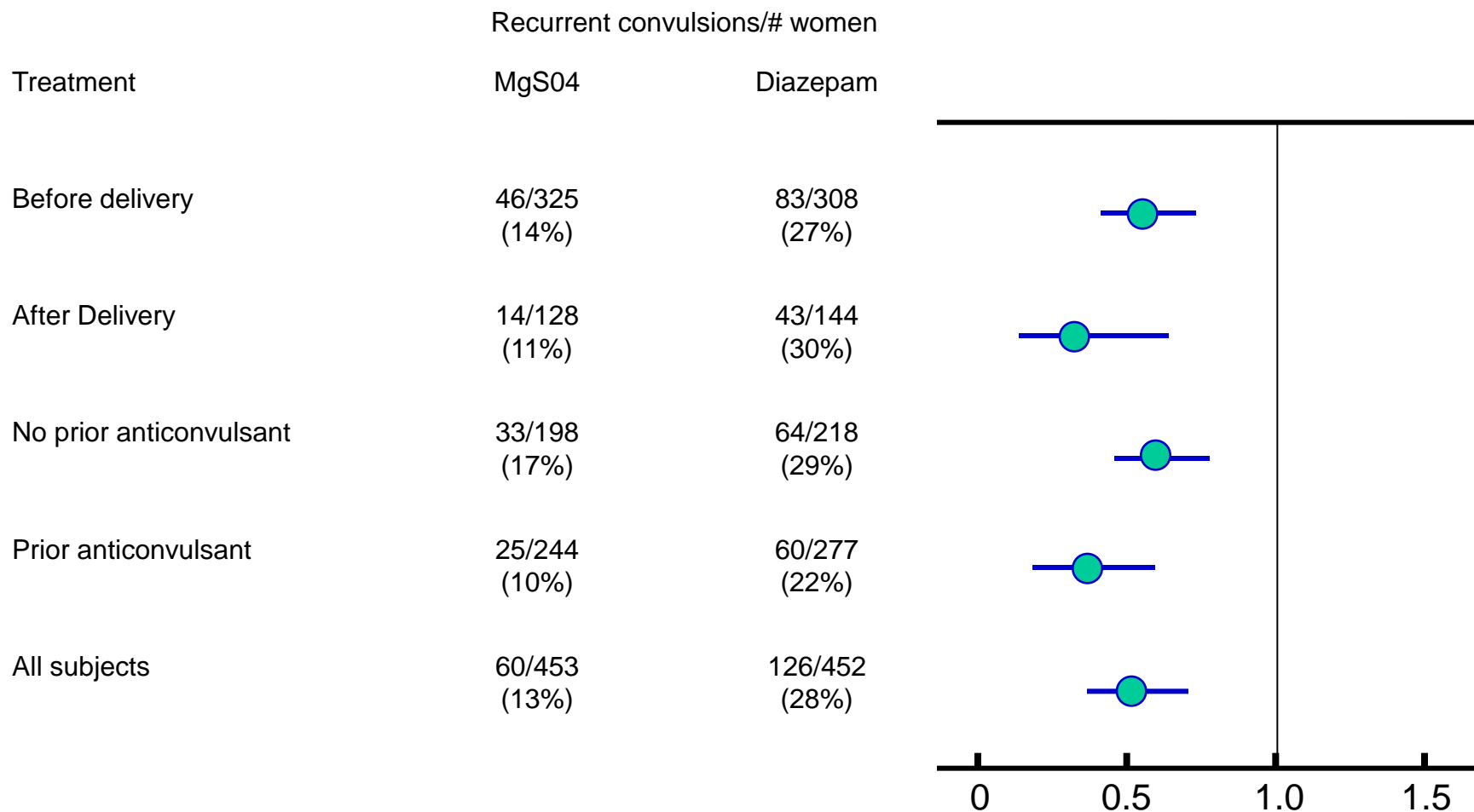


# Which anticonvulsant for women with eclampsia? Evidence from the Collaborative Eclampsia Trial

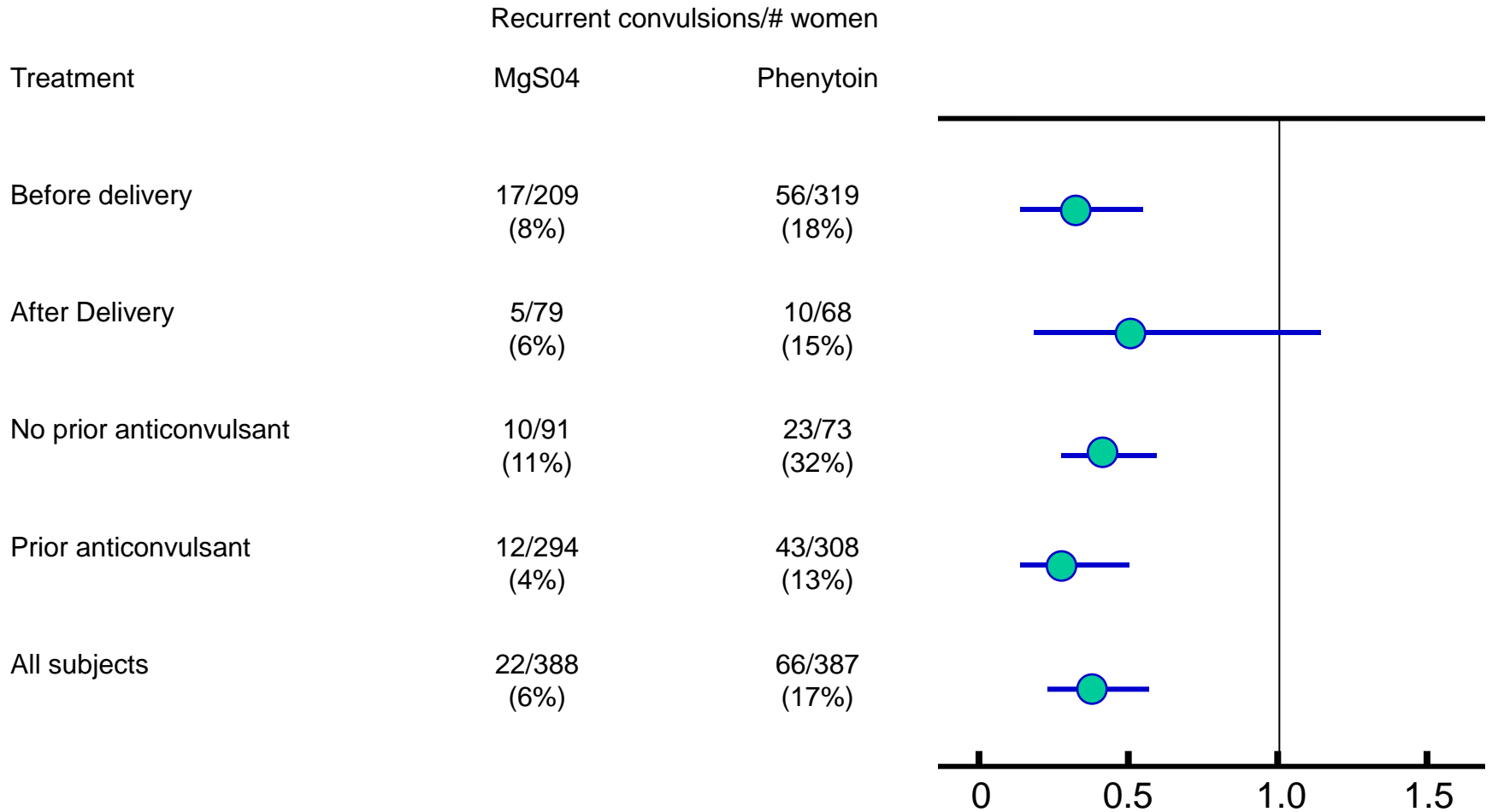
*The Eclampsia Trial Collaborative Group\**

- 1680 women with eclampsia randomized to
  - MgSO<sub>4</sub> (n=453) vs Diazepam (n=453)
  - MgSO<sub>4</sub> (n=388) vs. Phenytoin (n=387)

# Results



# Results



# Magnesium sulfate

- Used as both prophylaxis and treatment for eclampsia
  - All women with severe preeclampsia should receive magnesium
- Continuous infusion
  - 6 gram loading dose diluted in 100cc of IVF over 15-20 minutes
  - 2g/hr thereafter until 24 hours post partum
  - May consider Mg levels every 4-6 hours (4-6 mEq/L)
- Intramuscular
  - 10 grams of 50% MgSO<sub>4</sub> solution injected as divided dose into each buttock

# MgSO4 levels

- >25 mEq/L **Arrest**
- 15 mEq/L **Respiratory paralysis**
- 10 mEq/L **Loss of DTR**
- 5-10 mEq/L **EKG changes**
- 4-6 mEq/L **Seizure prophylaxis**

“Mag check” →

- ✓ Ask about lethargy, SOB
- ✓ Check O2 sats, UOP, DTR

# Persistent eclamptic seizures

- 10-15% have subsequent convulsion after initial MgSO<sub>4</sub> therapy
  - ✓ Consider additional 2g bolus of IV MgSO<sub>4</sub>
- If seizures are persistent
  - ✓ Other anticonvulsant drugs may be considered
  - ✓ Consider alternative diagnosis and imaging



# Differential Diagnosis

- consider if >48-72h PP or on MgSO<sub>4</sub>
- Brain tumor
- Encephalitis
- Meningitis
- Seizure disorder
- Metabolic disorders
  - Hypoglycemia
  - Hyponatremia
- CVA
  - Hemorrhage
  - Ruptured aneurysm
  - Embolism
  - Thrombosis
  - Angioma
- TTP
- Cerebral vasculitis

# HELLP Syndrome

- Hemolysis
  - LDH, peripheral smear, haptoglobin
- Elevated Liver enzymes
  - AST/ALT > 2x ULN
- Low Platelets
  - Plate count < 100,000

# HELLP Syndrome

- Can occur antepartum or postpartum
- If <33 6/7wks it is suggested that delivery be delayed for 24-48h if maternal and fetal condition remain stable to allow for corticosteroids
- For women at 34 0/7 weeks or more delivery soon after maternal initial stabilization

# CHTN with superimposed preeclampsia

- Superimposed preeclampsia develops in 13-40%
- Superimposed preeclampsia likely when:
  - A sudden increase in BP that was previously well controlled
  - New onset proteinuria or a sudden increase in proteinuria
- Stratified into 2 groups
  - Superimposed preeclampsia
  - Superimposed preeclampsia with severe features

# CHTN with superimposed preeclampsia

- For women without severe features and stable maternal and fetal condition expectant management until 37 0/7 weeks
- Paucity of data on outpt management
  - Home BP monitoring daily
  - Physician visits 1-2x/wk
  - Weekly laboratory testing
  - Fetal surveillance

# Superimposed preeclampsia with severe features

- Superimposed preeclampsia with severe features:
  - Severe hypertension despite escalation of antihypertensive therapy
  - Persistent cerebral or visual disturbances or RUQ pain
  - AST/ ALT > 2x/ULN
  - Platelets < 100,00
  - Pulmonary edema
  - Creatinine level above 1.1mg/d or doubling
- When severe features are present, magnesium sulfate is recommended during the intrapartum-postpartum period
- Expectant management beyond 34 0/7 weeks is not recommended

# Postpartum Management

- In women with the diagnosis of
  - Preeclampsia
  - Gestational hypertension
  - Superimposed preeclampsia

it is suggested that BP be monitored in the hospital for at least 72h postpartum and again 7-10 days after delivery
- BP usually decreases within 48h after delivery, but increases again 3-6 days postpartum
- For women with persistent SBP  $\geq 150$  or DBP  $\geq 100$  on at least 2 occasions that are 4-6h apart, antihypertensive therapy is suggested
- Persistent SBP  $\geq 160$  or DBP  $\geq 110$  should be treated within 1 hour

# Postpartum Hypertension

- BP remains labile for months postpartum, usually normalizing by the end of the first year
- For women who present after delivery with:
  - New-onset hypertension associated with HA or visual changes
  - Preeclampsia with severe hypertension

The parental administration of magnesium sulfate is recommended for at least 24h



# Postpartum management

- Education of patients on symptoms
- Education of health professional that preeclampsia can occur up to 4 weeks postpartum
- Contribution of NSAIDs to increase BP, consider replacing in women with hypertension that persists for more than 1 day postpartum

# Management of women with prior preeclampsia

- Preconception (can be done at 6wk PP visit)
  - Weight loss / Nutrition consult
  - Increased physical activity
  - Optimize control of BP and diabetes
  - Perform baseline metabolic profile and urinalysis
  - Recommend early establishment of prenatal care
- Antepartum
  - Early ultrasound for dating
  - Baseline labs
  - Frequent PNC visits to monitor symptoms, BP, proteinuria
  - Serial ultrasounds for fetal growth

# Prevention of preeclampsia

- Low dose aspirin was shown in a meta-analysis to provide a slight reduction in preeclampsia
  - >300,000 women from 31 trials
  - RR 0.90 (95% CI 0.84-0.97)
  - However larger trials did not show a benefit
  - No increase in major adverse effects
- Daily low-dose aspirin beginning in the late first trimester
  - History of early-onset preeclampsia requiring preterm delivery at less than 34 0/7 weeks
  - Preeclampsia in more than one prior pregnancy

# Prevention of preeclampsia

- Things that don't work
  - Vitamin C and E
  - Calcium
  - Fish oil
  - Bed rest/ Activity restriction
  - Salt restriction

# References

- American College of Obstetricians and Gynecologists. Task Force on Hypertension in Pregnancy, author. Hypertension in Pregnancy – Practice Guideline WQ 244