PREGNANCY RELATED HYPERTENSION AND DIABETES

Therapeutic Management

August 2021
Collaborators
More resources available at:
https://dchealth.dc.gov/dcrx
Course Overview

• Hypertensive Disorders of Pregnancy
  – Prevalence
  – Risk and screening
  – Management
  – Medications

• Gestational Diabetes
  – Prevalence
  – Risk and screening
  – Management
  – Medications
Presenters

• Rita W. Driggers
  – Medical Director, Maternal Fetal Medicine, Sibley Memorial Hospital, Johns Hopkins Medicine

• Tara Bastawrous, PharmD, BCPS, BC-ADM
  – Clinical Pharmacy Specialist, Kaiser Permanente Mid-Atlantic States

• Elaine Yip, PharmD, BCPS
  – Clinical Pharmacy Specialist, Kaiser Permanente Mid-Atlantic States
Advisors

• Tiffany R. Gray, DrPH, MPH
  – Public Health Advisor, DC Department of Health

• Danielle R. Waldrop, MD, FACOG, MBA, Med
  – OB/GYN, Moore Obstetrics and Gynecology
Conflicts of Interest

• None of the speakers or advisors have a conflict of interests to declare.
Important Information

The video will progress at its own pace.

Do not attempt to speed up the video.

The video can be paused and resumed later.
Hypertensive Disorders of Pregnancy

August 2021
Rita W. Driggers, MD
Medical Director, Maternal Fetal Medicine
Sibley Memorial Hospital, Johns Hopkins Medicine
Objectives

At the completion of this module, the learner should possess the knowledge to:

- Recognize and properly diagnose pregnancies complicated by chronic hypertension, gestational hypertension, and preeclampsia
- Counsel patients about the complications and risks associated with hypertensive disorders of pregnancy
- Manage or describe the management of and make appropriate referrals for pregnancies complicated by chronic hypertension, gestational hypertension, and preeclampsia
- Manage or describe the management of and make appropriate referrals for pregnancies complicated by hypertensive emergencies, and eclampsia
Impact/Prevalence

• Age-adjusted trend in hypertension prevalence among adults aged 18 and over, by sex: United States, 1999 -2018

NCHS Data Brief No. 364, April 2020
Impact/Prevalence

• Prevalence of hypertension among adults aged 18 and over, by sex and age: United States, 2017-2018
Impact/Prevalence

- Age-adjusted prevalence of hypertension among adults aged 18 and over, by race and Hispanic origin: United States, 2017-2018

NCHS Data Brief No. 364, April 2020
Impact/Prevalence

Prevalence of Hypertension, 2017
U.S. Adults Ages 20 and Older

Data Source:
BRFSS - Behavioral Risk Factor Surveillance System, CDC.

Self-report: “Have you ever been told by a doctor, nurse, or other health care professional that you have high blood pressure?” Excludes women who reported being told only during pregnancy and respondents who reported they had been told that their blood pressure was borderline high or pre-hypertensive.
Impact/Prevalence

Rate of hypertensive disorders per 10,000 delivery hospitalizations

Hypertensive disorders in pregnancy

Chronic hypertension

Impact/Prevalence

Direct Causes of Maternal Mortality

- Haemorrhage: 35%
- Hypertension: 18%
- Sepsis: 8%
- Abortion: 9%
- Other Direct: 12%
- Indirect: 18%

Deliveries by maternal health conditions

Distribution of DC-resident delivery hospital discharges by mother’s health conditions that complicated the pregnancy or delivery, 2016-2019

GESTATIONAL HYPERTENSION
- No: 88%
- Yes: 12%

PREEXISTING HYPERTENSION
- No: 96%
- Yes: 4%

Data Source: Hospital Discharge Data for 2016-2019, DC Hospital Association
Knowledge Check

Which of the following groups has the highest prevalence of hypertension

A. Non-Hispanic white adults
B. Non-Hispanic black adults
C. Hispanic adults
Definitions/Classifications

• Chronic hypertension
  – 2017 America College of Cardiology and the American Heart Association modified blood pressure categories:
    o Normal: Less than 120/80 mmHg
    o Elevated: Systolic between 120-129 and diastolic less than 80 mmHg
    o Stage 1: Systolic between 130-139 or diastolic between 80-89 mmHg
    o Stage 2: Systolic at least 140 or diastolic at least 90 mmHg
  – Resulted in increase in prevalence of hypertension from ~32% to ~46% in the US adult population

Definitions/Classifications

• Chronic hypertension in pregnancy
  – Defined as hypertension diagnosed or present before pregnancy or before 20 weeks of gestation
  – Hypertension that is diagnosed for the first time during pregnancy and that does not resolve in the typical postpartum period
  – Traditional BP criteria:
    o Systolic BP of 140 mmHg or higher
    o Diastolic BP of 90 mmHg or higher
  – Requires at least two readings at least 4 hours apart

ACOG Practice Bulletin #203, Jan 2019
Definitions/Classifications

• Preeclampsia
  – Systolic BP of 140 mmHg or higher or diastolic BP of 90 mm Hg or higher on two occasions at least 4 hours apart after 20 weeks in a woman with a previously normal blood pressure, and
  – Proteinuria
    o 300mg or higher on 24-hour urine collection
    o Protein: Creatinine ratio of 0.3 or more
    o Dipstick reading of 2+ protein
  – Preeclampsia may be diagnosed without proteinuria if severe features are present
Definitions/Classifications

- Preeclampsia with severe features
  - Systolic blood pressure of 160 mm Hg or higher, or diastolic blood pressure of 110 mm Hg or higher on two occasions at least 4 hours apart
  - Thrombocytopenia: Plt < 100k
  - Renal insufficiency: Cr > 1.1mg/dl or doubled
  - Impaired liver function: Liver transaminases twice upper limits of normal or severe persistent RUQ or epigastric pain
  - Pulmonary edema
  - Headache unresponsive to medication and not explained by alternative diagnosis
  - Visual disturbances

ACOG Practice Bulletin #222, Dec 2018
Definitions/Classifications

• Gestational hypertension
  – Defined as systolic BP 140 mmHg or higher OR diastolic BP 90 mmHg or higher on two occasions at least 4 hours apart after 20 weeks with previously normal BP
  – Considered severe when systolic BP reaches 160 mmHg or diastolic BP reaches 110 mmHg
  – Occurs without proteinuria or lab abnormalities
  – Develops after 20 weeks and resolves in the postpartum period
  – May not truly be distinct entity from preeclampsia

ACOG Practice Bulletin #222, Dec 2018
Definitions/Classifications

• Hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome
  – More severe form of preeclampsia
  – Associated with increased rates of maternal morbidity and mortality
  – Suggested diagnostic criteria:
    o AST or ALT more than twice upper limits of normal
    o Platelets < 100k
    o LDH ≥ 600 IU/L

ACOG Practice Bulletin #222, Dec 2018
Clin Perinatol 2004;31:807-33
Am J Obstet Gynecol 1990;162:311-16
Am J Obstet Gynecol 1999;180:1373-84
Am J Obstet Gynecol 1995;172:1876-8
Definitions/Classifications

• Eclampsia
  – Most severe manifestation of hypertensive disorders of pregnancy
  – New-onset seizures in absence of other causes
  – Significant cause of maternal mortality, especially in low-resource settings
  – Occurs in small proportion of patients:
    o 1.9% with preeclampsia
    o 3.2% with severe features

ACOG Practice Bulletin #222, Dec 2018
J Repro Med 1987;32:499-503
Lancet 2002;359:1877–90
Definitions/Classifications

• Eclampsia
  – Often preceded by signs of cerebral irritation
    o Severe occipital or frontal headache
    o Blurred vision/photophobia
    o Altered mental status
  – May occur before, during, or after labor
  – Up to 38% do not have hypertension or proteinuria prior to seizure

ACOG Practice Bulletin #222, Dec 2018
Semin Perinatol 2009;33:166–72
Knowledge Check

The primary difference between gestation hypertension and preeclampsia is:

A. Blood pressure levels
B. Whether proteinuria is present
C. Gestational age at diagnosis
D. Whether blood pressure levels return to normal in the postpartum period
Risk factors for chronic hypertension

• Age, sex, race/ethnicity
• Elevated BP: Systolic between 120-129 and diastolic less than 80 mmHg
• Diabetes
• Unhealthy diet
• Physical inactivity
• Obesity
• Too much alcohol
• Tobacco use
• Genetics and family history

www.cdc.gov/bloodpressure/risk_factors.htm
Risk factors for preeclampsia

- Nulliparity
- Multifetal gestations
- Preeclampsia in a previous pregnancy
- Chronic hypertension
- Pregestational diabetes
- Gestational diabetes
- Thrombophilia
Risk factors for preeclampsia

• Systemic lupus erythematosus
• Prepregnancy body mass index greater than 30
• Antiphospholipid antibody syndrome
• Maternal age 35 years or older
• Kidney disease
• Assisted reproductive technology
• Obstructive sleep apnea
Knowledge Check

Which of the following is NOT a risk factor for BOTH chronic hypertension AND preeclampsia:

A. Advancing age
B. Diabetes
C. Obesity
D. Thrombophilia
Maternal complications of chronic hypertension

• If poorly controlled:
  – Maternal mortality
  – Cerebrovascular accidents
  – Pulmonary edema
  – End-organ damage (heart, brain, kidneys)

• Gestational diabetes
• Superimposed preeclampsia
• Cesarean delivery
• Postpartum hemorrhage
Maternal complications of preeclampsia

• Progression to eclampsia
  – Seizures may lead to
    o Maternal hypoxia
    o Trauma
    o Aspiration pneumonia
  – Residual neurologic damage is rare

• Increased risk of chronic hypertension and cardiovascular disease
Fetal/neonatal complications of maternal chronic hypertension

- Stillbirth or perinatal death
  - Independent of other possible contributors
- Growth restriction (17%)
- Preterm birth (28%)
  - Indicated, not spontaneous
- Congenital anomalies
  - Cardiac, hypospadias, esophageal atresia
- Placental abruption

ACOG Practice Bulletin #203, Jan 2019
J Perinatol 1997;17:425–7
BJOG 2008;115:1436–42
BMJ 2014;348:g2301
BJOG 2015;122:1002–9
Fetal/neonatal complications of maternal preeclampsia

• Fetal growth restriction
• Oligohydramnios
• Placental abruption
• Non-reassuring fetal heart rate monitoring
• Preterm birth
  – Spontaneous or indicated

ACOG Practice Bulletin #222, Dec 2018
Ultrasound Obstet Gynecol 2012;40:373–82
Knowledge Check

Fetal/neonatal risks of BOTH chronic hypertension and preeclampsia include all of the following EXCEPT:

A. Fetal growth restriction
B. Placental abruption
C. Congenital anomalies
D. Preterm birth
Management – Chronic Hypertension

• Preconception
  – Evaluate for end-organ damage
  – Optimize maternal co-morbidities
  – Optimize BP control
  – Medication review
  – Explain maternal and fetal/neonatal risks
  – Evaluate for causes of secondary hypertension

ACOG Practice Bulletin #203, Jan 2019
Obstet Gynecol 2015;126:e112–26
Obstet Gynecol 2009;113:1405–13
Management – Chronic Hypertension

### Box 3. Historical Features Favoring Hypertension Cause

<table>
<thead>
<tr>
<th>Primary Hypertension</th>
<th>Secondary Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gradual increase in BP, with slow rate of rise in BP</td>
<td>BP lability, episodic pallor, and dizziness (pheochromocytoma)</td>
</tr>
<tr>
<td>Lifestyle factors that favor higher BP (e.g., weight gain, high-sodium diet, decreased physical activity, job change entailing increased travel, excessive consumption of alcohol)</td>
<td>Snoring or hypersomnolence (obstructive sleep apnea)</td>
</tr>
<tr>
<td>Family history of hypertension</td>
<td>Muscle cramps or weakness (hypokalemia from primary aldosteronism or secondary aldosteronism due to renovascular disease)</td>
</tr>
</tbody>
</table>

### Abbreviations: BP, blood pressure; NSAIDs, nonsteroidal antiinflammatory drugs.

Management – Chronic Hypertension

• Baseline evaluation
  – Serum aspartate aminotransferase and alanine aminotransferase
  – Serum creatinine
  – Serum electrolytes (specifically potassium)
  – Blood urea nitrogen
  – Complete blood count
  – Spot urine protein/creatinine ratio or 24-hour urine for total protein and creatinine
  – Electrocardiogram or echocardiogram as appropriate

• Usual BP changes in pregnancy

• Low-dose aspirin (81mg)
Management – Chronic Hypertension

• BP treatment goals during pregnancy
  – Studies evaluating tight versus less tight control of BPs
  – Tight control of hypertension
    o Conferred no benefit to the fetus
    o Had only marginal effects for the woman (reduced frequency of progression to severe hypertension)

• Initiate antihypertensive therapy for persistent chronic hypertension:
  – Systolic BP ≥ 160mmHg
  – Diastolic BP ≥ 110mmHg

• Treat at lower blood pressure thresholds with comorbidities
Management – Chronic Hypertension

• BP treatment goals during pregnancy
  – Limited data on ideal BP
  – Lowering BP too much may compromise uteroplacental blood flow
  – Current recommendations:
    o Systolic BP at or above 120mmHg but less than 160mmHg
    o Diastolic BP at or above 80mmHg but less than 110mmHg
    o Lower BPs for women with comorbid conditions

ACOG Practice Bulletin #203, Jan 2019
Management – Chronic Hypertension

• Maternal and fetal monitoring
  – Close monitoring of BPs
  – Assessment of fetal growth
  – Antenatal fetal surveillance

• Delivery timing
  – Delivery by 38+0-39+6 weeks with CHTN on no meds
  – Delivery by 37+0-39+6 weeks with CHTN controlled on meds
  – Delivery by 36+0-37+6 weeks with CHTN difficult to control
  – Delivery by 34 weeks or sooner with superimposed preeclampsia
Management – Chronic Hypertension

• Postpartum considerations
  – BP control continues to be an issue postpartum
  – After initial decline immediately after delivery, BPs rise
  – Severe hypertension or superimposed preeclampsia may develop
    o Outpatient follow up the first 1-2 weeks
    o Home BP monitoring
  – Goal BP postpartum:
    o Systolic BP ≤ 150mmHg
    o Diastolic BP < 100mmHg

ACOG Practice Bulletin #203, Jan 2019
Obstet Gynecol 2018;131:e140–50
Obstet Gynecol 2018;131:e140–50
Cochrane Database of Systematic Reviews 2013, Issue 4. Art. No.: CD004351
Hypertens Pregnancy 2010;29:294–300
Knowledge Check

Which of the following is TRUE about chronic hypertension during pregnancy?

A. Blood pressure goals during pregnancy are lower than when not pregnant
B. Blood pressure normally decreases in the 2nd trimester and this decrease may be more profound in patients with chronic hypertension
C. Very tight control of blood pressures improves fetal outcomes
D. Blood pressure goals immediately postpartum are the same as during pregnancy
Management – Gestational Hypertension or Preeclampsia

• Delivery is the only cure for GHTN/preeclampsia

• Delaying delivery increases likelihood that preeclampsia will progress (to severe preeclampsia, HELLP, or eclampsia)

• Initial evaluation:
  – Labs (CBC, Cr, LDH, AST, ALT, testing for proteinuria)
  – Ultrasound for estimated fetal weight and amniotic fluid index
  – Fetal monitoring

• Subsequent management depends on gestational age and test results
  – Must balance maternal and fetal risks

ACOG Practice Bulletin #222, Dec 2018
Management – Gestational Hypertension or Preeclampsia

• Mild preeclampsia or gestational hypertension ≥37 weeks
  – Delivery is recommended
  – Administration of intrapartum-postpartum magnesium sulfate to prevent eclampsia is not recommended as long as BPs are in mild range (SBP<160mm Hg and DBP <110mm Hg) and the patient is without symptoms
  – Monitor BPs in the hospital for at least 72 hours postpartum and again 7-10 days after delivery, earlier in women with symptoms

ACOG Practice Bulletin #222, Dec 2018
Management – Gestational Hypertension or Preeclampsia

• Mild preeclampsia or gestational hypertension <37 weeks
  – Close monitoring as follows:
    o Serial assessment of maternal symptoms and fetal movement (daily by the patient)
    o Twice weekly BP checks (at least once in office, once at home by patient)
    o Weekly assessment of platelet counts and liver enzymes
    o Once or twice weekly fetal monitoring

ACOG Practice Bulletin #222, Dec 2018
Management – Gestational Hypertension or Preeclampsia

• Mild preeclampsia or gestational hypertension <37 weeks
  – Do not treat SBP <160mm HG or DBP <110mm Hg (if BPs are greater than this, patient now has severe disease)
  – Strict bedrest is NOT recommended, but decreased activities may be indicated
  – Serial growth assessments every 3-4 weeks
Management – Gestational Hypertension or Preeclampsia

• Mild preeclampsia or gestational hypertension <37 weeks
  – Delivery is recommended at 37 weeks if not indicated prior for severe disease
  – Administration of intrapartum-postpartum magnesium sulfate to prevent eclampsia is not recommended as long as BPs are in mild range (SBP<160mm Hg and DBP <110mm Hg) and the patient is without symptoms
  – Monitor BPs in the hospital for at least 72 hours postpartum and again 7-10 days after delivery, earlier in women with symptoms

ACOG Practice Bulletin #222, Dec 2018
Management – Gestational Hypertension or Preeclampsia

• Severe preeclampsia or gestational hypertension ≥34 weeks
  – Delivery is recommended after maternal stabilization
  – Administration of intrapartum-postpartum magnesium sulfate to prevent eclampsia is recommended
  – For women undergoing cesarean delivery, the intraoperative administration of parenteral magnesium sulfate to prevent eclampsia is recommended
  – Monitor BPs in the hospital for at least 72 hours postpartum and again 7-10 days after delivery, earlier in women with symptoms

ACOG Practice Bulletin #222, Dec 2018
Management – Gestational Hypertension or Preeclampsia

• Severe preeclampsia or gestational hypertension <34 weeks
  – If stable maternal and fetal conditions, expectant management with close observation is recommended
  – Treat sustained systolic BPs > 160mmHg or diastolic BPs > 110mmHg
  – Give corticosteroids to decrease morbidities associated with prematurity
Management – Gestational Hypertension or Preeclampsia

• Severe preeclampsia or gestational hypertension < 34 weeks
  – Give corticosteroids to decrease morbidities associated with prematurity and deliver after 48 hours with any of the following:
    o PPROM
    o Labor
    o Platelets < 100,000 per microliter
    o Transaminases persistently twice or more the upper normal values
    o IUGR (EFW<5th percentile)
    o Severe oligohydramnios (AFI < 5cm)
    o Umbilical artery reversed end diastolic flow
    o New onset renal insufficiency (doubling of Cr or Cr > 1.1mg/dl)
Management – Gestational Hypertension or Preeclampsia

• Severe preeclampsia or gestational hypertension <34 weeks
  – Give corticosteroids but DO NOT delay delivery (after initial maternal stabilization) regardless of gestational age for any of the following:
    o Uncontrollable severe hypertension
    o Eclampsia
    o Pulmonary edema
    o Abruptio placentae
    o Disseminated intravascular coagulation
    o Non-reassuring fetal status
    o IUFD

ACOG Practice Bulletin #222, Dec 2018
Management – Gestational Hypertension or Preeclampsia

• Severe preeclampsia or gestational hypertension <34 weeks
  – Mode of delivery need not be cesarean delivery (determine by presentation, cervical exam, and maternal/fetal conditions)
  – Administration of intrapartum-postpartum magnesium sulfate to prevent eclampsia is recommended
  – For women undergoing cesarean delivery, the intraoperative administration of parenteral magnesium sulfate to prevent eclampsia is recommended
  – Monitor BPs in the hospital for at least 72 hours postpartum and again 7-10 days after delivery, earlier in women with symptoms

ACOG Practice Bulletin #222, Dec 2018
Management – Gestational Hypertension or Preeclampsia

• Severe preeclampsia or gestational hypertension prior to viability
  – Delivery after maternal stabilization is recommended
  – Monitor BPs in the hospital for at least 72 hours postpartum and again 7-10 days after delivery, earlier in women with symptoms
Management – Gestational Hypertension or Preeclampsia

• HELLP syndrome
  
  – If prior to fetal viability or $\geq34$ weeks, delivery should be undertaken shortly after initial maternal stabilization
  
  – If after viability but $<34$ weeks, delay delivery for 24-48 hours (to administer corticosteroids) if maternal and fetal condition remains stable
  
  – Monitor BPs in the hospital for at least 72 hours postpartum and again 7-10 days after delivery, earlier in women with symptoms

ACOG Practice Bulletin #222, Dec 2018
Management – Gestational Hypertension or Preeclampsia

• Postpartum gestational hypertension/preeclampsia
  
  - For women in the postpartum period who present with new-onset hypertension associated with headaches or blurred vision or preeclampsia with severe hypertension, the parental administration of magnesium sulfate is recommended

  - For women with persistent postpartum hypertension, SBP > 150 mmHg or DBP > 100 mmHg, on at least 2 occasions 4-6 hours apart, anti-hypertensive therapy is as needed for BP elevations above the cut off

  - SBP > 160 mmHg or DBP > 110 mmHg should be treated within 1 hour

  - Monitor BPs in the hospital for at least 72 hours postpartum and again 7-10 days after delivery, earlier in women with symptoms

ACOG Practice Bulletin #222, Dec 2018
Management – Gestational Hypertension or Preeclampsia

• Counseling for future pregnancies
  – Prone to hypertensive complications in future pregnancies
  – At increased risk of later life cardiovascular disease
  – The earlier preeclampsia occurred, the more likely it is to recur
  – Risk of recurrence:
    o 15% for women who had preeclampsia in one previous pregnancy
    o 30% for women who had preeclampsia in previous two pregnancies
    o 40% for nulliparous women who were diagnosed prior to 30 weeks
    o 5-7% for women with one episode of HELLP
Management – Gestational Hypertension or Preeclampsia

• Counseling for future pregnancies
  – With subsequent development of preeclampsia, there is high incidence of:
    o Preterm delivery
    o Fetal growth restriction
    o Placental abruption
    o Cesarean delivery
  – Initiate daily low-dose aspirin (81mg) beginning in the late first trimester is suggested
    o Therapy should be initiated prior to 16 weeks in order to improve trophoblast invasion which is typically complete by 20 weeks gestation
Knowledge Check

Which of the following statements is FALSE about the management of preeclampsia and gestational hypertension:

A. Mild preeclampsia or gestational hypertension prior to 37 weeks may be managed expectantly with close follow up

B. Delivery is indicated for severe preeclampsia at or beyond 34 weeks

C. If HELLP syndrome is diagnosed at 32 weeks, delivery is indicated after maternal stabilization

D. If preeclampsia with severe features is diagnosed prior to fetal viability, delivery is recommended after maternal stabilization
Conclusions/Summary

• Prevalence of hypertensive disorders of pregnancy is increasing
• Pregnancies complicated by hypertensive disorders of pregnancy are at increased risk for maternal and fetal/neonatal complications
• Recognizing and properly diagnosing pregnancies complicated by chronic hypertension, gestational hypertension, and preeclampsia is vital to reducing these complications
Conclusions/Summary

- Counseling patients about the complications and risks associated with hypertensive disorders of pregnancy will empower patients to seek medical advice when appropriate.

- Appropriate management of pregnancies complicated by chronic hypertension, gestational hypertension, and preeclampsia decreases maternal and fetal/neonatal complications.
Pharmacologic Management of Hypertension in Pregnancy

August 2021
Tara Bastawrous, PharmD, BCPS, BC-ADM
Elaine Yip, PharmD, BCPS
Clinical Pharmacy Specialists, Kaiser Permanente Mid-Atlantic States
Objectives

• Determine first line options for the treatment of hypertension in pregnancy
• Describe benefits and risks of therapies in the treatment of hypertension in pregnancy
• Recognize antihypertensive medications to be avoided during pregnancy
• Identify major patient counseling points on appropriate administration of medications and strategies to improve adherence
Is Pharmacotherapy Necessary?

• The American College of Obstetricians and Gynecologists (ACOG) recommends not initiating medication for mild chronic hypertension (>140/90 mmHg and <160/110 mmHg)
  – Consider discontinuing medication in women with mild hypertension who become pregnant and recommend lifestyle modifications

• Pharmacotherapy is recommended for pregnant women with severe hypertension (systolic BP >160 mmHg or diastolic BP ≥105-110 mmHg)
  – Initiate medications at BP ≥150/100 mmHg in women with end-organ involvement, such as cardiac or renal disease
## 1st Line Preferred Agents

<table>
<thead>
<tr>
<th></th>
<th>Labetalol</th>
<th>Nifedipine ER</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Class</strong></td>
<td>Combined Alpha and Beta blocker</td>
<td>Calcium Channel Blocker</td>
</tr>
</tbody>
</table>
| **Dosing**| Initial: 100mg twice daily, increase by 100mg twice daily every 2 to 3 days as needed  
     Usual effective dose: 200 to 800mg in 2 divided doses  
     Max total daily dose: 2400mg | Initial: 30 to 60mg once daily, increase at 7-14 day intervals  
     Usual effective dosage: 30 to 90mg once daily  
     Max total daily dose: 120mg |
| **Side effects**| Bronchoconstriction | Flushing, peripheral edema, heartburn, nausea, dizziness |
| **Data in pregnancy**| Crosses the placenta  
     May be associated with fetal growth restriction and neonatal bradycardia | Crosses the placenta  
     Increase in perinatal asphyxia, cesarean delivery, prematurity, and intrauterine growth retardation have been reported |
# 2nd Line Preferred Agents

<table>
<thead>
<tr>
<th>Class</th>
<th>Hydrochlorothiazide</th>
<th>Metyldopa</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diuretic</td>
<td>Central acting alpha agonist</td>
</tr>
</tbody>
</table>

## Dosing

- **12.5 to 25mg daily**
  - **Initial:** 250mg 2 to 3 times daily, increase every 2 days as needed
  - **Usual effective dosage:** 250 to 1000mg in 2 to 3 divided doses
  - **Max total daily dose:** 3000mg

## Side effects

- **Volume depletion**
- **Electrolyte disorders**
- **Sedation**
- **Depression**

## Data in pregnancy

- **Crosses the placenta**
- **May cause neonatal jaundice, thrombocytopenia, or other adverse events observed in adults**
- **Crosses the placenta**
- **Data shows use in pregnancy does not cause fetal harm and improves fetal outcomes**

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Adv Chronic Kidney Dis 2007; Am Fam Physician 2015; Lexicomp 2021

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## Alternative Agents

<table>
<thead>
<tr>
<th></th>
<th>Hydralazine</th>
<th>Clonidine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Class</strong></td>
<td>Vasodilator</td>
<td>Alpha2-Adrenergic Agonist</td>
</tr>
</tbody>
</table>
| **Dosing**           | - Initial 10mg orally 4 times daily, titrating 10 to 25mg/day every 2 to 5 days  
- Usual Effective Dose: 50-100mg orally in 2 to 4 divided doses  
- Max total daily dose: 200mg | - Initial 0.1mg twice daily, titrating in increments of 0.1mg/day weekly as needed/tolerated  
- Usual Effective Dose: 0.2 to 0.6mg/day in 2 divided doses  
- Max total daily dose: 2.4mg |
| **Side effects**     | - Reflex tachycardia  
- Edema  
- Nausea/Vomiting/Diarrhea | - Rebound hypertension if stopped suddenly  
- Orthostatic hypotension  
- Nausea/GI pain/Constipation |
| **Data in pregnancy**| - Crosses the placenta  
Pharmacokinetics may be altered due to pregnancy-induced physiologic changes and maternal acetylator status (NAT2 genotype) | - Crosses the placenta  
Pharmacokinetics may be altered due to increase in nonrenal clearance in pregnancy, possibly regulated by CYP2D6 genotype |
# Preferred Agents in Hypertensive Emergency

<table>
<thead>
<tr>
<th></th>
<th>Labetalol</th>
<th>Hydralazine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Class</strong></td>
<td>Combined Alpha and Beta Blocker</td>
<td>Vasodilator</td>
</tr>
<tr>
<td><strong>Dosing</strong></td>
<td>• 20mg IV gradually over 2 minutes</td>
<td>• 5mg IV gradually over 1 to 2 minutes</td>
</tr>
<tr>
<td></td>
<td>• Continuous infusion of 1 to 2mg/minute can be used instead of intermittent therapy, or started after initial 20mg dose</td>
<td></td>
</tr>
<tr>
<td><strong>Monitoring</strong></td>
<td>• Reassess BP at 10 minute intervals</td>
<td>• Reassess BP at 20 minute intervals</td>
</tr>
<tr>
<td></td>
<td>• If BP remains above target at 10 minutes, give 40mg IV over 2 minutes</td>
<td>• If BP remains above goal at 20 minutes, give 5 or 10mg IV over 2 minutes</td>
</tr>
<tr>
<td></td>
<td>• Reassess BP every 10 minutes thereafter. If continuously above target, then give 80mg IV over 2 minutes</td>
<td>• If BP remains above goal at 40 minutes, give 10mg IV over 2 minutes</td>
</tr>
<tr>
<td></td>
<td>• Cumulative max dose- 300mg.</td>
<td>• Cumulative max dose- 30mg</td>
</tr>
</tbody>
</table>

Obstet Gynecol 2017; Obstet Gynecol 2020
### Alternative Agents in Hypertensive Emergency

<table>
<thead>
<tr>
<th></th>
<th>Nifedipine ER</th>
<th>Nicardipine</th>
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<tbody>
<tr>
<td><strong>Class</strong></td>
<td>Calcium Channel Blocker</td>
<td>Calcium Channel Blocker</td>
</tr>
<tr>
<td><strong>Dosing</strong></td>
<td>• Initial 30mg orally</td>
<td>• Initial dose of 5mg/hour IV by infusion pump, can be increased to max of</td>
</tr>
<tr>
<td></td>
<td>• Repeat dose of 30mg if target dose is not achieved in 1-2 hours</td>
<td>15mg/hour</td>
</tr>
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<td></td>
<td></td>
<td>• Onset of action 5-15 minutes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Avoid rapid titration to minimize risk of overdosing</td>
</tr>
<tr>
<td><strong>Monitoring</strong></td>
<td>• If goal BP is not achieved after 2 doses, consider administering a different class of agents</td>
<td>• Adjust dose within above range to achieve targeted BP</td>
</tr>
</tbody>
</table>

Obstet Gynecol 2017; Obstet Gynecol 2020
Magnesium Sulfate

• Prevent convulsions in the setting of eclampsia/preeclampsia

• Initial IV: 4 to 6 g loading dose over 15-30 minutes at onset of labor or induction/cesarean delivery
  – 1 to 2g/hour continuous infusion for at least 24 hours after delivery (max infusion rate 3g/hour)
  – Administer bolus of 2 to 4g over at least 5 minutes if seizure occurs while administering magnesium
  – Max dose: 40g/24hours

• Calcium gluconate should be available to treat magnesium toxicity if needed
Antihypertensive Agents to Avoid

• ACEI, ARBs
  – Crosses the placenta
  – Increased risk of fetal malformations

• Mineralocorticoid receptor antagonists (eplerenone, spironolactone)
  – Crosses the placenta
  – May cause feminization of male fetus (spironolactone)
  – High doses have been associated with intrauterine growth restriction
Knowledge Check

JP has now become pregnant. Her provider does not want to further increase labetalol due to fear of further decreasing HR, however, her BP is not sufficiently controlled. Which medication would be the best to add on?

A. Thiazide
B. Nifedipine ER
C. Clonidine
D. Losartan
Conclusions

• Labetalol and nifedipine are the preferred antihypertensive agents in pregnancy

• Pharmacists are a valuable resource to ensure patients stay adherent to their medications for optimal outcomes for both mother and baby and to assist in choosing the safest medications
References


Gestational Diabetes

August 2021
Rita W. Driggers, MD
Medical Director, Maternal Fetal Medicine
Sibley Memorial Hospital, Johns Hopkins Medicine
Objectives

• At the completion of this module, the learner should possess the knowledge to:
  – Identify patients at increased risk for the development of gestational diabetes
  – Describe the most frequently used gestational diabetes testing protocols
  – Counsel patients about the risks of gestational diabetes to the mom and the baby
  – Properly manage a pregnancy complicated by gestational diabetes
Impact/Prevalence

1980
First International Workshop on GDM
GDM defined as “carbohydrate intolerance of variable severity recognized for the first time in pregnancy.” Recommended that all women be screened at 24-28 weeks using the 100g DOTT with O’Sullivan and Mahan’s diagnostic criteria.

1984
Second International Workshop on GDM
Proposed 50g oral glucose challenge test (OGCT)

1990
Third International Workshop on GDM
Minor modifications to screening and diagnostic criteria.

1997
Fourth International Workshop on GDM
Change screening criteria to identify low, average and high risk women. Modify diagnostic criteria to use Carpenter and Coustan’s cutoffs for the 100g OGTT and 75g OGTT.

1998
WHO Update Definition of GDM
WHO classifies any glucose levels above normal as indicative of GDM

2001
ACHOS RCT Published (1995-2003)
Treatment of women with gestational diabetes (dietary advice, blood glucose monitoring, insulin therapy) reduced rate of serious perinatal outcomes. Previously no conclusive evidence of the effect of treatment of GDM.

2008
HAPO RCT Published
Evidence of a strong, continuous association of maternal glucose levels with increased birth weight and increased cord blood serum C-peptide levels

2010
International Association of Diabetes and pregnancy Study Groups Consensus Panel
Modifies diagnostic criteria for GDM based on HAPO results.

Lavery BJOG 2017
Country-specific Prevalence of GDM

Median (interquartile range) prevalence (%) of GDM by World Health Organization region, 2005-2015

Prevalence of GDM Among Women with Live Birth in 2016

CDC MMWR Nov 2, 2018
Deliveries by maternal health conditions

Distribution of DC-resident delivery hospital discharges by mother’s health conditions that complicated the pregnancy or delivery, 2016-2019

**OBESITY**
- Yes: 13%
- No: 87%

**GESTATIONAL DIABETES**
- Yes: 5%
- No: 95%

Data Source: Hospital Discharge Data for 2016-2019, DC Hospital Association
Knowledge Check

Which of the following states/areas has the highest prevalence of gestational diabetes?

A. District of Columbia
B. South Dakota
C. Alabama
D. Georgia
Risk Factors

- Personal history of GDM
- Personal history of baby weighing > 9lb
- Family history of Type 2 DM
- Polycystic ovarian syndrome (PCOS)
- Obesity
- Glycosuria
- Age
- Race/ethnicity

https://www.cdc.gov/diabetes/basics/gestational.html
ACOG Practice Bulletin #190, February 2018
Risk Factors – Race/Ethnicity

- Non-Hispanic White
- Non-Hispanic Black
- Hispanic
- Asian
- Japanese
- Korean
- Chinese
- Vietnamese
- Filipina
- Asian Indian
- Other Asian

Weighted %

Race/Ethnicity

Racial/Ethnic Asian Subgroup
Risk Factors – Prepregnancy BMI

CDC.gov
Risk Factors - Age

- Non-Hispanic white (N=136,673)
- Asian (N=40,493)
- African American (N=20,204)
- Hispanic (N=50,810)

Care.diabetesjournals.org
Knowledge Check

Which of the following race/ethnicities has the highest prevalence of gestational diabetes with a normal BMI?

A. American Indian
B. Asian/Pacific Islander
C. Hispanic
D. Non-Hispanic Black
Screening/Diagnosis

• Universal versus risk-based screening
• Screening based on historic factors will fail to identify ½ of women with GDM
• Only 10% of pregnant women are low-risk
• In 2014, the US Preventive Services Task Force recommended screening all pregnant women for GDM at or beyond 24 weeks of gestation
• 1973 study proposed the use of the 50gm, 1-hour oral glucose tolerance test (OGTT) followed by 100gm 3-hour OGTT if abnormal
  – Most widely accepted screening test in US
  – Used by 95% of obstetricians in the US

ACOG Practice Bulletin #190, February 2018
Coustan DR. Obstet Gynecol 1989
O’Sullivan JB. Am J Obstet Gynecol 1973
Gabbe SG. Obstet Gynecol 2004
Moyer VA. Ann Intern Med 2014
Indications for early screening

• Overweight or obese (BMI > 25 or BMI > 23 in Asian Americans) with one or more of the following additional risk factors:
  
  • Physical inactivity
  • First-degree relative with diabetes
  • High-risk race or ethnicity
  • Previously infant weighing 4,000g (approximately 9lbs) or more
  • Previous gestational diabetes mellitus
  • Hypertension
  • History of cardiovascular disease
  
  • HDL cholesterol level less than 35 mg/dL, a triglyceride level greater than 250 mg/dL
  • Polycystic ovarian syndrome
  • A1C greater than or equal to 5.7%, impaired glucose tolerance, or impaired fasting glucose on previous testing
  • Other clinical conditions associated with insulin resistance

ACOG Practice Bulletin #190, February 2018
American Diabetes Association. Classification and Diagnosis of Diabetes. Diabetes Care 2017
Screening/Diagnosis

• Two-step approach most commonly used
• Thresholds for the 1-hour glucose challenge vary by institution
  – 130 to 140 mg/dl
  – Using 130 mg/dl
    o Higher screen positive rate, higher sensitivity but higher false positive rates.
  – Using 140mg/dl
    o Lower screen positive rate, lower sensitivity but also lower false positive rates.
## Screening/Diagnosis

### Table 1. Proposed Diagnostic Criteria for Gestational Diabetes Mellitus* ⇐

<table>
<thead>
<tr>
<th>Status</th>
<th>Plasma or Serum Glucose Level Carpenter and Coustan Conversion</th>
<th>Plasma Level National Diabetes Data Group Conversion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mg/dL mmol/L</td>
<td>mg/dL mmol/L</td>
</tr>
<tr>
<td>Fasting</td>
<td>95 5.3</td>
<td>105 5.8</td>
</tr>
<tr>
<td>1 hour</td>
<td>180 10.0</td>
<td>190 10.6</td>
</tr>
<tr>
<td>2 hours</td>
<td>155 8.6</td>
<td>165 9.2</td>
</tr>
<tr>
<td>3 hours</td>
<td>140 7.8</td>
<td>145 8.0</td>
</tr>
</tbody>
</table>

*A diagnosis generally requires that two or more thresholds be met or exceeded, although some clinicians choose to use just one elevated value.


ACOG Practice Bulletin #190, February 2018
Risk-based screening rather than universal screening for gestational diabetes is recommended because the majority of patients with gestational diabetes have risk factors.

A. True
B. False
Complications: Maternal

- Preeclampsia
- Cesarean delivery
- Developing Type 2 DM later in life
  - Up to 70% of women with GDM will develop diabetes within 22-28 years after pregnancy
    - Influenced by race, ethnicity, and obesity
    - 60% of Latin American women may develop Type 2 DM within 5 years

ACOG Practice Bulletin #190, February 2018
Yoge Y. Am J Obstet Gynecol 2004
Ehrenberg HM. Am J Obstet Gynecol 2004
O’Sullivan JB. JAMA 1982
Kim C. Diabetes Care 2002
Kjos SL. Diabetes 1995
Complications: Fetal/Neonatal

- Macrosomia
- Shoulder dystocia
- Birth trauma
- Neonatal hypoglycemia
- Hyperbilirubinemia
- Stillbirth
- Childhood and adult-onset obesity and diabetes

ACOG Practice Bulletin #190, February 2018
Rosenstein MG. Am J Obstet Gynecol 2012
Dabelea D. Diabetes 2000
Clausen TD. J Clin Endocrinol Metab 2009
Management - Benefits of treatment

- 2005 Australian Carbohydrate Intolerance Study in Pregnant Women trial
  - Reduction in rate of composite of serious newborn complications
    - perinatal death
    - shoulder dystocia
    - birth trauma
  - Preeclampsia
  - Large for gestational age
  - Birth weight greater than 4,000 g

ACOG Practice Bulletin #190, February 2018
Crowther CA. N Engl J Med 2005
Management - Benefits of treatment

• US Preventive Task Force systematic review
  – Preeclampsia
  – Shoulder dystocia
  – Macrosomia

• Treatment in most studies consisted of dietary counseling and exercise

ACOG Practice Bulletin #190, February 2018
Hartling L. Ann Intern Med 2013
Knowledge Check

Maternal complications of gestational diabetes that have been shown to be reduced with adequate treatment include:

A. Cesarean delivery
B. Preeclampsia
C. Developing Type 2 DM later in life
Management - Diet/nutrition counseling

- Little evidence evaluating different GDM diets
- Most recommend 3 meals and 2-3 snacks daily

What is the Diabetes Plate Method? (diabetesfoodhub.org)
Management - Diet/nutrition counseling

- Limit carbohydrate intake to 33-40% of calories, with the remaining calories divided between protein (20%) and fat (40%)
  - Breakfast: 10-20% (30 g carb)
  - Lunch: 20-30% (30 g carb)
  - Dinner: 30-40% (45 g carb)
  - Snacks: up to 30% (15 g carb)
Management - Exercise

• Women with uncomplicated pregnancies and without a medical reason to avoid pregnancy should be encouraged to exercise
• Physical inactivity is a risk factor for GDM
• Additional benefits of exercise, lower incidence of:
  – Excessive gestational weight gain
  – Gestational hypertensive disorders
  – Preterm birth
  – Cesarean birth

ACOG Committee Opinion #804, April 2020
# Management - Exercise

## Table 3. Characteristics of a Safe and Effective Exercise Regimen in Pregnancy

<table>
<thead>
<tr>
<th>When to Start</th>
<th>First Trimester, More Than 12 Weeks of gestation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of a session</td>
<td>30–60 minutes</td>
</tr>
<tr>
<td>Times per week</td>
<td>At least 3–4 (up to daily)</td>
</tr>
<tr>
<td>Intensity of exercise</td>
<td>Less than 60–80% of age-predicted maximum maternal heart rate*</td>
</tr>
<tr>
<td>Environment</td>
<td>Thermoneutral or controlled conditions (air conditioning; avoiding prolonged exposure to heat)</td>
</tr>
<tr>
<td>Self-reported intensity of exercise (Borg scale)</td>
<td>Moderate intensity (12–14 on Borg scale)</td>
</tr>
<tr>
<td>Supervision of exercise</td>
<td>Preferred, if available</td>
</tr>
<tr>
<td>When to end</td>
<td>Until delivery (as tolerated)</td>
</tr>
</tbody>
</table>

*Usually not exceeding 140 beats per minute.


ACOG Committee Opinion #804, April 2020
Management - Blood sugar monitoring and goals

- 4 times per day blood glucose monitoring
- American Diabetes Association suggests the following targets:
  - Fasting: 95 mg/dl or less
  - One hour after a meal (postprandial): 140 mg/dl or less
  - Two hours after a meal (postprandial): 120 mg/dl or less
- When targets cannot be achieved with diet and exercise, pharmacologic treatment is recommended
Knowledge Check

Which of the following are correct goals for carbohydrate intake and blood sugar values?

A. Fastings < 95mg/dl, 30gm of carbohydrates with snacks
B. 1 hour postprandial < 120mg/dl, 45gm of carbohydrates with dinner
C. 2 hour postprandial < 140mg/dl, 30gm of carbohydrates with lunch
D. 1 hour postprandial < 140mg/dl, 30gm of carbohydrates with breakfast
Management - Fetal monitoring

• BPP, modified BPP, growth assessments
• GDM well controlled with diet and exercise
  – No indication for antenatal testing prior to 40 weeks
• GDM controlled with medications
  – Once or twice weekly antenatal testing starting at 32 weeks
• Poorly controlled GDM
  – Twice weekly antenatal testing starting at 32 weeks

ACOG Committee Opinion #828, June 2021
Driggers RW. Obstet Gynecol. 2021 June
Management - Delivery

• Delivery timing
  – GDM well controlled with diet and exercise
    o 39-0/7 to 40-6/7 weeks
  – GDM well controlled on medications
    o 39-0/7 to 39-6/7 weeks
  – GDM poorly controlled
    o Individualized

• Mode of delivery
  – Women with GDM and estimated fetal weight 4500gm or more should be counseled regarding risks/benefits of cesarean delivery
Management - Delivery

• Rates of shoulder dystocia in pregnancies complicated by diabetes:
  – 8.4% for infants between 4000 and 4250 gm
  – 12.3% for infants between 4250 and 4500 gm
  – 19.9% for infants between 4500 and 4750 gm
  – 23.5% for infants between 4750 and 5000 gm

• If delivery was assisted by forceps or vacuum
  – 12.2% for infants between 4000 and 4250 gm
  – 16.7% for infants between 4250 and 4500 gm
  – 27.3% for infants between 4500 and 4750 gm
  – 34.8% for infants between 4750 and 5000 gm

Nesbitt et al, AJOG 1998
Management - Postpartum screening

Figure 1. Management of postpartum screening results. Abbreviations: FPG, fasting plasma glucose; OGGT, oral glucose tolerance test; IGT, impaired glucose tolerance. ☞

ACOG Practice Bulletin 180
Management - Counseling for future health and pregnancies

- Up to 70% will develop diabetes later in life
  - ACOG and ADA recommend repeat testing every 1-3 years
  - Maintain healthy weight and diet
- Increased risk of recurrent GDM
  - Can reduce risk by maintain healthy weight and diet
  - Early screening in subsequent pregnancies
  - Repeat at 24-28 weeks if early screening normal
Knowledge Check

All patients with gestational diabetes should be screened with either a fasting plasma glucose level or a 75gm, 2hr OGTT at 4-12 weeks postpartum

A. True
B. False
Summary

• US is seeing an increase in prevalence of pregnancies complicated by GDM
• Universal screening for GDM is recommended
• Poorly controlled GDM is associated with increased risk of maternal and fetal/neonatal complications
• Adequate control of blood sugars may decrease these risks
• Postpartum screening is recommended
• Regular screening by PCP every 1-3 years
Pharmacologic Management of Gestational Diabetes

August 2021

Tara Bastawrous, PharmD, BCPS, BC-ADM
Elaine Yip, PharmD, BCPS
Clinical Pharmacy Specialists, Kaiser Permanente Mid-Atlantic States
Objectives

• Determine first line options for the treatment of gestational diabetes (GDM)
• Describe benefits and risks of therapies in the treatment of GDM
• Recognize diabetes medications to be avoided during pregnancy
• Identify key areas for patient counseling
Is Pharmacotherapy Necessary?

• Lifestyle modifications are crucial component

• Initiation of pharmacotherapy for GDM has been shown to improve outcomes if the patient is unable to maintain blood glucose at goal with diet and lifestyle modifications

• 30% of women diagnosed with GDM require pharmacologic therapy
Insulin Production During Pregnancy

- Usual insulin production during pregnancy
- Shortage of insulin production during pregnancy with gestational diabetes

Segrue 2018
Insulin

• Preferred first line therapy for GDM
• Does not cross the placenta
• Highly effective
• Type of insulin and regimen used should be based on blood glucose patterns
  – Fasting hyperglycemia: Starting dose ~0.2 units/kg/day basal insulin
  – Fasting and post-prandial hyperglycemia: Starting total daily dose ~0.7-1.0 units/kg/day split between basal and bolus insulins and given in divided doses
• Side effects: hypoglycemia, weight gain

ACOG 2018, ADA 2021, SMFM 2018
## Basal Insulin

<table>
<thead>
<tr>
<th></th>
<th>NPH</th>
<th>Detemir</th>
<th>Glargine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type</strong></td>
<td>Intermediate</td>
<td>Long</td>
<td>Long</td>
</tr>
<tr>
<td><strong>Onset</strong></td>
<td>1-3 hours</td>
<td>1-3 hours</td>
<td>1-2 hours</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>13-18 hours</td>
<td>18-26 hours</td>
<td>24 hours</td>
</tr>
<tr>
<td><strong>Peak</strong></td>
<td>5-7 hours</td>
<td>Minimal peak at 8-10 hours</td>
<td>No peak</td>
</tr>
<tr>
<td><strong>Data in pregnancy</strong></td>
<td>• Most well studied for safety and effectiveness</td>
<td>• Acceptable safety • Similar outcomes to NPH • Studied more than glargine</td>
<td>• Acceptable safety • Similar outcomes to NPH</td>
</tr>
<tr>
<td><strong>Usual Frequency</strong></td>
<td>Once-twice daily</td>
<td>Once-twice daily</td>
<td>Once daily</td>
</tr>
<tr>
<td><strong>Formulations</strong></td>
<td>Vial, pen</td>
<td>Vial, pen</td>
<td>Vial, pen</td>
</tr>
</tbody>
</table>

ACOG 2018, ADA 2021, Lexicomp 2021, Pharmacist’s Letter 2019, SMFM 2018
# Bolus Insulin

<table>
<thead>
<tr>
<th></th>
<th>Lispro</th>
<th>Aspart</th>
<th>Regular</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type</strong></td>
<td>Rapid</td>
<td>Rapid</td>
<td>Short</td>
</tr>
<tr>
<td><strong>Onset</strong></td>
<td>1-15 min</td>
<td>1-15 min</td>
<td>30-60 min</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>3-5 hours</td>
<td>3-5 hours</td>
<td>6-8 hours</td>
</tr>
<tr>
<td><strong>Peak</strong></td>
<td>1-2 hours</td>
<td>1-2 hours</td>
<td>2-4 hours</td>
</tr>
</tbody>
</table>
| **Data in pregnancy** | • Acceptable safety  
• Lower risk of delayed hypoglycemia when compared to regular | • Acceptable safety  
• Lower risk of delayed hypoglycemia when compared to regular | • Least immunogenic  
• Most well studied for safety and effectiveness |
| **Usual Frequency** | Daily- 3 times daily (With meals) | Daily- 3 times daily (With meals) | Daily- 3 times daily (With meals) |
| **Formulations**    | Vial, pen  | Vial, pen  | Vial      |

ACOG 2018, ADA 2021, Lexicomp 2021, Pharmacist’s Letter 2019, SMFM 2018
Non-Insulin Options

• Metformin
• Glyburide
  – declining use
• Higher patient acceptance
• Up to 30% of patients may require insulin in conjunction
## Oral Agents

<table>
<thead>
<tr>
<th></th>
<th>Metformin</th>
<th>Glyburide</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Class</strong></td>
<td>Biguanide</td>
<td>Sulfonylurea</td>
</tr>
</tbody>
</table>
| **Dosing**           | Initial: 500 mg once or twice daily  
Max total daily dose: 2,550 mg (IR, as two divided doses)  
2,000 mg (XR)  | 1.25 to 20 mg/day given as single or divided doses |
| **Side effects**     | • GI upset      | • Hypoglycemia  
• Weight gain    | |
| **Data in pregnancy**| • Crosses placenta  
• Less maternal weight gain and neonatal hypoglycemia  
• Not associated with an increase in birth defects, but long-term safety data not available | • Crosses placenta  
• Neonatal hypoglycemia, macrosomia  
• Outcomes not equivalent to insulin or metformin  
• Long-term safety data not available |
Patient LS is 25 weeks pregnant and newly diagnosed with GDM. She has reservations about administering insulin injections. Which of the following could be considered for management of her GDM?

A. liraglutide  
B. metformin  
C. glipizide  
D. empagliflozin
How Do We Choose?

• Cost
• Timing of hyperglycemia
• Side effects
• Health literacy
Patient LS has been taking metformin 1000 mg twice daily, but as she progresses in her pregnancy, her fasting blood glucose has been running in the 160s-180s despite good adherence to medications and diet/lifestyle modifications. What would your next step be?

A. Discontinue metformin and initiate regular insulin
B. Discontinue metformin and initiate linagliptin
C. Add glyburide
D. Add NPH insulin
Pharmacist’s Role

• Address patient barriers to medication adherence
  – Complexity of regimen
  – Patient concerns about harm to baby
  – Adverse effects
  – Cost

• Proper administration and storage of medication
• Management of hypoglycemia
• Accessible follow-up
Knowledge Check

With the addition of NPH to her regimen, review of Patient LS’ blood glucose log reveals that her readings are now at goal. Which of the following should be included in the counseling provided to patient LS?

A. Since blood glucose is now at goal, patient will need minimal follow up as she can continue the same maintenance dose for the remainder of her pregnancy.

B. Patient will need careful follow up after delivery as insulin requirements usually increase rapidly post-partum.

C. Patient should continue to return for frequent follow-ups as insulin requirements can rapidly change as her pregnancy progresses.

D. If she experiences an episode of hypoglycemia, insulin should be discontinued.
Conclusion

• Insulin is the preferred first line option for management of GDM
• Metformin can be considered as an alternative if patient is unable to use insulin
• Due to potential risks, would consider use of therapies other than glyburide until additional data is available
• Other usual agents for DM management are generally not recommended for GDM due to limited safety data
References


5. Lexicomp Online, Lexi-Drugs, Hudson, Ohio: UpToDate, Inc.; 2021; July 1, 2021.


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Please close this window and return to the main module window to resume the course, complete the evaluation, and claim credit.