

Learning Objectives

- Describe Maternal-Fetal Metabolism in Normal and Diabetic Pregnancy
- Discuss Counseling of overt diabetics
- Review guidelines and treatment For Gestational Diabetes



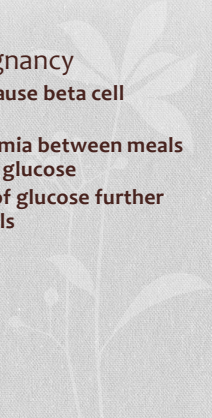
OUTLINE

- Pregnancy in the overt diabetic
- Rx recommendations
- Diagnosis and treatment GDM



Normal Changes with Pregnancy

- Increased levels of hormones cause beta cell hyperplasia
- Increase in maternal hypoglycemia between meals and at night due to fetus use of glucose
- Increase peripheral utilization of glucose further decrease maternal glucose levels
- Results in
 - lower fasting by 11 mg/dl
 - Unchanged post prandials



Continued changes

- Increased use of maternal fat stores are utilized for energy
- Levels of diabetogenic hormones rise during second and third trimesters causing increasing tissue resistance to maternal insulin
- If mother unable to increase and utilize insulin results in maternal and then fetal hyperglycemia

Elevation of Post Prandial levels

- Promotes storage of excess nutrients causing macrosomia
- Drives catabolism of the oversupply of fuel using energy and depleting fetal oxygen stores
- Episodic fetal hypoxia leads to outpouring of adrenal catecholamines
- This may cause fetal cardiac hypertrophy, stimulation of erythropoietin, increased hematocrit levels
- High hematocrits in turn lead to poor circulation and postnatal hyperbilirubinemia (jaundice)

Target Blood Sugars (ACOG)

- Fasting 60-90 mg/dl
- Preprandial 60-105 mg/dl
- 2 h postprandial ≤ 120 (1h < 130-140)
- 2 am- 6 am 60-90mg/dl
- Relative hypoglycemia may cause IUGR (intrauterine growth restriction)
- Ideal mean glucose for 7x/day testing: 87-104*

*Langer O, Levy J, Brusman L, Anyaegbunam A, Merkatz R, Divon M. Glycemic control in gestational diabetes mellitus-How tight is tight enough: Small for gestational age versus large for gestational age? Am J Obstet Gynecol 1989;161:646-53.

IDDM Effects on Pregnancy

- **Abortion**
- **Congenital Malformations**
- **Macrosomia**
- **Growth Retardation**
- **Perinatal Mortality**
- **Perinatal Morbidity**

Complications of IDDM

- **Retinopathy**
- **Nephropathy**
- **Hypertension**
- **Atherosclerotic heart disease**
- **DKA**

Diabetic Retinopathy

- **Leading cause blindness women 24-64 yo.**
- **Severity & duration DM best predicts progression risk.**
- **1/2 progress with pregnancy**
 - **Related to disease duration**
- **All partially regress postpartum**

Retinopathy: Management

- Good control prior to pregnancy
- Early ophthalmology exam
 - Minimum yearly
 - If early disease: q3-6 mos
 - Advanced disease: monthly
- Prompt laser proliferative changes
 - reduces progression to blindness 50%
- Vitreous hemorrhage
 - valsalva may cause retinal detachment
 - Limit second stage with forceps

Nephropathy

- > 500 mg protein or > 300 mg albumin 24 hrs
- Microangiopathic renal disease leading cause death and disability
 - Causes 30% deaths if onset < 31 yo
- Incidence: 40-45% of IDDM
 - Related to control

Nephropathy

- Pregnancy may worsen mod-severe disease
 - Partial regression post partum
- Second trimester improve

Nephropathy

- Third trimester worsen
- Difficult to identify preeclampsia
- Preeclampsia leading cause Preterm delivery
- Poor prognostic signs
 - >1 BP med 1 tri
 - serum Cr > 1.5
 - 24hr U Prot > 3 gm 1 trimester

Preeclampsia

- Disorder unique to pregnancy
- Characterized by poor perfusion of vital organs both of baby (vasospasm of placenta) and mother (headache, liver enzyme elevation, edema)
- These symptoms reversible with delivery
- Symptoms include: hypertension (B/P>140/90), proteinuria>300mg in 24 hour urine

Abortion

- Risk increases with elevation of HbA1C
- If well controlled no increase
- Theories of loss include: altered arachidonic acid levels, fetal hyperglycemia case formation of oxygen radicals in mitochondria of fetal tissues

Congenital Anomalies

- Most common cause Perinatal Morbidity (50%)
- No increase
 - Offspring diabetic fathers
 - True GDM
- Mechanism
 - Oxygen free radicals
 - Reece 1997: Rx with antioxidants decreases congenital malformation in diabetic animals
 - Yolk sac damage
 - Glycosylation of fetal tissues

Congenital Anomalies

- Increased by 2-3x
- correlates with HbA1C
- CNS (Central Nervous System) most common
 - spina bifida
 - anencephaly
- Congenital Heart Defect 1%
 - Fetal echocardiogram
- Sacral agenesis (Caudal regression syndrome), type of hypoplastic development lower spine

Perinatal Morbidity

- ↑ Pre Term Delivery due to complications
- ↑ Respiratory Distress Syndrome
 - maturity delayed from mean 34 wk. to 38 wk..
- Polycythemia
 - increased erythropoietin
- Hyperglycemia
 - hyperinsulinemia
- ↑ hypocalcemia
- hyperbilirubinemia
- Hypertrophic and congestive cardiomyopathy

Perinatal Mortality

- 2x increases non-diabetic
- 50% from Congenital Malformation
- Unexplained IUFD (Intrauterine fetal demise)
 - Hyperglycemia and hyperinsulinemia lead to progressive hypoxia, acidosis and death
- Respiratory distress
- Slower to achieve mature phospholipids

History of GDM

- 1979 First International Workshop on GDM
 - Def: Glucose intolerance with recognition of onset during pregnancy
- 1985 Second Workshop
 - Universal 50 gm screening with 140
 - Postpartum testing with 75 gm
 - Antepartum surveillance for poorly controlled patients
 - Increased obesity and IGT in offspring

History of GDM

- 1991 Third Workshop
 - Lowering 50 gm cut off increases sensitivity and decreases specificity
 - One abnormal 3 h GTT value may need Rx
 - Evidence of lg abdominal circum on ultrasound lead to more aggressive treatment
 - long-term implications GDM to child

History of GDM

- 1997 Fourth Workshop
- Long term consequences GDM
 - Mother
 - Fetus
- Strategies to prevent long term consequences

History of GDM

- 2007 Fifth Workshop
- All women with dx have 75 gram 2 hour GTT postpartum
- Encourage women to breastfeed
- May use oral agents to Treat (Glyburide)

Guidelines in a Nutshell

- Universal screening with 50 gm
- Coustan & Carpenter's 3 h GTT
- Diabetes Educator consult
- Medical Nutrition Therapy
 - Adjusted for BMI
- Home Glucose Monitoring for all GDM
- Insulin Therapy
- Intrapartum/Delivery Management
- Postpartum Follow-up

Coustan vs. O'Sullivan

- **O'Sullivan: whole blood using Somogyi-Nelson technique**
- **Plasma levels: 14% > than whole blood**
- **Enzymatic methods: 5 mg/dl < than Somogyi-Nelson**
- **Coustan: converted O'Sullivan and rounded to nearest 5 mg**

Carpenter M, Coustan D. Criteria for screening tests for gestational diabetes. Am J Obstet Gynecol 1982;144:768-73.

Why Switch?

- **More accurate conversion**
- **Coustan identifies 50% more GDM**
- **GDM by Coustan alone vs. O'Sullivan**
 - **Same proportion need insulin¹**
 - **Same outcome as O'Sullivan²**
 - **Same proportion of macrosomia (25%)³**
 - **Same long term risk of overt diabetes⁴**

1. Neiger R, Coustan D. The role of repeat glucose tolerance tests in the diagnosis of gestational diabetes. Am J Obstet Gynecol 1991;165:797-90.
2. Magee M, Walden C, Benedetti T, Knapp R. Influence of diagnostic criteria on the incidence of gestational diabetes and perinatal morbidity. JAMA 1993;269:609-15.
3. Berkus M, Langer O, Piper J, Luther M. Efficiency of lower threshold criteria for the diagnosis of gestational diabetes. Obstet Gynecol 1995;86:292-6.
4. Kaufmann R, Schleyhahn F, Huffman D, Amankwah K. Gestational diabetes diagnostic criteria: Long-term maternal follow-up. Am J Obstet Gynecol 1995;172:621-6.

Time	O'Sullivan	Coustan
Fasting	<105	<95
1 hr pp	<190	<180
2 hr pp	<165	<155
3 hr pp	<145	<140

Coustan vs. O'Sullivan

Pathogenesis Gestational Diabetes

- Delayed and blunted secretion of insulin
- Increased peripheral resistance
- Similar to Type II Diabetes
- Post receptor processing

Treating GDM is Important

- Decreased perinatal morbidity related to macrosomia
- Improve health-related quality of life
- Treatment with insulin in GDM reduces morbidity from macrosomia
- Improved glycolic control is associated with
 - Reduced rates of preeclampsia, gestational hypertension
 - Reduced cesarean delivery
- Less weight gain after dx with treatment

1Langer, O. et al. N Engl J Med. 2000;343:1134-1138
2. S. de Veciana M. N Engl J Med 1995;333:1237-41
3Crowther, C Effect of Treatment of GDM on Pregnancy Outcomes, NEJM 2005;352:352-2477-86
4Metzger, B Hyperglycemia and Adverse Pregnancy Outcomes, NEJM 2008;358:1991-2002.

Other Treatment Options

- New studies indication efficacy of treatment with Glyburide
- Start with 2.5mg 1-2x day with increase to 20mg
- Unable to control with oral medication will need insulin
- Outcomes similar

Langer, O. A comparison of Glyburide and Insulin in Women with Gestational diabetes. New England Journal of Medicine Oct. 19, 2000;1134-1138
Kremer, C. Glyburide for treatment of gestational diabetes. American Journal of Obstetrics and Gynecology May 2004; 1438-1439

Risk of Type 2 Diabetes

- 30-70% depending on length of f/u and population
- 70% incidence Prediabetes or DM over 12 years¹
- 30-50% over 3-5 years²
- 60-100% after 12-18 years²

1. Henry O, Beisher N. Long-term implications of gestational diabetes for the mother. *Baillieres Clin Obstet Gynaecol* 1991;5:461-83.
2. Gregory K, Kjos S, Peters R. Cost of non-insulin-dependent diabetes in women with a history of gestational diabetes: Implications for prevention. *Obstet Gynaecol* 1993;81:782-6.

Recurrence Risk GDM

- 30-50% recurrence
- If no recurrence, decreased risk Type 2 DM
- 3% vs. 30% over 16 years in Australia
- Each subsequent pregnancy with GDM increases risk of Type 2 DM

1. Henry O, Beisher N. Long-term implications of gestational diabetes for the mother. *Baillieres Clin Obstet Gynaecol* 1991;5:461-83.

Early Screening 12-16 weeks

- Obesity
- > 40 yo
- Hypertension
- Prior History of Insulin Requiring Gestational
- 3-4+ glycosuria
- Strong family history DM
- Repeat at 24-28 weeks if negative
- If positive consider undiagnosed pregestational DM and Rx accordingly

Effects of Carbohydrate Intolerance Don't Follow Cut Offs

- **↑ intolerance = ↑ adverse outcome**
- **1 abnl or 2nd value > 1st on O'Sullivan**
 - **↑ Preeclampsia, macrosomia, c/s, jaundice, ¹**
- **With no dx GDM, as 2nd value ↑:²**
- **↑ macrosomia, preeclampsia and cesarean section**
- **2nd value 120-164:**
 - **27.5% macrosomia**
 - **40% combined Preeclampsia or c/s**

1. Sermer M, Naylor C, Farine D, Kershole A, et al. The Toronto Tri-Hospital gestational diabetes project. Diabetes Care 1998;21:B33-42.
2. Tallarigo L, CiampelTRO O, Penno G, Miccoli R, Gregori G, Navalesi R. Relation of glucose tolerance to complications of pregnancy in nondiabetic women. N Engl J Med 1986;315:989-92.

1 abnormal by Coustan's Criteria

- **Re-test 4 weeks later**
- **34% will have 2 abnormal values**

Neiger R, Coustan D. The role of repeat glucose tolerance tests in the diagnosis of gestational diabetes. Am J Obstet Gynecol 1991;165:787-90.

Starting Insulin

- **ACOG criteria**
 - **Fasting > 105**
 - **2 hours > 120**
- **State NH Guidelines**
 - **More than 2 abnormal values in 1 week**
 - **>20% out of target range**
- **Experience**
 - **Wait a few days after starting diet**
 - **See if patient can identify cause of hyperglycemia**
 - **Follow weight closely**

Antenatal Testing

- Diet controlled gestational start 2x weekly Non Stress Testing at 40 weeks
- Insulin requiring gestational 2x weekly Non Stress Testing at 32 weeks
 - or if hypertension
 - or if prior still birth
- Fetal Movement Count for all at 28 weeks

Carr D, Gabbe S. Gestational Diabetes: Detection, management and implications. Clinical Diabetes 1998;16.

Delivery

- Must do an amniocentesis if prior to 39 weeks
- Consider amnio and delivery if poor control
- Diet controlled gestational may deliver at term
- Increased risk of shoulder dystocia due to atypical adipose distribution
- Consider c/s if estimated fetal weight > 4500gms

Postpartum

- Random blood sugar Postpartum day #2 or #2
 - (< 200 is normal)
- Discuss risk of type 2 DM
- Educate regarding prevention
- Educate S/Sx of diabetes
- Recommend visit diabetes educator
- 75 Gm at 6 -12 weeks postpartum
- Annual fasting

Postpartum testing

- **Who to test**
- **All patient with diagnosis**
- **Much recent work on different testing strategies**
- **FBS lacks sensitivity**
- **Recommend 75gm 2 hour GTT 6-12 weeks postpartum**

Greenger L, Moore T, Murphy H. Gestational diabetes mellitus: antenatal variables as predictors of postpartum glucose intolerance. *Obstet Gynecol* 1995;86:97-191.

Postpartum Screening Criteria

Diagnosis	Fasting glucose	Casual glucose	75 g 2-hour OGTT
IGT	≥ 110 and < 126		≥ 140 and < 200
Diabetes	≥ 126	≥ 200 + symptoms	≥ 200

(1997). "Report of the expert committee on the diagnosis and classification of diabetes mellitus." *Diabetes Care* 20: 1183-97.

Long Term Surveillance

- **All patient both diet and medication requiring**
- **Annual fasting glucose**
- **Average age onset 50-60 yo, so 20-30 yrs surveillance**
