

Gestational Diabetes

Definition

- Glucose intolerance that is first detected during pregnancy

Screening

- Identify clinical characteristics (see table)
- Screen those with HIGH RISK clinical characteristics at INITIAL VISIT and if negative REPEAT at 24-28 weeks

-Start with 50-g oral glucose-challenge test: serum/plasma glucose measured 1 hour after glucose challenge (performed anytime of day, w/o regard to meals)

>140mg/dL has 80% sensitivity

>130mg/dL has 90% sensitivity

Sensitivity is the likelihood that those with glucose >140 or >130 actually have gestational DM. Decreasing the glucose value may identify more women with GDM but it may also increase the number of false positives.

-If 50-g test high perform 100-g 3 hour oral glucose tolerance test or 75-g 2 hour oral glucose tolerance test*

Random	>200	DM I or II
Overnight fast	>126	DM I or II
Overnight fast	95	GDM
1 hour after test	180	
2 hours after test	155	
3 hours after test	140	

*Gestational DM if 2 or more values exceeded

*Fourth International Workshop-Conference on Gestational Diabetes

-If polyuria +/- polydipsia - fasting serum glucose may be sufficient for diagnosis

- Screen those without LOW RISK characteristics at 24-28 weeks
- DEBATE: Should ALL women without HIGH RISK characteristics be screened at 24-28 weeks? Arguments for screening all women are 1-2% of women with no risk factors develop diabetes and ADA guidelines add complexity to the screening process.

Risks

- To the mother
 - Increased frequency of hypertensive disorders
 - Preeclampsia
 - Pregnancy-induced hypertension
 - Increased frequency of c-section
- To the fetus
 - Congenital anomalies
 - Higher risk with severe maternal hyperglycemia and initial fasting glucose >120
 - Stillbirth
 - Prevent with maternal monitoring of fetal movements and fetal cardiotocography
 - Macrosomia
 - Only 20-30% with GDM have infants with macrosomia
 - Associated complications of L&D
 - Hypoglycemia
 - Other: jaundice, respiratory distress syndrome, polycythemia, hypocalcemia

Treatment

- Nutritional education and dietary treatment + exercise
 - Limit carbohydrate intake to 40% of total calories (40% fat, 20% protein)
 - Lower birth weights
 - Fewer c-sections
 - Carbohydrates with low glycemic index
 - Reduce total caloric intake for overweight/obese from 30-32kcal/kg/day to 25kcal/kg/day
 - Exercise can eliminate the need for insulin therapy
- Frequent measurement of maternal blood glucose concentrations
 - Postprandial hyperglycemia increases macrosomia risk
 - Pre and postprandial glucose monitoring with memory-capable meters
 - Measure fasting and 1-hour after each meal w/o insulin therapy
 - Measure fasting and pre/postprandial with insulin therapy
 - Blood glucose goal
 - <90 capillary, <105 plasma fasting
 - <95 preprandial
 - <140 1-hour postprandial
 - <120 2-hours postprandial
 - Better to have postprandial glucose <140 than preprandial glucose <95
 - If at risk for macrosomia by fetal US, goal preprandial glucose = 80
- Identify women with high fetal risk and institute aggressive treatment
 - Serum fructosamine to identify low risk
 - If not then insulin in the amniotic fluid to identify fetal hyperinsulinemia
 - Fasting serum glucose q1-2 weeks and if <105 low risk
 - If not then fetal abdominal circumference in early 3rd trimester to identify macrosomia
- Insulin Therapy- decreases frequency of fetal macrosomia and perinatal morbidity
 - Indication is capillary glucose >120 more than 2x in 2 week period (= to plasma of >140)
 - Indication is capillary glucose >90 fasting/plasma glucose >105 fasting
 - Tailor therapy to patient glucose

<u>Week of Gestation</u>	<u>Daily Insulin Dose (units)</u>
1-18	0.7xPPW-kg
18-26	0.8xPPW
26-36	0.9xPPW
36-40	1.0xPPW

- Combination of NPH (45%) and Lispro (55%)
 - NPH before breakfast and dinner
 - Lispro before each meal

After the pregnancy

- Fetal exposure increases risk of childhood obesity and abnormal glucose tolerance
 - Corresponds to high levels of fetal insulin
- Women with GDM have a 17-63% risk of non-GDM within 5-16 years after index pregnancy
 - Obesity
 - GDM diagnosed before 24 wks of gestation
 - Marked hyperglycemia during/soon after pregnancy
 - Significant weight gain during pregnancy and additional pregnancies
 - Contraception with progesterone-only OC during breast-feeding

Clinical Characteristics of Gestational Diabetes

HIGH RISK	Obesity DM in 1st degree relative Hx of glc intolerance Previous infant with macrosomia Current glycosuria
AVERAGE RISK	Neither HIGH nor LOW risk
LOW RISK	Age <25 Low risk race/ethnicity* No DM in 1st degree relative Normal prepregnancy weight Normal weight gain during pregnancy No hx of abnormal blood glc concentrations No prior poor obstetrical outcomes *Not Hispanic, black, Native American, South or East Asian, Pacific Islander, Indigenous Australian

Sulfonylureas

- Functional pancreatic beta cells must be present for activity.
- Excellent absorption, bound to protein, mainly albumin.
- All sulfonylureas bind to the same receptor.
- Increase the sensitivity of beta cells to glucose.
- Promote insulin release from beta cells by binding to “sulfonylurea receptor” that closes ATP dependent K⁺ channel, depolarizes membrane which opens Ca²⁺ channels, increases intracellular calcium, calcium binds to calmodium which causes exocytosis of insulin-containing secretory granules.
- Metabolized in liver to inactive or active compounds that are then excreted in urine.

Table of Sulfonylureas

First Generation	Trade Name	Dose	Duration of Action	Other	Metabolites
Acetohexamide	Dymelor Generic	500mg-1.5g (1g)	12-24h	Uricosuric, Less effective Pregnancy Category C	active
Chlorpropamide	Diabinese Generic	50-750mg (250mg)	1-3d	Pregnancy Category C	active
Tolazamide	Tolinase Generic	100mg-1g (250mg)	12-24h	Pregnancy Category C	inactive
Tolbutamide	Orinase Generic	500mg-3g (2g)	6-12h	Less effective Pregnancy Category C	inactive
Second Generation					
Glipizide	Glucotrol	2.5mg-40mg	10-24h	Pregnancy Category C	inactive
Glyburide	DiaBeta Glynase	1.25mg-20mg (2.5mg-10mg)	12-24h	Pregnancy Category B	inactive
	Micronase	0.75-12mg (1.5mg-6mg)			
Glimepiride	Amaryl	1-8mg	24h	Reduced hypoglycemic risk	
Usual dose in ().					

Sulfonylureas in Pregnancy

- First generation sulfonylureas cross placenta and cause fetal insulin secretion
- First generation: tolbutamide and chlorpropamide – profound and prolonged hyperinsulinemic hypoglycemia among neonates
- Excessive fetal growth (macrosomia) due to fetal hyperinsulinemia
Insulin is an anabolic hormone that causes accretion of fat, muscle, bone in the fetus
- Fetal hyperinsulinemia leading to fetal hypoxemia as a cause of late fetal deaths
- Congenital malformations: first trimester sulfonylurea therapy associated with major congenital malformations but women with poorest metabolic control received sulfonylureas and poor metabolic control is associated with congenital malformations.

References

- Langer O., Conway DL, Berkus MD, Elly MJ, et al. A comparison of glyburide and insulin in women with gestational diabetes mellitus. *N Engl J Med* 2000;343:1134-8.
- Greene MF. Oral hypoglycemic drugs for gestational diabetes {Editorial}. *N Engl J Med* 2000;343:1178-9.
- Kjos SL, Buchanan TA. Gestational diabetes mellitus. *N Engl J Med* 1999;341:1749-56.
- Jovanovic L. Controversies in the diagnosis and treatment of gestational diabetes. *Cleveland Clinic Journal of Medicine* 2000;67:481-88.
- Zimmerman BR. Current therapies for diabetes: sulfonylureas. *Endocrinology and Metabolism Clinics* 1997;26:511-19.