SWEET SUCCESS:
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We are looking for topics of interest, recurrent themes, and pictures of babies for future issues.
If you have anything to share, please email either:

Leona Dang-Kilduff
leonad@stanford.edu
Kristi Gabel
gabelkt@sutterhealth.org

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Oral Hypoglycemic Agents

By Sadie Sacks, RN, MSN and David Sacks, MD

Background

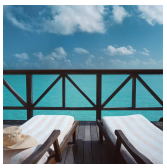
Historically, neonatal hypoglycemia secondary to oral antidiabetic drugs crossing the placenta has been the concern surrounding the use of oral hypoglycemic agents in pregnancy (Ho et al., 2007; Feig, et al. 2007). Although, insulin has been the treatment of choice for pregnant women with diabetes, in this decade with evolving new evidence (Elliott, 1991; Langer, 2000; Rowan et al., 2008) oral agents have enjoyed limited acceptance in the management of pregnant DM 2 and GDM women. Prior to Langer's randomized control trial (2000), there have been several reviews of the use of sulfonylureas, biguanides, and glucosidase inhibitors in the treatment of women with gestational diabetes. These earlier reports were heterogeneous (cohorts, retrospectives, a series of case reports or case cohort studies) with numerous confounders and had small numbers making them underpowered to demonstrate clear relationships between the drugs and neonatal outcomes. In early investigations of congenital malformations and their relationship to oral agents, investigators started to conclude that it was the hyperglycemia, a long recognized teratogen (Mills, et al., 1988; Kitzmiller et al., 1991), and its degree of control and not the oral agent that was responsible for the malformations (Sutherland, 1974; Towner et al., 1995; Homko et al., 2004).

Pharmacology

Trials were launched to determine the amount of hypoglycemic agents that were able to cross the placenta. Elliott et al. (1994, 1997) compared glyburide, glipizide, chlorpropamide and tolbutamide using a recirculating single cotyledon human placenta model. They found wide variation in transplacental transport among the drugs. The molecular properties (size, hydrophilic tendencies and protein-binding capability) of the drug molecules helped determine the amount of phamacologic agent crossing the placenta. Second generation sulfonylureas were found to allow for less drug passage via the placenta and thus decreased fetal exposure. Further study of the phenomenon was recommended.

Lactation

Regarding the safety of the group of oral hypoglycemic agents for breastfeeding, in general the information on oral hypoglycemic drugs as a group has been inconsistent and controversial. In early studies, first generation sulfonylureas, (tolbutamide and chlorpropamide) were found to be excreted into breast milk in significant quantities (American Academy of Pediatrics committee on Drugs, 2001; Moiel et al, 1967) but observations of the infants were not reported. In a more recent investigation, Feig et al. (2005) looked at glyburide and glipizide and their transfer to breastmilk and none of the drugs at the doses tested were found to be present in breast milk. The infants showed no signs of hypoglycemia as well. This led to the conclusion that these two drugs at the dosage tested are safe for breastfeeding.



SPECIFIC ORAL HYPOGLYCEMIC AGENTS

Glyburide

Pharmacology

Glyburide, (glibenclamide generic) is a second generation sulphonylurea which is more potent than the first generation drugs in this class. The

sulphonylureas bind directly to the β-cell receptors. As part of a complex biochemical reaction causing potassium to be retained in the cell and favoring cell membrane depolarization, calcium channels are opened allowing an influx of calcium which activates calcium-dependent proteins that control the release of insulin (Krentz et al., 2005). The sulphonylureas interact on the β-cell plasma membrane to allow immediate release of preformed insulin adjacent to the plasma membrane ('first phase' insulin response) [Rorsman et al., 2003]. The sulphonylureas prolong the 'second phase' starting approximately 10 minutes later during which newly formed insulin is moved to the cell membrane from inside the β-cell (Groop, 1992). Assuming the β-cell is working at capacity, the stimulation goes on as long as the drug is active, with or without food. Hence, this is cause for the hypoglycemia that is often seen with this drug. See specific comments below on dosing and food intake.

Safety

In his review of existing evidence that has come available in 2000-2007 on the safety and efficacy of the use of glyburide in pregnancy, Moore (2007) noted glyburide is not approved by the FDA for use in pregnancy. The rate of drug failure appears to be around 20% (Conway et al., 2004; Bertini et al., 2005; Kremer et al., 2004; Jacobson et al., 2005). Pregnant women with fastings >115 mg/dl were at increased risk for failure. The fact that mean maternal fasting and postprandial glucose values appear to be lower with use of glyburide would seem to offer patient advantages. Moore recommended larger randomized control trials to be done in the future with adequate power to prove or disprove any possible reduction of neonatal obesity that would be resulting from improved maternal glycemic control found by some investigators (Jacobson et al., 2005).

"...glyburide does seem to offer viable more user friendly options for medication treatments for 80% of patients..."

Drug Dosing

Glyburide dosing is somewhat problematic in that current dosing recommendations are based on investigations done with animals and non-pregnant patients (Moore, 2007). Since maximum drug peak in pregnancy occurs 2-4 hours after intake (Yin et al., 2005) with a prolonged 'second stage' response and glucose peak after a carbohydrate load is 90 minutes (Ben-Haroush et al., 2004), a reasonable recommendation for glyburide dosing would be to take the drug 1 hour preprandial. Because the half life of the drug in pregnant patients is 2-4 hours (not 10 hours as in the non-pregnant population), the drug might be reasonably given twice a day (Moore, 2007). Timely snacks are important in helping prevent hypoglycemia. Please see the Nutrition Section for specific recommendations on snacking. Large, randomized control trials in pregnant women are needed to verify the pharmacokinetics of such a regimen.

Adequacy of Blood Glucose Control

As previously stated, approximately 80% of women with GDM failing diet and exercise therapy are able to be adequately treated with glyburide leaving about 20% that will require intervention with insulin (Kremer et al.,2004; Bertini et al., 2005; Jacobson, et al., 2005; Moore, 2007). Several have tried to determine the antecedent factors that contribute to glyburide failure causing patients to be placed on an insulin regimen. Kahn et al.(2006) investigated patient characteristics that would predict glyburide failure. They found maternal age (> 34 years as compared to 29 years), earlier diagnosis of GDM (<25 weeks), higher gravidity and parity, and higher mean fasting glucose value (112mg/dl as compared to 100mg.dl) to be predictors. In her related study, Kremer (2004) also found obesity to be a harbinger of failure as did Jacobson et al., 2005). Rochon (2006) in a similar study found patients' glucose challenge test (GCT) outcomes to be significant predictors in that those who had a higher mean glucose value on the GCT (200.5 ± vs 176 ± 33.8) were more likely to need insulin as did Jacobson et al.(2005). These patients more frequently had a GCT ± 200 mg/dl.

Maternal Advantages/Side Effects

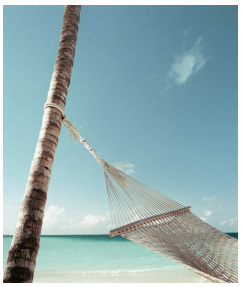
Maternal side effects that suggest more investigation into the safety of glyburide include Jacobson's finding of an increased rate of preeclampsia among his glyburide group when compared to patients receiving insulin (2005). Even after controlling for confounders such as race and ethnicity, the glyburide group had almost twice as much preeclampsia. Some have reported an increased maternal hypoglycemia (Kremer, 2004) possibly related to prolonged 'second stage' and unresolved dosing and food intake issues. Other drugs that can potentiate the hypoglycemic affect include salicylates, sulphonamides, warfarin, phenylbutazone, fibric acid derivatives, monamine oxidase inhibitors, chloramphenicol, phenylbutazone, probenecid, allopurinol and alcohol. In the presence of persistent hypoglycemic episodes, drug dosing, patient lifestyle habits including meals, snacks, exercise, alcohol intake, and other medications being taken simultaneously should be reviewed (Krentz et al., 2005).

Despite these cautions, glyburide does seem to offer viable more user friendly options for medication treatment for 80% of patients as compared to those on insulin only (Kremer at al., 2004; Bertini et al., 2005; Jacobson et al., 2005), especially those with fasting glucose values <115 mg/dl (Conway et al., 2004). Mean maternal glucose fasting and post prandial seem to be better controlled with glyburide than with insulin (Moore et al., 2007).

Neonatal Advantages/Side Effects

Neonatal side effects have been reported. Increased short term NICU admits, possibly from hypoglycemia and respiratory distress (Bertini et al., 2005; Rochon, 2006), and a greater incidence of photo therapy (Jacobson et al., 2005) have been observed. A higher rate of birth injuries in glyburide infants vs. insulin infants, though statistically insignificant, requires

closer investigation (Jacobson et al., 2005).



On a more positive note, glyburide seems to be compatible with lactation (Feig et al., 2005). In addition, there seems to be no relationship between fetal anomalies and use of oral agents (Towner et al., 1995).

Metformin

Pharmacology

Metformin is a biguanide or an insulin sensitizer. That is, it lowers blood glucose levels by blocking hepatic glucose production through gluconeogenesis. In addition, it increases insulin sensitivity at the cellular level, as well. Clinically this appears as increased glucose uptake, oxidation and glycogenesis by muscle, increased glucose metabolism to lactate by the intestine and possibly a reduced rate of intestinal glucose absorption (Bailey, 1993). Recent studies, ex vivo and in vivo, demonstrated that metformin, with its smaller molecular weight than glyburide, its hydrophilic tendencies and its lack of plasma protein binding ability, crossed the placental barrier in the laboratory into fetal circulation readily approaching concentrations similar to those in the maternal circulation (Bruce et al., 2006). The fetal consequences of this are, as yet, unknown. There was no difference in placental function and the drug disposition between diabetic and non-diabetic patients.

Safety

For a period of time in the 1970s the entire class of drugs had a tarnished reputation from phenformin's association with lactic acidosis, fetal anomalies in mice (Denno et al., 1994) and its ultimate withdrawal from the market. Metformin has demonstrated no such tendencies and, at present, is the only biguanide available in the US (Krentz at al., 2005). An early report, without controlling for obesity, attributed a higher rate of pre-eclampsia and maternal mortality to metformin as compared to both insulin and sulphonylurea (Hellmuth et al., 2000). However, Jakubowicz's retrospective study of polycystic ovarian syndrome (PCOS) patients conceiving on metformin and continuing throughout pregnancy helped establish the drug's safe use in pregnancy. The early pregnancy rate of loss was significantly lower in the metformin group as compared to the control group. This was true in the subgroup with a history of previous early pregnancy loss with a five-fold improvement (Jakubowicz et al., 2000). As an insulin sensitizer, metformin has been shown in a double blind randomized control trial to decrease circulating ovarian androgen concentration thus increasing ovulation (Moghetti, et al., 2002). Glueck et al. (2004) reported that women in their study who had the most insulin resistance preconception experienced the greatest benefit when given the drug prior to pregnancy.

Drug Dosing

In his review of metformin use in non-pregnant patients, Bailey (1996) recommended taking the drug with food and starting the dose at 500 mg or 850 mg in the a.m. or taking 500 mg. a.m. and p.m. He stressed increasing the drug slowly over a period of weeks with the maximum dose being 2550 mg per day. Hughes et al. (2006) studied a small number of patients acting as their own controls both when they were pregnant and at least 8 weeks postpartum. He found that metformin is cleared much more rapidly in the pregnant state because of greater renal elimination. This gives rise to the question of a need to adjust drug dosage in late pregnancy to maintain therapeutic level. Mean concentrations in pregnancy were 69% of that postpartum. This small study gives rise to the need for a larger study to answer the question of need to change dosing in late pregnancy.

While administering a dose of 1000-2000 mg/day to women with PCOS who are considered to be at increased risk for miscarriage during pregnancy, Khattab et al., found a three-fold decrease in early pregnancy loss in the intervention group (2006). The Metformin in Gestational Diabetes (MiG) trial used similar dosing with a range of 1750 mg to 2500 mg (Rowan, 2007; Rowan et al., 2008).

Adequacy of Glucose Control

Using the criteria applied earlier to glyburide of using the drug alone or requiring insulin, Rowan and colleagues (2008) in the MIG study found 92.6% of their study subjects continued on metformin and that almost half (46.3%) required the addition of insulin. Investigators' group outcomes into composite groups and the outcomes between the metformin only and the metformin and insulin group were similar. Patients in the metformin only group had a higher patient satisfaction in that more than ¾ would choose that therapy again. Moore et al. had shown similar results in a much smaller randomized study (2007).

Maternal Advantages/Side Effects

Though metformin is not FDA approved for preconception and pregnancy use, many prospective studies in PCOS patients found lower early pregnancy losses (Khattab et al., 2006), preconception weight loss with less weight gain in pregnancy, and decreased development of GDM (Glueck et al., 2001; Glueck et al., 2002; and Jakubowicz et al., 2005. In the MIG study (Rowan et al., 2008) investigators found lower weight gain in the period from enrollment at 36 weeks to the six weeks' postpartum visit as compared to the women taking insulin alone.

For women with DM 2, similar risks/benefits occur. Despite the fact that women in the metformin group had more risk factors for untoward pregnancy outcomes, Hughes and Rowan (2006) found no difference in perinatal loss between the metformin group and those on insulin.

Maternal risks for all groups include

hypoglycemia, though rare with metformin as compared to the sulfonylureas. Lactic acidosis was a side effect of earlier generation biguanides but is infrequent with metformin in the presence of adequate renal and cardiac functioning (Bailey et al., 1996). The drug is excreted unchanged by the kidney and the rate of acidosis has been set a 0.03 per 1000 patient years (Tran et al., 2004). Bauman's study (2002) on gastrointestinal side effects in a nonpregnant population gave rise to some discussion on the need for calcium B_{12} and calcium supplementation. Gastrointestinal side effects are sometimes seen with the introduction of the drug with hypothesized malabsorption concerns for the fetus but this complication lacks data from full investigation studies (McCarthy et al., 2004; Bauman et al., 2002).

Neonatal Advantages/Side Effects

The maternal drug activity findings above created a concern for the welfare of the fetus relative to the amount of drug crossing the placenta or the effect of the drug on placental function (Nanovskaya et al., 2006). Rowan et al. (2008) preliminarily answered some questions about fetal welfare or the fetus surrounded by high levels of circulating metformin. They found fewer episodes of severe neonatal hypoglycemia in study subjects taking metformin as compared to insulin alone. The incidence of neonatal complications was similar in both the metformin and the insulin only group. The authors do state that this investigation was underpowered to determine the advantages of combined treatment and insulin only. The offspring of this MIG study will be reassessed at two years of age. Glueck at al. (2004) had data on 18 month old offspring of 126 PCOS patients who conceived on metformin while continuing the drug through pregnancy. Their height, weight, growth and motor-social development did not differ from Center for Disease Control and Prevention data. As with glyburide, oral agents taken in pregnancy and continued through the lactation period have not been associated with fetal anomalies or side effects from the drug in mothers' milk (Towner et al., 1995; and Feig et al., 2005).

Acarbose

Acarbose is an α-glucosidase inhibitor that targets postprandial hyperglycemia. That is, its primary action is to hamper absorption of ingested carbohydrates in the gut (Merlob et al., 2002). Because of this, patients need to eat a diet rich in complex carbohydrates (Krentz et al., 2005). Few studies exist where acarbose was utilized during pregnancy. Wilton et al., in a report of pregnancy outcome relative to 35 newly marketed drugs in England (1998) reported that five pregnancies occurred with pregnancy exposure to acarbose through the first trimester only. Use was discontinued by all and pregnancy outcomes were two spontaneous abortions and three healthy newborns. Bertini et al., in a comparison of insulin, glyburide and acarbose (2005) found all the groups to be similar. Eight of 19 patients on acarbose required being switched to insulin. Neonatal outcomes were similar in the two groups with more neonatal hypoglycemia being seen in the glyburide group.

Based on the available data, use of acarbose during pregnancy appears to be safe, but minimal studies have looked at use of this agent during pregnancy. Its major drawback seems to be gastrointestinal discomfort and symptoms with a possible problem in pregnancy of malabsorption for the fetus.

Recommendations

Oral hypoglycemics continue to be evaluated as an efficacious alternative to insulin therapy or, in some cases, in combination with insulin. In the mean time the provider caring for a pregnant patient requiring drug intervention should discuss with the woman the risks and benefits of the agent's use during pregnancy and document this discussion in her chart.

Recommendations for the patient are:

- The woman should establish and maintain diet and exercise therapy.
- The woman should comply with recommended SMBG schedule.
- Conduct fetal surveillance as recommended for patients utilizing insulin therapy.
- Make all providers aware of significant health history in all major organ systems (i.e. heart, kidney, gastrointestinal, eye, etc)

REFERENCES available on request.

Table 1: Glyburide Initiation—Suggested Recommendations for Use During Pregnancy
• Begin at lowest dose (1.25—2.5 mg)
• Take Glyburide 1/2 hour to 45 minutes before meal that has elevated blood sugar or before bed if FBG is elevated
• Adjust every 3 days to weekly per blood glucose patterns
• Maximum 20 mg/day in split doses
• Do not use if patient has sulfa allergy
• Least effective with FBG > 110
• If unsuccessful in lowering BG's to desired levels, switch to insulin

Beyond the Numbers

By Charlene Canger, MFT, LCSW, Region 4 ccanger@stanford.edu

"...thank you, Sweet Success affiliates, for the commitment, knowledge, and skill you bring to your work with mothers, babies, and their families."

Reflecting a bit as our region's site visits near completion, it seems more than time to express appreciation for all that affiliates accomplish across the state on behalf of the mothers and babies. In our Behavioral Medicine teleconferences a frequent, and recurring topic is how affiliates in all the regions have fewer resources available to support THEM while there is increase in their clinical and data collection responsibilities for the women they serve.

All the Sweet Success affiliate staff's commitment and effort, regardless of their professional discipline, shows in their eagerness to know "how did we do?" when asking about the data findings. All of us want to know if we made a difference for the better in the well being of people's lives. Inherent also in asking about the outcome data is a desire to make program changes if needed.

The affiliates' work gets harder. There is more data to collect and on-going policy revisions. Reimbursement and staffing issues persist, as do coordination struggles with involved professionals. Mothers in the programs bring in unspoken and perhaps even unspeakable problems that the best Sweet Success care won't remedy. Funding cuts are a given and diminished community services result. This list is just a start.

Sweet Success outcome data reveals much about the improved quality of care offered and staff's commitment to the process. It is not only the Guidelines for Care that influence improved outcome but the manner that quality care is given. There is the protocol and then there is the artistry with which it is carried out.

If I may speak on behalf of all of us, thank you, Sweet Success affiliates, for the commitment, knowledge, and skill you bring to your work with mothers, babies, and their families.

"Silent gratitude isn't much use to any one" G.B. Stern

WEB WONDER

Have your patients sign up for weekly information, tips, and inspirational stories...they just have to type in their name, email, and due date.

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http://www.nichd.nih.gov/health/topics/Gestational_Diabetes.cfm

Has information about Gestational Diabetes, links to additional websites, clinical research and clinical trials, health education publications and materials.

Celiac Disease: Is it Important in Diabetes?

By Emmy Mignano, RD, CDE, Region 2 RD Consultant

WHAT is celiac disease?

Celiac disease (AKA gluten-sensitive enteropathy) is a lifelong digestive disease caused by an immune-mediated reaction to the protein gluten in certain foods. When gluten is eaten, the body's own immune system responds and damages the small intestine. The villi in the small intestine are damaged or destroyed, leading to problems with absorption.

WHAT are the complications of untreated celiac disease?

Due to nutrient malabsorption, people with celiac disease are at risk for several health problems associated with malnutrition, including anemia, osteoporosis and osteopenia, short stature, and infertility and recurrent miscarriage. In addition, celiac disease is linked to lymphoma and adenocarcinoma.

WHAT are the symptoms of celiac disease?

Not everyone with celiac disease has symptoms. Many of the symptoms are similar to those of other diseases such as irritable bowel syndrome, diverticulitis, Crohn's disease or gastroparesis. Symptoms *may* include: gas, recurring abdominal pain, chronic diarrhea, constipation, chronic fatigue or tooth discoloration or loss of enamel. (See references for a more complete list.) People with diabetes and celiac disease may experience unexplained hypoglycemia.

"Celiac disease…a lifelong digestive disease caused by an immune-mediated reaction to the protein gluten in certain foods."

WHO has celiac disease?

Celiac disease is considered to be an autoimmune disease that occurs in genetically susceptible individuals. Since type 1 diabetes is also an autoimmune disease, the incidence of celiac disease in people with type 1 is higher than in the general population (1-16% vs. .3-1%). In the United States, it is estimated that 1 in 133 people have celiac disease.

HOW is celiac disease diagnosed?

People with celiac disease have higher levels of certain autoantibodies. The American Diabetes Association recommends that people with type 1 who are symptomatic for celiac disease should have tissue transglutaminase or anti-endomysial antibodies measured, with documentation of normal serum IgA levels. Typically, people with positive antibodies are then referred to a gastroenterologist for a small intestinal biopsy. New research is suggesting that a biopy may not always be conclusive; work is progressing on using a serologic algorithm for diagnosis. Although many pediatric endocrine practices screen all patients for celiac with antibody testing, many adults with type 1 have never been screened and are unaware of the risk.

WHAT is the treatment?

A lifelong avoidance of foods with gluten is the recommended treatment. This means that foods made with wheat, rye, barley, triticale and other related cereals must be avoided, so traditional grain, pasta and cereal products must be avoided. Oats have been very controversial; currently, it is thought that small (up to ½ cup dry) pure, uncontaminated oats are tolerated by most people with celiac. Gluten may be hidden in foods when wheat products are used as thickeners and stabilizers. Contamination of non-gluten foods has also been a problem, since many factories that produce corn and rice products also process wheat products. Some medications and supplements have gluten as an inactive ingredient. However, more and more gluten free products are entering the market or are available online. A team approach is ideal: consultation with a registered dietitian specializing in treatment of celiac is recommended; local support groups can provide information about eating out and available products. Reading labels for carbohydrates is important in gluten-free products, since the carbohydrate content may not be similar to the "regular" products.

At diagnosis, screening for nutritional deficiencies is recommended. This should include bone density, parathyroid hormone, CBC, iron studies, folate, B12, vitamins A, E, D and K, electrolytes, albumin, total protein, liver enzymes and prothrombin time.

Experimental therapies include the use of proteases to degrade gluten to nontoxic fragments.

As the damage to the small intestine heals, absorption improves. Lactose intolerance may resolve; the absorption of oral medications may improve, so dosages may need adjustment.

WHAT'S next?

Annual visits should include serum antibodies to determine adherence to the gluten free diet. Screening for nutritional deficiencies and other autoimmune diseases is also recommended.

KEY POINTS:

- Since celiac disease is an autoimmune disease, people with type 1 diabetes are at greater risk;
- A gluten free diet is the current treatment for celiac disease;
- A team approach that includes the patient, MD, RD and a celiac support group is recommended;
- Absorption of lactose and oral medications may change with successful treatment.

REFERENCES available on request.

Highlights from the International Workshop Conference on Gestational Diabetes Diagnosis and Classification June 11-13, 2008

By Maribeth Inturrisi, RN, MS, CNS, CDE, Region 1 and 3 Coordinator

Over two hundred registrants from the International Association of Diabetes and Pregnancy Study Groups convened in Pasadena, California to review the results of the Hyperglycemia and Pregnancy Outcomes **(HAPO) study** published May 8 2008 in the *New England Journal of Medicine*.

The **primary focus** of the conference was to review the population-based data which link maternal glucose levels to fetal, neonatal, childhood, and maternal **outcomes.** The **purpose of the conference** was to **analyze** these data with a view to developing a **world-wide consensus** on the **diagnosis of GDM** or glucose intolerance of pregnancy.

A total of **25,505 pregnant women at 15 centers in nine countries underwent 75-g oral glucose-tolerance testing at 24 to 32 weeks of gestation. Data remained blinded** if the fasting plasma glucose level was 105 mg per deciliter or less and the 2-hour plasma glucose level was 200 mg per deciliter or less. **Primary outcomes** were birth weight above the 90th percentile for gestational age, primary cesarean delivery, clinically diagnosed neonatal hypoglycemia, and cord-blood serum C-peptide level above the 90th percentile. Secondary outcomes were delivery before 37 weeks of gestation, shoulder dystocia or birth injury, need for intensive neonatal care, hyperbilirubinemia, and preeclampsia.

RESULTS

For the **23,316 participants with blinded data**, we calculated adjusted odds ratios for adverse pregnancy outcomes associated with an increase in the fasting plasma glucose level of 1 SD (6.9 mg per deciliter [0.4 mmol per liter]), an increase in the 1-hour plasma glucose level of 1 SD (30.9 mg per deciliter [1.7 mmol per liter]), and an increase in the 2-hour plasma glucose level of 1 SD (23.5 mg per deciliter [1.3 mmol per liter]). See Table 2.

There were no obvious thresholds at which risks increased. Significant associations were also observed for secondary outcomes, although these tended to be weaker.

CONCLUSIONS

The results indicate strong, continuous associations of maternal glucose levels below those diagnostic of diabetes with increased birth weight and increased cord-blood serum C-peptide levels.

- **Some interesting findings: C-peptide** was selected as a primary outcome variable because in theory the higher the cord insulin the more likely it is that mother had high glucose concentrations which crossed to the fetus. Insulin levels were not used because hemolysis lowers plasma insulin concentrations, whereas it does not affect c-peptide. About 15% of cord specimens will hemolyze. There is a strong correlation between c-peptide (the part of the insulin molecule that links the a-chain with the b-chain) and insulin. Therefore, cord c-peptide levels serve as a proxy for fetal insulinemia.
- There was a strong association between **increasing maternal OGTT results at all three times; fasting, 1-hr, and 2 -hr** and **cord c-peptide levels** in the neonate but the **highest correlation was with fasting and the 1 hour after the load.**
- The **high c-peptide** production was associated with **neonatal hypoglycemia** following birth.
- There appeared to be agreement that the 75 gm (rather than the 100 gm) OGTT may be preferred for GDM diagnosis throughout the world and that only 1 abnormal result may be needed to diagnose GDM.
- There was no consensus on whether the diagnostic test should include the fasting and 1-hr or fasting and 1-hr and 2-hr. (i.e. whether the test should be 1 or 2 hours after the glucose load).
- Pregnant Fasting Plasma Glucose (FPG) less than 80 mg/dl had the least correlation with adverse outcomes but still had some correlation. Pregnant FPG > 90mg/dl had the highest correlation with adverse outcomes.
- One hour after a 75 gm load greater than 179mg/dl was associated with a significantly increased risk of adverse outcomes. Two hours after the 75 gm load greater than 140mg/dl was also associated with a significantly increased risk of adverse outcomes.
- There was also a majority opinion that within the definition of GDM there should be a designation of those who have overt DM (eg FPG >126mg/dl).Thus we should be able to diagnose type 2 (and rarely type 1) during pregnancy.

Table 2 : Adjusted Odds Ratios for Associations between Maternal Glycemia as a Continuous Variable and Primary Outcomes

Outcome	Plasma Glucose Level		
	Fasting	At 1 Hr	At 2 Hr
Primary Outcome	Odds Ratio (95% CI)		
Birth Weight > 90th percentile	1.38 (1.32-1.44)	1.46 (1.39-1.53)	1.38 (1.32-1.44)
Primary Cesarean Section	1.11 (1.06-1.15)	1.10 (1.06-1.15)	1.08 (1.03-1.12)
Clinical Neonatal Hypoglycemia	1.08 (0.98-1.19) ‡	1.13 (1.03-1.26)	1.10 (1.00-1.12)
Cord-Blood Serum C-Peptide > 90th percentile	1.55 (1.47-1.64)	1.46 (1.38-1.54)	1.37 (1.30-1.44)

A writing committee will convene to determine how to translate these research findings into a draft of clinical recommendations. Also, the calculations will be redone, using the mean or median glucose value rather than the lowest category of glucose results as the reference group. Stay tuned!

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August 2008

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Upcoming Educational Opportunities

August 19, 2008

Sweet Success Affiliate Training Region 2: Sutter Health University, Sacramento; contact Wendy Bang, Grant Program Secretary at 916-733-1705 or BangWS@sutterhealth.org for registration.

September 22 and 23

Sweet Success Affiliate Training Region 6.1; Center for Health Education Long Beach Memorial and Miller Children's Hospital, Long Beach. Contact CDAPP Region 6.1 at 562-595-6459.

October 13

Sweet Success Affiliate Sharing Day for Regions 1 and 4, San Francisco. Contact Leona Dang-Kilduff at leonad@stanford.edu or Maribeth Inturrisi at Maribeth.Inturrisi@nursing.ucsf.edu

November 6-8

Sweet Success Express 2008 Diabetes and Pregnancy National Research Conference, Facing Change and Challenge, Anaheim. Contact Professional Education Center at 800-732-2387 / www.sweetsuccessexpress.com / www.proedcenter.com

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