Over the past few years, oral agents have been reintroduced in the management of diabetes during pregnancy. There are several reviews of sulfonylureas, biguanides, and glucosidase inhibitors used primarily in pregnancies complicated by gestational diabetes. Oral agents were once thought to be associated with an increased incidence of congenital malformations. However, the issue of malformations may be more related to hyperglycemia. Hyperglycemia is a known teratogen. Inadequate blood glucose control using oral agents prior to pregnancy usually continues into the first trimester of pregnancy. For those women on oral agents with inadequate blood glucose control prior to conception, it is the hyperglycemia that is thought to be the teratogen. A meta-analysis of the safety of oral agents in the first trimester supports this contention. Human insulin and insulin analogs (with the exception of glargine) do not appear to be teratogens in human pregnancies and thus, continue to be recommended by ACOG and the ADA as the only pharmacologic antihyperglycemic agent for use during pregnancy.

Firm recommendations for oral agent use in pregnancy are limited by the paucity of level 1 evidence. Some providers do not believe these agents can achieve adequate glycemic control. As beta cell destruction increases, oral agents lose their ability to maintain euglycemia. Only glyburide has been studied in a prospective randomized control trial demonstrating that it did produce comparable maternal and neonatal outcomes to insulin in about 200 patients. Placental transfer of glyburide has been shown to be insignificant.

Metformin has widespread use among infertility specialists as a treatment for insulin resistance associated with the infertility experienced by women with polycystic ovarian syndrome (PCOS). When metformin is continued through the first trimester to avoid miscarriage, no increase in malformation rates have been reported. Women using metformin for fertility are generally insulin resistant but may not be hyperglycemic early in pregnancy thus eliminating the concern for glucose-mediated teratogenicity. Metformin is thought to cross the placenta but does not alter placental metabolism of glucose. Several other studies of metformin use throughout pregnancy in women with PCOS imply a reduced rate of GDM and preeclampsia without adverse effects on the fetus and newborn, up to 4 years of age. Breastfeeding with metformin appears to be safe with no difference between infants breastfed by women without metformin.

In 2000, there was a 0% utilization of oral agents reported by the California Diabetes and Pregnancy Program affiliates. Data summaries
from 2003 reveal a 5% utilization of oral agents. The long-term effects of these medications are not fully known. CDAPP continues to track the use of oral agents during pregnancy and has begun to link outcomes with certain agents. (2005 CDAPP data base)

During the recent 5th International Gestational Diabetes Workshop, glyburide was included as an option for treating gestational diabetes.

It may be prudent to keep in mind that:

- Most of the published data concern utilization of oral agents in pregnancy is in the GDM population. Oral agents alone may be effective in women with type 2 if the degree of beta cell impairment is minimal.
- No randomized control trials have been published concerning outcomes with glyburide use for type 2 women during pregnancy.

If glyburide is used, consider the following:

1. Discuss and document risks and benefits of the agent's use during pregnancy with the woman.
2. Establish and maintain diet and exercise therapy.
3. Comply with recommended SMBG schedule.
4. Conduct fetal surveillance as recommended for patients utilizing insulin therapy.
5. When using a glyburide:
   - Be aware that hypoglycemia can occur
   - Adhere to MNT meal and snack regimen to avoid hypoglycemia
   - Ensure that the woman can recognize and treat hypoglycemia
   - Monitor weight and assess for appropriate weight gain

Recommendations regarding the use of metformin in pregnancy are reserved until outcomes of the metformin in GDM (MIG) study are available in 2006.5
REFERENCES


REFERENCES


