

## Failed Glyburide Trial in Gestational Diabetes Not Tied to Long-Term Harm

BY TIMOTHY F. KIRN  
Sacramento Bureau

RENO, NEV. — Glyburide may successfully control gestational diabetes in all but about 20% of patients, and a failed trial of glyburide appears to cause no long-term harm, Meredith Rochon, M.D., of the department of obstetrics, gynecology, and reproductive science at Mount Sinai School of Medicine, New York, and colleagues reported.

Glyburide treatment has been shown to be effective and safe for gestational diabetes.

The investigators reviewed the records of all patients with class A2 gestational diabetes treated with glyburide at a diabetes clinic over a period of 2 years to ensure that there were no ad-

verse effects when the treatment failed.

The study found no reason to avoid using glyburide instead of insulin as first-line therapy, the researchers wrote in a poster presented at the annual meeting of the Society for Maternal-Fetal Medicine.

Of 83 patients identified, 18 (22%) were patients who underwent a trial of glyburide but failed to reach the target of fasting and postprandial-glucose levels of 60-90 mg/dL and 120 mg/dL, respectively, even when treated with a dose of 20 mg daily. Consequently, those patients were switched to insulin.

Despite their initial lack of blood glucose control, the pregnancy outcomes in the patients who failed treatment—including birth weight, mode of delivery, and incidence of macrosomia—were no different from those who were successfully managed on glyburide.

The sole difference in outcome was in the patients who were successfully treated with glyburide. Those patients had more neonates who required admission to the neonatal intensive care unit (NICU) than did the women who had been switched to insulin (35% vs. 11%).

The most common reason for the admission was hypoglycemia (10 of 23 admissions).

In an interview, Dr. Rochon said the finding was a surprise and something of a mystery, since glyburide does not cross the placenta, and previous studies have not noted this potential association.

The hypoglycemia was not considered by the investigators to be a serious adverse effect because it was transient in all cases. However, if it proves to be true that glyburide treatment does produce a higher rate of hypoglycemic neonates who need NICU admission, it may have significant cost implications, Dr. Rochon said.

The mean length of stay was 8 days for all the babies that were admitted to the NICU and 4 days for those admitted with hypoglycemia. ■

### Pregnancy Outcomes by Glyburide Treatment Success or Failure

|                                  | Success<br>(n = 65) | Failure<br>(n = 18) |
|----------------------------------|---------------------|---------------------|
| Mean gestational age at delivery | 38.3 weeks          | 37.9 weeks          |
| Cesarean section                 | 37%                 | 39%                 |
| Mean birth weight                | 3,404 g             | 3,410 g             |
| Macrosomia                       | 14%                 | 12%                 |
| 5-minute Apgar <7                | 0%                  | 0%                  |
| Admission to NICU                | 35%                 | 11%                 |

Source: Dr. Rochon

## Pregnancy History Cuts Risk of Unprovoked VTE

BY MITCHEL L. ZOLER  
Philadelphia Bureau

ORLANDO, FLA. — Having a child cuts a woman's risk of unprovoked venous thromboembolism, according to results of an epidemiologic study with more than 19,000 women.

Compared with women who were never pregnant, women with a history of at least one pregnancy had a 41% reduced risk of venous thromboembolism (VTE) in a multivariate model that was adjusted for several potential confounders, Christiana Iyasere, M.D., told attendees during the annual meeting of the American College of Cardiology.

The difference in risk was statistically significant, said Dr. Iyasere, a cardiologist at Brigham and Women's Hospital in Boston.

The overall incidence of unprovoked VTE in nulliparous women was about 0.8%, compared with a rate of about 0.5% in women who had at least one pregnancy.

This means that, on average, a history of pregnancy cut the population risk for unprovoked VTE by about 3 cases per 1,000 people.

The study used data collected in the Women's Health Study, which re-

cruited postmenopausal women in the health professions with a primary goal of assessing the safety and efficacy of both aspirin and vitamin E for the primary prevention of cardiovascular disease.

Dr. Iyasere and her associates used data collected by questionnaire from the nearly 40,000 women who participated in this study to evaluate the impact of endogenous hormones on VTE risk.

They excluded women with a history of VTE, known hypercoagulable states, a history of prolonged immobility, a history of malignancy, or recent trauma.

The analyses were done using data collected from the remaining 19,219 women.

The researchers found no detectable association between VTE risk and age of menarche, age of menopause, and total duration of menses.

There was also no significant association between VTE risk and parity when the women were subdivided into four categories based on their child-

bearing history: nulliparous, one or two pregnancies, three or four pregnancies, or five or more pregnancies. But a statistically significant association existed when the comparison was made between nulliparous women and those with any pregnancy.

Among 2,635 nulliparous women, 21 reported having an unprovoked VTE.

**Compared with women who were never pregnant, women with a history of at least one pregnancy had a 41% reduced risk of VTE.**

Among 16,584 women who were pregnant at least once, 86 had an unprovoked VTE.

The fully adjusted multivariate model corrected the hazard ratio for age, history of exogenous hormone use, body mass index, history of diabetes, history of hypertension, history of smoking, and degree of exercise activity.

The researchers were surprised to find no apparent link between other measures of endogenous hormone exposure and VTE risk because exogenous hormones, in the form of oral contraceptives and hormone therapy, are proven risk factors for an increased VTE incidence, Dr. Iyasere commented at the meeting. ■

## Morbidity Still A Concern in Fetal Surgeries

BY ROBERT FINN  
San Francisco Bureau

RENO, NEV. — Newer, less invasive techniques have decreased morbidity associated with fetal surgery, but morbidity is still a concern in these surgeries, Robert H. Bell, M.D., said at the annual meeting of the Society for Maternal-Fetal Medicine.

The morbidity data come from a retrospective study of all fetal surgeries at the University of California, San Francisco, between July 1985 and May 2003, said Dr. Bell of the university.

During the early days of fetal surgery, most of the procedures involved open hysterotomy. Then fetal endoscopy (FETENDO) became popular, and now ultrasound-guided radiofrequency ablation (RFA) is the dominant procedure.

In all, 187 women with a mean maternal age of 29 (range 19-43) were treated during this period. Nine cases were marked by procedure-related fetal demise. Of the remaining 178 procedures, 79 involved a laparotomy and hysterotomy, 68 involved FETENDO, and 31 involved RFA.

Indications for the procedures included congenital diaphragmatic hernia in 38% of cases, monozygotic twin complications in 31%, hydrops in 11.8%, meningomyelocele in 8.6%, teratomas in 6.4%, and urinary obstruction in 2.1%.

The average gestational age for both hysterotomy and FETENDO was about 25 weeks, but RFA was done significantly earlier, at an average gestational age of about 21 weeks.

There were no significant differences in gestational age at delivery, with hysterotomy patients delivering at an average of 30.1 weeks, FETENDO patients delivering at 30.4 weeks, and RFA patients delivering at 32.7 weeks.

"Premature delivery, sadly, at this point is [a matter of] 'when' and not 'if,'" Dr. Bell said, although he pointed out that the data, averaged over a number of years of surgical experience, do not reflect recent improvements in lengthening pregnancies.

Premature rupture of membranes (PROM) is the primary cause of preterm delivery in these cases, and the rates of PROM are 52% in hysterotomy patients, 44% in FETENDO patients, and a significantly lower 13% in RFA patients.

About a quarter of the hysterotomy and FETENDO patients suffered pulmonary edema, a complication Dr. Bell attributed to deep inhalational anesthesia in the hysterotomy patients and the use of tocolytics in both hysterotomy and FETENDO patients.

None of the RFA patients suffered pulmonary edema (a statistically significant difference), reflecting recent changes in the treatment algorithm for preterm labor.

Another impressive improvement occurred in the average length of the patient's hospital stay. Although Dr. Bell said that clinicians at his institution are very cautious in managing patients in terms of surveillance and limitations of movement, the average length of stay has declined significantly from 11.9 days in the hysterotomy patients, to 7.9 days in the FETENDO patients, to 2.5 days in the RFA patients. And this understates the degree of improvement, since many RFA patients can now go home within 24 hours. ■