Glyburide was as safe and effective as insulin in gestational diabetes

Langer O, Conway DL, Berkus MD, Xenakis EM-J, Gonzales O. **A comparison of glyburide and insulin in women with gestational diabetes mellitus.** N Engl J Med. 2000 Oct 19;343:1134-8.

QUESTION

Is glyburide as effective and safe as insulin in women with gestational diabetes mellitus?

DESIGN

Randomized (allocation concealed*), unblinded,* controlled trial.

SETTING

Maternal health clinics in San Antonio, Texas, United States.

PATIENTS

404 women (mean age 29.5 y) who were between 11 and 33 weeks of gestation with a singleton pregnancy and who had gestational diabetes and fasting blood glucose levels ≥ 5.3 mmol/L and < 7.8 mmol/L. Follow-up was 100%.

INTERVENTION

404 women were allocated to receive glyburide (n = 201) or insulin (n = 203). Glyburide was started at an oral dose of 2.5 mg and increased to 20 mg as needed. Insulin was started at a dose of 0.7 U/kg of actual body weight, given subcutaneously 3 times/d, and increased as needed. All women were given standard nutritional instructions for 3 meals and 4 snacks daily.

MAIN OUTCOME MEASURES

The primary outcome was the achievement of prespecified levels of glycemic control. Secondary outcomes were maternal and neonatal complications.

MAIN RESULTS

Analysis was by intention to treat. At a mean of 10.5 weeks of testing, the glyburide and insulin groups did not differ for mean daily blood glucose levels (5.9 vs 5.9 mmol/L, P = 0.99) or mean glycosylated hemoglobin (5.5% vs 5.4%, P = 0.12). The glyburide and insulin groups did not differ for the rate of infants who were large for gestational age (12% vs 13%, P = 0.76), had macrosomia defined as a birthweight ≥ 4000 g (7% vs 4%, P = 0.26), or had hypoglycemia (9% vs 6%, P = 0.25) or for those who had cord-serum insulin levels (15 vs 15 μU/mL, P = 0.84). 8 women in the glyburide group (4%) were switched to insulin therapy because the maximal glyburide dose failed to produce good glycemic control.

CONCLUSION

Glyburide was as safe and effective as insulin in the treatment of women with gestational diabetes mellitus.

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*See Glossary.

COMMENTARY

Diet counseling is the appropriate initial approach to managing gestational diabetes mellitus. If hyperglycemia persists in these patients, insulin is the current recommended treatment. Older studies have shown that transplacental passage of some hypoglycemic agents and consequent neonatal hypoglycemia occur (1).

The elegant study by Langer and colleagues shows that glyburide does not cross the placenta and, therefore, would not increase the risk for neonatal hypoglycemia or large-for-gestational-age infants. The higher molecular weight of glyburide is likely the reason for the lack of transplacental passage. Groups did not differ for glucose control; however, fewer episodes of maternal hypoglycemia occurred in the glyburide than in the insulin group (2% vs 20%, P = 0.03). The starting dose of insulin was large, and a lower initial dose given 4 times daily may have reduced the episodes of maternal hypoglycemia and led to better glucose control (2). Although not statistically significant, both neonatal hypoglycemia and macrosomia tended to occur less often in the insulin group; larger numbers may be required to examine whether this trend is real.

What should we tell patients with gestational diabetes? The few patients who develop new-onset diabetes in the first trimester should not be given oral hypoglycemic drugs because of possible teratogenicity. Metformin is contraindicated for gestational diabetes because of the associated increased risk for perinatal mortality (3). Patients with gestational diabetes who have fasting hyperglycemia after the first trimester now have a choice in their therapy. If they wish to avoid insulin injections (a mode of therapy that has a known safety profile, gives greater flexibility, and with insulin pens is easy to use), glyburide appears to be a reasonable option.

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