

Treatment of Gestational Diabetes Mellitus

Reviewed by Madeleine B. Chollet and David J. Pettitt, MD

STUDY

Crowther CA, Hiller FE, Moss JR, McPhee AJ, Jeffries WS, Robinson JR, for the Australian Carbohydrate Intolerance Study in Pregnant Women Trial Group: Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. *N Engl J Med* 352:2477–2486, 2005

SUMMARY

Objective. To determine whether treatment of women with mild gestational diabetes mellitus (GDM), i.e., GDM that would meet the criteria for impaired glucose tolerance (IGT) in the nonpregnant state, decreases the risk of perinatal complications and to assess the effects of treatment on maternal outcome, mood, and quality of life.

Design. At the time this trial was initiated, the World Health Organization (WHO) recommended that the management of IGT during pregnancy should be the same as for diabetes,¹ a recommendation that differed from that of the National Diabetes Data Group.² The trial reported by Crowther et al. and reviewed here enrolled only women who fit into this controversial category.

Researchers at multiple centers in Australia and the United Kingdom randomly assigned 1,000 women who were diagnosed with GDM at 24–34 weeks of gestation to either an intervention group or a routine-care group. They admitted to the study only women with one or more risk factors for diabetes or a positive 50-g oral glucose challenge test in addition to a fasting glucose of < 140 mg/dl and a 75-g oral glucose tolerance test 2-

hour glucose concentration of 140–199 mg/dl. The intervention group received individualized dietary advice, instructions on glucose self-monitoring and insulin therapy, and routine primary care, whereas the routine-care group received only routine primary care.

End points. End points included the rate of serious perinatal outcomes, defined as death, shoulder dystocia, bone fracture, and nerve palsy, as well as less-serious outcomes, including admission to the neonatal nursery, jaundice, induction of labor, cesarean birth, and maternal anxiety, depression, and health status.

Results. This study revealed a significantly lower rate of serious perinatal outcomes among infants born to mothers in the intervention group. Specifically, there were 7 serious complications (1%) among infants in the intervention group and 23 (4%) serious complications among infants in the routine-care group ($P = 0.001$). This included five perinatal deaths and three nerve palsies and bone fractures in the routine-care group compared with none in the intervention group. The only serious outcome in the intervention group was shoulder dystocia ($n = 7$), which was not significantly different from the number ($n = 16$) in the routine-care group.

Women in the intervention group were older, less likely to be white, and more likely to have had induction of labor. Infants born to these women were more likely to be admitted to the neonatal nursery for special care, had significantly lower birth weights, and were born at an earlier average gestational

age. According to the Edinburgh Postnatal Depression Scale, more women in the routine-care group (17%) than in the intervention group (8%, $P = 0.001$) had a score indicative of depression.

Conclusions. Treatment of women with GDM appears to reduce the rate of serious perinatal outcomes from 4 to 1% without increasing the rate of cesarean delivery. Infants born to mothers who receive care for GDM are significantly less likely to have macrosomia, and despite increased admission to the neonatal nursery, these infants demonstrate no significant differences in secondary clinical outcomes.

An increased use of labor induction in the mothers and an increased rate of admission to the neonatal nursery for the infants, both of which are associated with knowledge of the diagnosis of GDM, probably contributed to the benefits ascribed to the intervention group. In addition, this study indicates that women who receive treatment for GDM have a better health-related quality of life during the antenatal period and 3 months after childbirth, as well as a reduced likelihood of experiencing depression after childbirth.

COMMENTARY

This study addresses a vital issue in prenatal care and has the potential, with further analysis, to be a landmark study in the field of GDM care. Crowther et al. designed and implemented a multi-site research proposal that directly and efficiently addressed the study's objective to determine the effect of treatment on women with GDM. Although stringent

enough to fulfill the study's objectives, the research design was also flexible enough to permit possible future research on the continuing health of the mothers and their infants.

The research team recruited 1,000 patients over a 10-year period, making this one of the largest and most rigorous investigations on this topic to date. The statistical analyses directly account for this wide array of individuals by adjusting for maternal age, race or ethnic group, and parity, and the researchers demonstrated critical foresight by designing a project that was able to be executed consistently over nearly a decade.

However, the researchers failed in one significant way: they did not take into account the new parameters for the diagnosis of diabetes, adopted by both the WHO and the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus,³⁻⁵ which changed the threshold for treatment of abnormal glucose tolerance in pregnancy. This study was designed to address the question of whether to treat pregnant women who have IGT. Originally, this condition was defined as a fasting glucose < 140 mg/dl and a 2-hour concentration of 140–199 mg/dl. In 1998, the fasting glucose concentration for diabetes in the nonpregnant state was lowered to 126 mg/dl.^{3,4} Today, any woman in the study with a fasting glucose

between 126 and 139 mg/dl would be indisputably diagnosed with diabetes by these standards and receive appropriate intervention.

The authors emphasize that, despite the new definition of GDM, "there remained uncertainty as to the level of glucose impairment associated with adverse perinatal outcomes." They have left this critical question unresolved by including women with GDM as well as those with gestational IGT. An additional analysis should be conducted that excludes these individuals to determine whether perinatal consequences are still reduced by treatment of the subset of women with fasting glucose concentrations in the lower range.

Without this information, the study is difficult to interpret. If most adverse perinatal outcomes were among infants of women with fasting glucose concentrations in the upper range, then treatment of pregnant women with glucose intolerance in the lower range would be unnecessary. However, if adverse outcomes were distributed more evenly across the range of glucose levels, then universal screening and treatment are warranted. The large multinational Hyperglycemia and Pregnancy Outcome Study,⁶ when completed, will shed light on this vital question, but Crowther et al. have the data to complete this analysis today. This study has the potential of

answering one of the most elusive questions to confront physicians treating women who, during pregnancy, develop IGT.

REFERENCES

- ¹World Health Organization: *Diabetes Mellitus: Report of a WHO Study Group*. Geneva, World Health Org., 1985 (Tech. Rep. Ser., no. 727). p. 1–113
- ²National Diabetes Data Group: Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. *Diabetes* 28:1039–1057, 1979
- ³The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus: Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 20:1183–1197, 1997
- ⁴Alberti KG, Zimmet PZ: Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1. Diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med* 15:539–553, 1998
- ⁵Metzger BE, Coustan DR: Summary and recommendations of the fourth international workshop-conference on gestational diabetes mellitus. *Diabetes Care* 21:B161–B167, 1998
- ⁶HAP0 Study Cooperative Research Group: The Hyperglycemia and Adverse Pregnancy Outcome Study. *Int J Gynecol Obstet* 78:69–77, 2002

Madeleine B. Chollet is a senior at Rice University in Houston, Texas, and served as an intern during the summer of 2005 at Sansum Diabetes Research Institute in Santa Barbara, Calif. David J. Pettitt, MD, is a senior scientist at the Sansum Diabetes Research Institute.