



## Does *myo*-inositol supplementation reduce the rate of gestational diabetes in pregnant women with a family history of type 2 diabetes?

**Yes.** In this 2-year, prospective, randomized, open-label, placebo-controlled trial, women who took *myo*-inositol (2 g daily) had a lower incidence of gestational diabetes mellitus (GDM), compared with those allocated to placebo (6% vs 15.3%, respectively;  $P = .04$ ). They also experienced a statistically significant reduction in the rate of fetal macrosomia.

*D'Anna R, Scilipoti A, Giordano D, et al. myo-inositol supplementation and onset of gestational diabetes mellitus in pregnant women with a family history of type 2 diabetes. Diabetes Care. 2013;36(4):854-857.*

### ► EXPERT COMMENTARY

**E. Albert Reece, MD, PhD, MBA**, Vice President for Medical Affairs at the University of Maryland, Baltimore; John Z. and Akiko K. Bowers Distinguished Professor; and Dean of the University of Maryland School of Medicine in Baltimore, Maryland.

**I**nositol has generated increasing attention as a treatment for conditions related to pregnancy, including polycystic ovary syndrome<sup>1</sup> and neural tube defects.<sup>2,3</sup> In this study, pregnant women with a family history of type 2 diabetes were randomly allocated to:

- folic acid alone (400 µg daily)—**placebo group**
- folic acid plus *myo*-inositol (400 µg and 4 g daily, respectively)—**treatment group**.

The goal was to determine whether the addition of *myo*-inositol could prevent GDM and macrosomia. Because the study was conducted in Italy, GDM was diagnosed using

*The author reports no financial relationships relevant to this article.*

### WHAT THIS EVIDENCE MEANS FOR PRACTICE

Current standards for identifying GDM include appropriate screening. Methods for prevention of GDM including dietary counseling and advice on an exercise program to reduce fetal macrosomia, but no interventions, to date, have effectively controlled GDM.

The concept of using a dietary supplement to prevent GDM is intriguing, and the results of this trial, coupled with a second recent report on the beneficial effects of *myo*-inositol to prevent GDM,<sup>10</sup> are promising. However, the many concerns raised here—especially the use of IADPSG criteria—make it difficult to apply these findings to traditional diagnostic criteria for US practitioners. Follow-up, large-scale trials are needed to determine how effective this supplement is in preventing GDM and whether its effects translate into benefits for women at increased risk of developing diabetes. The routine use of *myo*-inositol in patients with a family history of type 2 diabetes should await further studies, including the aforementioned trials.

►► **E. ALBERT REECE, MD, PHD, MBA**

### FAST TRACK

**Women who took *myo*-inositol were less likely to develop gestational diabetes or have a macrosomic fetus**

CONTINUED ON PAGE 24



recommendations from the International Association of Diabetes and Pregnancy Study Groups (IADPSG).<sup>4</sup>

Of the 197 women who completed the study, those given *myo*-inositol had a lower incidence of GDM than those given placebo: 6 of 99 women in the treatment group developed GDM, compared with 15 of 98 in the placebo group ( $P = .04$ ). None of the women in the treatment group gave birth to a macrosomic infant ( $>4,000$  g), compared with seven women in the placebo group ( $P = .007$ ). However, other adverse outcomes, such as cesarean delivery, gestational hypertension, shoulder dystocia, preterm delivery, and fetal respiratory distress syndrome occurred at similar frequencies in the two groups.

### Strengths and limitations of the study


Investigators conducted a prospective, randomized, placebo-controlled trial, one of the first moderately sized trials to examine the therapeutic effects of *myo*-inositol in pregnant women who had a family history of type 2 diabetes (in one or both parents). This study builds upon a previous report from the same investigators of the positive effects of *myo*-inositol in reducing insulin resistance in a smaller group of women ( $n = 69$ ) with GDM.<sup>5</sup>

Another strength is that the investigators focused on a compound, inositol, readily found in foods, which suggests that women could derive benefits from a diet fortified with this supplement.

However, there are several concerns, also touched upon in a previous commentary about this study,<sup>6</sup> which include:

- Only white women were included in the study. (As an ethnic group, white women have a lower risk of GDM.)
- All of the women enrolled in this trial had a prepregnancy body mass index within the normal range. Women who have a family history of type 2 diabetes who are also obese are a significant population to study.
- More work is needed to understand the

mechanism of action of *myo*-inositol to help determine the optimal concentration to administer and the route of administration (ie, in pill form or as part of a diet plan).

Another important point: Investigators used IADPSG criteria to diagnose GDM; these criteria tend to identify significantly more cases of diabetes than the Carpenter and Coustan criteria, which are currently used in the United States.<sup>7,8</sup> Indeed, a National Institutes of Health expert panel recommended continuing use of the Carpenter and Coustan criteria to diagnose GDM in the United States until more data are collected to show correlation between changing the diagnostic threshold and improved fetal and maternal outcomes.<sup>9</sup> 

### References

1. Morgante G, Orvieto R, Di Sabatino A, Musacchio MC, De Leo V. The role of inositol supplementation in patients with polycystic ovary syndrome, with insulin resistance, undergoing the low-dose gonadotropin ovulation induction regimen. *Fertil Steril*. 2011;95(8):2642–2644.
2. Khandelwal M, Reece EA, Wu YK, Borenstein M. Dietary *myo*-inositol therapy in hyperglycemia-induced embryopathy. *Teratology*. 1998;57(2):79–84.
3. Cavalli P, Tonni G, Grosso E, Poggiani C. Effects of inositol supplementation in a cohort of mothers at risk of producing an NTD pregnancy. *Birth Defects Res A Clin Mol Teratol*. 2011;91(11):962–965.
4. International Association of Diabetes and Pregnancy Study Groups Consensus Panel. International Association of Diabetes and Pregnancy Study Groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. *Diabetes Care*. 2010;33(3):676–682.
5. Corrado F, D'Anna R, Di Vieste G, et al. The effect of *myo*inositol supplementation on insulin resistance in patients with gestational diabetes. *Diabet Med*. 2011;28(8):972–975.
6. Coustan DR. Can a dietary supplement prevent gestational diabetes mellitus? *Diabetes Care*. 2013;36(4):777–779.
7. Reece EA, Moore T. The diagnostic criteria for gestational diabetes: To change or not to change? *Am J Obstet Gynecol*. 2013;208(4):255–259.
8. Langer O, Umans JG, Miodovnik M. Perspectives on the proposed gestational diabetes mellitus diagnostic criteria. *Obstet Gynecol*. 2013;121(1):177–182.
9. National Institutes of Health Draft Consensus Development Panel. Draft Statement: National Institutes of Health Consensus Development Conference Statement: Diagnosing Gestational Diabetes Mellitus; March 4–6, 2013; Bethesda, Maryland. <http://prevention.nih.gov/cdp/conferences/2013/gdm/files/DraftStatement.pdf>. Published March 6, 2013. Accessed May 17, 2013.
10. Matarrelli B, Vitacolonna E, D'Angelo M, et al. Effect of dietary *myo*-inositol supplementation in pregnancy on the incidence of maternal gestational diabetes mellitus and fetal outcomes: a randomized controlled trial [published online ahead of print March 1, 2013]. *J Matern Fetal Neonatal Med*. doi:10.3109/14767058.2013.766691.



**This study's use of IADPSG diagnostic criteria for gestational diabetes makes it difficult to apply the findings to US obstetric practice**