Nutrition Therapy in Gestational Diabetes Mellitus: Time to Move Forward

Teri L. Hernandez[1] *and Jennie C. Brand-Miller*[2]

Diabetes Care 2018;41:1343–1345 | https://doi.org/10.2337/dci18-0014

Nutrition therapy remains the conventional first-line approach to treatment of gestational diabetes mellitus (GDM). It will reach every woman with GDM across differing diagnostic criteria (1) and phenotypic heterogeneity (2). The goal of nutrition in pregnancy is to support maternal, placental, and fetal metabolic needs, and it may be the first introduction to a lifetime of healthy eating (3). In this way, nutrition therapy in GDM becomes an early-stage intervention in the vicious cycle of intergenerational obesity and diabetes (4). Importantly, because the prevalence of GDM has reached an alarming ≥20% of pregnancies (5), a cost-effective approach to management is urgently needed. While controlling fetal exposure to maternal hyperglycemia and overnutrition, effective nutrition can treat GDM in a way that is fiscally reasonable and culturally sensitive, ultimately reducing the need for medication and intensified health care resource use (1).

The importance of nutrition therapy in GDM is a premise unlikely to be contested. Yet, the widely accepted approach rooted in carbohydrate restriction was challenged more than a decade ago based on concerns related to higher fat intake and exacerbation of maternal insulin resistance by free fatty acids (6,7). The dietary management of diabetes in pregnancy has remained in limbo ever since, with no specific guidelines for nutrition therapy in GDM, a travesty that has resulted in non–evidence-based, fragmented, and inconsistent approaches globally (8–12). Action is necessary not only because of the powerful influence of nutrition on fetal programming and development (13,14) but also because of the ability to positively impact the health of millions of mother-infant dyads. Currently, nutrition therapy appears to have become our Achilles heel, such that despite our strength, we have limped forward in generating clinical evidence to substantiate the potential for nutrition in GDM. More than 13 years after the last American Diabetes Association international conference on GDM (7), we have made minimal progress. Perhaps the new meta-analysis by Yamamoto et al. (15) in this issue of *Diabetes Care* represents a turning point.

Over a century of lessons from diabetes was prologue to treatment of GDM. The original approach to treatment of type 1 diabetes was extreme carbohydrate restriction in the preinsulin era, when Allen and Joslin recognized that a low-carbohydrate/high-fat diet (8–10% carbohydrate/70% fat) was more powerful than available medications, such as opioids, arsenic, or potassium bromide (16). After the discovery of insulin, and through the World War II era, restricted carbohydrate intake remained a key component of therapy in pregnancies affected by diabetes (17). Recognition of glucose intolerance in pregnancy outside of preexisting diabetes by O'Sullivan and Mahan (18) in the 1960s underscored the emergence of a GDM phenotype that in no way could have foreshadowed the later explosion of GDM in parallel with the obesity epidemic. By 1990, it made sense based on decades of clinical experience that nutrition in GDM should be rigidly restricted in carbohydrates (19). Suggested in 1990 by Jovanovic-Peterson and Peterson (19), it was recommended that calories be sufficient to avoid starvation ketosis, with carbohydrates limited to 30–40% of total calories (vs. >50% in national dietary guidelines) (20) in order to limit postprandial hyperglycemia (19). Using this approach clinically in 300 women with GDM (19), no macrosomia occurred. That seminal article (19) and two small studies (20,21) (only one of which was randomized) supported the prevailing basis for restriction of dietary carbohydrates in GDM. The rationale was logical enough: restriction of carbohydrate would reduce postprandial hyperglycemia, decrease fetal glucose exposure, and lessen the risk for macrosomia (19).

From that point on, clinical experience and additional nonrandomized studies justified the use of rigid carbohydrate restriction to manipulate maternal metabolism and attenuate fetal overgrowth. Glycemic control could be achieved using diet plus insulin (17),

[1]*Division of Endocrinology, Metabolism and Diabetes, Department of Medicine, University of Colorado Anschutz Medical Campus, Aurora, CO*
[2]*Charles Perkins Centre and School of Life and Environmental Sciences, University of Sydney, Sydney, Australia*

Corresponding author: Teri L. Hernandez, teri.hernandez@ucdenver.edu.

See accompanying article, p. 1346.
See accompanying articles, pp. 1337, 1339, 1362, 1370, 1378, 1385, 1391, and e111.

although consumption of <42% energy as carbohydrate helped avoid the need for insulin therapy (22). Importantly, women with GDM who attained a fasting glucose ≤95 mg/dL (≤5.4 mmol/L) within 2 weeks of diet prescription were less likely to require insulin or oral medication (23,24), demonstrating that nutrition alone could successfully treat GDM.

In the meantime, however, the quest to compare carbohydrate restriction to more liberal carbohydrate consumption became a focus. In well-designed randomized controlled trials (RCTs), more liberal consumption of "complex" carbohydrates in GDM was found to effectively control maternal glycemia compared with carbohydrate restriction (25–29). Moreover, consuming low–glycemic index compared with higher–glycemic index carbohydrates could reduce the need for insulin therapy (30) and control maternal glycemia (31). Yet beneath all of these RCTs were important limitations that undermined the evidence: lack of control for insulin or oral medication, poor compliance, significant study heterogeneity, differences in gestational age at delivery, and inconsistent reporting of gestational weight gain and fetal growth (1). Results from systematic reviews have been mixed, and no approach to nutrition therapy has been found to be superior in terms of maternal and infant outcomes (32). Thus, significant study heterogeneity in combination with uncontrolled confounding factors has rendered the evidence of low quality, preventing adoption of uniform guidelines for nutrition therapy in GDM. Indeed in 2008, the first report (33) that maternal lipids might better predict fetal growth than glucose in women with well-controlled GDM fueled concerns about dietary carbohydrate restriction with compensatory higher fat intake (1,8).

In hindsight, we missed asking the most basic question first: does nutrition therapy in GDM reduce maternal hyperglycemia and attenuate fetal growth patterns? It was this question that Yamamoto et al. (15), commissioned by the International Life Sciences Institute Europe (ILSI Europe), addressed in a high-quality, robust systematic review and meta-analysis published in this issue of *Diabetes Care*. Unlike previous meta-analyses of this subject, they considered RCTs of any nutrition intervention in GDM (vs. control) in the context of maternal postprandial glucose and medication use, as well as neonatal outcomes including birth weight, macrosomia, and large for gestational age. In 18 RCTs with >1,000 mothers, modification of nutrition in GDM resulted in a greater reduction in postprandial glucose and a lesser need for medication. Across 16 studies with >800 infants, modified diets were associated with substantially lower infant birth weight (−170 g) and ~50% reduced risk of macrosomia.

Although there are many strengths to this analysis, a significant underlying limitation to the nutrition studies is that diets could not be blinded to the women themselves. This introduces a significant source of bias because of the reasonable expectation that any novel treatment could be considered superior to usual care. This bias is a universal limitation of most dietary studies, and realistically, it cannot be overcome in free-living individuals.

Nonetheless, for the first time, we have good evidence to suggest there is room for improvement in the usual nutrition advice for women with GDM. Although this gives us cause for hope, we still do not know which diet should be prescribed for women diagnosed with GDM. Perhaps several alternatives are to be expected: humans evolved in a variety of habitats that predicated diets of different composition. The modern diet, however, is based on an abundance of animal foods and plant foods that are very different in chemical and physical structure to those available prior to agriculture (34). The resulting increase in maternal fuels may be the source of overnutrition that precipitates both GDM and an epidemic of large babies (35). Studies such as that by Yamamoto et al. (15) are vital to establishing well-designed future prospective investigations. Indeed, it is time for nutrition therapy in GDM to move forward so we may generate evidence to reveal its true potential to improve mother and infant health.

Funding. T.L.H. has received funding from National Institutes of Health National Institute of Diabetes and Digestive and Kidney Diseases (R01 DK101659). J.C.B.-M. has received research funding from the National Health and Medical Research Council (Australia), Food Innovation Australia Limited, and the Glycemic Index Foundation. She is the president and director of the Glycemic Index Foundation and oversees a glycemic index testing service at the University of Sydney. She has received royalties for books about nutrition and health.

Duality of Interest. T.L.H. has received funding from Janssen Research & Development. She has a collaborative association with Janssen; however, Janssen played no role in the development of this work. No other potential conflicts of interest relevant to this article were reported.

References

1. Hernandez TL, Mande A, Barbour LA. Nutrition therapy within and beyond gestational diabetes. Diab Res Clin Pract. In press
2. Powe CE, Allard C, Battista MC, et al. Heterogeneous contribution of insulin sensitivity and secretion defects to gestational diabetes mellitus. Diabetes Care 2016;39:1052–1055
3. Barker DJ, Thornburg KL. The obstetric origins of health for a lifetime. Clin Obstet Gynecol 2013; 56:511–519
4. Dabelea D, Mayer-Davis EJ, Lamichhane AP, et al. Association of intrauterine exposure to maternal diabetes and obesity with type 2 diabetes in youth: the SEARCH Case-Control Study. Diabetes Care 2008;31:1422–1426
5. Sacks DA, Hadden DR, Maresh M, et al.; HAPO Study Cooperative Research Group. Frequency of gestational diabetes mellitus at collaborating centers based on IADPSG consensus panel-recommended criteria: the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study. Diabetes Care 2012;35:526–528
6. Sivan E, Homko CJ, Whittaker PG, Reece EA, Chen X, Boden G. Free fatty acids and insulin resistance during pregnancy. J Clin Endocrinol Metab 1998;83:2338–2342
7. Metzger BE, Buchanan TA, Coustan DR, et al. Summary and recommendations of the Fifth International Workshop-Conference on Gestational Diabetes Mellitus. Diabetes Care 2007;30 (Suppl. 2):S251–S260
8. Hernandez TL. Carbohydrate content in the GDM diet: two views: view 1: nutrition therapy in gestational diabetes: the case for complex carbohydrates. Diabetes Spectr 2016;29:82–88
9. Committee on Practice Bulletins—Obstetrics. Practice bulletin no. 180: gestational diabetes mellitus. Obstet Gynecol 2017;130:e17–e37
10. Academy of Nutrition and Dietetics. Gestational diabetes: full recommendations and supporting evidence [Internet]. Available from http://www.andeal.org. Accessed 30 March 2017
11. The Royal Australian College of General Practitioners. Gestational diabetes mellitus [Internet], 2016. Available from https://www.racgp.org.au/your-practice/guidelines/diabetes/13-diabetes-and-reproductive-health/133-gestational-diabetes-mellitus. Accessed 14 March 2018
12. National Institute of Health and Care Excellence. Diabetes in pregnancy: management from preconception to the postnatal period [Internet], 2015. Available from https://www.nice.org.uk/guidance/ng3/chapter/1-Recommendations#gestational-diabetes-2. Accessed 14 March 2018
13. Hanson MA, Gluckman PD. Early developmental conditioning of later health and disease: physiology or pathophysiology? Physiol Rev 2014; 94:1027–1076
14. Freinkel N. Banting Lecture 1980. Of pregnancy and progeny. Diabetes 1980;29:1023–1035
15. Yamamoto JM, Kellett JE, Balsells M, et al. Gestational diabetes mellitus and diet: a systematic review and meta-analysis of randomized controlled trials examining the impact of modified dietary interventions on maternal glucose control and neonatal birth weight. Diabetes Care 2018;41:1346–1361

16. Westman EC, Yancy WS Jr, Humphreys M. Dietary treatment of diabetes mellitus in the pre-insulin era (1914-1922). Perspect Biol Med 2006; 49:77–83
17. Mestman JH. Historical notes on diabetes and pregnancy. Endocrinologist 2002;12:224–242
18. O'Sullivan JB, Mahan CM. Criteria for the oral glucose tolerance test in pregnancy. Diabetes 1964;13:278–285
19. Jovanovic-Peterson L, Peterson CM. Dietary manipulation as a primary treatment strategy for pregnancies complicated by diabetes. J Am Coll Nutr 1990;9:320–325
20. Peterson CM, Jovanovic-Peterson L. Percentage of carbohydrate and glycemic response to breakfast, lunch, and dinner in women with gestational diabetes. Diabetes 1991;40(Suppl. 2):172–174
21. Ilic S, Jovanovic L, Pettitt DJ. Comparison of the effect of saturated and monounsaturated fat on postprandial plasma glucose and insulin concentration in women with gestational diabetes mellitus. Am J Perinatol 1999;16:489–495
22. Major CA, Henry MJ, De Veciana M, Morgan MA. The effects of carbohydrate restriction in patients with diet-controlled gestational diabetes. Obstet Gynecol 1998;91:600–604
23. McFarland MB, Langer O, Conway DL, Berkus MD. Dietary therapy for gestational diabetes: how long is long enough? Obstet Gynecol 1999; 93:978–982
24. Barnes RA, Wong T, Ross GP, et al. A novel validated model for the prediction of insulin therapy initiation and adverse perinatal outcomes in women with gestational diabetes mellitus. Diabetologia 2016;59:2331–2338
25. Nolan CJ. Improved glucose tolerance in gestational diabetic women on a low fat, high unrefined carbohydrate diet. Aust N Z J Obstet Gynaecol 1984;24:174–177
26. Cypryk K, Kamińska P, Kosiński M, Pertyńska-Marczewska M, Lewiński A. A comparison of the effectiveness, tolerability and safety of high and low carbohydrate diets in women with gestational diabetes. Endokrynol Pol 2007;58:314–319
27. Asemi Z, Tabassi Z, Samimi M, Fahiminejad T, Esmaillzadeh A. Favourable effects of the Dietary Approaches to Stop Hypertension diet on glucose tolerance and lipid profiles in gestational diabetes: a randomised clinical trial. Br J Nutr 2013;109:2024–2030
28. Hernandez TL, Van Pelt RE, Anderson MA, et al. A higher-complex carbohydrate diet in gestational diabetes mellitus achieves glucose targets and lowers postprandial lipids: a randomized crossover study. Diabetes Care 2014;37: 1254–1262
29. Hernandez TL, Van Pelt RE, Anderson MA, et al. Women with gestational diabetes mellitus randomized to a higher-complex carbohydrate/low-fat diet manifest lower adipose tissue insulin resistance, inflammation, glucose, and free fatty acids: a pilot study. Diabetes Care 2016;39:39–42
30. Moses RG, Barker M, Winter M, Petocz P, Brand-Miller JC. Can a low-glycemic index diet reduce the need for insulin in gestational diabetes mellitus? A randomized trial. Diabetes Care 2009;32:996–1000
31. Hu ZG, Tan RS, Jin D, Li W, Zhou XY. A low glycemic index staple diet reduces postprandial glucose values in Asian women with gestational diabetes mellitus. J Investig Med 2014;62:975–979
32. Han S, Middleton P, Shepherd E, Van Ryswyk E, Crowther CA. Different types of dietary advice for women with gestational diabetes mellitus. Cochrane Database Syst Rev 2017;2:CD009275
33. Schaefer-Graf UM, Graf K, Kulbacka I, et al. Maternal lipids as strong determinants of fetal environment and growth in pregnancies with gestational diabetes mellitus. Diabetes Care 2008; 31:1858–1863
34. Cordain L, Eaton SB, Sebastian A, et al. Origins and evolution of the Western diet: health implications for the 21st century. Am J Clin Nutr 2005;81:341–354
35. Archer E. The childhood obesity epidemic as a result of nongenetic evolution: the maternal resources hypothesis. Mayo Clin Proc 2015;90: 77–92