Nutrition Therapy in Gestational Diabetes Mellitus: Time to Move Forward

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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),...
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 glycaemia 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 glycaemia (31). Yet beneath all of these RCTs were important limitations that underlined 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 hyperglycaemia 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’s 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.

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