The Potential for Dietary Intervention Postpartum in Women With Gestational Diabetes

Gestational diabetes mellitus (GDM) identifies premenopausal women at risk for diabetes, predominately type 2 diabetes (1,2). The rapidity of diabetes onset after a GDM pregnancy depends on the population. While >50% of Hispanic-American women become diabetic within 5 years after a GDM pregnancy (3), <30% of women of white European ancestry are diabetic within 20 years (4). However, in these lower-risk populations the frequency of diabetes continues to increase above background 30 years after a GDM pregnancy. Alongside ethnicity, other nonmodifiable risk factors for future type 2 diabetes include age, family history, and degree of glucose intolerance in pregnancy (3); while the known modifiable risk factors include obesity, weight gain, and future pregnancies (5). The work by Moses et al. in this issue of *Diabetes Care* (6) suggests that dietary fat may be another potentially modifiable risk factor.

Women with a history of gestational diabetes mellitus (GDM) have evidence of β-cell dysfunction both during and after pregnancy (7–9). These women are metabolically vulnerable, with insufficient β-cell reserve to offset the physiological decrease in insulin sensitivity that occurs in late pregnancy. Many women are also insulin resistant, both during and after pregnancy (10). Lifestyle changes that improve insulin sensitivity postpartum should theoretically preserve β-cell function and slow the progression to type 2 diabetes. Large epidemiological studies show that weight loss, increased physical activity, and low-fat, high-carbohydrate diets all independently improve insulin sensitivity and lessen the risk of diabetes (11–16). Women with previous GDM should also benefit from these lifestyle patterns.

In a 16-year follow-up study of GDM women from Boston, MA, diabetes developed in 48% of obese women, compared with 28% for the nonobese women (1). To date, no retrospective or prospective studies have examined the influence of physical activity or dietary composition on future diabetes in this at-risk group. The work by Moses et al. (6) starts to redress this omission. Dietary histories of women between an index GDM pregnancy and a subsequent pregnancy were compared according to whether or not GDM recurred. The Moses et al. (6) report states that the recurrence of GDM was greater in women who consumed more fat between pregnancies. The use of recurrence of GDM in a subsequent pregnancy rather than type 2 diabetes as the primary endpoint allows this retrospective study to be conducted over a shorter time frame (i.e., <5 years) than that required for the development of type 2 diabetes, which in a predominately white population would require a 30-year study. GDM recurs in 30–60% (17) of subsequent pregnancies, a similar rate to impaired glucose tolerance (IGT) outside pregnancy being confirmed after retesting (18). Future type 2 diabetes is greatest in individuals who retest positive for either GDM or IGT; however, those who revert to normal glucose tolerance retain an increased lifetime risk (18). Some of the advantages of using the recurrence of GDM as a surrogate endpoint for future diabetes are offset by the large number of initial GDM pregnancies required, because only a minority of women will have a subsequent pregnancy. Obtaining accurate dietary histories is always problematic. However, if the finding is accepted that the total energy derived from dietary fat influences the recurrence of GDM in a subsequent pregnancy, we are left with four possible explanations, none mutually exclusive of the others.

First, women who modified their dietary fat intake between pregnancies lessen their risk of subsequent GDM. Reduction in dietary fat would be anticipated to result in an increase in dietary carbohydrate and in an overall reduction in total energy consumption (19), changes that would promote weight reduction and improved insulin sensitivity. Continuation of this diet up until retesting for GDM in a subsequent pregnancy would optimize glucose tolerance, even in people with limited β-cell reserve.

The second explanation is that these women made no conscientious dietary changes between pregnancies, and dietary histories reflected their habitual adult diet. Population studies show that habitual high-fat diets are associated with hyperinsulinemia, suggesting an increased insulin resistance (20) and an increased risk for type 2 diabetes (16,21,22). Previous GDM women who habitually consumed a high-fat diet would have insulin resistance predating and continuing after an initial GDM pregnancy. Long-standing insulin resistance would have an adverse cumulative effect on their β-cell reserve, increasing their susceptibility to the recurrence of GDM in any subsequent pregnancy. Dietary fat is central in the pathogenesis of insulin resistance (23,24); its metabolite nonesterified fatty acid (NEFA) competes with glucose as an oxidative fuel. Cellular uptake of NEFA inhibits intracellular glucose metabolism, which reduces GLUT4 expression that could potentially compromise glucose tolerance (25,26).

A third explanation would be that it is the carbohydrate constituency of the diet and not the fat content that is important (27). Habitual high-fat diets by inference are low-carbohydrate diets. Both the American Nurses and the Health Professionals follow-up studies have shown that high-carbohydrate diets characterized by high-fiber, low–glycemic index diets reduce the risk of NIDDM (28,29). Low–glycemic index diets improve insulin sensitivity in subjects with insulin-resistant syndromes, including diabetes, obesity, ischemic heart disease, and those at risk of heart disease (30–33). The metabolic benefits of low–glycemic index foods result from their ability to prolong carbohydrate absorption and attenuate the insulin response. Postprandially, NEFA levels are lower because of longer suppression of hormone-sensitive lipase, which preferentially favors glucose uptake. Low–glycemic index diets, similar to low-fat diets, should therefore increase GLUT4 expression in addition to reducing hepatic gluconeogenesis (34).

The fourth explanation could be that women with a subsequent pregnancy not

complicated by GDM were not only consuming less dietary fat but had adopted other healthier lifestyle behavioral traits, which included increased exercise (35) and reduced smoking habits (36,37), changes known to improve insulin sensitivity.

Preventive measures to delay the onset of type 2 diabetes are encouraging. The DaQing Study reported a 30%, 6-year reduction in the progression of IGT to NIDDM in Chinese men and women adopting a low-fat, high-carbohydrate diet with or without the addition of exercise (38). The Diabetic Prevention Program, which includes previous GDM women, is currently evaluating lifestyle and therapeutic interventions on the 4.5-year progression of IGT to NIDDM (39). GDM women are an ideal group for diabetic prevention, because they are by selection mothers of young families, often responsible for the shopping and the preparation of the family meals. Behavioral intervention in this group has the potential to favorably influence younger family members at risk for diabetes.

Despite this optimism, it is becoming apparent that there is a time in the progression of IGT to type 2 diabetes when lifestyle intervention is unable to reverse the metabolic inevitable decline to diabetes. In the high-risk Hispanic population, it is the degree of postpartum glucose intolerance rather than postpartum weight loss or weight maintenance that predicts the onset of diabetes (3). Results of the multicentered Fasting Hyperglycemia Study Group have shown little benefit 1 or 3 years after the introduction of reinforced healthy living advice, including low-fat, high-carbohydrate diets (40,41), in nondiabetic subjects with increased fasting plasma glucose (5.5–7.7 mmol/l). This study implies that when fasting glucose passes a given threshold, β-cell dysfunction has deteriorated to a level that lifestyle changes are unable to reduce insulin sensitivity sufficiently to maintain or improve glucose tolerance.

With the above reservations, the findings of Moses et al. (6) complement the epidemiological and clinical investigational studies that show that lifestyle behavioral patterns, including diet, can modify an individual's risk of type 2 diabetes. The potential benefits of lessening the progression to diabetes in previous GDM women by encouraging a low-fat, high-carbohydrate diet and regular exercise postpartum are enormous. However, they will remain only potential benefits until the necessary prospective interventional studies with diet and exercise are done. It will be necessary to show that advice postpartum can change lifestyle habits for women sufficiently to reduce not only the recurrence rate of GDM in further pregnancies but delay and prevent the later development of diabetes.

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