Carbohydrate Content in the GDM Diet: Two Views

View 1: Nutrition Therapy in Gestational Diabetes: The Case for Complex Carbohydrates

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Nutrition therapy is the most formative approach to treating gestational diabetes mellitus (GDM). In pregnancy, a prevailing maternal metabolic adaptation is the shift in glucose metabolism from insulin sensitivity to insulin resistance, exemplified by higher circulating lipids, heightened postprandial glucose, and increased β-cell demand/response (1,2). These intriguing exacerbations of human physiology are recognized to be additive to the prepregnancy phenotype (3), now largely characterized by overweight and obesity (4). When women cannot adapt to the glycemic demands of pregnancy, hyperglycemia and glucose intolerance manifest by the late second trimester, and this is recognized as GDM (5). There is hope that optimal nutrition therapy can offer a lower-cost treatment strategy for the rising number of women with GDM, which is anticipated to encompass 18% of all pregnancies after new diagnostic criteria are adopted (6,7). A treatment approach that circumvents expensive medication, reduces intensified fetal surveillance, and favorably affects both maternal and infant health is crucial.

The conventional approach to nutrition therapy in GDM has focused on carbohydrate restriction (8). Although effective based on clinical experience, this approach is perhaps the most challenging component to treatment adherence in GDM. Moreover, the paucity of evidence supporting carbohydrate restriction or any diet prescription in GDM has now been recognized. With carbohydrate restriction comes the potential for increased dietary fat intake, and mounting evidence supports a strong association between maternal lipids (i.e., triglycerides and free fatty acids [FFAs]) and excess fetal growth (9).

Accordingly, in 2005, the American Diabetes Association withdrew nutrition therapy guidelines for GDM (10). To date, there is no consensus on the optimal diet for women with GDM, emphasizing the need for highly controlled randomized trials (10–12).

A more contemporary understanding of dietary complex carbohydrate has underscored a differential impact on postprandial glucose, wherein some polysaccharides and starches (primarily from whole grains, starchy vegetables, and legumes) tend to mitigate a sharp rise in postprandial glucose (13). This raises the possibility that nutrition therapy in GDM may safely include more complex, nutrient-dense carbohydrate than the conventional restrictive approach has.
allowed. The purpose of this article is to review the background, evidence, and rationale for a balanced liberalization of complex carbohydrate within nutrition therapy regimens for women with GDM.

Potential of Nutrition Therapy to Break a Relentless Cycle

A balanced, effective macronutrient diet composition in GDM could improve maternal glycemia, but simultaneously could prevent worsening of maternal metabolic parameters that lead to excessive fetal growth. GDM has the potential to create a relentless cycle of obesity and diabetes prevalence. Up to 50% of mothers with GDM will develop type 2 diabetes within 10–20 years of their pregnancy (14–17). Moreover, the offspring of women with GDM are at risk for being large for gestational age (LGA) (18), having increased adiposity (19,20), and developing impaired glucose tolerance (21,22), metabolic syndrome (23), and type 2 diabetes (15,16,24–26). Strong positive associations between infant birth weight and later BMI support that larger newborns are more likely to become obese adults (18,27), and females born LGA (≥90th percentile) have a doubled risk for delivering an LGA infant themselves (28). Because the risk is attributed to in utero exposure to diabetes or GDM (26,29,30), women with GDM perpetuate a cycle of obesity and diabetes prevalence through generations when affected daughters become pregnant (31). Overweight and obesity currently affect up to 75% of young women in the United States (32), and, as GDM prevalence increases, the GDM intrauterine metabolic environment is expected to further fuel the risk of offspring obesity and glucose intolerance (33). Nutrition therapy holds great potential to effectively treat this growing population of mothers and offspring.

Stress, Anxiety, and Fear as Barriers to GDM Nutrition Therapy Treatment

A GDM diagnosis generates stress, anxiety, and fear, all of which may undermine any approach to nutrition therapy. Until the diagnosis at ~28 weeks’ gestation, most women have experienced a “normal” pregnancy, during which the development of GDM has occurred asymptotically (34). The diagnosis suddenly necessitates a high-risk pregnancy label, adherence to nutrition therapy, and heightened surveillance. Anxiety and depression in these women may stem from self-blame (34), feelings of loss of control (35,36), fear of macrosomia or infant complications (36,37), feelings of being misunderstood by their partner (38), and fear of future type 2 diabetes (34), all of which are magnified by the confining high-risk pregnancy label and controlled or restrictive nature of nutrition therapy (36–38).

Women with GDM have expressed feeling an intense moral obligation to the health of their unborn child, motivating them to endure intensified management (38). Although they are motivated to modify their lifestyle, adherence to nutrition therapy has been identified as the most arduous, confining component of treatment (34,36,37). Nutrition therapy has been described as intrusive (34) and an infringement on cultural/social roles, beliefs, and diet practices (35,36,39). Quick adaptation to a new diet composition late in pregnancy is challenging (34,40). Many women do not understand food properties (i.e., types of carbohydrates and types of fats), making food choices mentally taxing (40). In our clinic, women with GDM were so fearful of macrosomia that they followed extreme carbohydrate-restricted diets, opting to replace calories from carbohydrates with calories from fat. Although this practice resulted in controlled glycemia, mounting evidence supports a potential deleterious intrauterine programming effect of FFAs on aberrant fetal growth and long-term infant health outcomes (41,42).

Unintended Consequences of Carbohydrate Restriction in GDM?

Nutrition therapy is the first line of treatment for women with GDM. If effective, glycemia is controlled, and adequate weight gain and nutritional status are supported (12,43). Twenty years ago, it was reported based on clinical experience that a carbohydrate-restricted diet (40%) in GDM blunted postprandial glucose excursions (8). This observation fueled the focus on dietary carbohydrate and was corroborated when a strong association between maternal postprandial glycemia and infant size was reported (44,45). Although there is a rationale for carbohydrate restriction (i.e., glucose control), it also creates a context for unbalanced macronutrient intake. In obesogenic environments, a focus on carbohydrate restriction facilitates an increase in dietary fat due to the abundance and cost-effective availability of saturated fats and processed foods (46,47). A large increase in protein is unlikely because it is consumed consistently in humans (46). An unbalanced increase in protein (i.e., without appropriate micronutrient intake) within pregnancy diets has been linked to reduced birth weight (48).

A diet-induced worsening of maternal insulin resistance (49,50) could further increase nutrient delivery to the fetus and worsen fetal hyperinsulinemia (51). Emerging data in animal and nonhuman primate models support an intrauterine influence of dietary fat in promoting offspring adiposity, hepatic steatosis, and metabolic syndrome (42,52). In humans, maternal triglyceride and FFA levels may be stronger predictors of excess fetal fat accretion than maternal glucose (9,53), raising the question of whether glycemia should constitute the only focus for therapy in GDM (54).
Restriction of dietary carbohydrate has been the cornerstone of diabetes treatment for >100 years. Before insulin, a diet prescription of ~8% carbohydrate and ~70% fat nearly eliminated glycosuria (58). Early 20th century pioneers in diabetes management established that a low-carbohydrate diet prescription required individualization but is generally ≤40% of total calories (58). As early management protocols for diabetes in pregnancy emerged to focus on “good” glycemic control to reduce maternal and fetal complications (59,60), nutrition therapy for GDM evolved to focus on control of maternal glucose. Data from later, nonrandomized trials supported carbohydrate restriction (61) by demonstrating blunted insulin secretion in response to a meal high in saturated fatty acids (62) and less need for insulin therapy with a carbohydrate intake <42% (63). However, carbohydrate restriction to <39% has been linked to the highest infant birth weights (64). Most studies of nutrition therapy in GDM are riddled with confounding insulin use, lack of compliance, heterogeneity in outcome reporting, and the absence of reported infant outcomes (i.e., birth weight and body composition) (11,12).

Grounded in the concern about increased fat intake, we asked a question to challenge the dogma emphasizing carbohydrate restriction in GDM. What if nutrition therapy in GDM focused on liberalization of complex carbohydrate instead of restriction of all carbohydrate? A salient finding across the few published randomized, controlled trials was that diets that were higher in complex carbohydrate and low–glycemic index foods (55–70% carbohydrate) were well tolerated (65–67). In fact, in GDM, diets higher in unrefined/complex carbohydrate have effectively blunted postprandial hyperglycemia (65,68), reduced the need for insulin therapy (66), lowered fasting LDL cholesterol levels (65,69) and FFAs (65), and improved insulin sensitivity (70), A1C (69), and systolic blood pressure (69).

Thus, we developed a diet to challenge the low-carbohydrate diet for GDM (13). We have named this diet CHOICE (Choosing Healthy Options in Carbohydrate Energy), emphasizing an overall cardiometabolically healthy, nutrient-dense eating plan (57) that encourages choosing the right kinds of carbohydrate to control glycemia (unrefined/complex/nutrient-dense), instead of restricting total carbohydrate. Recently, we demonstrated in a controlled, randomized crossover study (all food provided, diet-controlled GDM), that, compared to a low-carbohydrate diet (40% carbohydrate/45% fat), the CHOICE diet (60% carbohydrate/25% fat) effectively controlled glycemia to...
within current treatment targets (13). Although more high-quality, randomized studies are needed, all of the evidence to date suggests that liberalization of complex carbohydrate in nutrition therapy for GDM meets management goals, may be effective in optimizing maternal and infant metabolic outcomes, and may help mitigate rising insulin resistance with advancing gestation in women with diet-controlled GDM.

**Diet and Insulin Action: The Case for Complex Carbohydrates**

Maternal insulin resistance is a key regulator of fetal nutrient exposure. Might it be possible to mitigate adipose tissue insulin resistance using nutrition therapy in GDM? If effective, this would result in optimal nutrient delivery and avoid the intrauterine overnutrition that programs aberrant growth patterns (42).

One of the greatest concerns in GDM is the risk for fetal LGA status and increased adiposity, historically linked to maternal hyperglycemia (25,71) and recently confirmed (72,73). Freinkel (51) described the intrauterine environment as an “incubation medium” shaped by all maternal nutrients—not only glucose. It is now understood that maternal glucose, lipids (triglycerides, FFAs), and amino acids are all potent fuels...
for fetal growth. In normal late pregnancy, maternal insulin resistance increases to ensure rapidly increasing fetal-placental energy requirements and fetal growth. However, overweight and obese women who develop GDM enter pregnancy with chronic preexisting insulin resistance (74) and insufficient β-cell reserve (1,3). These women display worsened insulin resistance in skeletal muscle (75), liver, and adipose tissue (2,3,76,77) by the third trimester. Diets high in fat may promote insulin resistance in part through elevation of tumor necrosis factor α (78) and FFAs, resulting in impaired insulin signaling (76,79). Elevated FFAs may also promote a β-cell defect (76), and evidence suggests that higher pre- and early pregnancy intake of animal fats and cholesterol (80) are associated with increased risk for GDM, implicating an effect of dietary fat and cholesterol on exacerbation of insulin resistance. Thus, there is concern that a low-carbohydrate diet that facilitates an unbalanced increase in fat may actually worsen maternal insulin resistance in GDM, contributing to intrauterine overnutrition.

Insulin is a hormone with many functions beyond glucose control. It serves as a suppressor of FFA release (lipolysis) from stored triglyceride in adipose tissue. With better insulin action, there is better insulin suppression of lipolysis, less FFA exposure over time, and improved tissue sensitivity to insulin.

We have learned important lessons about diet and fuel metabolism from our controlled studies, both outside and within pregnancy. For example, after following a low-carbohydrate, high-fat diet (20 g carbohydrate/day) for 6 weeks, men and women secreted minimal insulin over 24 hours, resulting in an almost complete lack of FFA suppression by insulin (a marker of insulin resistance) and sustained elevated FFA levels over 24 hours (Figure 1A and B) (81). Our crossover study in diet-controlled GDM (13) showed that, after a controlled breakfast on the CHOICE diet, there was a higher insulin response, resulting in lower postprandial FFAs. The low-carbohydrate diet resulted in less insulin secretion (as seen in our nonpregnant participants) and worse suppression of lipolysis/increased postprandial FFAs (Figure C and D).

Humans are postprandial much of the day, and if the patterns seen in Figures 1A and B were similar in mothers with GDM, there would be high fetoplacental lipid exposure over 24 hours on a low-carbohydrate diet. In diet-controlled GDM, if the responses in Figures 1C and D were similar across meals, the low-carbohydrate diet would result in nearly 20% more lipid exposure than with the CHOICE diet. Importantly, early evidence also showed that 6–7 weeks of therapy with the CHOICE diet resulted in lower fasting glucose and FFAs, better insulin suppression of FFAs in adipose tissue, less adipose tissue inflammation, and a trend for less neonatal adiposity, all of which suggest better insulin action despite the rising insulin resistance of pregnancy (82). The case for including complex carbohydrates in nutrition therapy for GDM, then, is that, if the degree of maternal insulin resistance is a key regulator in controlling maternal glucose, lipids, and amino acids to the fetal-placental unit, and it can be lessened by balanced liberalization of complex nutrient-dense carbohydrate and reduced dietary fat, then excessive fetal growth and potential programming effects could be strongly modifiable by nutrition therapy in GDM.

Conclusion
Adherence to a low-carbohydrate diet is one of the most challenging components to therapy for GDM. It is possible that a less restrictive approach to nutrition therapy will lessen feelings of confinement in GDM. Although more high-quality, randomized trials are needed, there is evidence that a balanced liberalization of complex carbohydrate as part of an overall nutrient-dense eating plan in GDM meets treatment goals and may mitigate maternal adipose tissue insulin resistance, both of which may promote optimal metabolic outcomes for mothers and their offspring.

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Duality of Interest
No potential conflicts of interest relevant to this article were reported.

References
1. Di Cianni G, Miccoli R, Volpe L, Lencioni C, Del Prato S. Intermediate metabolism in normal pregnancy and in gestational diabetes. Diabetes Metab Res Rev 2003;19:259–270
2. Butte NF. Carbohydrate and lipid metabolism in pregnancy: normal compared with gestational diabetes mellitus. Am J Clin Nutr 2000;71:1256S–1261S
3. Buchanan TA, Xiang AH. Gestational diabetes mellitus. J Clin Invest 2005;115:485–491
4. Nicklas JM, Barbour LA. Optimizing weight for maternal and infant health: tenable, or too late? Expert Rev Endocrinol Metab 2015;10:227–242
5. American College of Obstetricians and Gynecologists. Gestational diabetes mellitus (Practice Bulletin No. 137). Obstet Gynecol 2013;122:406–416
6. Sacks DA, Hadden DR, Maresh M, et al. 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
7. Metzger BE, Gabbe SG, Persson B, et al. International Association of Diabetes and Pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care 2010;33:676–682
8. Jovanovic-Peterson L, Peterson CM. Dietary manipulation as a primary treatment strategy for pregnancies complicated by diabetes. J Am Coll Nutr 1999;9:320–325
9. Schaefer-Graf UM, Graf K, Kolbacka 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
10. Metzger BE, Buchanan TA, Coustan D, et al. Summary and recommendations of the Fifth International Workshop-Conference on Gestational Diabetes Mellitus. Diabetes Care 2007;30(Suppl 2):S251–S260
11. Han S, Crowther CA, Middleton P, Heatley E. Different types of dietary advice for women with gestational diabetes mellitus. Cochrane Database Syst Rev 2013;3:CD009527
12. Hernandez TL, Anderson MA, Chartier-Logan C, Friedman JE, Barbou LA. Strategies in the nutritional management of gestational diabetes. Clin Obstet Gynecol 2013;56:803–815
13. 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
14. American Diabetes Association. Gestational diabetes mellitus. Diabetes Care 2004;27(Suppl 1):S88–S90
15. Barbou LA. New concepts in insulin resistance of pregnancy and gestational diabetes: long-term implications for mother and offspring. J Obstet Gynecol 2003;23:545–549
16. Ferrara A, Kahn HS, Quesenberry CP, Riley C, Hedderson MM. An increase in the incidence of gestational diabetes mellitus: Northern California, 1991–2000. Obstet Gynecol 2004;103:526–533
17. Lauenborg J, Hansen T, Jensen DM, et al. Increasing incidence of diabetes after gestational diabetes: a long-term follow-up in a Danish population. Diabetes Care 2004;27:1194–1199
18. Rogers I. The influence of birthweight and intrauterine environment on adiposity and fat distribution in later life. Int J Obes Relat Metab Disord 2003;27:755–777
19. Catalano PM, Thomas A, Huston-Presley L, Amini SB. Increased fetal adiposity: a very sensitive marker of abnormal in utero development. Am J Obstet Gynecol 2003;189:1698–1704
20. Vohr BR, McGarvey ST, Tucker R. Effects of maternal gestational diabetes on offspring adiposity at 4–7 years of age. Diabetes Care 1999;22:1284–1291
21. Silverman BL, Landsberg L, Metzger BE. Fetal hyperinsulinism in offspring of diabetic mothers: association with the subsequent development of childhood obesity. Ann N Y Acad Sci 1993;699:36–45
22. Silverman BL, Metzger BE, Cho NH, Loebl CA. Impaired glucose tolerance in adolescent offspring of diabetic mothers: relationship to fetal hyperinsulinism. Diabetes Care 1995;18:611–617
23. Boney CM, Verma A, Tucker R, Vohr BR. Metabolic syndrome in childhood: association with birth weight, maternal obesity, and gestational diabetes mellitus. Pediatrics 2005;115:e296–e296
24. Dabelea D, Mayer-Davis EJ, Lecomphane 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
25. Jovanovic L. Gestational diabetes mellitus: the case for euglycemia. Can J Diabetes 2005;29:428–432
26. Silverman BL, Rizzo TA, Cho NH, Metzger BE. Long-term effects of the intrauterine environment: the Northwestern University Diabetes in Pregnancy Center. Diabetes Care 1999;21(Suppl 2):B142–B149
27. Wells JC, Chomtho S, Fettwrell MS. Programming of body composition by early growth and nutrition. Proc Nutr Soc 2007;64:423–434
28. Ahlsson F, Gustafsson J, Tuvemo T, Lundgren M. Females born large for gestational age have a double risk of giving birth to large for gestational age infants. Acta Paediatr 2007;96:358–362
29. Dabelea D, Knowler WC, Pettitt DJ. Effect of diabetes in pregnancy on offspring: follow-up research in the Pima Indians. J Matern Fetal Med 2000;9:83–88
30. Dabelea D, Hanson RL, Lindsay RS, et al. Intrauterine exposure to diabetes conveys risks for type 2 diabetes and obesity: a study of discordant sibships. Diabetes 2000;49:2208–2211
31. Barbou LA. Changing perspectives in pre-existing diabetes in pregnancy and gestational diabetes: implications on maternal and infant short- and long-term outcomes. Curr Opin Endocrinol Diabetes Obes 2014;21:264–270
32. Flegal KM, Carroll MD, Kit BK, Ogden CL. Prevalence of obesity and trends in the distribution of body mass index among US adults, 1999–2010. JAMA 2012;307:491–497
33. Heerwagen MJ, Miller MR, Barbou LA, Friedman JE. Maternal obesity and fetal metabolic programming: a fertile epigenetic soil. Am J Physiol Regul Integr Comp Physiol 2010;299:R711–R722
34. Lawson EJ, Rajaram S. A transformed pregnancy: The psychosocial consequences of gestational diabetes. Sociol Health Illn 1994;16:536–562
35. Devsam BU, Bogossian FE, Peacock AS. An interpretive review of women’s experiences of gestational diabetes mellitus: proposing a framework to enhance midwifery assessment. Women Birth 2013;26:e69–e76
36. Hui AL, Sevenhuysen G, Harvey D, Salamon E. Food choice decision-making by women with gestational diabetes. Can J Diabetes 2014;38:26–31
37. Lapolla A, Di Cianni G, Di Benedetto A, et al. Quality of life, wishes, and needs in women with gestational diabetes: Italian DAWN Pregnancy Study. Int J Endocrinol 2012;784726
38. Evans MK, O’Brien B. Gestational diabetes: the meaning of an at-risk pregnancy. Qual Health Res 2005;15:66–81
39. Smith-Morris CM. Diagnostic controversy: gestational diabetes and the meaning of risk for Pima Indian women. Med Anthropol 2005;24:145–177
40. Hui AL, Sevenhuysen G, Harvey D, Salamon E. Food choice decision-making by women with gestational diabetes. Can J Diabetes 2014;38:26–31
41. Innis SM. Metabolic programming of long-term outcomes due to fatty acid nutrition in early life. Matern Child Nutr 2011;7(Suppl 2):112–123
42. Friedman JE. Obesity and gestational diabetes mellitus pathways for programming in mouse, monkey, and man: where do we go next? Diabetes Care 2013;38:1402–1411
43. Gunderson EP. Gestational diabetes and nutritional recommendations. Curr Diab Rep 2004;4:377–386
44. Combs CA, Gunderson E, Kitzmiller JL, Gavrin LA, Main EK. Relationship of fetal macrosomia to maternal postpartum glucose control during pregnancy. Diabetes Care 1992;15:1251–1257
45. de Veciana M, Major CA, Morgan MA, et al. Postparturial versus prepartum blood glucose monitoring in women with gestational diabetes mellitus requiring insulin therapy. N Engl J Med 1995;333:1237–1241
46. Simpson SJ, Raubenheimer D. Obesity: the protein leverage hypothesis. Obes Rev 2005;6:133–142
47. Booth SL, Sallis JF, Ritenbaugh C, et al. Environmental and societal factors affect food choice and physical activity: rationale, influences, and leverage points. Nutr Rev 2001;59:S21–S39
48. Barker DJ, Thornburg KL. The obstetric origins of health for a lifetime. Clin Obstet Gynecol 2013;56:511–519
49. Lichtenstein AH, Schwab US. Relationship of dietary fat to glucose metabolism. Atherosclerosis 2000;150:227–243
50. Reer J, Koska J, Ovias M, Reaven P. Dietary models of insulin resistance. Metabolism 2015;64:163–171
51. Freinkel N. Banting Lecture 1980: Of pregnancy and progeny. Diabetes 1980;29:1023–1035
52. McCurdy CE, Bishop JM, Williams SM, et al. Maternal high-fat diet triggers lipotoxicity in the fetal livers of nonhuman primates. J Clin Invest 2009;119:323–335
53. Harman KA, Gerard L, Jensen DR, et al. Continuous glucose profiles in obese and normal-weight pregnant women on a-
trolled diet: metabolic determinants of fetal growth. Diabetes Care 2011;34:2198–2204
54. Barrett HL, Dekker NM, McIntyre HD, Callaway I.K. Normalizing metabolism in diabetic pregnancy: is it time to target lipids? Diabetes Care 2014;37:1484–1493
55. Blumer I, Hadar E, Hadden DR, et al. Diabetes and pregnancy: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2013;98:4227–4249
56. Eckel RH. Role of glycemic index in the context of an overall heart-healthy diet. JAMA 2014;312:2508–2509
57. Eckel RH, Jakicic JM, Ard JD, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 2014;129(25 Suppl.2):S76–S99
58. 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
59. Nestman JH. Historical notes on diabetes and pregnancy. Endocrinologist 2002;12:224–242
60. Hernandez TL. Glyceric targets in pregnancies affected by diabetes: historical perspective and future directions. Curr Diab Rep 2015;15:565–576
61. 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
62. 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
63. 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
64. Romon M, Nuttens MC, Vambergue A, et al. Higher carbohydrate intake is associated with decreased incidence of newborn macrosomia in women with gestational diabetes. J Am Diet Assoc 2001;101:897–902
65. Nolan CJ. Improved glucose tolerance in gestational diabetic women on a low fat, high refined carbohydrate diet. Aust N Z J Obstet Gynaecol 1984;24:174–177
66. 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
67. Louie JC, Markovic TP, Perera N, et al. A randomized controlled trial investigating the effects of a low-glycemic index diet on pregnancy outcomes in gestational diabetes mellitus. Diabetes Care 2011;34:2341–2346
68. Cypryk K, Kaminska P, Kosinski M, Pertynska-Marzewska M, Lewinski 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
69. 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
70. Lauszus FF, Rasmussen OW, Henriksen JE, et al. Effect of a high monounsaturated fatty acid diet on blood pressure and glucose metabolism in women with gestational diabetes mellitus. Eur J Clin Nutr 2001;55:436–443
71. Jovanovic L. What is so bad about a big baby? Diabetes Care 2001;24:1317–1318
72. Metzger BE, Lowe LP, Dyer AR, et al. Hyperglycemia and adverse pregnancy outcomes. N Engl J Med 2008;358:1991–2002
73. Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study Group. Associations with neonatal anthropometrics. Diabetes 2009;58:453–459
74. Catalano PM, Huston L, Amini SB, Kalhan SC. Longitudinal changes in glucose metabolism during pregnancy in obese women with normal glucose tolerance and gestational diabetes mellitus. Am J Obstet Gynecol 1999;180:903–916
75. Barbour LA, McCurdy CE, Hernandez TL, Friedman JE. Chronically increased S6K1 is associated with impaired IRS1 signaling in skeletal muscle of GDM women with impaired glucose tolerance postpartum. J Clin Endocrinol Metab 2011;96:1431–1441
76. Sivan E, Homko CJ, Whitaker PG, Reee EA, Chen X, Boden G. Free fatty acids and insulin resistance during pregnancy. J Clin Endocrinol Metab 1998;83:2338–2342
77. Sivan E, Chen X, Homko CJ, Reee EA, Boden G. Longitudinal study of carbohydrate metabolism in obese pregnant women. Diabetes Care 1997;20:1470–1475
78. Kirwan JP, Hauguel-de Mouzon S, Lepercq J, et al. TNF-alpha is a predictor of insulin resistance in human pregnancy. Diabetes 2002;51:2207–2213
79. Barbour LA, McCurdy CE, Hernandez TL, Kirwan JP, Catalano PM, Friedman JE. Cellular mechanisms for insulin resistance in normal pregnancy and gestational diabetes. Diabetes Care 2007;30(Suppl. 2):S81–S88
80. Bowers K, Tobias DK, Yeung E, Hu FB, Zhang C. A prospective study of prepregnancy dietary fat intake and risk of gestational diabetes. Am J Clin Nutr 2012;95:446–453
81. Hernandez TL, Sutherland JP, Wolfe P, et al. Lack of suppression of circulating free fatty acids and hypercholesterolemia during weight loss on a high-fat, low-carbohydrate diet. Am J Clin Nutr 2010;91:578–585
82. Hernandez TL, van Pelt RE, Anderson MA, et al. Women with gestational diabetes 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
83. Evert AB, Boucher JL, Cypress M, et al. Nutrition therapy recommendations for the management of adults with diabetes. Diabetes Care 2013;36:3821–3842