TYPE 2 DIABETES AND THE KETOGENIC DIET

Fall Research Review

Samantha Inman

OBJECTIVES

1. Purpose
2. Brief summary of type 2 diabetes
3. Brief summary of ketogenic diet
4. Review of 3 research articles
5. Research summary
6. Additional discussion
7. Takeaways
8. Questions

WHY?

SUMMARIES

TYPE 2 DIABETES

Disease state:

- Inability to use or produce insulin to allow cells to uptake glucose from the blood stream
- Most common form, often in middle-aged or older persons
- Results in other chronic disease states

Terms:

- **HbA1c:** glycated hemoglobin
  - Measure of average plasma glucose over previous 3 mos.
  - 6.5% is clinically significant value for diagnosis of diabetes

National Center for Biotechnology Information. (n.d.). Use of glycated haemoglobin (HbA1c) in the diagnosis of diabetes mellitus: Abbreviated report of a WHO consultation. Retrieved from https://www.ncbi.nlm.nih.gov/books/NBK304271/

National Institute of Diabetes and Digestive and Kidney Diseases. (n.d). Type 2 diabetes. Retrieved from https://www.niddk.nih.gov/health-information/diabetes/overview/what-is-diabetes/type-2-diabetes

KETOGENIC DIET

HIGH FAT

MODERATE PROTEIN

LOW CARBOHYDRATES

Gordon, Barbara. (2019, May 15). What is the ketogenic diet? Retrieved from https://www.eatright.org/health/weight-loss/fad-diets/what-is-the-ketogenic-diet

IMPROVEMENT IN GLYCEMIC AND LIPID PROFILES IN TYPE 2 DIABETICS WITH A 90-DAY KETOGENIC DIET

Study 1

PURPOSE

To determine whether a 90-day low carbohydrate diet could improve markers of insulin resistance and type 2 diabetes

Primary outcome: HbA1c

Secondary outcomes: body weight, blood pressure, liver enzymes, blood lipids

Walton, C. M., Perry, K., Hart, R. H., Berry, S. L., & Bikman, B. T. (2019). Improvement in glycemic and lipid profiles in type 2 diabetics with a 90-day ketogenic diet. *Journal Of Diabetes Research*, *2019*, 8681959. https://doi-org.ezproxy.uwgb.edu:2443/10.1155/2019/8681959

Study 1

METHODOLOGY

- **Design:** Cohort
- **n = 11**
- **Inclusion criteria:** age 18-45, recent diagnosis of type 2 diabetes (HbA1c ≥6.5%), and any feature of metabolic syndrome including hypertension and dyslipidemia
- **Exclusion criteria:** medication use for diabetes, previous disease diagnoses, pregnant or nursing

Walton, C. M., Perry, K., Hart, R. H., Berry, S. L., & Bikman, B. T. (2019). Improvement in glycemic and lipid profiles in type 2 diabetics with a 90-day ketogenic diet. *Journal Of Diabetes Research*, *2019*, 8681959. https://doi-org.ezproxy.uwgb.edu:2443/10.1155/2019/8681959

METHODOLOGY

- 90 days
  - Weekly visits
    - Diet education
    - Weekly measurements of plasma ketones

Study 1

8.9%
→
5.6%

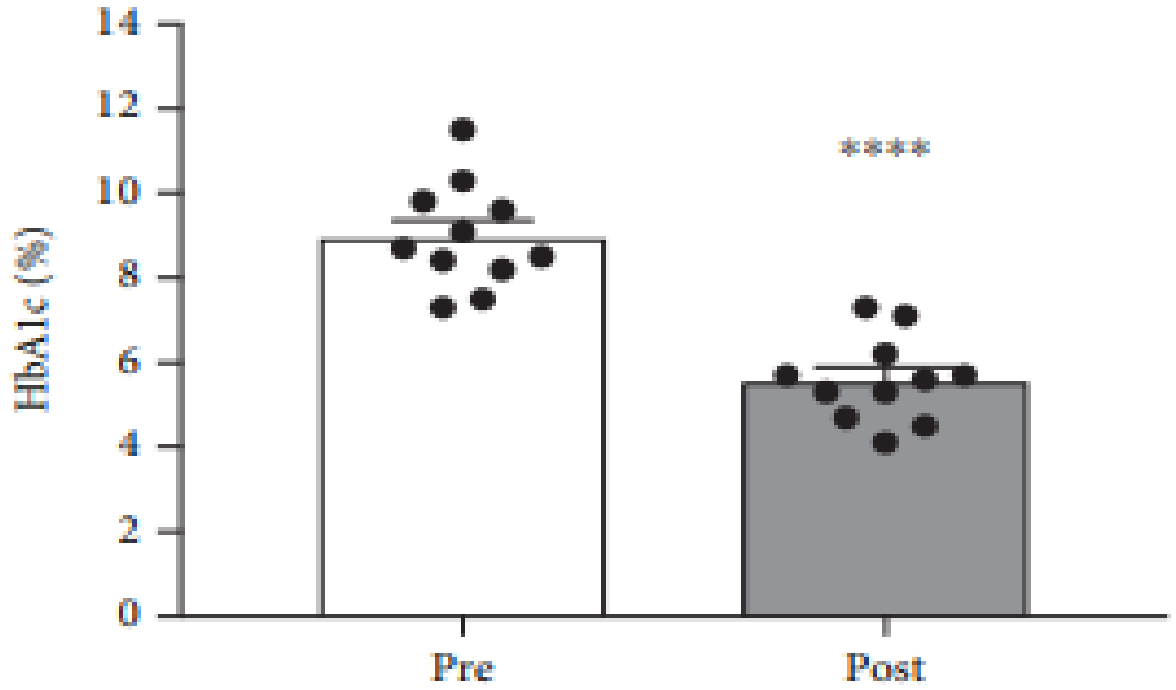


FIGURE 3: The effect of a 90-day low-carbohydrate diet on HbA1c in women ($n = 11$; $^{****}p < 0.0001$).

Walton, C. M., Perry, K., Hart, R. H., Berry, S. L., & Bikman, B. T. (2019). Improvement in glycemic and lipid profiles in type 2 diabetics with a 90-day ketogenic diet. *Journal Of Diabetes Research*, *2019*, 8681959. https://doi-org.ezproxy.uwgb.edu:2443/10.1155/2019/8681959

Study 1

RESULTS

Significant reductions in body weight ($p<0.0001$), BMI ($p<0.0001$), systolic ($p<0.0001$) and diastolic ($p<0.005$) blood pressure , and triglycerides ($p <0.005$)

Significant increase in HDL cholesterol ($p<0.005$)

Non-significant changes in LDL cholesterol, AST, and ALT values

Walton, C. M., Perry, K., Hart, R. H., Berry, S. L., & Bikman, B. T. (2019). Improvement in glycemic and lipid profiles in type 2 diabetics with a 90-day ketogenic diet. *Journal Of Diabetes Research*, *2019*, 8681959. https://doi-org.ezproxy.uwgb.edu:2443/10.1155/2019/8681959

Study 1

CONCLUSION

Diet induces a favorable metabolic state, particularly in reduction of HbA1C; additional benefits of body weight and blood pressure reductions unlike insulin medications.

Strengths: measured adherence to the diet; 0% attrition

Limitations: sample size; ability to generalize; no plasma insulin data

EAL Grade: Minus/Negative (-)

Walton, C. M., Perry, K., Hart, R. H., Berry, S. L., & Bikman, B. T. (2019). Improvement in glycemic and lipid profiles in type 2 diabetics with a 90-day ketogenic diet. *Journal Of Diabetes Research*, *2019*, 8681959. https://doi-org.ezproxy.uwgb.edu:2443/10.1155/2019/8681959

TWELVE-MONTH OUTCOMES OF A RANDOMIZED TRIAL OF A MODERATE-CARBOHYDRATE VERSUS VERY LOW-CARBOHYDRATE DIET IN OVERWEIGHT ADULTS WITH TYPE 2 DIABETES MELLITUS OR PREDIABETES

Study 2

PURPOSE

Comparison of the health impacts of a very low-carbohydrate diet compared to a moderate carbohydrate calorie restricted diet on type 2 diabetes

Primary outcome: HbA1c

Secondary outcomes: lipids, insulin resistance, and weight

Saslow, L. R., Daubenmier, J. J., Moskowitz, J. T., Kim, S., Murphy, E. J., Phinney, S. D., Hecht, F. M. (2017). Twelve-month outcomes of a randomized trial of a moderate-carbohydrate versus very low-carbohydrate diet in overweight adults with type 2 diabetes mellitus or prediabetes. *Nutrition & Diabetes*, 7(12), 304. https://doi-org.ezproxy.uwgb.edu:2443/10.1038/s41387-017-0006-9

Study 2

METHODOLOGY

- **Design:** Randomized Controlled Trial
- **n = 34**
- **Inclusion criteria:** age 18 or older, BMI of 25 or above and HbA1C of 6.0% or greater
- **Exclusion criteria:** use of insulin, more than three glucose-lowering medications, did not speak English, mental health or other medical conditions, taking weight loss medications, pregnant/planning to become pregnant, nursing, history of or planned weight loss surgery, vegan, or unwilling to do home glucose monitoring

Saslow, L. R., Daubenmier, J. J., Moskowitz, J. T., Kim, S., Murphy, E. J., Phinney, S. D., Hecht, F. M. (2017). Twelve-month outcomes of a randomized trial of a moderate-carbohydrate versus very low-carbohydrate diet in overweight adults with type 2 diabetes mellitus or prediabetes. *Nutrition & Diabetes*, 7(12), 304. https://doi-org.ezproxy.uwgb.edu:2443/10.1038/s41387-017-0006-9

Study 2

METHODOLOGY

INTERVENTION

- 12 mos.
  - Behavioral intervention
  - Very low-carbohydrate diet, 20-50 grams of carbohydrates per day
  - Twice weekly measurements of plasma ketones

CONTROL

- 12 mos.
  - Behavioral intervention
  - Moderate carbohydrate, calorie restricted diet

Study 2

6.6% → 6.1%

Results from Table 1: Estimated Marginal Mean (EMM) ± 95% CI at baseline to 6 and 12 months

HbA1c	Intervention	Control	P value (group differences in changes relative to baseline)
Baseline	6.6 (6.3, 6.9)	6.9 (6.6, 7.2)	-
6 mos.	6.0 (5.7, 6.3)	6.7 (6.4, 6.9)	.001
12 mos.	6.1 (5.8, 6.4)	6.7 (6.4, 7.0)	.007

Walton, C. M., Perry, K., Hart, R. H., Berry, S. L., & Bikman, B. T. (2019). Improvement in glycemic and lipid profiles in type 2 diabetics with a 90-day ketogenic diet. *Journal Of Diabetes Research*, *2019*, 8681959. https://doi-org.ezproxy.uwgb.edu:2443/10.1155/2019/8681959

Study 2

RESULTS

Significant reductions in HbA1c ($p=0.007$), body weight ($p<0.001$), and BMI ($p<0.001$)

Significant decrease in LDL cholesterol ($p=0.003$) at 6 mos. ONLY

Non-significant changes in triglycerides, HDL, or insulin resistance

Saslow, L. R., Daubenmier, J. J., Moskowitz, J. T., Kim, S., Murphy, E. J., Phinney, S. D., Hecht, F. M. (2017). Twelve-month outcomes of a randomized trial of a moderate-carbohydrate versus very low-carbohydrate diet in overweight adults with type 2 diabetes mellitus or prediabetes. *Nutrition & Diabetes*, 7(12), 304. https://doi-org.ezproxy.uwgb.edu:2443/10.1038/s41387-017-0006-9

Study 2

CONCLUSION

Overweight adults with prediabetes or type 2 diabetes may be able to improve glycemic control with less medication by following a very low-carbohydrate diet

Strengths: retention rates, fair dietary adherence

Limitations: sample size; limited understanding of the effect of dietary intervention alone

EAL Grade: Minus/Negative (-)

Saslow, L. R., Daubenmier, J. J., Moskowitz, J. T., Kim, S., Murphy, E. J., Phinney, S. D., Hecht, F. M. (2017). Twelve-month outcomes of a randomized trial of a moderate-carbohydrate versus very low-carbohydrate diet in overweight adults with type 2 diabetes mellitus or prediabetes. *Nutrition & Diabetes*, 7(12), 304. https://doi-org.ezproxy.uwgb.edu:2443/10.1038/s41387-017-0006-9

AN ONLINE INTERVENTION COMPARING A VERY LOW-CARBOHYDRATE KETOGENIC DIET AND LIFESTYLE RECOMMENDATIONS VERSUS A PLATE METHOD DIET IN OVERWEIGHT INDIVIDUALS WITH TYPE 2 DIABETES: A RANDOMIZED CONTROLLED TRIAL

Study 3

PURPOSE

Comparison of the health impacts of a very low-carbohydrate diet compared to a moderate carbohydrate calorie restricted diet on type 2 diabetes

Primary outcomes: HbA1c and body weight

Secondary outcomes: blood lipids and aspects of psychological health

Saslow, L. R., Mason, A. E., Kim, S., Goldman, V., Ploutz-Snyder, R., Bayandorian, H., Moskowitz, J. T. (2017). An online intervention comparing a very low-carbohydrate ketogenic diet and lifestyle recommendations versus a plate method diet in overweight individuals with type 2 diabetes: A randomized controlled trial. *Journal Of Medical Internet Research*, *19*(2), e36. https://doi-org.ezproxy.uwgb.edu:2443/10.2196/jmir.5806

Study 3

METHODOLOGY

- **Design:** Randomized Controlled Trial
- **n = 25**
- **Inclusion criteria:** age 18 or older, BMI of 25 or above and HbA1C between 6.5-9% and regular access to the internet
- **Exclusion criteria:** use of diabetes medication other than metformin

Saslow, L. R., Mason, A. E., Kim, S., Goldman, V., Ploutz-Snyder, R., Bayandorian, H., Moskowitz, J. T. (2017). An online intervention comparing a very low-carbohydrate ketogenic diet and lifestyle recommendations versus a plate method diet in overweight individuals with type 2 diabetes: A randomized controlled trial. *Journal Of Medical Internet Research*, *19*(2), e36. https://doi-org.ezproxy.uwgb.edu:2443/10.2196/jmir.5806

Study 3

METHODOLOGY

INTERVENTION

- 32 weeks
  - Behavioral intervention
  - Very low-carbohydrate diet, 20-50 grams of carbohydrates per day
  - Once weekly measurements of plasma ketones

CONTROL

- 32 weeks
  - No behavioral intervention
  - Low-fat, emphasis on green vegetables, lean protein, and limited sweet/starchy foods

Study 3

RESULTS

Greater reduction in HbA1c ($p=0.002$) and body weight ($p<0.001$)

Significant decrease in triglycerides ($p=0.01$) at 32 weeks ONLY

Non-significant changes in HDL or LDL

Saslow, L. R., Mason, A. E., Kim, S., Goldman, V., Ploutz-Snyder, R., Bayandorian, H., Moskowitz, J. T. (2017). An online intervention comparing a very low-carbohydrate ketogenic diet and lifestyle recommendations versus a plate method diet in overweight individuals with type 2 diabetes: A randomized controlled trial. *Journal Of Medical Internet Research*, *19*(2), e36. https://doi-org.ezproxy.uwgb.edu:2443/10.2196/jmir.5806

Study 3

CONCLUSION

An online intervention supporting a very low-carbohydrate ketogenic diet with lifestyle modification could result in lower HbA1c, body weight, and triglyceride levels

Strength: measured adherence to the diet, although subject reported

Limitations: sample size; attrition rate; no lifestyle intervention provided to control group

EAL Grade: Minus/Negative (-)

Saslow, L. R., Mason, A. E., Kim, S., Goldman, V., Ploutz-Snyder, R., Bayandorian, H., Moskowitz, J. T. (2017). An online intervention comparing a very low-carbohydrate ketogenic diet and lifestyle recommendations versus a plate method diet in overweight individuals with type 2 diabetes: A randomized controlled trial. *Journal Of Medical Internet Research*, *19*(2), e36. https://doi-org.ezproxy.uwgb.edu:2443/10.2196/jmir.5806

RESEARCH SUMMARY

Study	n=	Duration	HbA1c	Body Weight	Blood Pressure	BMI	HDL	LDL	Triglycerides
1	11	90 days	↓	↓	↓	↓	↑	-	↓
2	34	12 mos.	↓	↓	N/A	↓	-	-	-
3	25	32 weeks	↓	↓	N/A	N/A	-	-	↓

* Only significant results shown

APPLICATIONS IN PRACTICE

ADDITIONAL DISCUSSION

- Updated Diabetes Standards of Care
  - "research indicates that low-carbohydrate eating plans may result in improved glycemia and have the potential to reduce antihyperglycemic medications for individuals with type 2 diabetes"
- Metformin
  - Oral medication used to help lower blood sugar levels
  - Side effects
  - Average 1.5% reduction in HbA1c

American Diabetes Association (2019). Introduction: Standards of Medical Care in Diabetes – 2019. Diabetes Care, 2019(42), S1-S2. https://doi.org/10.2337/dc19-Sint01
The Johns Hopkins Patient Guide to Diabetes (n.d.) Metformin. Retrieved from http://hopkinsdiabetesinfo.org/medications-for-type-2-diabetes-metformin/

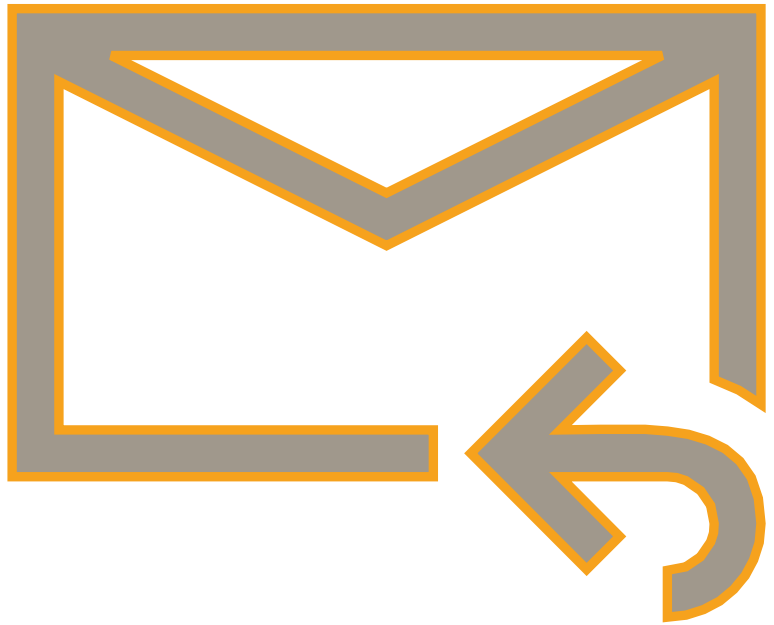
TAKEAWAYS

- Advantages of plasma ketone measurement
- Lifestyle intervention is effective
- Meeting patients where they're at
- Future studies:
  - Increase sample size
  - Make population demographics more generalizable
  - More defined control group and separation from lifestyle intervention

QUESTIONS?

RESOURCES

- **Contact:**
  - Samantha Inman
    - inmasl25@uwgb.edu
- **Presentation:**
  - https://uwgbresearchreviews.weebly.com/fall-presentations-2019.html



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