The effect of type and amount of dietary carbohydrate on biomarkers of glucose homeostasis and inflammation in healthy adults: Results from the OmniCarb trial

Stephen P Juraschek; Edgar R Miller III; Elizabeth Selvin; Vincent J Carey; Lawrence J Appel; Robert H Christenson; Frank M. Sacks
Author Disclosure Information

• None

• Asahi Kasei Corporation donated reagents for the glycated albumin assays, but were otherwise not involved in this study
Quantity & Quality of Dietary Carbohydrates

- **Quantity**
  - Proportion of calories from carbohydrates
  - Note: as % kcal from carb decreases, there is a corresponding increase in protein and/or fat

- **Quality**
  - Glycemic index (GI) is one measurement of quality
  - Estimated from 2hr glucose AUC after standardized serving
    - High GI → greater glucose release in blood
    - Low GI → lower glucose release in blood
Examples of Glycemic Index

- White rice: 126
- Baked potato: 121
- White bread: 101 (reference)
- Long-grain rice: 72
- Oat bran bread: 68
Original Investigation

Effects of High vs Low Glycemic Index of Dietary Carbohydrate on Cardiovascular Disease Risk Factors and Insulin Sensitivity
The OmniCarb Randomized Clinical Trial

Frank M. Sacks, MD; Vincent J. Carey, PhD; Cheryl A. M. Anderson, PhD, MPH; Edgar R. Miller III, PhD, MD; Trisha Copeland, MS, RD; Jeanne Charleston, RN, BSN; Benjamin J. Harshfield, BA; Nancy Laranjo, BA; Phyllis McCarron, MS, RD; Janis Swain, MS, RD; Karen White, MS, RDN; Karen Yee, MS, RD; Lawrence J. Appel, MD, MPH
OMNICARB Trial

- **Objective:** To determine whether reduced GI (and reduced %carb) would improve insulin sensitivity and CVD risk factors
- **Results:** GI did not improve
  - Insulin sensitivity (increased fasting glucose)
  - Lipid levels
  - Systolic blood pressure
- **Conclusion:**
  
  "In the context of an overall DASH-type diet, using glycemic index to select specific foods may not improve cardiovascular risk factors or insulin resistance."
Rationale for this Ancillary

- Insulin sensitivity
  - Based on a fasting glucose curve representing a single time point
  - Not average (aggregate) glycemia

- Unknown dietary effects on inflammation
  - A hypothesized pathway in early pathogenesis of CVD risk factors
Glucose peaks versus average levels

Average glycemia is a stronger predictor of health outcomes
Objectives

To determine the effects of reducing GI and/or %carb on:

1. Markers of 2-3 week glycemia:
   • Glycated Albumin
   • Fructosamine

2. Inflammation:
   • High sensitivity C-reactive protein
Hypotheses

• Reducing GI and/or %carb would lower 2-3 week glycemia

• Reducing GI and/or %carb would lower inflammation
Study Population

• Study participants:
  – Adults
  – Overweight or obese
  – Normal or stage I hypertension

• Excluded:
  – Diabetes
  – Chronic kidney disease
  – Cardiovascular disease
# Dietary Interventions

## Glycemic Index (GI)

<table>
<thead>
<tr>
<th>Proportion Carbohydrate (%carb)</th>
<th>High Carb 58%</th>
<th>Low Carb 40%</th>
</tr>
</thead>
</table>

## Dietary Interventions

<table>
<thead>
<tr>
<th>Glycemic Index (GI)</th>
<th>High GI ≥65</th>
<th>Low GI ≤45</th>
</tr>
</thead>
<tbody>
<tr>
<td>CG</td>
<td>cG</td>
<td>Cg</td>
</tr>
<tr>
<td>cG</td>
<td></td>
<td>cg</td>
</tr>
</tbody>
</table>
## Healthy Diets

<table>
<thead>
<tr>
<th>Diet</th>
<th>Carb</th>
<th>Prot</th>
<th>Fat</th>
<th>Glycemic Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>CG</td>
<td>58</td>
<td>15</td>
<td>27</td>
<td>≥65</td>
</tr>
<tr>
<td>Cg</td>
<td></td>
<td></td>
<td></td>
<td>≤45</td>
</tr>
<tr>
<td>cG</td>
<td>40</td>
<td>23</td>
<td>37</td>
<td>≥65</td>
</tr>
<tr>
<td>cg</td>
<td></td>
<td></td>
<td></td>
<td>≤45</td>
</tr>
</tbody>
</table>

The DASH Diet was 55% Carb with GI of 68, most similar to the CG diet.
Design:
Randomized crossover trial

163 participants randomized to 1 of 8 sequences

Screening & Baseline Visits

Period 1
5 weeks

Washout Periods
2 wk

Period 2
5 weeks

Period 3
5 weeks

Period 4
5 weeks

Plasma collected at baseline and at the end of each feeding period
Outcomes & Analyses

• Markers of 2-3 week glycemia
  – Glycated albumin, fructosamine
  – Similar to hemoglobin A1c
    • Glucose bound to blood protein
    • Shorter duration based on protein turnover
  – Excluded 15% of specimens due to hemolysis

• Marker of inflammation:
  – High-sensitivity C-reactive protein

• Statistical analysis:
  – Comparison of end-of-period measurements
  – Generalized estimating equation models
# Population Characteristics

(N = 163)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Mean or %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>53</td>
</tr>
<tr>
<td>Male, %</td>
<td>48</td>
</tr>
<tr>
<td>Black, %</td>
<td>50</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>32</td>
</tr>
<tr>
<td>Fasting glucose, mg/dL</td>
<td>104</td>
</tr>
<tr>
<td>Insulin, μU/mL</td>
<td>58</td>
</tr>
<tr>
<td>Triglycerides, mg/dL (median)</td>
<td>105</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>132</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>80</td>
</tr>
<tr>
<td>Glycated albumin, %-point</td>
<td>14.9</td>
</tr>
<tr>
<td>Fructosamine, μmol/L</td>
<td>236</td>
</tr>
<tr>
<td>High sensitivity C-reactive protein, mg/dL (median)</td>
<td>1.8</td>
</tr>
</tbody>
</table>
# Glycated Albumin

## Reducing glycemic index

<table>
<thead>
<tr>
<th>Condition</th>
<th>N</th>
<th>Difference, 95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>In a low %carb diet</td>
<td>117</td>
<td>0.08 (-0.07, 0.24)</td>
<td>0.29</td>
</tr>
<tr>
<td>In a high %carb diet</td>
<td>117</td>
<td>-0.03 (-0.19, 0.13)</td>
<td>0.73</td>
</tr>
</tbody>
</table>

## Reducing carbohydrate & increasing protein and fat

<table>
<thead>
<tr>
<th>Condition</th>
<th>N</th>
<th>Difference, 95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>In a low GI diet</td>
<td>112</td>
<td>-0.10 (-0.25, 0.06)</td>
<td>0.23</td>
</tr>
<tr>
<td>In a high GI diet</td>
<td>106</td>
<td>-0.21 (-0.40,-0.02)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

## Combined effects

<table>
<thead>
<tr>
<th>Condition</th>
<th>N</th>
<th>Difference, 95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reducing both GI &amp; %carb</td>
<td>110</td>
<td>-0.13 (-0.31, 0.06)</td>
<td>0.18</td>
</tr>
<tr>
<td>Increasing GI &amp; reducing %carb</td>
<td>108</td>
<td>-0.18 (-0.36,-0.01)</td>
<td>0.04</td>
</tr>
</tbody>
</table>
## Fructosamine

### Reducing glycemic index
- **In a low %carb diet**
  - N: 117
  - Difference, 95% CI: -0.33 (-2.89, 2.23)
  - P: 0.80

- **In a high %carb diet**
  - N: 117
  - Difference, 95% CI: 2.42 (-0.79, 5.63)
  - P: 0.14

### Reducing carbohydrate & increasing protein and fat
- **In a low GI diet**
  - N: 112
  - Difference, 95% CI: -3.86 (-6.39, -1.33)
  - P: 0.003

- **In a high GI diet**
  - N: 106
  - Difference, 95% CI: -1.11 (-4.52, 2.30)
  - P: 0.52

### Combined effects
- **Reducing both GI & %carb**
  - N: 110
  - Difference, 95% CI: -1.44 (-4.58, 1.69)
  - P: 0.37

- **Increasing GI & reducing %carb**
  - N: 108
  - Difference, 95% CI: -3.53 (-6.23, -0.82)
  - P: 0.01

---

μmol
### High Sensitivity C-reactive Protein

<table>
<thead>
<tr>
<th>Reducing glycemic index</th>
<th>N</th>
<th>% Difference, 95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>In a low %carb diet</td>
<td>144</td>
<td>3.5 (-10.6, 19.8)</td>
<td>0.64</td>
</tr>
<tr>
<td>In a high %carb diet</td>
<td>145</td>
<td>-4.7 (-14.4, 6.1)</td>
<td>0.38</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reducing carbohydrate &amp; increasing protein and fat</th>
<th>N</th>
<th>% Difference, 95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>In a low GI diet</td>
<td>139</td>
<td>4.5 (-8.0, 18.8)</td>
<td>0.50</td>
</tr>
<tr>
<td>In a high GI diet</td>
<td>133</td>
<td>-3.8 (-16.3, 10.6)</td>
<td>0.59</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Combined effects</th>
<th>N</th>
<th>% Difference, 95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reducing both GI &amp; %carb</td>
<td>136</td>
<td>-0.4 (-12.4, 13.2)</td>
<td>0.95</td>
</tr>
<tr>
<td>Increasing GI &amp; reducing %carb</td>
<td>136</td>
<td>1.0 (-12.2, 16.1)</td>
<td>0.89</td>
</tr>
</tbody>
</table>

*Performed on log-scale*
Limitations & Strengths

• Limitations
  – Brief feeding periods → no clinical events
  – Potentially underestimated effects:
    • Excluded people with diabetes, chronic kidney disease, cardiovascular disease
    • All diets were healthy

• Strengths
  – Randomized trial with a diverse population
  – High follow-up rates
  – Repeat measures
  – Tightly controlled and isocaloric diets
  – Alternative markers of glycemia
Conclusions

- Reducing GI had no effect on 2-3 week glycemia
- Reducing %carb lowered glycated albumin or fructosamine (in low or high GI context)
- Neither GI or %carb affected inflammation
- Implications: low carbohydrate diet more effectively lowers glycemia in adults at risk for diabetes
Thank You

- Study team and participants
- Main Results: Sacks F et al, JAMA 2014; 312(23): 2531-2541
- Editorial: Eckel RH, Role of Glycemic Index in the Context of an Overall Heart-Healthy Diet. JAMA 2014; 312(23): 2508-2509
OMNICARB Study Team

Boston Center, Frank Sacks PI and Study Chair
- Trisha Copeland, Project Manager; Jackie Gallagher and Cassandra Carrington
- Janis Swain and Karen Yee, Dietary Core
- Jeremy Furtado, Lipid Core Laboratory

Data Coordinating Center
- Vincent Carey, Ph.D, Director
- Nancy Laranjo, BJ Harshfield

Baltimore Center, Lawrence Appel, PI, and Study Co-Chair
- Drs. Pete Miller and Cheryl Anderson
- Jeanne Charleston and Letitia Thomas, Project Managers
- Phyllis McCarron and Karen White, Dietary Core

Consultant: David Ludwig
QUESTIONS?

Email: spj@jhmi.edu