DIETARY ISSUES IN DIABETES

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Presenter Disclosure

• Funding
  • NIH, CDC, Abbott Diabetes Care, Eli Lilly, Sanofi
Outline

- Goals for medical nutrition therapy (MNT) for diabetes
- Evidence and current recommendations for dietary intake
- Effective behavior change strategies
MNT Goals

• Achieve and maintain:
  • Blood glucose levels in the normal range
  • Lipid/lipoprotein profile that reduces the risk for vascular disease
  • Blood pressure levels in the normal range

• Prevent, or slow rate of development of, chronic complications

• Address individual nutrition needs, taking into account personal and cultural preferences and willingness to change

• Maintain pleasure of eating by only limiting food choices when indicated by scientific evidence

ADA, Position Statement on Nutrition-2008
A NOTE ON WEIGHT LOSS

Focus on the Look AHEAD Trial
Weight Loss Recommendations

- Weight loss is recommended for all overweight or obese individuals who have or are at risk for diabetes

- For weight loss, low-CHO, low-fat calorie-restricted, or Mediterranean diets may be effective in the short-term (up to 2 years)

ADA, Standards of Medical Care in Diabetes-2012
Look AHEAD Trial

- Does sustained weight loss in people with diabetes reduce CVD risk?

- N=5143 randomized to:
  - Intensive Lifestyle Intervention (ILI)
    - Diet + physical activity to achieve 7% weight loss in 1 year
    - Calorie-controlled, < 30% energy fat, < 10% energy saturated, ≥ 15% energy protein, meal replacements; portion controlled
    - 175 minutes/week of physical activity (brisk walking intensity)
  OR
  - Diabetes Support and Education (DSE)
    - 3 group sessions/year

Look AHEAD Trial

• After 4 years of follow-up*:  
  - ILI lost 5% of baseline body weight (vs. 1% DSE)  
  - ILI had improved glycemic control, blood pressure, HDL-c and TG

• After up to 11 years of follow-up:  
  - Early stop (Fall 2012) due to futility --  
  - No evidence for reduced risk of CV events in ILI  
  - However, ILI needed less intensive medication regimens

MNT FOR DIABETES

Goals and ADA Recommendations
An Unusual Challenge

• No “Diabetic Diet”

• Need to individualize
  • Role of nutrition in daily blood glucose management
    • Mostly involves total CHO (but not entirely)
    • Depends on diabetes medication regimen
  
  • Role of nutrition in long-term CVD risk management
    • Mostly involves dietary fats (but not entirely)
    • Depends on CVD risk profile

• May or may not include weight loss

• Need for day-to-day and lifelong adherence
### Historical Perspective

<table>
<thead>
<tr>
<th>Year</th>
<th>CHO (%)</th>
<th>Protein (%)</th>
<th>Fat (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before 1921</td>
<td>Starvation Diets</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1921</td>
<td>20</td>
<td>10</td>
<td>70</td>
</tr>
<tr>
<td>1950</td>
<td>40</td>
<td>20</td>
<td>40</td>
</tr>
<tr>
<td>1971</td>
<td>45</td>
<td>20</td>
<td>35</td>
</tr>
<tr>
<td>1986</td>
<td>≤60</td>
<td>12-20</td>
<td>&lt;30</td>
</tr>
<tr>
<td>1994</td>
<td>Based on assessment &amp; treatment goals</td>
<td>10-20</td>
<td>Based on goals &lt; 10% saturated fat</td>
</tr>
<tr>
<td>2002</td>
<td>Comment on GI</td>
<td>15-20 (usual)</td>
<td>Based on goals &lt; 7% saturated fat Minimize trans fats</td>
</tr>
<tr>
<td>2008</td>
<td>Recommendation that low-CHO diets should not be used for management of diabetes removed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2012</td>
<td>Recommendation that use of GI &amp; GL may provide additional benefit for glycemic control removed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2013</td>
<td>Recommendations under review / revision</td>
<td></td>
<td></td>
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</tbody>
</table>
ADA Systematic Review: 2012

- Focus on literature published since 2001 relating to macronutrients, eating patterns, and individual foods independent of weight loss
- Results of this review currently being used to update the most recent comprehensive nutrition position paper (2008 ADA Position Statement on Nutrition)

Wheeler et al. Diabetes Care 2012;35:434-45
Results: Low-CHO diets

- Low-CHO defined as < 40% of total kcal as CHO
- 11 clinical trials evaluated
  - 3 single-arm; 7 parallel randomized; 1 crossover
  - All in adults with type 2 diabetes
  - All weight-loss studies and most compared low-CHO to low-fat

<table>
<thead>
<tr>
<th>Study Characteristic</th>
<th>Range</th>
<th>Additional Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample Size</td>
<td>10-55</td>
<td>Per study arm</td>
</tr>
<tr>
<td>Duration</td>
<td>14 days-1 yr</td>
<td>9/11 were ≥ 3 mos</td>
</tr>
<tr>
<td>Retention</td>
<td>58-100%</td>
<td>6/11 were ≥ 80%, including both 1-year studies 2/11 were 100%, both metabolic unit studies</td>
</tr>
<tr>
<td>Achieved CHO in intervention group</td>
<td>21-120 g/day</td>
<td>7/11 were very low CHO (21-70 g/day) → only 4/7 achieved very low CHO 4/11 were low CHO (30-&lt;40% kcal as CHO)</td>
</tr>
</tbody>
</table>

Wheeler et al. *Diabetes Care* 2012;35:434-45
Results: Low-CHO diets

- Results:
  - Improvements in markers of glycemic control and insulin sensitivity
  - Improvements in HDL-c
    - Improvements in other lipoproteins, but not consistently better than control

<table>
<thead>
<tr>
<th>Amount CHO</th>
<th>Total # Studies</th>
<th>Improved Glycemic Control(^1,) (2)</th>
<th>Improved TG(^1)</th>
<th>Improved HDL-c(^1)</th>
<th>Improved LDL-c(^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very low CHO</td>
<td>21-70 g/day</td>
<td>7</td>
<td>4(*)</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Low CHO</td>
<td>30-&lt;40%</td>
<td>4</td>
<td>3(†)</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>

\(^1\)Number of studies reporting significant effect (p < 0.05) relative to baseline or control.
\(^2\)A1C, FBG, or fasting insulin.
\(*\)3/4 had retention rates < 80%.
\(†\)1/3 had retention rate < 80%.

Wheeler et al. *Diabetes Care* 2012;35:434-45
Low-CHO study example

• Highest quality study evaluated given:
  • Design (parallel randomized)
  • Duration (1 year)
  • Retention (> 80%)
  • Adherence (~33% kcal CHO at 6 and 12 mos in intervention compared to ~50% in controls)

• Compared low-CHO and low-fat diets
  • Overweight adults with type 2 diabetes (intent-to-treat analysis)
    • 55 intervention (low-CHO)
    • 50 control (low-fat)
  • Primary outcomes: weight and A1C
  • Secondary outcomes: blood pressure and lipids

Davis et al. Diabetes Care 2009;32:1147-52
Low-CHO study example

• Results:
  • Weight loss faster on low-CHO diet but similar weight reduction at 1 year
  • No significant changes in A1C at 1 year in either group
  • Significantly greater increase in HDL-c on low-CHO diet at 1 year

• Conclusion: relationship between low-CHO diet and glycemic control is more unclear than cumulative evidence may suggest

Davis et al. Diabetes Care 2009;32:1147-52
Results: Low-GI diets

- 8 clinical trials evaluated
  - 5 parallel randomized; 3 crossover
  - All in adults with type 2 diabetes
  - Control diets were variable (high-GI, high-fiber, traditional, very-low-CHO)

<table>
<thead>
<tr>
<th>Study Characteristic</th>
<th>Range</th>
<th>Additional Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample Size</td>
<td>12-67</td>
<td>Per study arm</td>
</tr>
<tr>
<td>Duration</td>
<td>4 wks-1 yr</td>
<td>4/8 were ≥ 3 mos</td>
</tr>
<tr>
<td>Retention</td>
<td>58-100%</td>
<td>5/8 were ≥ 80%, including both 1-year studies 3/8 were 100%, all free-living</td>
</tr>
<tr>
<td>Achieved GI in intervention group</td>
<td>39-77 units</td>
<td>Wide range; no consistent definition; confounding by high-fiber</td>
</tr>
</tbody>
</table>

Wheeler et al. *Diabetes Care* 2012;35: 434-45
Results: Low-GI diets

- In general, there is little difference in glycemic control and CVD risk factors

<table>
<thead>
<tr>
<th>Low GI</th>
<th># Studies</th>
<th>Improved Glycemic Control(^1,2)</th>
<th>Improved TG(^1)</th>
<th>Improved HDL-c(^1)</th>
<th>Improved LDL-c(^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>8</td>
<td>3(^*)</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

\(^1\)Number of studies reporting significant effect (p<0.05) relative to baseline or control.
\(^2\)A1C or FBG.
\(^*\)2/3 had retention rates <80%.

Wheeler et al. *Diabetes Care* 2012;35:434-45
Low-GI study example

- Highest quality study evaluated given:
  - Design (randomized, controlled)
  - Duration (6 mos)
  - Retention (74%; compare to 58% in other 6-mos trial)
  - Adherence (achieved GI of 69.6 compared to 83.5 among controls)

- Compared low-GI and high-fiber diets
  - Overweight adults with type 2 diabetes (intent-to-treat analysis)
    - 57 intervention (low-GI)
    - 67 control (high-fiber)
  - Primary outcome: A1C
  - Secondary outcomes: FBG and lipids

Jenkins et al. *JAMA* 2008;300:2742-53
Low-GI study example

• Results:
  • A1C decreased by 0.5 in low-GI compared to 0.2 in high-fiber
  • HDL-c increased by 1.7 mg/dL in low-GI compared to decrease of 0.2 mg/dL in high-fiber

• Key limitation:
  • Low-GI diet had *higher* fiber than High-fiber diet at 6 mos:

<table>
<thead>
<tr>
<th></th>
<th>Low-GI Diet</th>
<th>High-fiber Diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fiber (g/1000 kcal)</td>
<td>18.7 (17.3-20.0)</td>
<td>15.7 (14.7-16.7)</td>
</tr>
<tr>
<td>Glycemic Index</td>
<td>69.6 (67.7-71.4)</td>
<td>83.5 (82.4-84.7)</td>
</tr>
</tbody>
</table>

Jenkins et al. *JAMA* 2008;300:2742-53
Saturated fat (recommend < 7% kcal)

• Increasing focus on specific fatty acids:
  • Stearic acid (C18:0): ~1/3 of saturated fat intake (meat, dairy), converted, in part to oleic acid (C18:1) potentially explaining neutral effect on total cholesterol, LDL and HDL
  • Palmitic acid (C16:0): primary saturated fat (vegetable oil, meat, dairy) and primary endogenously produced fatty acid
  • Lauric (C12:0), Myristic (C14:0) and Palmitic (C16:0) have adverse effects on lipids

• Food perspective: high correlation between stearic and palmitic acid (both meat, dairy sources)

• Several recent studies suggest limited evidence for saturated fat in relation to CVD outcomes although replacement with PUFA may be beneficial

Micha *Lipids* 2010; Mente *Arch Int Med* 2009; Flock *Curr Opin Clin Nutr Metab Care* 2012, Astrup, *AJCN* 2011
Omega-3 fatty acids

• 3 parallel RCTs evaluated in Wheeler systematic review:
  • Supplementation does not improve A1c but may decrease TG
  • Effects on HDL-c and LDL-c are unclear

• ORIGIN doubled-blind trial*
  • Eligibility: impaired fasting glucose, IGT, or diabetes
  • Randomized to 900mg omega–3 suppl (N=6319) or placebo (N=6292)
  • Primary endpoint: death from CV causes
  • Median follow-up 6.2 yrs
  • No effect of omega-3 suppl on CV death: HR (95% CI), 0.98 (0.87-1.10)
  • Too late in the natural history of atherosclerosis??
  • Supplements may not be the issue….range of intake available from food may be most relevant

*ORIGIN Trial Investigators NEJM 2012;367:309-18
Omega-6 and \textit{trans} fatty acids

- Omega-6 FA’s (e.g., vegetable oil) can be converted to arachidonic acid and may exert pro-inflammatory response
  - Ratio of omega-6 to omega-3 is uncertain however omega-6 still preferred to saturated fat

- \textit{Trans} fatty acids: minimize intake (although naturally occurring \textit{trans} fat from dairy, \textit{trans}-palmitolic acid, may be beneficial)
Results: Mediterranean diet

- 5 clinical trials evaluated
  - 4 parallel randomized; 1 crossover
  - All in adults with type 2 diabetes

<table>
<thead>
<tr>
<th>Study Characteristic</th>
<th>Range</th>
<th>Additional Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample Size</td>
<td>10-108</td>
<td>Per study arm</td>
</tr>
<tr>
<td>Duration</td>
<td>4 wks-4 yrs</td>
<td>4/5 were 4 wks</td>
</tr>
<tr>
<td>Retention</td>
<td>91-100%</td>
<td>4/5 were 100%, all 4-wk trials</td>
</tr>
<tr>
<td>Achieved intake in intervention group</td>
<td>44-53% CHO</td>
<td>No clear definition of “Mediterranean Diet”</td>
</tr>
<tr>
<td></td>
<td>10-15% Saturated fat</td>
<td></td>
</tr>
<tr>
<td></td>
<td>17-21% MUFA</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4-11.5% PUFA</td>
<td></td>
</tr>
<tr>
<td></td>
<td>15-19% Protein</td>
<td></td>
</tr>
</tbody>
</table>

Wheeler et al. *Diabetes Care* 2012;35:434-45
Results: Mediterranean diet

- Results:
  - No advantage of Mediterranean Diet over other diets for glycemic control
  - Mediterranean Diet may improve HDL-c and TG

<table>
<thead>
<tr>
<th></th>
<th># Studies</th>
<th>Improved Glycemic Control</th>
<th>Improved TG</th>
<th>Improved HDL-c</th>
<th>Improved LDL-c</th>
</tr>
</thead>
<tbody>
<tr>
<td>Med Diet</td>
<td>5</td>
<td></td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

1Number of studies reporting significant effect (p<0.05) relative to baseline or control.
2A1C, FBG, or postprandial glucose.

Wheeler et al. *Diabetes Care* 2012;35:434-45
Mediterranean Diet: Update

• PREDIMED trial
  • Eligibility: type 2 diabetes mellitus or ≥ 3 risk factors: smoking, hypertension, high LDL-c, low HDL-c, overweight or obesity, family history of premature coronary heart disease
  • Randomized to 1 of 3 diets: Mediterranean supplemented with extra-virgin olive oil (N=2543), Mediterranean supplemented with mixed nuts (N=2454), or control (advice to reduce fat; N=2450)
  • Primary endpoint: myocardial infarction, stroke, or death from cardiovascular causes
  • Median follow-up 4.8 yrs

Estruch et al. NEJM 2013
Mediterranean study example

- Results:

<table>
<thead>
<tr>
<th>(n, events)</th>
<th>MeDiet +EVOO Adjusted* HR (95% CI)</th>
<th>MeDiet+Nuts Adjusted* HR (95% CI)</th>
<th>Control Adjusted* HR (95% CI)</th>
<th>P-value interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>(7447, 288)</td>
<td>0.70 (0.54-0.92)</td>
<td>0.72 (0.54-0.96)</td>
<td>0.70 (0.54-0.92)</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>(3833, 98)</td>
<td>0.69 (0.43-1.12)</td>
<td>0.66 (0.40-1.07)</td>
<td>0.69 (0.43-1.12)</td>
</tr>
<tr>
<td>Yes</td>
<td>(3614, 190)</td>
<td>0.69 (0.50-0.97)</td>
<td>0.74 (0.51-1.06)</td>
<td>0.69 (0.50-0.97)</td>
</tr>
</tbody>
</table>

*Adjusted for sex, age, smoking, and family history of early CHD

Estruch et al. *NEJM* 2013
BEHAVIOR CHANGE STRATEGIES

Behavioral science as relates to dietary adherence
Why don’t patients eat what I want them to eat?

• Viewing patients as “obedient adopters of facts and recommendations” is too simplistic

• **Individual perspective** – Many characteristics play a role in food and beverage choices
  • Biological
  • Psychological
  • Cultural
  • Economic

• **Context** – Individuals interact reciprocally with their environment
  • Eating behaviors of family and friends
  • Neighborhood and workplace food and built environment
  • Local, state, and national policies relating to health

Marrero et al. *Diabetes Care* 2013;36:463-70
Recommendations for Clinicians

• Need to change approach to establishing therapeutic goals
  • *Empower* patients through *collaborative* goal setting and *shared* decision making
    • Be open-minded about patient choices, even if they conflict with what you consider to be “best practice”
  • *Motivational interviewing* can help identify *patient ambivalence* about behavior change and resolve *discrepancies between patient goals and behaviors*

Marrero et al. *Diabetes Care* 2013;36:463-70
Recommendations for Clinicians

- Ensure that the patient receives adequate training to encourage self-management
  - Review laboratory data as part of goal setting

- Ongoing support is critical for sustaining behavior change
  - Renew or revise the plan at each visit
  - Peer support programs and new technologies may help

- **Recognize that the behaviors involved in managing diabetes are dynamic and multidimensional**

Marrero et al. *Diabetes Care* 2013;36:463-70
CONCLUSION

Challenges and Future Directions
Key Nutrition Recommendations

- **Weight loss is recommended** for all overweight or obese individuals who have or are at risk for diabetes.

- Individuals who have or are at risk for diabetes should receive **individualized** MNT as needed to achieve treatment goals.

- The **mix of CHO, protein, and fat may be adjusted to meet the metabolic goals** and individual preferences of the person with diabetes.

- The **Mediterranean Diet** holds promise – but needs to be further evaluated with consideration of culture and context of patients’ lives.

- **Watch for Update late in 2013**

ADA, Standards of Medical Care in Diabetes-2012
Future Directions

- We need a better understanding of differences in individual response to diet
  - May explain mixed results throughout the literature
  - Future research should involve post-hoc analyses of existing data to generate hypotheses and use of innovative genetic tools

- We need to improve our understanding of the biochemical mechanisms underlying nutrition-related CVD risk
  - For example, role of fiber and omega-3 fatty acids in inflammatory response

- We need a more integrated understanding of individual nutrient effects in the context of dietary patterns
THANK YOU