Effects of macronutrients on insulin resistance and insulin requirements

Dr Duane Mellor RD
Assistant Professor in Dietetics,
The University of Nottingham, UK
Outline of Discussion

- Issues of determining macronutrient balance
- Macronutrients or total energy?
- Evidence from the literature
- Practical Implications
- Recommendations for research and future practice
Considering Macronutrient Balance…

…consider a basic logic puzzle

- A farmer has a wolf, a goat and a cabbage.
- He needs to move all 3 across the river, the can move a maximum of 1 on their boat at a time, he cannot leave the wolf alone with the goat otherwise the goat will be eaten. Similarly the goat cannot be left alone with the cabbage.
However to make it more like macronutrients

- Based on EFSA DRVs for carbohydrate, fat and protein
- If Wolf = Carbohydrate
- Cabbage = Fat
- Goat = Protein

(Note not trying to draw metabolic comparisons)
However

- Carbohydrate can be ‘simple’/ high glycaemic index

- Or ‘complex’ / low glycaemic index
Additionally fats and protein are not a singular entity. Different compositions can have differing biological effects.

**Different fatty acid**

**Different amino acids**
This is all based on individual nutrients. Foods consist of varying compositions.

- So when considering what the optimal macronutrient composition for managing diabetes
- It is important to recognise the number of variables changing when attempting to manipulate the proportions of macronutrients in the diet
- This can add confounding to the original studies, and bias when interpreting the results for application in clinical practice.
Points to consider

• Is there a benefit from restricting carbohydrate in type 2 diabetes?
• Does reducing saturated fat intake reduce cardiovascular risk?
• Is energy restriction more important than macronutrient profile?
• What is the overall effect on mortality
Nutritional Modulation of Insulin Resistance

- Recent reviews by ADA (Evert et al., 2013) and Diabetes UK (Dyson et al., 2011) both agree that for most individuals as the insulin resistance is associated with obesity, weight loss is the most effective way to reduce insulin resistance.
- Multiple diabetes prevention studies have demonstrated the benefits of modest weight loss.
- Most used a low fat, high carbohydrate diet along with physical activity as the intervention.
## Does weight loss always help?

<table>
<thead>
<tr>
<th>Study Year Location</th>
<th>Type of study</th>
<th>Size</th>
<th>Age (year)</th>
<th>Duration of diabetes (years)</th>
<th>Mortality follow-up (years)</th>
<th>Mean BMI</th>
<th>Treatment</th>
<th>Weight change</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knatterud et al 1982 US</td>
<td>Randomized Controlled Trial</td>
<td>608</td>
<td>55% &lt;55</td>
<td>Newly diagnosed</td>
<td>12.5 (mean)</td>
<td>13.4%</td>
<td>-Insulin variable dose</td>
<td>-5% placebo (no change in insulin arms)</td>
<td><img src="up" alt="arrow" /></td>
</tr>
<tr>
<td>Bloom et al 1987 USA (abstract only)</td>
<td>Prospective</td>
<td>1854</td>
<td>61-74</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>-1.0 lbs</td>
<td><img src="up" alt="arrow" /></td>
</tr>
<tr>
<td>Lean et al 1990 Scotland</td>
<td>Retrospective</td>
<td>233</td>
<td>65</td>
<td>8.6 (median)</td>
<td>6.5 (mean)</td>
<td>23</td>
<td>Dietary instructions (patients on insulin excluded)</td>
<td>NA</td>
<td><img src="down" alt="arrow" /></td>
</tr>
<tr>
<td>Erikssson et al 1991 Sweden</td>
<td>Non randomized Clinical Trial</td>
<td>6734</td>
<td>47-49</td>
<td>Newly diagnosed</td>
<td>6 (mean)</td>
<td>27</td>
<td>Diet and physical activity intervention</td>
<td>-2.3% -3.7% (BMI)</td>
<td><img src="up" alt="arrow" /></td>
</tr>
<tr>
<td>Manson et al 1990 USA (Pima Indians)</td>
<td>Prospective</td>
<td>814</td>
<td>45 (median)</td>
<td>4.7</td>
<td>8 (median)</td>
<td>NA</td>
<td>Observational</td>
<td>0.8 Kg/year</td>
<td><img src="up" alt="arrow" /></td>
</tr>
<tr>
<td>Chabrievski et al 1996 Europe</td>
<td>Prospective</td>
<td>992</td>
<td>35.56</td>
<td>8.5</td>
<td>8 (mean)</td>
<td>25%</td>
<td>Observational (questionnaire)</td>
<td>50% ±2 BMI 16% &gt;±2 BMI 25% &lt;2 BMI</td>
<td><img src="up" alt="arrow" /></td>
</tr>
<tr>
<td>Williamson et al 2000</td>
<td>Prospective</td>
<td>4970</td>
<td>40-65</td>
<td>NA</td>
<td>12.8 (median)</td>
<td>&lt;27</td>
<td>Observational (questionnaire)</td>
<td>34% Intentional 13% unintentional</td>
<td><img src="down" alt="arrow" /></td>
</tr>
<tr>
<td>Swedish Obesity Study 2012</td>
<td>Prospective</td>
<td>607</td>
<td>45 (mean)</td>
<td>3</td>
<td>13.3 (mean)</td>
<td>41</td>
<td>Bariatric surgery</td>
<td>NA</td>
<td><img src="up" alt="arrow" /></td>
</tr>
<tr>
<td>LOOK AHEAD 2013</td>
<td>Randomized Controlled Trial</td>
<td>5145</td>
<td>59 (mean)</td>
<td>5 (median)</td>
<td>6.6 (median)</td>
<td>35</td>
<td>Intense lifestyle vs diet advice</td>
<td>6% vs 3.5% weight loss</td>
<td><img src="up" alt="arrow" /></td>
</tr>
</tbody>
</table>
Is the dietary approach important?

- Multiple meta-analyses suggest macronutrient profile is not the key, adherence to energy restriction is for weight loss, is this the same for diabetes?
- Diogenes suggested moderately increased protein and low glycaemic index preferable with respect to weight, insulin resistance less clear
- Suggestion that carbohydrate restriction should be the nutritional strategy of choice for diabetes (Feinman et al. 2014)
Figure 2. Change in homeostasis model assessment of insulin resistance over the 6-month randomized diet period (between post-intervention and post-low calorie diet test day), represented as mean together with the 95% confidence interval (analysis of variance $p = 0.357$). Statistically relevant differences are indicated in the figure, the remaining comparisons did not reach the $p < 0.10$ statistical value.
Views of Dr Eric Westman

• “Prior to the discovery of medical treatment for diabetes, carbohydrate-restriction was the predominant treatment recommendation to treat diabetes mellitus.”
• “At the end of our clinic day, we go home thinking, "The clinical improvements are so large and obvious, why don't other doctors understand?"
• “Carbohydrate-restriction is easily grasped by patients: because carbohydrates in the diet raise the blood glucose, and as diabetes is defined by high blood glucose, it makes sense to lower the carbohydrate in the diet.”
• “By reducing the carbohydrate in the diet, we have been able to taper patients off as much as 150 units of insulin per day in 8 days, with marked improvement in glycaemic control—even normalization of glycaemic parameters.”
Could this be rephrased?

• Why did the farmer have a wolf?

• If diabetes is a condition of carbohydrate why consume carbohydrate?
Challenges of interpreting research on carbohydrate restricted diets

• What is a low carbohydrate diet?
  – <40% energy from carbohydrate
  – <25g carbohydrate
  – Some focus on glycaemic index or load
• What is the remainder of the energy made up from, is it protein or fat?
• Is the diet truly ad libitum or is it restricted energy?
Dietary carbohydrate restriction positively affecting CVD risk and metabolic syndrome

Fig. 1 Schematic of hepatic metabolic regulation induced by a low-carbohydrate diet. Restriction in dietary carbohydrate, even in the presence of high saturated fatty acids, decreases availability of ligands (glucose, fructose, and insulin) that activate lipogenic and inhibit fatty acid oxidative pathways.
Should dietary carbohydrate restriction be the 1\textsuperscript{st} approach in diabetes management?


- **Case proposed:**
  - Hyperglycaemia is the salient feature of diabetes, dietary carbohydrate restriction is the best way to reduce hyperglycaemia
  - Population increases in diabetes and obesity have occurred as carbohydrate intakes have risen
  - Benefits not linked to weight loss
  - Low carbohydrate diets better for weight loss
  - Adherence equivalent or better compared to other approaches
  - Replacement of carbohydrate with protein is generally beneficial
Should dietary carbohydrate restriction be the 1st approach in diabetes management?

• Case proposed (continued):
  – Total Dietary Fat and Saturated fat do not correlate with CVD
  – Plasma saturated fat effected more by dietary carbohydrate than lipids
  – Carbohydrate restriction best way to reduce triglycerides and increase HDL cholesterol
  – Patients on carbohydrate regimens need less medication
Should dietary carbohydrate restriction be the 1st approach in diabetes management?

Low-carbohydrate diet better for weight loss, glucose control, HDL, triglycerides.

Counter position to Feinman et al. (2014)

• Type 2 diabetes is perhaps more about the metabolic disturbances, it is only characterised by hyperglycaemia?
• Carbohydrate restriction may increase NEFA which increases CVD risk?
• Energy restriction is essential to reduce the ectopic fat in the liver and pancreas associated with insulin resistance and reduced insulin secretion
• Increased protein may have satiating benefits and influence a number of pathways
• There is mixed data on link between saturated fat and CVD risk, it is what it is replaced with that is possibly as important
• Some carbohydrate sources, e.g. resistant starches have benefits in metabolic syndrome and diabetes
Are carbohydrate restrictions useful?

- **Example**
  - Individual consuming 3000kcal - 40% energy from carbohydrate
  - Is consuming 300g carbohydrate
  - If reduce energy intake to 2000kcal - 50% energy from carbohydrate
  - Will consume 250g carbohydrate
  - Is energy restriction perhaps the key?
  - Perhaps reducing fat alone is not enough?
What about fat?

- Fat accumulation – ectopic fat is linked with insulin resistance and deficiency of insulin secretion
- Omega 3 fatty acids associated with improved insulin sensitivity
- Animal models suggest that saturated fatty acids are associated with insulin resistance and cardiovascular risk
- Picture with humans less clear cut, possible benefits from novel fatty acids in dairy products e.g. CLA and odd number chain fatty acids
Protein?

- Data suggests increasing protein may improve satiety, but unclear if that brings about long term benefits?
- Some amino acids may influence endocrine pathways e.g. incretin, which suppresses glucagon and improves insulin secretion and cholecystokinin
- Evidence emerging linked to insulin signalling pathways (mTOR) and brain chemistry
- However, high intake of protein in type 1 diabetes may need insulin to reduce postprandial glycaemia
Alcohol

- Is alcohol a macronutrients
- It is an energy source and is consumed by many adults
- It suppresses gluconeogenesis/glycogenosis in the liver
- It can in excess increase blood pressure and levels of liver fat
Implications for practice

- Carbohydrate restrictions can be an effective way to reduce insulin resistance
- Weight loss can be effective and achieved by other approaches
- Adherence is perhaps more important than the nutrient profile
- When changing amounts of a macronutrient, think about what it is or might be replaced with
Recommendations for research

- Clear definitions for low carbohydrate, carbohydrate restriction
- Transparent reporting of dietary intakes achieved and how they were administered
- Development of metabolomics, do some individuals benefit from different approaches?
- Need long term follow up and mortality data
Recommendations for practice

- The best approach is one which can be adhered to
- Consider what may replace the food you recommend that the person eats less of?
- Consider if you recommend a food to be eaten, has consumption of other foods been reduced
- Talk and base advice on foods rather than nutrients
- Should weight loss the primary goal, are behaviours more important? Will improved health behaviours lead to reduced risk of complications?
Thank you for listening...

Duane Mellor PhD RD
Assistant Professor in Dietetics
Division of Nutritional Sciences
The University of Nottingham
Sutton Bonington Campus
Leicestershire, LE12 5RD, UK.

Email: duane.mellor@nottingham.ac.uk
Twitter: @MellorDuane

"God sent Adam and Eve out of the garden because of the apple. Apples have carbs and carbs are evil!"
References


