Dietary Carbohydrate Intake and Mitochondrial Content in Mice

Diane Royalty
Mentor: Dr. Jon Ramsey

Introduction

Mitochondria are important for energy supply and metabolism in the cell. Enzyme reactions of the Krebs cycle, electron transport chain, beta-oxidation, and ketone body formation occur and are regulated in the mitochondria. Mitochondria may also regulate the process of aging through redox metabolism. Dietary composition affects metabolic processes, content, and aging of mitochondria. Low carbohydrate and ketogenic diets result in an increase in beta-oxidation and ketogenesis. Since beta-oxidation and ketone body formation both occur in the mitochondria, low carbohydrate and ketogenic diets may cause an increase in mitochondrial biogenesis.

Hypothesis

Mice consuming a low carbohydrate or a ketogenic diet will have a greater mitochondrial content than mice fed a high carbohydrate diet in liver and skeletal muscle.

Materials and Methods

27 twelve month old male mice were divided into three groups of nine mice:

- Group 1: Fed a standard high carbohydrate control diet
- Group 2: Fed a low carbohydrate diet
- Group 3: Fed a ketogenic diet

All mice consumed 11.2 g food/day.

Mice were weaned at 2 to 3 months of age, and were eating their respective diets for one month.

Liver and skeletal muscle were analyzed for mitochondrial content.

<table>
<thead>
<tr>
<th>Diet Type</th>
<th>Carbohydrate</th>
<th>Protein</th>
<th>Fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Carbohydrate (control)</td>
<td>65%</td>
<td>18%</td>
<td>17%</td>
</tr>
<tr>
<td>Low Carbohydrate</td>
<td>10%</td>
<td>20%</td>
<td>70%</td>
</tr>
<tr>
<td>Ketogenic</td>
<td>0.7%</td>
<td>10%</td>
<td>89.3%</td>
</tr>
</tbody>
</table>

Mitochondrial content was determined by measuring biomarkers of mitochondrial activity. The biomarkers used to assess mitochondrial content included:

- Enzyme activities of:
  - Citrate synthase
  - Complex I of the electron transport chain
  - Complex IV of the electron transport chain

- Voltage-Dependent Anion Channel (VDAC) protein content
- Mitochondrial DNA to nuclear DNA ratio

Citrate synthase and complex I activity are considered to be the markers most strongly correlated to mitochondrial content in skeletal muscle.

Results

Enzyme activity in liver samples. There were no statistically significant changes in complexes I and IV.

Liver Results

VDAC protein content in liver samples. The control and low carb diets had greater VDAC protein content than the ketogenic diet.

Skeletal Muscle Results

Enzyme activity in skeletal muscle samples. Citrate synthase activity was higher in the low carb diet than in the ketogenic diet. The ketogenic diet’s citrate synthase activity was not significantly different from the control and low carb diets' citrate synthase activity. There were no statistically significant changes in complexes I and IV.

VDAC protein content in skeletal muscle samples. There were no significant changes in VDAC protein content between the diet groups.

Conclusions

Markers of mitochondrial content responded differently in liver and skeletal muscle. Results obtained from skeletal muscle were more consistent with the hypothesis than results from liver. In muscle, citrate synthase and mtDNA/nDNA were increased (p < 0.05) in the low carb diet compared to the control diet, with the ketogenic diet showing values intermediate to the other diet groups. Trends in complex I in skeletal muscle and complex IV in liver were also compatible with the hypothesis. Liver results for VDAC did not support the hypothesis. Changes in citrate synthase in the liver were likely correlated to low carb and ketogenic animals being in a gluconeogenic state rather than with changes in mitochondrial content. Overall the data collected neither supported nor disproved the hypothesis. Changes in citrate synthase depended upon the diet consumed and the tissue and mitochondrial compartment analyzed.

Further research is needed to determine how dietary carbohydrate intake effects mitochondrial content and activity as well as aging. This project is part of a long-term study. Another group of mice will consume the same diets for fourteen months and have mitochondrial content determined for liver and skeletal muscle. This second group of mice will provide more information on how long-term consumption of low carbohydrate and ketogenic diets effects mitochondrial content, composition, and aging.

References


