Obesity in Phenylketonuria

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Rates of overweight including obesity in different OECD countries in children 5-17 years of age (OECD update 2012)


Statlink: http://dx.doi.org/10.1787/888932523994
Additional risk for obesity in PKU by increased protein/glycemic load?
Role of high protein supply, on insulin secretion and development of obesity

High protein intake

- Increased insulinogenic amino acids
  - Enhanced secretion of insulin and IGF1
    - \( \uparrow \text{Leptin} \)
    - \( \downarrow \text{Adiponectin} \)
    - \( \uparrow \text{Insulin} \)
      - \( \uparrow \text{glucagon} \)
      - \( \uparrow \text{cortisol} \)
    - \( \uparrow \text{Lipogenesis} \)
      - \( \uparrow \text{TG} \) & \( \uparrow \text{FFA} \)
      - \( \uparrow \text{Acetyl-CoA} \)
      - \( \uparrow \text{ghrelin and other hormones} \)
    - \( \uparrow \text{Appetite} \)
    - \( \uparrow \text{BP} \)
    - \( \uparrow \text{SNS} \)
    - \( \uparrow \text{Alcosterol} \)
    - \( \uparrow \text{ACR} \)

- \( \uparrow \text{Obesity} \)
- Fatty liver, endothelial dysfunction & Other co-morbidities

- \( \uparrow \text{Insulin resistance} \) & \( \uparrow \text{metabolic syndrome} \)

High protein intake:

- Increased insulinogenic amino acids
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Consequences of high glycemic index/high glucose intake on insulin and development of insulin resistance

- ↑GI → ↑glucose
- ↑glucose → ↑glucagon
- ↑glucagon → ↑cortisol
- ↑cortisol → ↑appetite
- ↑appetite → ↑ghrelin and ? other hormones

- ↑GI → ↑Insulin
- ↑Insulin → ↑Lipogenesis
- ↑Lipogenesis → ↑TG & FFA
- ↑TG & FFA → ↑ACR

- ↑ACR → ↑BP
- ↑BP → ↑Alcosterol
- ↑Alcosterol → ↑SNS

- ↑SNS → ↑Leptin
- ↑Leptin → ↑appetite

- ↓Adiponectin → Fatty liver, endothelial dysfunction & Other co-morbidities
- ↓Adiponectin → Obesity

Insulin resistance & metabolic syndrome

- ↑Insulin → ↓Adiponectin
- ↓Adiponectin → Fatty liver, endothelial dysfunction & Other co-morbidities

- ↑Insulin → ↑Lipogenesis
- ↑Lipogenesis → ↑TG & FFA
- ↑TG & FFA → ↑ACR

- ↑ACR → ↑BP
- ↑BP → ↑Alcosterol
- ↑Alcosterol → ↑SNS

- ↑SNS → ↑Leptin
- ↑Leptin → ↑appetite

- ↓Adiponectin → Fatty liver, endothelial dysfunction & Other co-morbidities
What we know about PKU and obesity from publications
Trends in overweight and obesity – PKU

- **Holm, 1979 / White, 1982:**
  - Excess body weight at 4y
- **McBurnie, 1991:**
  - Increased weight > 4y in females
- **Schaefer, 1994:**
  - Significant longitudinal (0-6y) weight-for height increase
- **Dhondt, 1995:**
  - Excessive weight gain with diet relaxation at 8y
- **Acosta, 2003:**
  - A trend for increased BMI-zs (2-12y)
- **Dobbelaere, 2003:**
  - No evidence of increased weight-zs vs. reference population (< 7y)
- **Scaglioni, 2004:**
  - ~25% overweight at 8y
Trends in overweight and obesity – PKU

- **Huemer, 2007:**
  - BMI and body composition similar to controls

- **Albersen, 2010:**
  - Similar BMI in patients and controls
  - Increased body fat % in females > 11y

- **Belanger-Quintana, 2011:**
  - Some patient groups significantly heavier than general population
    - Classical PKU females > 13y
    - Classical PKU males > 18y

- **Burrage, 2012:**
  - 40% overweight or obese
  - a trend for increased prevalence of overweight in females > 11y
Dietary treatment in phenylketonuria does not lead to increased risk of obesity or metabolic syndrome

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<table>
<thead>
<tr>
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<th>Patients (n=89)</th>
<th>Controls (n=79)</th>
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<tbody>
<tr>
<td>Prevalence of OVW / OBE</td>
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<tr>
<td>Females</td>
<td>32.6%</td>
<td>24.1%</td>
<td>0.293</td>
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<tr>
<td>Males</td>
<td>41.5%</td>
<td>23.9%</td>
<td>0.129</td>
</tr>
<tr>
<td>BMI (kg/m²) mean (SD)</td>
<td>20.1 (4.3)</td>
<td>21.1 (5.1)</td>
<td>0.323</td>
</tr>
<tr>
<td>Waist circumference (cm) mean (SD)</td>
<td>73.2 (14.4)</td>
<td>75.2 (15.2)</td>
<td>0.376</td>
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## Potentially modifiable factors associated with infant/child overweight

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<thead>
<tr>
<th>Factor</th>
<th>General population</th>
<th>PKU evidence</th>
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<tbody>
<tr>
<td>Breast feeding</td>
<td>- ve association with breast feeding duration/exclusivity and toddler/school age weight</td>
<td>Long term breast feeding commonly reported. No data on long term weight gain</td>
</tr>
<tr>
<td>Early age of weaning</td>
<td>+ ve associated with overweight in infants, toddlers, preschool children</td>
<td>Age of weaning not described in PKU</td>
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## Diet quality and quantity

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<th>Factor</th>
<th>General population</th>
<th>PKU evidence</th>
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| Energy intake               | +ve association with energy intake with infant/childhood overweight | Limited data
Classical PKU 200 kcal/day higher than hyperphe (Rocha et al 2012)
105% of EAR (MacDonald et al 1999)
92% of DACH RDA (Ronde et al 2012) |
| Intake of sweetened beverages | +ve association with energy intake with infant/childhood overweight | Dietary pattern analysis not reported in PKU
Aspartame issue |
| Fruit and vegetable consumption | +ve association with high consumption and desirable body weight | Free use of fruit and veg do not improve their intake in PKU (Ronde et al 2012) |
Diet relaxation

- relaxed diet associated with excess weight gain (Dhont et al. 1995)

- ↑ in adiposity in 6/11 patients on Sapropterin/normal diet (Lambruschini et al. 2005)

- ↑ blood phe: poor cooking skills, poor budgeting, poor food choices, little exercise
Conclusions

- Obesity prevalence similar to general but may be more common in women
- Many PKU dietary factors may predispose to obesity although none proven
- Little data describing dietary patterns in PKU
- Nutritional profiling of many low protein foods could be improved
- ... there is much work left to do