Refeeding Low Weight Adolescents with AN

Graeme O’Connor RD
PhD Research Student - UCL
Specialist paediatric Dietitian
Great Ormond Street Hospital Foundation Trust
Pathophysiology of starvation

1. Insufficient energy
   ↓ insulin  ↑ glucagon

2. Depleted glycogen stores in muscles and liver

3. Activation of hormone sensitive lipase.

4. Adipose tissue breakdown

5. ↑ Fatty acids + glycerol delivered to the liver → ketone production

6. Gluconeogenesis
   Amino acid and glycerol = glucose
   Brain, retina and nephrons

7. Shift to ketone and glucose metabolism

8. Serum electrolytes maintained:
   Bone and tissue catabolism
   Increased renal tubular reabsorption
   Dehydration

9. Muscle wasting – amino acid production

10. Autonomic nervous system disturbances – bradycardia, QT Interval prolongation.
Perceived Risk factors of RS

- Rate of weight loss prior to refeeding (Crook, Hally et al. 2001; Boateng, Sriram et al. 2010; Raj, Keane-Miller et al. 2012);
- The extent of malnutrition (Ornstein, Golden et al. 2003; Raj, Keane-Miller et al. 2012);
- Method of refeeding (enteral verse Parenteral) (Weinsier and Krumdieck 1981; Diamanti, Basso et al. 2008);
- Carbohydrate load (Kohn, Madden et al. 2011; O'Connor and Goldin 2011);
- Rate at which nutrition is introduced (Kohn, Golden et al. 1998; Whitelaw, Gilbertson et al. 2010).

- The rate at which nutrition is introduced has received much attention and tends to be the focal point of refeeding guidelines (Golden, Katzman et al. 2003; NICE February 2006; RCP July 2005).
## Literature Review – Refeeding malnourished children

<table>
<thead>
<tr>
<th>Author/Country</th>
<th>Age</th>
<th>Kcal/ kg</th>
<th>Calculated intake for a 30kg child</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia/ WHO</td>
<td>&lt;16</td>
<td>50-75</td>
<td>1500-2250kcal</td>
</tr>
<tr>
<td>USA/ Canada 2006</td>
<td>&lt;18</td>
<td>30-40</td>
<td>900-1200kcal</td>
</tr>
<tr>
<td>UK MARSIPAN - NICE - 2006</td>
<td>Adult</td>
<td>5-20</td>
<td>150-600kcal</td>
</tr>
<tr>
<td>Adult</td>
<td>5-20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Junior MARSIPAN 2012</td>
<td>Adult</td>
<td>15-20</td>
<td>450-600kcal</td>
</tr>
<tr>
<td>European – Stanga 2008</td>
<td>Adult</td>
<td>10-15</td>
<td>300-450kcal</td>
</tr>
</tbody>
</table>

Institute of Child Health/ UCL - Nutrition Unit
Research Proposal

• **Aim**
  Identify whether there is a correlation between energy intake and cardiovascular, biochemical and anthropometric outcomes:

• **Outcome Measure**
  - Cardiovascular – QTc interval/ QT dispersion/ HR
  - Biochemical - PO4, K, Ca, Mg, FBC
  - Anthropometrics – Weight/ %BMI

• Identify potential predictive markers for the refeeding Hypophosphatemia.

• Develop International evidence based refeeding guidelines
Methodology

• **Inclusion criteria**
  
  • DSM IV Restrictive anorexia nervosa
  • <75%mBMI (healthy 95-105%)
  • Weight losing trajectory (>0.2kg/ week)
  • Admission to paediatric unit

• **Randomisation:**
  
  • Control group 500kcal/ day (10-20kcal/ kg) – low calorie
  • Treatment group 1200kcal/ day (30-40kcal/ kg) – high calorie

  – stratification for %BMI and feeding route (oral or enteral)
  (SIMS computer programme)

36 participants recruited over 2 years

Institute of Child Health/ UCL - Nutrition Unit
Methodology

- Once randomised - 200kcal increments daily until at 80% of EAR (1800-1900kcal/ day) – meal plan templates.

- Thiamine 200mg/ day from day 1

- ECG 12 lead (on day 1 and 4)

- Fasting biochemistry inc insulin, glucose, FBC (day 1,2,4,6,10)

- Vital signs – HR, BP, Temp (4 x daily)
Day 4 Mean diff 0.4kg (P=0.06; CI -0.9, 0.03)
Day 10 Mean Diff 0.5kg (95% CI -1.1, 0.1kg; P=0.09)
QT Interval

Institute of Child Health/ UCL - Nutrition Unit
### QTc interval >440ms

<table>
<thead>
<tr>
<th>Event</th>
<th>500KCAL</th>
<th>1200KCAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>QTc interval prolongation</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>QTc interval prolongation (post feeding)</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Total Refed</td>
<td>18</td>
<td>18</td>
</tr>
</tbody>
</table>

Odds Ratio 0.5 (95% CI 0.04, 5)

Institute of Child Health/ UCL - Nutrition Unit
### Hypophosphatemia <0.8mmol/l

<table>
<thead>
<tr>
<th>Event</th>
<th>500KCAL</th>
<th>1200KCAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypophosphatemia (&lt;0.8mmol/l)</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Total Refed</td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td>Odds Ratio 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(95% CI 0.5, 18)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Institute of Child Health/ UCL - Nutrition Unit
Relationship between energy intake and post feeding phosphate
%mBMI Marker for RH

For every 1% decrease in mBMI serum PO4 drops by 0.02 (P=0.03; 95%CI 0.001 to 0.039mmol/l)
WBC marker for RH

For every $1 \times 10^9$ drop in WBC, serum PO4 values were on average 0.1 mmo/l lower with a 95% CI 0.02, 0.2; P=0.01
Mechanisms contributing to RH

- Ghrelin
- Leptin
- Cortisol
- GH-IGF1 axis disturbance
- Body fat and %BMI

Disrupted Mesenchymal Stem Cell Function

- Osteoblast Formation
- Haematopoietic formation

- Bone Mineral Density/Bone Mass
- Bone stores of PO₄ and Ca
- Bone Marrow Adipose Tissue
- Bone Marrow Adipose Tissue

- Low Carbohydrate intake
- High Protein intake
- Serum WBC's

Amenorrhea

REFEEDING

- Digestive Juices (PO₄ 3mg/kg/day)
- PO₄ Utilisation
- Glucose Oxidation ATP Formation

- Serum PO₄

- Stimulates PTH and Calcitonin for bone resorption of PO₄

- Depleted bone stores

REFEEDING HYPOPHOSPHATEMIA
Refeeding recommendations

- Refeeding malnourished adolescents with AN at 1200kcal/day (30-40kcal/kg) elicits greater weight gain and had no adverse effect on cardiac function.

- No association between energy intake or carbohydrate intake was linked to refeeding hypophosphatemia.

- Patients that are very low weight <70%BMI may be at increased risk of developing refeeding hypophosphatemia.

- Patients that have low WBC’s <3.8 x 10^9/L may be at increased risk of developing refeeding hypophosphatemia (caveat raised CRP).

- Patients at higher risk of refeeding complications should commence prophylactic phosphate at 2-3mmol/kg (phosphate sandoz =16mmol)
References


• Refeeding Syndrome: Guidelines. (March 2007) Cape Town Metropole Paediatric Interest Group