Identification and management of patients with Refeeding Syndrome

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Malnutrition among hospital inpatients

- Incidence between 20-50%

- Beaumont Hospital – factors affecting nutritional status
  - 53% patients had no recorded weight
  - 5% had incorrect meal provision

- Analysis of contributing factors (750 patients in 3 centres)
  - Lack of malnutrition screening

- BAPEN Nutritional Screening Week 2010
  - 1 in 3 Irish patients malnourished on admission
Refeeding Syndrome

• Potentially fatal shifts in fluids and electrolytes that may occur in malnourished patients receiving feeding resulting in hormonal and metabolic changes causing serious clinical complications.

• True incidence unknown due to lack of universally accepted definition.

• 34% of ICU patients in one prospective cohort study
  – 236 patients
  – Mehanna et al. 2008
Refeeding Syndrome

- The metabolic and hormonal changes caused by rapid refeeding.
- Protein and fat as main energy source
- BMR reduces by 20-25
- Muscle and tissues decrease use of ketone bodies – fatty acids as energy source.
- Brain – uses ketones as main energy source.
- Liver – reduces rate of gluconeogenesis.
- Several intracellular minerals severely depleted.
Glycaemia leads to increased insulin secretion and decreased glucagon secretion.

PO4, Mg and cofactors such as thiamine are consumed.

Insulin stimulates potassium absorption into cells through sodium-potassium ATPase transporter.

Water follows by osmosis.

Reduced serum levels of potassium, magnesium and phosphate which are already depleted.
Phosphorus

• Predominantly intracellular mineral
• Essential for intracellular processes and integrity of cell membrane.
• Enzymes and second messengers activated by phosphate binding.
• Energy storage as ATP
• Regulates affinity of Hb for oxygen and regulates delivery to tissues
• Renal acid-base buffer system
Phosphorus

• Chronic whole body depletion.

• Insulin surge causes greatly increased uptake and use in cells.

• Deficit in intracellular and extracellular phosphorus.

• Widespread dysfunction of cellular processes affecting almost every physiological system.
Potassium

• The major intracellular cation

• Anabolism leads to increased intracellular uptake, as well as uptake due to direct action of insulin

• Deranged electrochemical membrane potential
Magnesium

- Predominantly intracellular cation

- Cofactor in most enzyme systems
  - Oxidative phosphorylation
  - ATP production

- Structural integrity of ribosomes, DNA and RNA

- Affects membrane potential
Complications

Respiratory
Failure or ventilator dependency
- Pulmonary oedema
- Retention of carbon dioxide

Cardiovascular
- Arrhythmia
- Congestive Heart Failure
- Digoxin toxicity
- Hyper/Hypotension
- Reduced cardiac contractility
- Sudden death
Complications

Renal
• Osmotic diuresis
• Pre renal azotemia
• Inability of renal tubules to concentrate urine.

Neurological
• Paraesthesia
• Weakness
• Altered mental state
• Paralysis
• Ataxia
• Tremor
• Tetany
• Seizures
• Wernickes Encephalopathy
Audit on identification of patients at risk of Refeeding Syndrome

- 102 patients
- 78.5% not at risk
- 21.5% at high risk
  - 11.2% - 2 minor risk factors
  - 9% - at least 1 major risk factor

- 2 patients – Refeeding Syndrome
- 32% of those at high risk treated according to guidelines
Patients at high risk

2 minor criteria

- Drugs and unintentional weight loss
- Alcohol abuse and little nutritional intake
- Drugs and little nutritional intake for > 5 days
- BMI < 18.5 and unintentional weight loss
- Chemotherapy and little nutritional intake for > 5 days

Patients with major risk factors

- Electrolyte imbalance
- BMI 13.5
- Little or no p.o. intake for > 2 weeks
Management of patients with major risk factors

- 3 patients – No Pabrinex
  No electrolyte monitoring
- 4 patients – No Pabrinex
  Electrolytes monitored
- 3 patients – Pabrinex
  Electrolytes monitored

- 8 patients were referred to dietician service

- 2 patients (9%) progressed to refeeding syndrome
Optimising nutritional care 2009-2012

- Department of Gastroenterology & Hepatology
  - Karen Boland
  - Prof. Frank Murray
- Department of Nutrition and Dietetics
  - Grainne Corrigan
  - Carmel O Hanlon
  - Paula O Connor
- Department of Pharmacy
  - Damodar Solanki
- Nursing Practice Committee
  - Marie Hennigan
NICE Guidelines

2 or more minor risk factors
• BMI < 18.5
• Unintentional weight loss of >10% over previous 3-6 months
• Little nutritional intake for >5 and < 10 days
• History of alcohol abuse or drugs including antacids, insulin, diuretics or chemotherapy

1 major risk factor
• BMI < 16
• Unintentional weight loss >15% of body weight over previous 3-6 months
• Little nutritional intake over previous 10 days
• Low potassium, phosphate or magnesium prior to refeeding
High risk patients

- Anorexia nervosa
- Chronic alcoholism
- Oncology patients
- Postoperative patients
- Elderly - reduced physiological reserve
- Uncontrolled diabetes mellitus
- Marasmus
- Prolonged fasting
- Morbid obesity with profound weight loss
- Malabsorption
- Long term diuretic users
- Long term antacid users
Issues around phosphate repletion

• Typical regimens require multiple infusions based on weight with frequent monitoring of serum phosphate.

• Intracellular nature of phosphate makes prediction of amount required to replenish stores difficult

• 30 patients with refeeding syndrome and normal renal function and PO4 <0.5mmol/L treated with 50mmol PO4 over 24 hours.
• 93% (n=28) achieved level >0.5mmol/L after 4 days.
  – Terlevich et al 2003

• Optimal regime still has to be confirmed with RCT
Prevention – NICE CG32

• Start nutritional support at maximum of 10kcal/kg/day. Increase levels slowly to meet requirements at 4-7 days.
• Use 5kcal/kg/day in extreme cases, monitoring cardiac rhythm continuously.
• Restore circulatory volume and maintain fluid balance
• Immediately before and during first 10 days, oral thiamine 200-300mg and trace element supplement.
• Correction of electrolytes.
Phosphate replacement:

- In hypophosphataemic patients at high risk of refeeding syndrome with normal renal function, give 500ml of Phosphate Polyfusor® over 6 - 12 hours, with close monitoring for complications.
- Phosphates Polyfusor® 500ml contains; 50mmol PO₄³⁻, 9.5mmol K⁺, 81 mmol Na⁺.
Schematic for publication on intranet and wards.

Nutritional Screening
• Scales audit
• Further training for nursing staff
• Addition of patient weights to nursing care plan

• Available on wards, intranet and interns handbook
• Education through Grand Rounds
• Development of Electrolyte Guidelines

SECTION 3: PROCEDURE FOR MANAGEMENT OF AT RISK PATIENTS

Figure 2: Management of patients at risk of refeeding syndrome, adapted from NICE Guidelines on Nutrition Support in Adults, February 2006.

<table>
<thead>
<tr>
<th>High risk: 1 or more major risk factors</th>
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<tbody>
<tr>
<td>• BMI &lt; 16kg/m²</td>
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<tr>
<td>• Unintentional weight loss of &gt;15% in the previous 3-6 months</td>
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<tr>
<td>• Little or no nutritional intake for &gt;10 days</td>
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<tr>
<td>• Low levels of potassium, phosphate and magnesium prior to refeeding</td>
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<table>
<thead>
<tr>
<th>Extreme risk: one of the following</th>
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<tbody>
<tr>
<td>• BMI &lt; 14 kg/m²</td>
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<tr>
<td>• Very little or no nutrient intake for &gt;15 days</td>
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<tr>
<th>High risk: 2 or more minor risk factors</th>
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<tbody>
<tr>
<td>• BMI &lt; 18.5 kg/m²</td>
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<tr>
<td>• Unintentional weight loss of &gt;10% in the previous 3-6 months</td>
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<tr>
<td>• Little or no nutritional intake for &gt;5 days</td>
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<tr>
<td>• History of alcohol abuse* or recent chemotherapy, *See Beaumont Hospital’s Management of Alcohol Withdrawal Guidelines (Department of Psychiatry, September 2011) for patients with alcohol dependency.</td>
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Moderate risk: 1 of the above factors

Risk by patient category
Alcoholics.
Elderly living alone.
Chronic GI symptoms.
Chronic debilitating disease.
Eating disorders.
Chronic dieters – severe restriction.
Mental illness.
Obviously malnourished.
Chronic use of diuretics, antacids, or insulin.

Patient identified as high risk according to NICE guidelines;
Check electrolytes

Slow initiation of feeding according to risk category

Dietitian referral
Extreme risk: 5kcal/kg
High risk: 10kcal/kg
Moderate risk: 20kcal/kg
Monitor fluid balance

IV Pabrinex 1 & 2
Once per day for 3 days, and general micronutrient supplement

Electrolyte replacement if required and ECG monitoring

Daily U&E, Ca²⁺, PO₄³⁻, K⁺ and Mg²⁺ for 5 days, then 3 times weekly until stable

Phosphate replacement:
• In hypophosphataemic patients at high risk of refeeding syndrome with normal renal function, give 500ml of Phosphate Polyfusor® over 6 - 12 hours, with close monitoring for complications.
• Phosphates Polyfusor® 500ml contains; 50mmol PO₄³⁻, 9.5mmol K⁺, 81 mmol Na⁺.
Audit of factors affecting nutritional intake at Beaumont Hospital

- Fasting inappropriately
- Meal insufficient
- Required feeding assistance and did not receive
- Required high protein - high calorie diet and received regular meal
- Required diabetic diet - received regular diet
Audit of factors affecting nutritional intake at Beaumont Hospital

- 53% of patients with prescribed special diets had documentation of requirements at end-of-bed.

- 47.4% of patients had record of recent weighing.

- 12.5% were non-compliant with oral nutritional supplements
<table>
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<tr>
<th>Serum potassium level</th>
<th>Guideline for repletion</th>
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<tr>
<td><strong>Critical deficit</strong></td>
<td>Likely to require replacement in intensive setting, seek specialist advice</td>
</tr>
<tr>
<td>K(^+) &lt; 2mmol/L or K(^+) &lt; 2.5mmol/L with ECG changes characteristic of hypokalaemia</td>
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<tr>
<td><strong>Severe Deficit</strong></td>
<td>Intravenous replacement via peripheral line(^{10,11}) 1.40mmol K(^+)/L premixed solution(^*) of potassium and fluid, given at 125mL per hour dependent on fluid status of patient. 2. Check serum potassium after 8 hours of commencement of infusion. 3. If serum potassium not corrected to normal levels, repeat step 1. Correct serum potassium to normal levels. 80mmol K(^+) usually required in cases of severe deficit.</td>
</tr>
<tr>
<td>K(^+) 2-2.5mmol/L without critical conditions or ECG changes</td>
<td></td>
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<tr>
<td><strong>Moderate deficit</strong></td>
<td>Intravenous replacement via peripheral line(^{10,11}) 1.40mmol K(^+)/L in premixed solution(^*) at 125mL per hour, dependent on patient fluid status. 2. Check serum potassium level after 8 hours. 3. If not corrected to normal levels, give further 20mmol K(^+)/500mL fluid. 4. Check serum potassium level 4 hours after last dose. Repeat infusion at step 3 as necessary to correct serum potassium to normal level.</td>
</tr>
<tr>
<td>Serum K(^+) 2.5-3.0mmol/L</td>
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<tr>
<td><strong>Mild deficit</strong></td>
<td>Oral replacement:(^10) Slow K(^<em>) – 2 tabs tds (8mmol K(^+)/tablet) Sando-K(^</em>) - 2 tabs bd (12mmol K(^+)/tablet) Kay-Cee-L(^<em>) – 10mL bd (1mmol K(^+)/mL) or Intravenous replacement with premixed solution(^</em>) of 20mmol K(^+)/500mL.</td>
</tr>
<tr>
<td>Serum K(^+) 3.1-3.5mmol/L</td>
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<tr>
<td>Serum calcium (corrected) level</td>
<td>Guideline for repletion</td>
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| **Acute severe hypocalcaemia**  | 1.1g calcium gluconate injection in 50mL glucose 5% infused over 20-30 minutes.  
Then  
1. Solution of ~10mg/mL calcium gluconate made by diluting 11g calcium gluconate in 1 litre glucose 5% or normal saline and infused at a rate of 50mL/hour. This can be adjusted to maintain the calcium level at the lower limit of normal.  
Serum calcium level should be closely monitored during infusion.  
Calcium gluconate injection 10% (1g in 10mL) |
| Symptomatic hypocalcaemia and Ca\(^{2+}\) <2.12mmol/L or Ca\(^{2+}\)<1.9mmol/L |                             |
| **Acute mild  hypocalcaemia**   | 1500-2000mg elemental calcium daily in divided doses between meals.  
Calcichew\(^\circledR\) (Calcium 500mg) - 2 tablets bd  
Sandocal 400\(^\circledR\) (Calcium 400mg) - 3 tablets bd |
<p>| Asymptomatic hypocalcaemia      | 1.9mmol/L &lt; Ca(^{2+}) &lt; 2.12mmol/L |</p>
<table>
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<tr>
<th>Serum magnesium level</th>
<th>Guideline for repletion</th>
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<tr>
<td><strong>Acute or Severe Hypomagnesaemia</strong></td>
<td>5g magnesium sulphate injection diluted in 500mL Sodium Chloride 0.9%. Infuse over a minimum of 5 hours for 3 to 5 days, depending on serum levels.¹⁶,¹⁷ Often requires oral magnesium to maintain at normal serum levels.</td>
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<tr>
<td>Mg²⁺ &lt;0.7mmol/L + symptoms or Mg²⁺ &lt;0.4mmol/L</td>
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<tr>
<td><strong>Mild Hypomagnesaemia</strong></td>
<td>Give by mouth 20 to 24mmol Mg²⁺ per day in divided doses for 5 days.¹⁰ Magnesium Verla® 2 sachets bd</td>
</tr>
<tr>
<td>Mg²⁺ 0.5 – 0.7mmol/L no symptoms</td>
<td></td>
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<tr>
<td>Serum phosphate level</td>
<td>Guidelines for repletion</td>
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| **Severe hypophosphataemia with refeeding syndrome** | Intravenous therapy  
50mmol PO$_4^{3-}$ over 6 – 12 hours. (i.e. Phosphate Polyfusor$^*$)$^{19}$ |
| **Severe defecit PO$_4^{3-}$<0.4mmol/L** | Intravenous replacement via peripheral line.  
1. Calculate phosphate requirement of 0.16mmol/kg$^{20}$ and administer over 6 hours in patients who are unwell or have multiple risk factors for hypophosphataemia. *i.e. in 70kg patient, give 20mL potassium phosphate or sodium phosphate injection diluted in 500mL Sodium Chloride 0.9% or Glucose 5% over 6 hours.*$^{11}$  
2. In critically unwell patients, increase to 0.24mmol/kg$^{21}$ over 6 hours. *i.e. in 70kg critically ill patient, give 28mL sodium phosphate injection diluted in 500mL Sodium Chloride 0.9% or Glucose 5% over 6 hours.*$^{11}$  
3. Recheck serum phosphate after 6 – 12 hours following infusion and repeat if necessary. Maximum of 50mmol PO$_4^{3-}$ in 24 hours.$^{19}$  
4. Check serum phosphate levels daily for 48 hours following infusion.  
5. Stop infusions when serum phosphate levels > 0.8mmol/L. |
| **Moderate deficit PO$_4^{3-}$ = 0.41-0.6mmol/L** | Intravenous replacement via peripheral line.  
1. Calculate phosphate requirement of 0.08mmol/kg$^{20}$ over 6 hours in patients who are unwell or have multiple risk factors for hypophosphataemia. *i.e. in 70kg patient, give 10mL of potassium phosphate or sodium phosphate injection diluted in 500mL Sodium Chloride 0.9% or Glucose 5% over 6 hours.*$^{4}$  
2. Recheck serum phosphate after 6 – 12 hours following infusion and repeat if necessary. Maximum of 50mmol PO$_4^{3-}$ in 24 hours.$^{19}$  
3. Check serum phosphate levels daily for 48 hours following infusion.  
4. Stop infusions when serum phosphate level > 0.8mmol/L. |
| **Mild deficit PO$_4^{3-}$ = 0.61-0.79mmol/L** | Oral replacement therapy  
1000mg phosphorus /day (32.2mmol/day)  
Phosphate -Sandoz$^*$ 1 tablet bd can go up to 6 tablets daily in divided doses.$^{10}$ |
Summary

- Identify patients at risk – NICE guidelines
- Order appropriate investigations
- Thiamine
- Appropriate electrolyte replacement
- Early referral to dietician service
- Repeat ECG or cardiac monitoring in at risk patients
- Low threshold for monitoring and treating patients with liver disease
Acknowledgements

• Professor Murray and Department of Gastroenterology and Hepatology

• Grainne Corrigan, Dietician
• Carmel O Hanlon, Dietician
• Paula O Connor, Dietician

• Damodar Solanki, Pharmacy

• Marie Hennigan, Nurse Practice Development

• Dr Diarmuid Smith, Endocrinology
• www.ispen.ie

• www.nice.org.uk

• www.espen.org