BAPEN
Putting patients at the centre of good nutritional care

Top Tips for Preventing and Managing Refeeding Syndrome

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Key points

1. Refeeding syndrome describes the clinical and biochemical problems that may result from feeding malnourished patients (orally, enterally or parenterally).
2. Hypophosphatemia is the most commonly used marker of refeeding syndrome. It commonly occurs when artificial nutritional support is started (especially with carbohydrate) and can very occasionally cause death. Hypomagnesaemia, hypokalaemia and hypo (or hyper) glycaemia also occur.
3. Orally/enterally fed patients are more likely to develop refeeding hypophosphataemia than those given parenteral nutrition.
4. Confusion can be due to thiamine deficiency (Wernicke's encephalopathy) and if untreated may lead to a permanent loss of short-term memory (Korsakoff psychosis).
5. Sodium/water retention (oedema) is common with refeeding especially with carbohydrate and can lead to cardiac failure.
6. Due to difficulties with definitions the patients at high risk can be hard to determine. UK NICE guidelines are helpful but not a completely reliable predictor so need careful consideration. Clinicians need to be aware of refeeding problems and assume most malnourished patients are at risk.
7. When feeding malnourished patients, carbohydrate must be introduced slowly (non-protein energy usually 50% CHO and 50% lipid). Additional phosphate, B vitamins, potassium and magnesium should be given at the same time as the feeding. Little or sometimes no sodium is given.
8. Nutritional support to the at-risk patient should start at no more than 50% of estimated needs for the first 24-48 hours. In patients at very high risk, UK NICE guidelines suggest initially being even more cautious (10 kcal/kg/24 hrs) (PENG suggest 10-20 kcal/kg/24 hour) but increasing quickly with appropriate monitoring.
9. Health professions experienced in refeeding problems (for the severe cases a multidisciplinary nutritional support team (NST)) should manage these patients. As they may fall, the phosphate, potassium, magnesium and glucose must be monitored (especially after the first feed and daily until stable).

Explanations

1. Refeeding deaths were first described when food became available to the inhabitant of a town/city that had been surrounded and starved into submission. The earliest record relates to the Siege of Jerusalem by the Romans in AD 70. Evidence of deaths with parenteral nutrition is scarce and relates to large amounts of glucose provision with inadequate electrolytes.
2. The start of refeeding with carbohydrate or glucose causes insulin secretion and this activated the glycolytic pathway and the decarboxcylic acid cycle so that phosphate is rapidly used and moves from the extracellular space to the intracellular one causing serum levels to fall. Blood phosphate levels below 0.32 mmol/L are considered severe in the literature.

   Hypophosphataemia has many effects including muscular weakness (especially of the diaphragm leading to respiratory failure), biventricular cardiac failure and arrhythmias, a low white cell count with dysfunctional white cells, abnormal liver function tests and many neurological problems, including cranial nerve palsies, a lower motor neuron type paralysis, ataxia, tremor, fits and coma.
3. Oral/enteral feeding is more commonly associated with hypophosphataemia than parenteral nutrition probably because of the 'incretin' effect of carbohydrate in the bowel. If the same amount of glucose is given on separate occasions orally and intravenously; the amount of insulin released is much greater after the oral glucose. This may be due to the secretion of upper gut peptide hormones (gastric inhibitory peptide (GIP) and glucagon like peptide-1 (GLP-1)). The high insulin levels will cause more glucose to enter the cells and be used to make ATP and thus further exacerbate the hypophosphataemia.
4. Thiamine is used in the glycolytic and decarboxycylic acid cycles and with their reactivation circulating thiamine is utilised. Thiamine deficiency can lead to the development of Wernicke's encephalopathy which is a triad of encephalopathy, ataxia and ocular dysfunction (nystagmus). In the long-term this may progress to the irreversible Korsakoff's syndrome, which is characterised by permanent short-term memory loss.

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5. The release of insulin (largely by glucose) and the availability of energy (ATP) reactivates the cell membrane Na+/K+ pump which expels sodium from the cell and allows magnesium and potassium in. The expulsion of sodium into the interstitial space is followed by water and may result in oedema. Serum potassium and magnesium concentrations may fall further, so close monitoring is needed.

   Patients at high risk of refeeding problems should receive about 20 ml fluid/kg and <1 mmol/kg sodium. Sodium excretion is limited in refeeding and excess provision combined with that liberated from cells can lead to circulatory overload (heart failure and severe oedema), which is dangerous in combination with cardiac atrophy from malnutrition and/or arrhythmias. Extreme caution should be observed when giving electrolytes in 0.9% NaCl (154 mmol Na/l) due to the risk of sodium and fluid overload and if using 5% dextrose the energy content needs to be taken into consideration (200 kcal/l). Ideally electrolytes should be added to the parenteral nutrition bag and oral preparations in water should be used where possible for oral and enteral tube feeding. However, it is important to remember that intestinal failure patients may need additional sodium and fluid to replace gastrointestinal losses from stomas, fistulas, drains or enteral tubes.

6. The UK NICE guidelines (below), while good, are not completely reliable at identifying those who develop refeeding problems; hence there must be a high degree of clinical suspicion. There are publications that support for a low serum magnesium or low IGF-1 improving their sensitivity.

   UK NICE risk factors for developing refeeding syndrome
   One or more of the following:
   - BMI <16 kg/m^2
   - Unintentional weight loss >15% within last 3-6 months
   - Little or no nutritional intake for more than 10 days
   - Low potassium, magnesium or phosphate prior to feeding.

   Two or more of the following:
   - BMI <18.5 kg/m^2
   - Unintentional weight loss >10% within last 3-6 months
   - Little or no nutritional intake for more than 5 days
   - A history of alcohol abuse or drugs including insulin, chemotherapy, antacids or diuretics.

7. The UK NICE guidelines are considered by many to be cautious in the amount of energy given when feeding first begins. The non-protein energy is generally given as 50% carbohydrate and 50% lipid to reduce the initial carbohydrate load though it is not always easy to do this if relying on standard products. The UK NICE guideline also recommends that B vitamins and a balanced multivitamin/trace element supplement are given immediately before and during the first 10 days of feeding. Intravenous B vitamins are usually given for 3-5 days.

8. Patients considered to have a high risk of refeeding problems should start feeding very cautiously, especially those fed enterally. Malnourished patients are likely to be intracellularly depleted of K, Mg and PO4. This depletion might not be reflected in pre-feeding plasma electrolytes levels which may appear normal. For this reason, UK NICE Guidelines recommend generous levels of electrolytes (except sodium) should be provided prophylactically where possible (2-4 mmol/kg K, 0.3-.06 mmol/kg PO4 and 0.2-0.4 mmol/kg mg) unless plasma levels are high in accordance with expert supervision.

9. Close monitoring is required to identify hypophosphataemia, hypomagnesaemia, hypokalaemia and hypoglycaemia (or hyperglycaemia) so that prompt replacement therapy may be given. This is important especially in those enterally/orally fed in whom monitoring is often not performed as meticulously as in those receiving parenteral nutrition. The expertise in monitoring and treating these patients lies with healthcare professionals with training and experience. This is usually a dietitian but in more severe cases the hospital's multidisciplinary NST.

Suggested reading

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