Clinical Guideline

REFEEDING SYNDROME

SETTING Trustwide – Bristol and Weston Sites

FOR STAFF Medical staff, Nursing staff, Dietitians, Pharmacists

PATIENTS All adult patients.

GUIDANCE

Definition:
Refeeding syndrome (RFS) can be characterised as **biochemical refeeding syndrome**; where electrolyte disturbances are observed with no adverse clinical symptoms, or **symptomatic refeeding syndrome**; where clinical symptoms are observed.

Pathway of Refeeding:

Malnutrition/Starvation
- Gluconeogenesis
- Weight Loss
- Water, vitamin and mineral depletion

Refeeding
- Increased carbohydrate intake
- Insulin release
- Increased cellular glucose uptake and increased protein synthesis
- Rapid cellular uptake of phosphate, magnesium and potassium
- Increased utilisation of thiamine (co-enzyme in carbohydrate metabolism)
- Biochemical and clinical symptoms of refeeding syndrome

Main Features:
- Fluid retention
- Altered glucose metabolism
- Hypophosphataemia
- Hypomagnesaemia
- Hypokalaemia

The clinical consequences can range from being generalised symptoms such as muscle weakness to life threatening cardiac arrhythmias.
Due to the potential severe consequences of refeeding syndrome health professionals need to raise awareness and aim for prevention in refeeding at risk patients.

Nutritional treatment of patients at risk of RFS should be provided by healthcare practitioners with adequate training in Nutrition Support (NICE 2006).

Risk of Refeeding Syndrome

- The evidence for identifying risk of refeeding syndrome is limited. These risk factors are a guideline only and should be used with caution
- Due to homeostatic mechanisms, serum concentrations of potassium, magnesium and phosphate may be normal prior to feeding and this should not be used as evidence of low risk of refeeding syndrome.
- NB. Diuretics, chemotherapy and rehydration are all potential causes for low electrolytes and biochemical monitoring alone should not be used as a risk factor.
- The presence of urinary ketones in the absence of diabetes may indicate starvation, but the absence of ketones does not exclude risk of refeeding syndrome.
- Even when oral or enteral nutrition intake appears to be sufficient to minimise risk of refeeding syndrome, consideration should be given to the extent of any vomiting or malabsorption that may result in metabolic starvation.

Patients at risk and extremely high risk:

At Risk: Any patient who has had very little or no food intake for >5 days

High Risk:

- **Patients with 1 or more of the following:**
  - BMI < 16 kg/m^2
  - Unintentional weight loss of >15% in the past 3 - 6 months
  - Very little or no nutritional intake for more than 10 days, or history of prolonged fasting including Anorexia Nervosa
  - Low plasma concentrations of potassium, phosphate or magnesium prior to feeding

- **Or with 2 or more of the following:**
  - BMI < 18.5 kg/m^2
  - Unintentional weight loss of >10% in the past 3 - 6 months
  - Underfed for 5-10 days with evidence of stress and depletion
  - History of alcohol or drug abuse or some drugs including insulin, chemotherapy, antacids or diuretics

Extremely High Risk:

- Very low BMI (<14 kg/m2) / negligible intake for >15 days / recent starvation

Special Consideration:

- Malnourished patient with sepsis
- Malnourished / dehydrated / kidney impairment

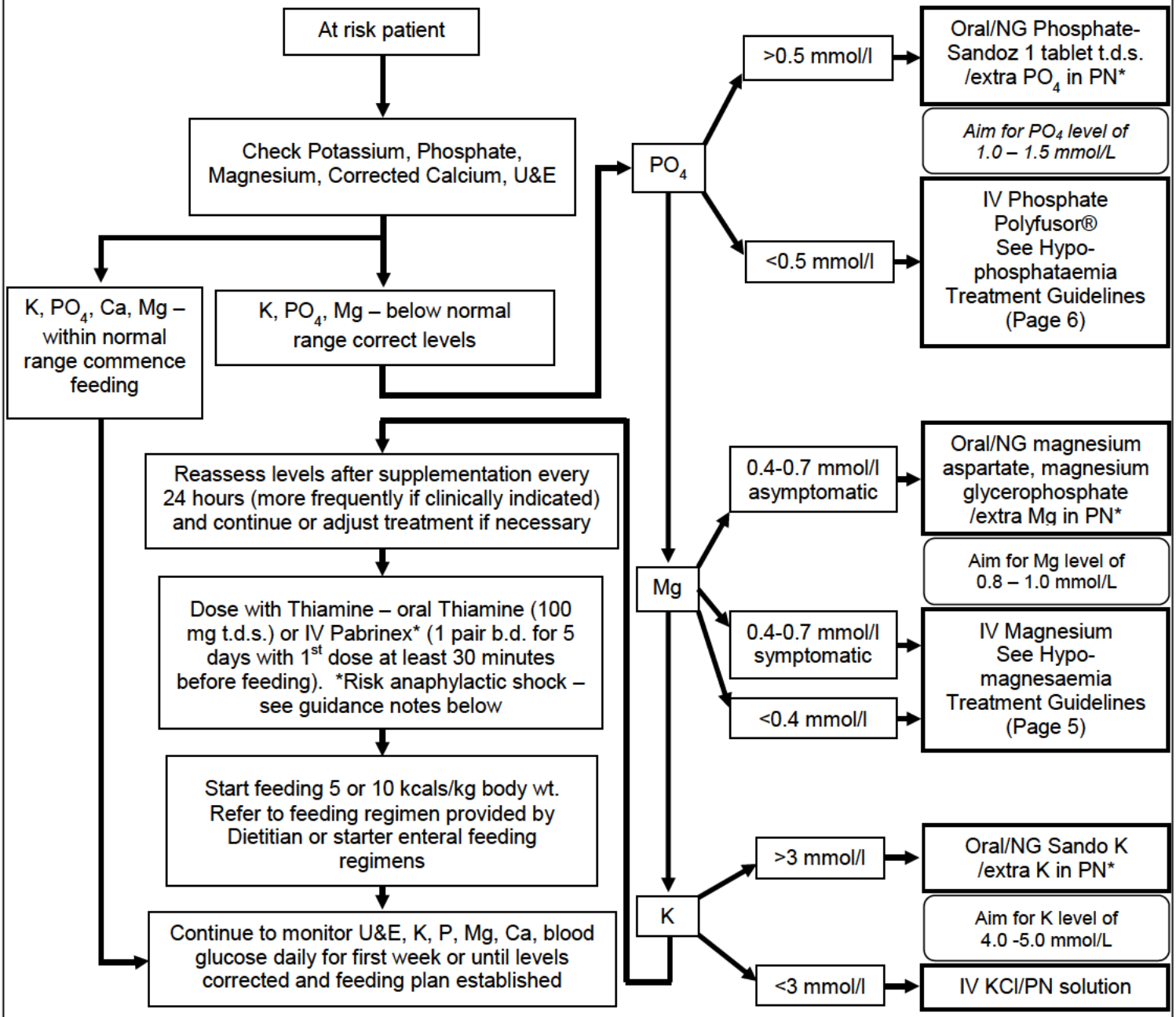
Prevention and Management of Refeeding Syndrome

How to prevent and manage refeeding syndrome:

- Be aware of risk category of patient (see above)
- Test and correct electrolytes ideally before starting nutrition support (See flow chart page 4)
- Feeding should start with 10-20 kcals/kg body weight/day, increasing levels slowly to meet full needs only after 4–7 days or in accordance with dietitian plan, if biochemical monitoring allows.
- Avoid overfeeding in obese patients (use Ideal Body Weight/Adjusted Body Weight rather than Actual Body Weight
- Initial rate of feeding and progression of calorie provision should be based on thorough assessment of the risk of refeeding syndrome.
- The risk of refeeding syndrome should be balanced with the ongoing risk of undernutrition and level of pre-existing malnutrition.
- Patients with known risk factors for re-feeding syndrome, such as severe anorexia nervosa, very low BMI, pre-existing electrolyte or renal abnormalities, infection and other medical complications, should be given fewer calories (5–10 kcal/kg/day) but frequently assessed (at least 12 hourly) so that calories can be increased in the absence of re-feeding syndrome and underfeeding syndrome can be avoided. Monitor cardiac rhythm continually in these people and any others who already have or develop any cardiac arrhythmias
- Continue to monitor electrolytes during the first week of refeeding and until stable.
- The first 72 hours after initiation of feeding is crucial in the potential development of RFS, therefore requires closer monitoring of signs / symptoms of RFS.
- Restore circulatory volume and monitor fluid balance and overall clinical status closely
- Provide immediately before and during the first 10 days of feeding: oral thiamine 100 mg t.d.s. or IV Pabrinex 1 pair b.d. for 5 days and a balanced multivitamin/trace element supplement once daily (e.g. Forceval capsule/soluble or Sanatogen A to Z complete)
- Provide oral, enteral or intravenous supplements of potassium (likely requirement 2–4 mmol/kg/day), phosphate (likely requirement 0.3–0.6 mmol/kg/day) and magnesium (likely requirement 0.2 mmol/kg/day intravenous, or 4 mmol/kg/day oral) unless pre-feeding plasma levels are high. Pre-feeding correction of low plasma levels will be guided by biochemical monitoring and determined by individual patient requirement.

NB. Consider the carbohydrate load of oral nutritional supplements when prescribing for patients with very poor oral nutritional intake who fall in to any of the risk categories above.

Refeeding Syndrome Flowchart



*Adding electrolytes to parenteral nutrition is unlikely to be possible in the majority of cases. Please discuss with the BRI Nutrition Team for advice on parenteral nutrition additions for patients at the BRI.

Guidance Notes for Refeeding Syndrome Flowchart

- ***Phosphate*** Hypophosphataemia <0.5mmol/l should be corrected with IV Phosphate Polyfusor®. However caution should be exercised and further advice sought if patient has renal failure or hypercalcaemia.
- ***Magnesium*** There is a risk of cardiac arrhythmias with IV administration of magnesium and thus requires close monitoring, consider the use of a cardiac monitor.
- ***Potassium*** Hypokalaemia may be associated with hypomagnesaemia, which will need to be corrected alongside potassium replacement.
- ***Pabrinex*** Anaphylactic shock rarely occurs during or shortly after administration, therefore facilities for treating anaphylaxis must be available when Pabrinex is administered (see Injectable medicines guide (Medusa), reference on Page 7). Pabrinex should be given over 30 minutes.
- ***Multivitamin***: a balanced multivitamin/trace element supplement should be prescribed once daily (e.g. Forceval capsule/soluble or Sanatogen A to Z complete) if oral intake allows.

Treatment Guidelines for Hypomagnesaemia in Refeeding Syndrome / Malnourished Patients

NHS University Hospitals Bristol and Weston NHS Foundation Trust

Magnesium Replacement Guidelines for Adults

Mg^{++} < 0.7mmol/L [0.7-1.0]

Yes

diarrhoea & vomiting, fistula, stoma loss, NG aspiration, short bowel syndrome, dietary deficiencies, malabsorption, TPN

Investigate route of Mg^{++} loss

diuretics, glycosuria, aminoglycosides, cyclosporin, chemotherapeutics, chronic alcoholism, diabetes mellitus

Mg^{++} < 0.4 mmol/L

Mg^{++} 0.4 - 0.7 mmol/L

asymptomatic

symptomatic

asymptomatic

REDUCE MAGNESIUM DOSE BY HALF IF eGFR <30 mL/min/1.73m^2

daily regimen:

Suggest, give 20mmol (=10ml 50% concentration $MgSO_4$) no faster than 4mmol/hr.

5 day regimen:

Day 1: 20mmol (=10 ml $MgSO_4$) over 3 hours followed by additional 20 mmol $MgSO_4$ over 21 hours.

Day 2-5: 20mmol (=10 ml $MgSO_4$) over 24 hours.

Review levels daily and stop when >0.8 mmol/L

Oral Replacement:

1. Magnesium Supplementation. Magnesium salts are not well absorbed from the gut, which explains their use as osmotic laxatives. Reduce dose if diarrhoea develops. Aim to provide approximately 24mmol/day in divided doses using one of the following options[1]:

a. 1st Line: Magnesium –L-aspartate 6.5g oral POWDER. Dissolve one sachet in water to give 10mmol. Suggest start at 1 sachet twice daily.

b. 2nd Line: Magnesium glycerophosphate: 4mmol CHEWABLE TABLET (suggest start at 8mmol three times daily) or 1mmol/ml LIQUID

2. Consider using/adding magnesium sparing diuretics e.g. Amiloride or Triamterene.

iv replacement:

Magnesium sulphate ($MgSO_4$) is the only parenteral supplement available.
It is contraindicated in severe renal failure, heart block and myasthenia gravis. $MgSO_4$ 50% ampoules contain 2mmol magnesium per ml.
Ampoules to be diluted with 500 ml of 5% glucose or sodium chloride 0.9%.
The total magnesium deficit may be as high as 1mmol/kg of body weight.

RE-CHECK MAGNESIUM LEVELS DAILY

Effects of toxicity:

Too rapid $MgSO_4$ administration: flushing, sweating, mild bradycardia, hypotension

Hypermagnesaemia: headache, muscle weakness, hyporeflexia, respiratory depression, pulmonary oedema

Antidote: Calcium Gluconate 1 gram iv slowly.

Reference:
UKMI_QA_How_is_acute_hypomagnesaemia_treated_in_adults_update_Nov_2020.pdf (sps.nhs.uk)

Treatment Guidelines for Hypophosphataemia in Refeeding Syndrome / Malnourished Patients

- Identify patient at risk of hypophosphataemia.
- Measure serum phosphate (together with other electrolytes and renal function) prior to feeding. If the patient is significantly hypophosphataemic (i.e. PO_4 <0.5 mmol/l) start treatment to correct this at the same time as starting feeding (enteral/parenteral).
- Suggested starting dose for correction of hypophosphataemia:
  - Serum Phosphate >0.5 mmol/l: Phosphate Sandoz 1 tablet t.d.s.
  - Serum Phosphate <0.5 mmol/l: 500ml Phosphate Polyfusor® over 24 hours (contains Na 81mmol, K 9.5mmol, PO_4 50mmol) via an infusion pump at 20ml/hour via a dedicated iv cannula (other drugs can precipitate in line).
- Phosphate Polyfusor® should be prescribed in the fluids section of the drug chart and can be obtained from the emergency drugs cupboard.
- A single 24 hour infusion is usually sufficient.
- Measure serum phosphate concentration daily for first week or until normal concentration is achieved.
- ***For patients with impaired renal function (eGFR <60 ml/min/1.73m^2), reduce the dose by at least 50% and consider monitoring more frequently. Seek further advice before treating if eGFR <30 ml/min/1.73m^2.***
- ***For further information on treatment of individual patients contact any member of the nutrition team.***

Useful Contacts

The Nutrition Team should be contacted for all patients who require parenteral nutrition and can be contacted to give advice on feeding patients who have complex medical, surgical and nutritional needs and are at significant risk of refeeding syndrome.

In the first instance the Nutrition Nurses or Dietitian should be contacted.

Members of the team

Bristol contacts:

- Consultant Gastroenterologist – [redacted]
- Nutrition Nurses – [redacted]
- Senior Dietitian – [redacted]
- Consultant Clinical Biochemist – [redacted]
- Pharmacist – [redacted]

Weston site contacts:

- Dietetic Department ext [redacted] / bleep [redacted]
- Pharmacist ext [redacted]
- Consultant Clinical Biochemist [redacted] ([redacted]).
- Biochemistry Dept. ext [redacted]

RELATED DOCUMENTS

Anaphylaxis Clinical Guidelines
[redacted]
Medch M13 Intravenous Injection of Strong Potassium Solutions
[redacted]
NICE Clinical Guideline 32: Nutrition Support in Adults
https://www.nice.org.uk/guidance/cg32/resources/guidance-nutrition-support-in-adults-pdf
Injectable medicines guide (Medusa)
UKMI_QA_How_is_acute_hypomagnesaemia_treated_in_adults_update_Nov_2020.pdf (sps.nhs.uk)
Royal College of Psychiatrists, Royal College Physicians, Royal College of Pathologists (2014) MARSIPAN: Management of Really Sick Patients with Anorexia Nervosa (2nd edn) (College Report CR189). Royal College of Psychiatrists. [Accessed 14 August 2021]
https://www.rcpsych.ac.uk/docs/default-source/improving-care/better-mh-policy/college-reports/college-report-cr189.pdf?sfvrsn=6c2e7ada_2
Todorovic, V.E. and Mafrici, B. eds. (2018) A Pocket Guide to Clinical Nutrition. 5th ed. (no place). PENG Parenteral and Enteral Nutrition Specialist Group of the British Dietetic Association.

QUERIES

Please contact a relevant member of the nutrition team using the contact details above.