

Refeeding Syndrome - Full Clinical Guideline

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Aim and purpose

This document provides a guideline to ensure appropriate identification and management of adult patients who are at risk of developing refeeding syndrome (RFS) at UHDB.

Abbreviations

RFS Refeeding Syndrome

NICE National Institute of Clinical Excellence

U & E Urea and electrolytes

Mg²⁺ Magnesium, PO₄³⁻ Phosphate, Ca Calcium, Zn Zinc K potassium

LFT Liver Function Tests

BM Blood glucose Monitoring

IV intravenous

Keywords Refeeding syndrome, malnutrition, nutrition, magnesium, potassium, phosphate hypophosphataemia, thiamine, pabrinex.

Introduction

What is refeeding syndrome?

Refeeding syndrome (RFS) describes a series of metabolic and biochemical changes that occur as a consequence of reintroduction of feeding after a period of starvation or fasting (Khan et al, 2011). RFS leads to severe fluid and electrolyte shifts (most notably hypophosphataemia), with related metabolic and potentially life threatening complications. In hospital practice, malnourished patients commencing any form of nutritional support (oral, enteral or parenteral) are most at risk.

Causes of RFS

During starvation, the use of glucose (from carbohydrate digestion) is reduced leading to the catabolism of protein and release of free fatty acids from fat stores to mobilise non-carbohydrate sources for energy production (Friedi et al, 2018). There

is a resultant loss of body fat and protein, and depletion of water, micronutrients and electrolytes. Notably there is a depletion of total body potassium, magnesium and phosphate. Although serum concentrations are maintained, intracellular stores are depleted (PENG, 2018).

Refeeding of patients after a time period of starvation causes a shift in metabolism from a catabolic to an anabolic state. There is a consequential release of insulin to support carbohydrate metabolism and this drives glucose, potassium, phosphate and magnesium to the intracellular compartment. There is also a rapid depletion of thiamine, a co-factor in carbohydrate metabolism (Stanga et al 2008). Subsequently, this may result in; hypophosphatemia, hypokalaemia, hypomagnesaemia, hypocalcaemia, thiamine deficiency and/or retention of sodium and water (Mehanna et al 2008).

Risk factors for RFS

NICE guidelines 32 provides a useful framework for identifying risk of RFS; however it is recognised that risk factors are only true risk factors in the presence of starvation (NICE, 2006)

During any initial assessment the following patients should be considered for risk of RFS:

- Patients with very poor dietary intake prior to admission
- Any malnourished patient planned to commence nutritional supplementation (enteral, including oral, or parenteral)
- Any inpatient who has had prolonged periods of being nil by mouth including post-operative patients for >7 days
- Any patient with a compromised nutritional status due to increased nutrient losses or decreased nutrient absorption, such as prolonged (over 4-10 days) diarrhoea or vomiting, chronic pancreatitis, dysfunction/inflammation of the GI tract, or post bariatric surgery
- Anorexia nervosa. For further guidance please refer to Trust guidelines for management of eating disorders
- Patients with a history of high alcohol intake
- Oncology patients undergoing treatment such as chemotherapy
- Patients with insulin dependent diabetes

Clinical features of RFS

RFS occurs when there is an unbalanced and too rapid reintroduction of nutrition in at risk patients. This typically occurs within 72hours after feeding recommences (either oral or artificial) and therefore close monitoring is recommended during the first 4 days of re-feeding (Friedli et al, 2017). The symptoms of RFS can be wide ranging and have a systemic effect. Some of these features can be seen below

(Table 1). Due to their non- specific nature, RFS should be suspected in any patient who exhibits signs of deterioration after re-feeding commences.

	Features
Hypophosphataemia	Altered myocardial function, arrhythmia, congestive heart failure, acute ventilatory failure, lethargy, weakness, seizures, confusion, coma, paralysis, acute renal failure, nausea, anorexia.
Hypokalaemia	Arrhythmia, cardiac arrest, respiratory distress, paralysis, weakness, rhabdomyolysis, polyuria, polydipsia, decreased GFR, constipation, ileus, glucose intolerance.
Hypomagnesaemia	Arrhythmia, tachycardia, ataxia, muscle tremors, confusion, weakness, tetany, respiratory depression, diarrhoea, constipation, abdominal pain, hypokalaemia, hypocalcaemia.
Thiamine deficiency	Congestive heart failure, lactic acidosis, Wernicke-Korsakoff syndrome, muscle weakness.
Hypernatraemia	Heart failure and arrhythmia, respiratory failure, pulmonary oedema, renal failure, muscle cramps, fluid retention and oedema

Table 1: Key clinical presentations of the biochemical abnormalities seen in RFS (Khan et al 2010)

Prevention of RFS (based on NICE 2006)**1. Assess risk:**

Identify patient at risk of RFS via presence of one or more of the following:

- BMI < 16 kg/m²
- Unintentional weight loss of greater than 15% in ≤ 6 months
- Very little or no food for > 10 days
- Low levels of potassium, phosphate or magnesium prior to feeding
- BMI < 18.5 kg/m²

Or presence of two or more of the following:

- Low levels of potassium, phosphate or magnesium prior to feeding
- BMI < 18.5 kg/m²
- Unintentional weight loss of greater than 10% in ≤ 6 months
- Very little or no food for > 5 days



2. Check electrolyte levels: Prior to feeding check serum; sodium, potassium, urea, creatinine, magnesium, phosphate, and albumin adjusted calcium levels. Replace electrolytes if low according to serum levels.



3. Prescribe and administer vitamins: Route of administration will depend up on the severity of RFS risk and access available. Prescribe and administer B vitamins at least 30 minutes before feeding re commences, for 7-10 days* as follows:

Intravenous access:

- Pabrinex ampoules: One pair daily for 72 hours
- After 72 hours change to enteral Thiamine/Vitamin B Compound Strong 2 tablets OD; crushed to administer via an enteral tube
- If no enteral access, continue Pabrinex until an enteral route is established

Enteral access:

- Thiamine 200mg/day Pabrinex ampoules: One pair daily for 72 hours.
- Vitamin B Compound Strong (as above)

If nutrition is unlikely to meet vitamin and mineral requirements consider a balanced multivitamin/trace element supplement such as Forceval.

**once patients meet their full requirements by feeding ongoing supplementation is unlikely needed.*



4. Introduce feed slowly: Commence feeding as per Dietitian advice. For patients requiring parenteral nutrition, refer to and follow Nutrition Team advice



5. Replace electrolytes: Correct electrolyte levels if: K < 3.5 mmol/l, PO₄ < 0.50 mmol/l, Mg < 0.50 mmol/l. See section on 'Treatment: Replacement of electrolytes'



6. Monitor: See section on 'Monitoring: Patients at risk or exhibiting signs of RFS'

Treatment: Replacement of electrolytes

Exclusions to the following recommendations may apply to patients with renal failure or critical care patients. Please discuss these patients with the relevant team and/or Pharmacist.

Electrolyte	Parental replacement	Enteral replacement
Phosphate	<ul style="list-style-type: none"> • If <0.32mmol. (Can also be considered if levels of 0.32-0.5mmol if compliance/access issues) • Give PHOSPHATES POLYFUSOR: 500ml infused over 12 hours at 40ml/hr, via a dedicated cannula. A single 12 hour infusion is usually sufficient but must be repeated daily if phosphate remains low until phosphate > 0.50mmol/l. 	<ul style="list-style-type: none"> • If 0.32-0.5mmol with enteral access • Give Phosphate Sandoz 2 tablets TDS
Magnesium	<ul style="list-style-type: none"> • If <0.5mmol OR 0.5-0.7mmol and symptomatic. (Can be considered if levels of 0.5-0.7mmol and compliance/access issues) • 20mmol magnesium sulphate available as 10mmol in 500ml 0.9% sodium chloride infused over 12 hours. • 10mmol may be given over 2 hours if symptomatic. Cardiac monitoring recommended. • In patients who are fluid restricted 10mmol may be given in 100ml 0.9% sodium chloride. • A preparation can be made in 5% glucose if hypernatraemia is a concern. 	<ul style="list-style-type: none"> • If 0.5-0.7mmol with enteral access and asymptomatic • Give Co-MAGADROX 195/220 Suspension 10-20ml QDS for 5 days.
Potassium	<ul style="list-style-type: none"> • If <2.5mmol. (Can also be considered if 2.5-3.0mmol) • Give 40mmol potassium chloride (KCl) in 1litre 0.9% sodium chloride or 5% glucose, infused over 4 hours via peripheral cannula. (Maximum 3mmol/kg per day.) • Give oral potassium IN ADDITION to IV • A more concentrated solution of potassium may be available when patients cannot tolerate these volumes for administration via central access on Critical Care. 	<ul style="list-style-type: none"> • If 2.5-3.5mmol with enteral access • Give Sando K, 2 tablets B.D-TDS (Initial dose).

Table 2: Guidance for replacement of deranged electrolytes (Terlevich et al 2003).

General guidance:

- Monitor electrolytes daily for at least first 5 days of feeding.
- Pre-feeding, normalisation of electrolytes is not necessary and may extend the period without nutrition (NICE 2006).
- Continue feeding whilst correcting any deranged electrolyte level. Do not stop the feeding plan whilst correcting electrolyte abnormalities
- Avoid long term phosphate replacement in patients with Chronic Renal Failure.
- Up to 160mmol of Mg^{2+} \geq 5 days may be required to correct hypomagnesaemia.
- Ensure low magnesium is corrected to ensure hypokalaemia responds to replacement.
- For additional guidance, see Trust guidelines for treatment of hypomagnesaemia and hypokalaemia.

Monitoring: Patients at risk or exhibiting signs of RFS**Monitoring of blood results:**

- Check for electrolyte disturbances daily for at least 5 days after feeding is commenced, during replacement therapy, and until results are stable.
- Note that biochemical measures may be within normal levels prior to feeding, but could decrease during refeeding.
- Be aware of malnourished, dehydrated patients with renal impairment and consequently normal or high electrolyte levels.

Monitoring of clinical condition:

- Ensure careful, appropriate restoration of circulatory volume, whilst monitoring pulse and fluid balance.

	Baseline	Daily for at least 5 days or until stable	Weekly until discharge
Bloods	FBC, U&E, Mg^{2+} , PO_4^{3-} , Ca.	U&E, Mg^{2+} , PO_4^{3-} , Ca.	U&E, Mg^{2+} , PO_4^{3-} , Ca.
Observations	Body weight, neurological signs or symptoms of RFS.	Temperature (4 hourly), blood glucose (BM once daily), pulse & respirations (once daily), body weight.	Body weight.
Food intake & fluid balance	Accurate input & output charts.	Accurate input & output charts.	

Table 3: Monitoring parameters specific for RFS (Based on NICE 2006)

References

Crook MA, Hally V, Panteli JV (2001) The importance of the refeeding syndrome. *Nutrition*.17 (8) 632-7

Friedli N, Stanga Z, Culkin A, Crook M, Laviano A, Sobotka L, Kressig R, Kondrup J, Mueller B, Schuetz, P (2018) Management and prevention of refeeding syndrome in medical inpatients: An evidence-based and consensus-supported algorithm. *Nutrition*. 47 13-20

Friedli N, Stanga Z, Sobotka L, Culkin A, Kondrup J, Laviano A, Mueller B, Schuetz, P (2017) Revisiting the refeeding syndrome: Results of a systematic review. *Nutrition* 35. 151-160

Khan LUR Ahmed J Khan S Macfie J (2011) Refeeding Syndrome: A literature review. *Gastroenterology Research and Practice*. Article ID 410971 1-6.

Mehanna HM Moledina J Travis J (2008) Refeeding Syndrome: What is it, and how to prevent and treat it. *British Journal of Medicine*. 336 1459-1458.

National Institute of Clinical Excellence (2006) Nutrition support in adults; oral nutrition support enteral tube feeding and parenteral nutrition. *Clinical Guideline 32*. London: NICE.

Parenteral and Enteral Nutrition Group (PENG): A pocket guide to Clinical Nutrition, (2018) 5th Edition, British Dietetic Association

Stanga Z, Brunner A, Leuenberger M, Grimble RF , Shenkin A, Allison SP and Lobo DN (2008) Nutrition in clinical practice-the refeeding syndrome illustrative cases and guidelines for prevention and treatment. *European Journal of Clinical Nutrition*. 62(6) 687- 694

Terlevich A, Hearing SD, Woltersdorf WW, Smyth C, Reid D, McCullagh E, Day A, Probert CS (2003) Refeeding syndrome: effective and safe treatment with phosphates polyfusor. *Alimentary Pharmacology & Therapeutics*. 17(10) 1325-9.

Documentation Controls

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