Refeeding Syndrome : A Systematic Review
By : Hjh Rohani Hj Matnor,
Kulliyyah of Pharmacy
International Islamic University Malaysia
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Part of Old Mining Town
: Sungai Lembing Kuantan
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Out-line

- Time-line : 1940's; 1997; 2004; 2006.
- Definition
- Pathophysiology
- Patient criteria
- Risk Management
- Take home message

Refeeding Syndrome : A Timeline

- Refeeding syndrome was first described in Far East prisoners of war after the second world war.
- Misadventures occurred during World War II in Leningrad and Netherland ; as well as Japanese prisoners of war.
- Minnesota Experiment dated back as early as 1940's
- Starting to eat again after a period of prolonged starvation seemed to precipitate cardiac failure.
- The refeeding syndrome has become popular topic in medical literature with the advent of total parenteral nutrition (TPN) in the 70's and 80's.

Scenario 1

- Starvation in times of famine and shortage of food supplies.
- Normal oral feeding was resumed.
- Orally fed after prolonged starvation with ‘NORMAL’ meal by the WELL- MEANING liberators of P.O.W
- Only to see deaths within a few days irony to being starved for a protracted period.

Scenario 2 : Final year medical student lost in snow clad mountain in Himalaya.

- A physically fit 84kg young man became lost in the Himalaya in winter and survived for 41 days at an elevation of 3000meters by eating only melted snow.
- He lost almost one quarter of total body weight and sustained neurological damage .
- Average loss of 3.3kg/wk (vs 2kg/wk)

REFEEDING??

Desire for food increased during first 20 days that leveled off, persistent dream for food.

By 6th week : Difficulty to keep warm*; persistent nausea; urinary urgency but* was often unable to void; inability to walk.

Upon rescue : gaunt; extremely fatigue; emotionally labile; lucid (with excellent memory).

2nd day of hospitalization weighed 61kg.

Fluid Resuscitation

- Normal saline 2000mL/d IV (discontinued after 2/7)
- Liquids 1500mL/d PO
- Dextrose IV after 1st dose of parenteral Thiamine
- D6→ developed third heart sound and tachycardia
- ***Food in small aliquots, increasing from 2000- 4000kcal/d***

Nutrition support

- People who have little or nothing for more than 5 days should have nutrition support introduced at no more than 50% of requirements for the first 2 days.
- Feeding rates should be increased to meet full requirements for fluid, electrolytes, vitamins and minerals if clinical and biochemical monitoring reveals no refeeding syndrome.

http://www.bmj.com/cgi/content/full/328/7445/908?ck=nck

Refeeding Syndrome:Definition

- A potentially fatal complication of the nutritional management of severely malnourished patients which almost always develop during the early stages of refeeding
- It can be associated with a severe derangement in electrolyte and fluid balance, and resulting in significant morbidity and mortality.
  - Afzal (2002) : Clinical Nutrition 21(6): 515-20

Refeeding Syndrome

- Occurrence of severe fluid and electrolyte shifts and their associated complications in malnourished patients undergoing feeding orally, enterally or parenterally.
- Refeeding can occur in any severely malnourished individuals but are particularly common in those who have eaten nothing for a protracted periods.

Refeeding Syndrome

- Severe electrolyte and fluid shifts associated with metabolic abnormalities in malnourished patients undergoing refeeding including abnormalities of fluid balance, glucose metabolism, hypophosphataemia, hypomagnesamia, hypokalaemia and vitamin deficiency

Crook et al (2001)
Protocol for management of hypophosphatemia;
King's College-London

Refeeding Syndrome

- Series of metabolic events precipitated by the provision of nutrients, primarily carbohydrate, to a patient in a nutritionally compromised state.
- It is associated with hypophosphataemia, hypokalaemia and hypomagnesemia; fluid retention and micronutrient deficiencies, including thiamine.
- If severe, it may result in respiratory, cardiac, and neuromuscular dysfunction especially in the stressed, elderly, or severely malnourished patient.

Metabolic complication

- Early complications, usually occurs within 4 days of starting to feed; also categorized as nutritional complication.
- Intracellular movement of electrolytes along with fall in the serum electrolytes including phosphate, potassium, magnesium, glucose and thiamine.
- Develop fluid and electrolyte disorders especially hypophosphataemia
- Complications : confusion, coma, convulsions and death

Pathophysiology

- During starvation, Na^{+}/K^{+} activated ATP-ase pump, protein synthesis, and immune response decrease.
- Anabolic and catabolic steroid activity altered.
- The same physiologic adaptations may be a source of danger when feeding is recommenced because the heart is ill-prepared for the stress of fluid, calories, and protein

Serum Phosphate

- Normally ranges from 0.80-1.40mmol/L
- The concentration fluctuates with a mean diurnal variation of 0.2 ± 0.03 mmol/L, with a NADIR at 1100, rising to a plateau at 1600 and peaking in the early night

Gaasbeek & Meinders (2005)
Protocol for management of hypophosphatemia;
King's College-London

Hypophosphataemia

- Mild : 0.65 – 0.80mmol/L
- Moderate : 0.32 – 0.65 mmol/L
- Severe : < 0.32mmol/L
- Mild to moderately severe hypophosphataemia is usually asymptomatic
- Major clinical sequelae usually occur only in severe hypophosphataemia

Bugg & Jones (1998),Gaasbeek & Meinders (2005), Amanzadeh & Reily (2006)
Protocol for management of hypophosphatemia;
King's College-London

- Malnourished patients' intracellular phosphate stores can be depleted despite normal serum phosphate concentrations.
- When they start to feed a sudden shift from fat to carbohydrate metabolism occurs and secretion of insulin increases.
- This stimulates cellular uptake of phosphate, which can lead to profound hypophosphataemia.
- This phenomenon usually occurs within four days of starting to feed again.

- Phosphate is necessary for the generation of ATP from ADP and AMP and other crucial phosphorylation reactions.
- Serum phosphate concentrations of less than 0.50 mmol/L can produce the clinical features of refeeding syndrome.
- Rhabdomyolysis, leucocyte dysfunction, respiratory failure, cardiac failure, hypotension, arrhythmias, seizures, coma, and sudden death.
- Importantly, the early clinical features of refeeding syndrome are non-specific and may go unrecognised.

Scenario 3 : 2004

- Thirty patients with refeeding syndrome, normal renal function, and a phosphate concentration of less than 0.50 mmol/l were treated with 50 mmol intravenous phosphate over 24 hours (500 ml Phosphates Polyfusor, Fresenius Kabi, Warrington, United Kingdom).
- This treatment was effective; 93% (28/30) achieved a serum phosphate concentration of 0.50 mmol/l or more after four days.

Stephen D Hearing, *consultant gastroenterologist*
Department of Gastroenterology, Staffordshire General Hospital
Weston Road, Stafford ST16 3SA (stephen.hearing@msgh-tr.wmids.nhs.uk)

- Five patients required further phosphate as severe hypophosphataemia recurred after initial correction.
- The treatment seemed safe; no patient developed renal failure, although three patients developed mild transient hyperphosphataemia and four asymptomatic hypocalcaemia.
- All patients were managed on general wards.
- Although this study is uncontrolled, it is the largest published series of the treatment of severe hypophosphataemia due to refeeding syndrome.

Recognize patients at risks

- anorexia nervosa,
- classic kwashikor or marasmus,
- chronic malnutrition,
- chronic alcoholism,
- prolonged fasting,
- prolonged IV hydration.

- When these patients require artificial feeding (enteral or parenteral), this should be started at a reduced calorific rate (25-50% of estimated requirements) to reduce the risk of refeeding syndrome developing.
- Serum phosphate, magnesium, calcium, potassium, urea, and creatinine concentrations should be measured before feeding and repeated daily for four days after feeding is started.
- When hypophosphataemia occurs it should be corrected in addition to other electrolyte abnormalities, such as hypokalaemia and hypomagnesaemia.

Management of Refeeding

- Correct electrolyte abnormalities before starting nutritional support.
- Administer volume and energy slowly
- Monitor pulse, I/O, electrolytes closely
- Provide appropriate vitamin supplementation
- Avoid overfeeding

Scenario 4:Enteral Refeeding Syndrome after long-term TPN

- 100 patients with GI fistula (Apr 2001-July2002)
- Clinical data collected : fasting time, daily stool frequency , body temperature, blood chemistries, liver enzymes and systemic inflammatory reaction score (SIRS).
- All patients received TPN during fasting stage before Enteral Nutrition (EN).
- SPSS 10.0 was used to analyze data.

Ren Jian-an (2006) : Enteral Refeeding syndrome after long-term total parenteral nutrition; Chin Med 119(22) :1856-1860

- Enteral refeeding syndrome (ERS) , a subtype of refeeding syndrome (RS), is different from RS in the sense that RS is characterized by hypophosphataemia, while ERS is featured with fever, abnormal liver function, and diarrhea early after EF in patients with long-term lack of lumen nutrition with or without malnutrition.
- Mainly caused by cholestasis and atrophy or edema of intestinal mucosa from long-term fasting

Take home message : Roland 1980

- TPN has already proven to be one of the major advances in medicine, many times being life saving for patients who would otherwise have died of malnutrition.
- With the availability of this new tool, our awareness and understanding of human nutrient requirements and their interactions have rapidly increased.
- The potential dangers have been recognized too, thus don't let this become a disservice to the patients who can otherwise within hours of initiation of TPN rapidly develop cardiopulmonary failure resulting in death.

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