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Jose Gerald Aragon
Rowan University

Mohammed A. Rattu
Jefferson Health NJ

Alex Gechlik
Jefferson Health NJ

Nicolas Coan
Jefferson Health NJ

James A. Espinosa
Jefferson Health NJ

See next page for additional authors

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Jose Gerald Aragon OMS-3[1], Mohammad Rattu DO[2], Alex Gechlik DO[2], Nicolas Coan DO[2], James Espinosa MD[2], Alan Lucerna DO[3]

1Rowan-Virtua SOM Medical School
2Department of Emergency Medicine, Rowan University SOM/Jefferson - Stratford NJ, USA
3Program Director, Emergency Medicine, Jefferson NJ/Rowan University SOM, Stratford NJ USA

Abstract:

Here we briefly review the definition, epidemiology, pathophysiology, clinical risk scenarios, prevention and treatment of the refeeding syndrome. Refeeding syndrome is a condition which arises when a severely malnourished individual has been restarted with increased nutrition in a relatively short period of time. The refeeding process can lead to shifts in a number of fluids and electrolytes. The hallmark feature is hypophosphatemia. The true incidence of refeeding syndrome is unknown. This is said to be partly due to the lack of a universally accepted definition. Populations that are likely to experience this syndrome include patients with maladaptive eating disorders, chronic diseases such as renal failure on hemodialysis and poorly controlled diabetes, chronic alcoholism, and oncological conditions. As the body continues to experience starvation or malnutrition, existing stores of electrolytes and vitamins can be depleted to sustain metabolic activity. Muscle and other tissues decrease their use of ketones and use fatty acid as a major source of energy. This response can be seen as early as 72 hours after complete fasting. During the refeeding process, glucose loads lead to increased levels of insulin. Glucagon is decreased. The process of synthesis of glycogen (as well as the synthesis of protein) leads to the depletion of phosphate, magnesium and thiamine. Along with ATP and DNA synthesis, phosphate plays a role in the activity of the heart's electrical transduction. Decreased levels of phosphate are associated with decreased cardiac contractility and arrhythmias along with decreased 2,3- DPG production Potassium can also be depleted. The mechanism of hypomagnesemia in the refeeding syndrome is still not entire clear. (The introduction of carbohydrate can lead to a decrease in the renal excretion of sodium and water. Thiamine (B1) depletes in patients who undergo starvation or severe malnourishment Overall, hypophosphatemia is a surrogate marker for refeeding syndrome. However, hypophosphatemia has many causes and is not, in itself, diagnostic of the refeeding syndrome. Guidelines exist for the prevention and treatment of refeeding syndrome. Treatment and management vary by guidelines.

What is Refeeding Syndrome?

Refeeding syndrome is a condition which arises when a severely malnourished individual has been restarted with increased nutrition in a relatively short period of time. The refeeding process can lead to shifts in a number of fluids and electrolytes. The hallmark feature is hypophosphatemia [1] The refeeding response by the body can be mild, moderate or severe [2]. The syndrome was first reported among patients who had been malnourished in concentration camps in World War 2 and underwent an immediate process of oral refeeding[3,4].

Incidence: The true incidence of refeeding syndrome is unknown. This is said to be partly due to the lack of a universally accepted definition[1,2]. The syndrome is said to be relatively poorly identified [5].

Clinical scenarios:

The issue does not arise from feeding the patient, it is the rate at which the patient is being fed. Situations that lead to the abnormal reduction in nutritional intake or diseases that poorly manage bodily levels of electrolytes, minerals, or vitamins are prone to this syndrome. Refeeding syndrome has been described in a number of scenarios. Populations that are likely to experience this syndrome include patients with maladaptive eating disorders, chronic diseases such as renal failure on hemodialysis and poorly controlled diabetes, chronic alcoholism, and oncological conditions [1]. There a many of these conditions, but they can be grouped into significant unintentional weight loss (such a patients with certain oncological conditions), low nutrient intake (such as patients with chronic alcoholism) and increased nutrient losses/malabsorption (such as some post-bariatric surgery patients) [3], In-patients with anorexia nervosa are at risk for refeeding syndrome [6,7]. The symptoms of refeeding syndrome are variable and include nausea and vomiting, weakness, delirium, hypotension and dysrhythmias [2].

Pathophysiology

What is significant to note about refeeding syndrome is the loss of electrolytes/minerals/vitamins secondary to the underlying nutritional deficit. As the body continues to experience starvation or malnutrition, existing stores of electrolytes and vitamins can be depleted to sustain metabolic activity. Muscle and other tissues decrease their use of ketones and use fatty acid as a major source of energy [1]. This response can be seen as early as 72 hours after complete fasting [2]. During the refeeding process, glucose loads lead to increased levels of insulin. Glucagon is decreased. The process of synthesis of glycogen (as well as the synthesis of protein) leads to the depletion of phosphate, magnesium and thiamine. Along with ATP and DNA synthesis, phosphate plays a role in the activity of the heart's electrical transduction. Decreased levels of phosphate are associated with decreased cardiac contractility and arrhythmias along with decreased 2,3- DPG production [5]. The significance of 2,3-DPG is that it aids in the off-loading of oxygen in tissues. Hence, patients who present with refeeding syndrome can also be at increased risk for developing tissue hypoxia as it affects the hemoglobin-dissociation curve [4]. Potassium can also be depleted. Patients can develop hypokalemia, which results in cardiac arrhythmia and weakness given that potassium is necessary for the electrical activity of the SA node and myocardial cells. Metabolic alkalosis can occur secondary to hypokalemia due to potassium and hydrogen ions opposing movements between intracellular and extracellular environments. The mechanism of hypomagnesemia in the refeeding syndrome is still not entire clear [5]. The introduction of carbohydrate can lead to a decrease in the renal excretion of sodium and water [5].Proteolytic pathways activated by starvations states are complex[8]. Thiamine (B1) depletes in patients who undergo starvation or severe malnourishment. B1 is important as it plays a supplemental role in glucose metabolism, more specifically, during the pyruvate oxidation phase. Given the importance of B1 in glucose metabolism, if ATP is depleted, this can lead to tissue damage especially in highly aerobic tissues such as the brain or heart. Glucose administration without adequate B1 levels has been said to lead to tissue damage in those highly aerobic regions of the body[1]. Overall, hypophosphatemia is a surrogate marker for refeeding syndrome. However, hypophosphatemia has many causes and is not, in itself, diagnostic of the refeeding syndrome[2,6,9].

Diagnosis

For supportive findings, a complete metabolic panel can aid in diagnosing a patient with refeeding syndrome in addition to history and physical examination findings pertaining to severe starvation or malnourishment such as muscle wasting or fatigue. Patients with refeeding syndrome may manifest with hypokalemia, hypomagnesemia, hypophosphatemia, thiamine deficiency, and hypoglycemia. Electrolytes, vitamins, and macronutrients can be lost in the process of starvation and malnourishment. Patients with refeeding syndrome present with various systemic symptoms ranging from bradycardia, arrhythmia, low blood pressure, peripheral edema, respiratory difficulties, nausea, vomiting, muscle weakness, kidney dysfunction, paresthesia, or altered mental status. Thiamine depletion can lead to Wernicke encephalopathy, with symptoms of confusion, ophthalmoplegia, and ataxia.

Prevention:

Refeeding can be started at 50% of energy requirements in patients who have had little to eat for five or more days [1]. For patients who have had little or nothing to eat for 14 days or more, guidelines exist for caloric intake [1]. Such patients are said to require cardiac monitoring. Vitamin supplementation can be started immediately. Fluids and electrolytes can be administered.

Treatment

When providing nutritional support to a patient who has been severely malnourished for an extended period, it is important to be mindful of how refeeding syndrome can arise.

Treatment and management vary by guidelines. The general consideration of supplemental infusion before oral feeding has been the traditional consensus. In a hospital setting, malnourished patients can be provided intravenous hydration along with electrolyte and vitamin replacement. Some guidelines suggest low caloric intake early in the course, with nutritional calculations found in the specific guidelines [1,7,10]. Depleted supplies of electrolytes/minerals/vitamins can be repleted intravenously, while the patient can slowly be re-introduced to oral feeding[10].

Conclusions:

Here we briefly review the definition, epidemiology, pathophysiology, clinical risk scenarios, prevention and treatment of the refeeding syndrome. Guidelines exist for the prevention and treatment of refeeding syndrome. Treatment and management vary by guidelines.

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