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Review Article

REFEEDING SYNDROME: CLINICAL AND NUTRITIONAL RELEVANCE

Qual é a importância clínica e nutricional da síndrome de realimentação?

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ABSTRACT – ***Introduction*** - Feedback syndrome is characterized clinically by neurological alterations, respiratory symptoms, arrhythmias and heart failure few days after refeeding. It happens due to severe electrolyte changes, such as hypophosphatemia, hypomagnesemia and hypokalemia associated with metabolic abnormalities that may occur as a result of nutritional support (oral, enteral or parenteral) in severely malnourished patients. ***Objetive*** – To evaluate its causes and the preventive dietary measures aiming to reduce the morbimortality. ***Methods*** – Was conducted literature review in SciELO, LILACS, Medline / Pubmed, Cochrane Library and government websites in Portuguese, English and Spanish. The survey was about the last 15 years, selecting the headings: refeeding syndrome, malnutrition, hypophosphatemia, hypokalemia, hypomagnesemia. ***Conclusion*** - The monitoring of metabolic parameters and electrolyte levels before starting nutritional support and periodically during feeding should be based on protocols and the duration of therapy. Patients at high risk and other metabolic complications should be followed closely, and depletion of minerals and electrolytes should be replaced before starting the diet. A multidisciplinary team of nutrition therapy can guide and educate other health professionals in prevention, diagnosis and treatment of the syndrome.

HEADINGS - Refeeding syndrome. Malnutrition. Hypophosphatemia. Nutritional therapy.

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RESUMO - ***Introdução*** - A síndrome de realimentação caracteriza-se por alterações neurológicas, sintomas respiratórios, arritmias e falência cardíacas, poucos dias após a realimentação. Ocorre em consequência do suporte nutricional (oral, enteral ou parenteral) em pacientes severamente desnutridos. ***Objetivo*** - Avaliar de suas causas e a aplicação das medidas dietéticas profiláticas apropriadas visando a prevenção e diminuição da morbimortalidade desta condição. ***Métodos*** – Foi realizado levantamento bibliográfico na SciELO, LILACS, Medline/Pubmed, Biblioteca Cochrane e sites governamentais nos idiomas português, inglês e espanhol. Os levantamentos foram sobre os últimos 15 anos, selecionando os descritores: síndrome de realimentação, desnutrição, hipofosfatemia, hipocalemia, hipomagnesemia. ***Conclusão*** - O acompanhamento de parâmetros metabólicos e de níveis de eletrólitos antes do início do suporte nutricional e periodicamente durante a alimentação deve ser baseado em protocolos, no estado da doença subjacente e na duração da terapia. Equipe multidisciplinar de terapia nutricional pode orientar e educar outros profissionais de saúde na prevenção, diagnóstico e tratamento dessa síndrome.

DESCRITORES - Síndrome de realimentação. Desnutrição. Hipofosfatemia. Terapia nutricional.

INTRODUCTION

The refeeding syndrome was first described in East prisoners of World War II, fed after prolonged periods of fasting, when they presented heart failure[29].

This potentially lethal condition can be defined as clinical complex, which includes electrolytic changes associated with metabolic abnormalities that can occur as a result of nutritional support (oral, enteral or parenteral)[12,30], in severely malnourished patients. Nowadays, there are patients with severe malnutrition after bariatric operations. It is clinically characterized by neurological and respiratory symptoms, arrhythmias and heart failure, few days after refeeding[12]. Its cause is due to overload in caloric intake and reduced capacity of the cardiovascular system[9,22,26,31].

Although previous studies have emphasized the severe hypophosphatemia as a predominant factor of refeeding syndrome, it became clear that there are other metabolic consequences. The important changes are water and glucose imbalance, certain vitamin deficiencies, hypokalemia and hypomagnesemia[9].

Since it has been recently identified as a disease, it appears that diagnosis and treatment are limited. The importance of control of serum phosphate is not recognized[26].

The previously recommended protocols for the treatment of severe hypophosphatemia were developed primarily from experience in treating a small number of critically ill patients. Usually, multiple infusions are recommended based on weight, with frequent monitoring of serum phosphate[32].

The aim of this review was to evaluate the causes and the application of prophylactic and therapeutic dietary measures to prevent and to reduce the morbidity and mortality of this syndrome.

METHOD

Literature review based on SciELO, LILACS, Medline / Pubmed, Cochrane Library and government websites in Portuguese, English and Spanish. The revision was made over the last 15 years, selecting the headings: refeeding syndrome, malnutrition, hypophosphatemia, hypokalemia, hypomagnesemia.

Risk groups and pathogenesis

The refeeding syndrome is seen in: patients with marasmus or kwashiorkor, those with weight loss exceeding 10% over a period of two months, in patients fasting for seven to 10 days, in the presence of stress and depletion, loss of significant weight in obese individuals after disabsortive bariatric operations, in patients undergoing chemotherapy, feedback in malnourished elderly, patients in the post-operative period of major surgeries, chronic alcoholism, prolonged intravenous fluid repletion and eating disorders, nervous anorexia[8.4,13,14,17].

It has been established that, in fasting, insulin secretion is reduced and increased the glucagon concentrations. Fat and protein stores are mobilized to be transformed in energy via gluconeogenesis. Adipose tissue provides large amounts of fatty acids and glycerol as the muscular tissue degraded provides amino acids. In these circumstances ketone bodies and free fatty acids replace glucose as major energy source. This mobilization of energy results in loss of body mass and loss of intracellular electrolytes, particularly phosphate buffer whose intracellular malnourished patients may be depleted despite normal plasma concentrations[7,8].

In the early feedback, shift occurs in glucose and lipid metabolism increasing insulin secretion, which stimulates the migration of glucose, phosphate, potassium, magnesium, water and protein synthesis to the intracellular environment, and may result in metabolic and electrolyte imbalance[8]. This phenomenon usually occurs within four days after the start of the feedback[17].

The metabolic abnormalities, particularly electrolytic resulting from syndrome feedback, can affect several body functions, the same way as the hyperglycemia feedback can reduce the excretion of sodium and water. Feedback of hyperlipidemia can result in weight loss and urinary sodium excretion, generating a negative sodium balance[8,15].

In critically ill patients, dietary protein levels may also result in hypertonic dehydration associated with hypernatremia, azotemia and metabolic acidosis[10].

It is known that both the intravenous and dietary intake of glucose can suppress gluconeogenesis, resulting in decreased mobilization of aminoacids (mainly alanine) and mitigating the negative nitrogen balance. However, infusion may lead to hyperglycemia metabolic consequence including a hyperosmolar non ketonic coma, and metabolic acidosis, ketosis, osmotic diuresis and dehydration[8,30,33].

It is known that glucose can be converted to fat through lipogenesis, causing hypertriglyceridemia, hepatic steatosis, liver function abnormalities and other systemic changes[8]. It is important that the lipid administration does not exceed the maximum capacity of elimination of fat on basis of 3.8 g lipid / kg body weight by day[10].

There is a consensus that a deficiency of thiamine (vitamin B1) may be associated with feedback[30].

Malnourished patients have vitamin several changes, including hypotiaminemia. In advanced stages may induce brain disorders such as Wernicke-Korsakoff[25] syndrome, also observed in obese undergoing bariatric operations[1].

In feedback, the mobilization of carbohydrates leads to the intracellular environment using thiamine as a cofactor in several enzymatic activities. The provision of intravenous thiamine before feedback can reduce the risk of acute hypotiaminemia[6,8,15,30] and its symptoms.

The predominant manifestation of refeeding syndrome is hypophosphatemia rapidly progressive[9,12,20,30].

Phosphorus

The phosphate is the major intracellular anion and moves between the intracellular and extracellular compartments. This transcellular movement can result from ingestion of carbohydrates, lipids and acid-base changes[20].

Phosphate is essential for cellular function and has many physiological actions. Among them, acts

in metabolic pathways of carbohydrate, lipid and protein. The phosphorylated high-energy components are responsible for all production and storage of energy in the body, also important for bone structure, collagen synthesis and calcium homeostasis[4,8].

In advance of malnutrition, many other conditions have been associated with hypophosphatemia, such as post-operative bariatric surgery[1], alcoholism[15], and gastrointestinal fistulas[11] in critically ill patients[19].

Hypophosphatemia is generally considered severe when serum inorganic phosphate concentration is <1.5 mg / dl (normal: 2.5 to 3.5 mg / dl). Can result in clinical manifestations, although most often are not clinically significant 15. However, it can produce acute rhabdomyolysis, hematological dysfunction, respiratory failure, heart disease[17] and neurological alterations[8,11,15,18,30].

Magnesium

Magnesium is the most abundant intracellular cation and essential for proper cell function[3], is involved as a metal cofactor in approximately 300 enzymatic reactions. Thus, it participates in many metabolic processes, including those related to carbohydrate metabolism involved in the regulation of secretion and insulin action[28].

The refeeding syndrome is associated with hypomagnesemia by a mechanism yet unknown and possibly multifactorial, resulting from movement through the intracellular ion due to diets high in carbohydrates and low of this cation[8,33]. However prior low serum concentrations of magnesium may exacerbate the degree of hypomagnesemia[30].

Analogous to hypophosphatemia, hypomagnesemia in many cases is not clinically significant, but when severe, defined as serum Mg <1.0 mEq / L may result in clinical cardiac complications, abdominal pain, anorexia and neuromuscular events[8,33].

Potassium

Monovalent cation is essential in maintaining intracellular action of the cell membrane. Its concentration is regulated by the kidneys, increasing aldosterone, with hyperkalemic dietary and increased sodium the distal tubule[8].

Hypokalemia can be considered severe with plasma concentration below 3.0 mEq / L levels at which clinical symptoms can manifest[8]. As in hypophosphatemia and hypomagnesemia, the clinical manifestations are rare unless the deficit is severe[8]. However, electrolyte abnormalities present potential risks to life[8,23]. The consequences are numerous, the most important being cardiac arrhythmia and intestinal hypomotility[3,16].

Prevention and treatment

The plasma electrolytes, particularly sodium, potassium, magnesium and phosphate should be monitored before and during the feedback at least[5,8] for four days. Plasma glucose and urinary electrolytes as well. Urinary sodium less than 10 mmol / L indicates salt depletion, while the determination of magnesium, potassium phosphate and urine can help to identify the loss of body electrolytes[3,5,19].

Before the feedback, electrolytic disorders must be corrected and carefully restored circulatory volume[2]. In clinical practice, these measures may delay the resumption of power, but can generally be completed within 12 to 24 hours[27].

In regard to the deficiency of trace elements and vitamins, is required correction specifically of thiamine given with intravenous doses of 50 to 250 mg at least 30 minutes before the diet be set[16]. There is no consensus on what is the exact dose of the thiamine to be supplied initially. The oral dose can be 100 mg tablet once a day[8]. Some clinicians suggest folate (5 mg) daily, which does not necessarily prevent refeeding syndrome[8].

In planning the energy needs, it is important that the calorie intake must be done slowly in oral, enteral or parenteral ways, approximately 20 Kcal / kg / day, or an average of 1000 Kcal / day initially 8, or 25% of calories requirements daily, advancing three to five days for the total value[16,21,27]. The daily protein requirements should be 1.2 to 1.5 g / kg / day or 0.17 g nitrogen / kg / day, using the ideal weight in protein-energy malnutrition and weight adjusted in obese individuals[33].

Studies suggest that treatment of hypophosphatemia is not usually necessary unless the plasma concentration of phosphate is less than 1.5 mg / dl or the patient is symptomatic. It is known that measurement of serum phosphate is not reliable because it is predominantly an intracellular ion. Thus, no relation exists with the total body stores[8].

Current recommendations for the treatment of severe hypophosphatemia suggests potassium intravenous administration with 2 mg / kg in six hours with the 5% glucose solution, at doses ranging from seven to 10 mg / kg, or up to 20mg/kg/day, stopping the infusion when the plasma concentration exceeds 1.5 mg / dl[8,33].

Regarding the treatment of hypomagnesemia, it is recommended oral administration of magnesium salts. However they are poorly absorbed and cause gastrointestinal disorders. Venous replacement is often performed with magnesium sulfate (50% solution containing 2.1 mmol / ml). This treatment is a facilitator for the correction of refractory hypokalemia[26].

Hypokalemia can be corrected by careful intravenous administration of potassium. The replacement should not exceed 20 mmol / h and concentration of the solution does not exceed 40 mmol / L [26,33].

CONCLUSIONS

The feedback syndrome is observed in clinical practice and is poorly recognized or understood. The pathophysiological process includes disorders of glucose, imbalance of fluid and electrolyte disorders that involve mainly intracellular ions, phosphate, potassium and magnesium, with a higher prevalence of hypophosphatemia. This syndrome is associated with nutritional support (oral, enteral or parenteral) offered inappropriately in patients at risk of malnutrition or severely malnourished. In this context, nutritional support is very important. Measures advocated initially reduced calorie intake, progressing according to the results of daily monitoring of serum electrolytes, vital signs and fluid balance.

Nutrition teams can guide and educate other health professionals in the management of the refeeding syndrome. However, more research is needed to provide detailed information about this syndrome, especially with respect to preventive protocols and therapeutic measures.

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