‘Refeeding Syndrome’ in a Kuwaiti Child: Clinical Diagnosis and Management

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Introduction

Refeeding malnourished patients may appear to be straightforward by just feeding them adequately in order to put on weight. However, there is a real danger in refeeding as the body adjusts from its pathophysiological starved or semistarved state.

Refeeding syndrome is a potentially lethal condition and is defined as severe electrolyte and fluid shifts associated with metabolic abnormalities in malnourished patients undergoing refeeding orally, enterally or parenterally [1]. Patients at risk for developing refeeding syndrome are those with marasmus, protein energy malnutrition, following prolonged starvation, massive weight loss in obese patients, prolonged intravenous fluid repletion and anorexia nervosa [1].

Key Words
Refeeding syndrome · Hypophosphatemia · Hypokalemia · Hypomagnesemia

Abstract
Objective: To report a case of refeeding syndrome in a Kuwaiti child, its clinical presentation and management. Clinical Presentation and Intervention: A 13-month-old Kuwaiti boy presented with acute severe malnutrition in the form of marasmic kwashiorkor. On admission, blood sugar and serum electrolytes were normal but on the 3rd day he developed typical biochemical features of refeeding syndrome in the form of hyperglycemia, severe hypophosphatemia, hypokalemia, hypocalcemia and hypomagnesemia. The child then received treatment appropriate for refeeding syndrome in the form of lower calorie intake with gradual increase, as well as supplementation of electrolytes, thiamine and vitamins and he eventually made a safe recovery.

Conclusion: This case showed that during rehabilitation of a malnourished child, a severe potentially lethal electrolyte disturbance (refeeding syndrome) can occur. Careful monitoring of electrolytes before and during the refeeding phase was needed and helped to detect this syndrome early. We suggest that slow and gradual calorie increase in the ‘at-risk’ patient can help prevent its occurrence.

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The predominant features of refeeding syndrome are severe hypophosphatemia together with fluid-balance abnormalities, altered glucose metabolism, hypokalemia, and hypomagnesemia and thiamine deficiency, consequently, leading to serious cardiac, pulmonary, hematological or central nervous system complications [1, 2]. Electrolyte disturbances can manifest within the first week of treatment, while delirium and other neurological features generally occur later [3, 4]. We report the case of a 13-month-old Kuwaiti boy with marasmic kwashiorkor.

**Case Report**

Our patient is a 13-month-old Kuwaiti boy who on previous admission at the age of 2 months with chronic diarrhea, vomiting and abdominal distension was diagnosed as having cow’s milk protein allergy. His condition resolved on Neocate milk formula (hydrolyzed protein formula) on which he was discharged and he was growing well with height and weight progressing along the 50th centile. At the age of 13 months, he was admitted with a history of watery diarrhea for the last 2 weeks, decreased oral intake and lethargy. Two months earlier, his mother on her own accord had stopped the Neocate formula and had replaced it with normal milk formula after which he developed loose motions, which became severe over the last 2 weeks. On examination, he was miserable, mildly dehydrated and edematous. On the lower limbs there was a dry dark scaly skin rash and pitting edema. His height was 76 cm (50th centile), weight was 7.6 kg (below 3rd centile) and body mass index was 13.2 (below 0.4th centile). Chest and cardiac examination were normal. His abdomen was distended with positive ascites. There was generalized hypotonia, with hyporeflexia. Investigations done at admission showed normal complete blood count and serum sodium. Serum creatinine, potassium, magnesium, phosphate and calcium were normal (table 1). Serum albumin was low (10 g/l, normal: 35–50 g/l) and serum immunoglobulin values were in the lower normal level range. Sweat test was normal. The patient was started on intravenous (i.v.) fluids (0.45 saline + 5% dextrose) and antibiotic and was assessed by our diettian. Neocate formula was recommenced. Total calorie intake was started with 70 kcal/kg/day (as in WHO protocol), however, as the watery diarrhea continued with an increasing serum creatinine level and persistence of clinical dehydration, fluid intake was increased and salt-free albumin was given on day 2. His blood sugar, which was normal on admission, increased through days 2 and 3: 11.2 and 16 mmol/l, respectively, with significant metabolic acidosis. He was treated with a low-dose insulin infusion for 18 h. Blood sugar from day 4 was within the lower normal range despite high total glucose intake (10 mg/kg/min). Serum phosphate that was normal on admission was decreased to a significant level (0.21 mmol/l) on day 3 (normal range: 1.25–2.1 mmol/l). At this point, the development of ‘refeeding syndrome’ was considered. High-dose oral phosphate (4 mmol/kg/day) was started on day 3 but despite this, phosphate level continued to be low till day 7 when an i.v. phosphate infusion (2 mmol/kg) was given for 24 h, then he remained on oral phosphate (2 mmol/kg/day). Serum calcium was normal on admission but he became hypocalcemic on day 5 after starting high-dose phosphate. Serum calcium then stabilized with intravenous then oral calcium (delivering 2.3 mEq/kg/day). Serum magnesium, normal on admission, decreased gradually and was treated with regular i.v. and oral magnesium (1 mmol/kg/day). Serum potassium decreased on day 3 and was treated accordingly. Serum sodium was normal on admission and remained normal all the time. Total calorie intake, calculated to give 70 kcal/kg/day on day 1, was gradually increased to 100 kcal/kg through the following 7 days as in the

**Table 1. Serum calcium, phosphate, magnesium, potassium, glucose, creatinine and total calorie intake**

| Days  | Calcium (2.2–2.6 mmol/l) | Phosphate (1.2–2.1 mmol/l) | Mg (0.6–1.05 mmol/l) | K (3.6–5.2 mmol/l) | Glucose (3.9–6.1 mmol/l) | pH | Creatinine (27–62 μmol/l) | Calories kcal/kg |
|-------|--------------------------|---------------------------|---------------------|------------------|------------------------|----|--------------------------|----------------|
| Day 1 | 2.53                     | 1.50                      | 0.80                | 4.1              | 5.5                    | 7.06 | 105                      | 70             |
| Day 2 | 3.70                     | 0.46                      | 1.12                | 2.5              | 16.0                   | 7.28 | 55                       | 90             |
| Day 3 | 2.30                     | 0.21                      | 0.62                | 2.5              | 16.0                   | 7.28 | 55                       | 70             |
| Day 4 | 2.24                     | 0.21                      | 0.50                | 3.3              | 4.9                    | 7.28 | N                        | 80             |
| Day 5 | 1.73                     | 0.29                      | 0.83                | 4.1              | 3.3                    | 7.38 | 80                       | 80             |
| Day 6 | 1.74                     | 0.49                      | 0.35                | 3.7              | 4.8                    | 7.38 | 80                       | 80             |
| Day 8 | 1.81                     | 1.26                      | 0.48                | 4.2              | 7.37                   | 90   | 90                       |                |
| Day 9 | 1.64                     | 1.06                      | 0.84                | 3.0              | 100                    |      | 100                      |                |
| Day 10| 2.05                     | 0.67                      | 0.59                | 2.6              | 100                    |      |                          |                |
| Day 11| 1.85                     | 1.07                      | 0.9                 | 3.6              | 100                    |      |                          |                |
| Day 12| 1.95                     | 1.14                      | 0.59                | 4.3              | 100                    |      |                          |                |
| Discharge| 2.17                    | 1.14                      | 0.71                | 5.7              | 4.5                    | 100  |                          |                |

Normal ranges are given in parentheses.
WHO protocol for the management of malnourished children. High-dose thiamine (200 mg) and multivitamins were given from day 4. His condition gradually improved, his diarrhea ceased, he tolerated orally well, his skin rash resolved and the edema subsided as well as his abdominal distention and ascites. His cardiopulmonary status was normal throughout his stay and remained stable. His laboratory profiles normalized and he was discharged after 15 days in a good general condition.

Discussion

Patients at risk of refeeding syndrome include those with chronic malnutrition (underfeeding), marasmus, kwashiorkor, anorexia nervosa, prolonged fasting and hunger strikes, morbid obesity with massive weight loss and cancer [5]. The manifestations of syndrome include the development of hypophosphatemia, hypokalemia and hypomagnesemia, hyperglycemia, fluid and sodium retention, neurological and hematological complications [6] as in our patient on day 2 of admission (table 1). During refeeding, a glucose load evokes insulin release causing increased cellular uptake of glucose, phosphate, magnesium and water and protein synthesis with subsequent hypophosphatemia [1] as evident in our case on day 2. Carbohydrate refeeding causes also increased cellular thiamine utilization and thiamine deficiency which may result in Wernicke’s encephalopathy or Korsakoff’s syndrome [7]. The electrolyte and fluid disturbances can cause cardiac failure, dehydration or fluid overload, hypotension, prerenal failure and sudden death [5]. Severe hypophosphatemia (<0.3 mmol/l) is the predominant feature of refeeding syndrome, which can result in a plethora of clinical manifestations such as dyspnea, respiratory failure, hypotension, shock, arrhythmias, cardiac failure and sudden death [5]. Refeeding with carbohydrate may reduce water and sodium excretion, resulting in expansion of the extracellular fluid compartment and edema [1]. Refeeding syndrome is most commonly reported in those who received total parenteral nutrition but can occur also in patients who received intravenous saline-dextrose, tube feeding or an oral diet [5] as in our patient who received (i.v.) fluids besides oral feeding. There are no accepted comprehensive guidelines for the management of refeeding syndrome in children. The key for successful management lies in a thorough nutritional assessment, continuous monitoring, cautious delivery of nutritional support and adequate supplementation of electrolytes and vitamins [5]. Stanga et al. [8] in their clinical review suggested a protocol for the prevention and management of refeeding syndrome in adults in which it is important to: always be aware of the circumstances in which the syndrome is likely to develop; refeed slowly and build up the macronutrient content of the feed over several days; monitor the patient frequently; anticipate additional requirements, particularly of phosphate, potassium, magnesium and thiamine [8]. The WHO guidelines for the management of malnourished children advise gradual increase of calorie intake starting at 80–100 kcal/kg/day for patients <7 years as was in our patient. These energy intake values may need to be adjusted by as much as 30% [9]. With our patient, it was difficult to make precise calculations of calorie intake during the first 2 days as the child had severe watery diarrhea. A low calorie intake (70 kcal/kg/day) was initiated and increased gradually to 100 kcal/kg/day by day 10. Afzal et al. [10] proposed evidence-based guidelines for the management of refeeding syndrome with enteral nutrition in children. They recommended the following supplement doses: sodium 1 mmol/kg/day, potassium 4 mmol/kg/day, magnesium 0.6 mmol/kg/day, phosphate up to 1 mmol/kg/day i.v. with oral supplements up to 100 mmol/day for children over 5 years [10]. Thiamine, folic acid, riboflavin, ascorbic acid, pyridoxine as well as fat-soluble vitamins A, D, E and K should be supplemented [10]. Our patient was admitted with normal serum calcium, phosphorus, potassium, magnesium, glucose and creatinine on day 1. Glucose and electrolytes were checked daily and correction of their disturbances was done accordingly. By the 15th day, our patient was discharged in good general condition with normal blood sugar and serum electrolytes.

Conclusion

This case showed that during rehabilitation of a malnourished child, a severe potentially lethal electrolyte disturbance (reefing syndrome) can occur. Careful monitoring of electrolytes before and during the refeeding phase was needed and helped to detect this syndrome early. Adequate precautions should be taken prior to commencing of feeding. We suggest that slow and gradual calorie increase in the ‘at-risk’ patient can help prevent its occurrence.
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