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Case Report

Refeeding Syndrome: A Case Report

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Abstract

We report the case of 46-year-old male who presented with acute confusion, severe electrolyte disturbances and lactic acidosis following a 25-day of fasting. He was found to have Refeeding syndrome with acute thiamine deficiency and was admitted to intensive care unit (ICU). He was managed supportively with fluid, electrolyte and nutritional support as per National Institute for Health and Care Excellence (NICE) guidelines, and made an excellent recovery within a week of admission.

Keywords: *Refeeding Syndrome; Electrolyte; Lactic Acidosis; National Institute for Health and Care Excellence (NICE)*

Background

Refeeding syndrome (RFS) broadly encompasses a severe electrolyte disturbance and metabolic abnormalities in undernourished patients undergoing refeeding whether orally, enterally, or parenterally [1]. The prevalence of RFS has been variably quoted with estimations as wide as 0.43% to 34% in different hospital populations [1]. RFS is characterised by low serum levels of phosphate, magnesium, and potassium as well as acute thiamine deficiency. The clinical presentation is related to these ion deficits and vitamin depletion, mainly vitamin B1 which leads to Wernicke's encephalopathy [1]. The following are clinical criteria for the determination of patients at risk of developing RFS (NICE guidelines) [1,2,6]:

- Patient s with 1 or more:
    1. BMI < 16 kg/m^2.
    2. Unintentional weight loss > 15% in past 3 - 6 months.
    3. Minimal or no nutritional intake for 10 days.
    4. Low levels of plasma potassium, phosphate, or magnesium before feeding.
- Patients with 2 or more:
    1. BMI < 18.5 kg/m^2.
    2. Unintentional weight loss > 10% in past 3 - 6 months.
    3. Minimal or no intake for > 5 days.
    4. History of alcohol misuse or drugs abuse.

Case Presentation

Mr XY was a 46 year old male mechanical engineer, known with hypertension on amlodipine 5 mg daily. His wife reported that he was fasted for 25 days prior to presentation and that he only ingested water for that period. He initially presented to a private clinic with a history of tiredness and was found to be hypoglycaemic with a blood glucose of 3.5 mmol/L (normal value 4.0 to 6.0 mmol/L). He was given 100 ml of 50% dextrose intravenously and subsequently became extremely confused and restless. He was then transferred to New Somerset Hospital (NSH) for further work-up. At NSH he was found to have a Glasgow Coma Scale (GCS) of 14/15, was delirious and severely

dehydrated. He was haemodynamically stable with a blood pressure of 125/85 mmHg and a pulse of 82 beat/minuet and his oxygen saturation was 100%. He was apyrexial, and his chest and abdominal examinations were unremarkable. His chest x-ray (CXR) was normal and his Electrocardiography (ECG) showed features of hypokalaemia. Table 1 below are his initial blood results at time of presentations.

	Normal value	Patient result
White Cell Count	3.90 - 12.60 X10^9/L	10 X 10^9/L
Haemoglobin	12.0 - 15.0 g/dL	16.9 g/dL
Platelets	186 - 454 x10^9/L	137 x 10^9/L
Sodium	136 - 145 mmol/L	138 mmol/L
Potassium	3.5 - 5.1 mmol/L	2.4 mmol/L
Urea	2.1 - 7.1 mmol/L	6.5 mmol/L
Creatinine	49 - 90 umol/L	162 umol/L
Calcium	2.15 - 2.50 mmol/L	1.7 mmol/L
Magnesium	0.63 - 1.05 mmol/L	0.45 mmol/L
Inorganic phosphate	0.78 - 1.42 mmol/L	0.53 mmol/L
Albumin	35 - 52 g/L	30 g/L
Alanine transaminase	7 - 35 U/L	89 U/L
Gamma-glutamyl transferase	< 40 U/L	100 U/L
Total bilirubin	5 - 21 umol/L	103 umol/L
Arterial blood pH	7.38 - 7.42	7.19
Bicarbonate	22 - 28 mEq/L	10 mEq/L
Arterial blood Lactate	<2.0 mmol/L	15.7 mmol/L
Base excess	-5 - +3 mEq/L	-19.9 mEq/L
Partial pressure of carbon dioxide	5.1 - 5.6 kPa	4.6 kPa
Partial pressure of oxygen	10.5 - 13.5 kPa	12.1 kPa
Blood Glucose	4.0 - 6.0 mmol/L	25 mmol/L

Table 1: *Show patient initial blood results.*

Based on his history of fasting as well as the hypokalaemia, hypocalcaemia, hypomagnesaemia, hypophosphatemia and severe lactic acidosis, a diagnosis RFS and Wernicke's encephalopathy was made clinically. The patient was intubated to maintain his airway due to his low GCS. Management of his RFS was started in consultation with a dietician and was in accordance with the latest NICE guidelines. He was started on nasogastric feeds @5 ml/hr (2 kcal/ml) for 1st 6 hrs then 25 ml/hr for 24 hrs followed by 35 ml/hr for next 48 hrs. He also received intravenous thiamine, vitamin B complex, potassium, magnesium and calcium. Rehydration fluid was administered at rate of 110 ml/hr and he was placed on an Insulin sliding scale. On day 4 post intubation he started waking up and extubated himself table 2 below showed results at that time. On day 5 he was transferred to the medical ward and on day 6 he was started on slow oral feeds. By day 7 he had made a complete clinical recovery and was discharged on oral vitamin supplements. He was seen 2 weeks later at our outpatient's clinic and was found to be in good health as results showed on table 2.

	Normal value	Day 4 ICU	2 weeks after discharge
White Cell Count	3.90 - 12.60 X 10^9/L	6 X 10^9/L	8.06 X 10^9/L
Haemoglobin	12.0 - 15.0 g/dL	15.3 g/dL	16 g/dL
Platelets	186 - 454 x 10^9/L	140 X 10^9/L	220 X 10^9/L
Sodium	136 - 145 mmol/L	139 mmol/L	137 mmol/L
Potassium	3.5 - 5.1 mmol/L	3.6 mmol/L	4.1 mmol/L
Urea	2.1 - 7.1 mmol/L	12.7 mmol/L	2.5 mmol/L
Creatinine	49 - 90 umol/L	124 umol/L	75 umol/L
Calcium	2.15 - 2.50 mmol/L	2.18 mmol/L	2.33 mmol/L
Magnesium	0.63 - 1.05 mmol/L	1.06 mmol/L	0.86 mmol/L
Inorganic phosphate	0.78 - 1.42 mmol/L	0.65 mmol/L	0.9 mmol/L
Albumin	35 - 52 g/L	29 g/L	42 g/L
Alanine transaminase	7 - 35 U/L	162 U/L	12 U/L
Gamma-glutamyl transferase	< 40 U/L	72 U/L	21 U/L
Total bilirubin	5 - 21 umol/L	100 umol/L	18 umol/L
Arterial blood pH	7.38 -7.42	7.39	
Bicarbonate	22 - 28 mEq/L	23 mEq/L	
Arterial blood Lactate	< 2.0 mmol/L	2.1 mmol/L	
Base excess	-5 - +3 mEq/L	-1.5	
Partial pressure of carbon dioxide	5.1 - 5.6 kPa		
Partial pressure of oxygen	10.5 - 13.5 kPa	11.0 kPa	
Blood Glucose	4.0 - 6.0 mmol/L	7.1 mmol/L	5 mmol/L

Table 2: *Show blood results on day 4 admission and 2 weeks after discharge.*

Discussion

RFS is caused by rapid refeeding after period of undernutrition. The body cells shifts metabolic status from a catabolic state to an anabolic one. There are several risk factors associated with the development of RFS [1,2] as in table 3.

Anorexia nervosa
Older age (> 70 years)
Prolonged fasting
Chronic alcoholism or drug abuse
Chronic infection (e.g., HIV)
Inflammatory bowel disease
Malabsorption syndrome
Malignant disease
Protracted vomiting
Bariatric surgery
Kwashiorkor and marasmus

Table 3: *Show risk factors associated with the development of RFS [1,2].*

Pathophysiology

Starvation lasting weeks to months causes the body to shift its energy needs from carbohydrate metabolism to fat and protein metabolism [1,3]. Plasma insulin concentrations decrease while glucagon levels increase during starvation, resulting in the rapid conversion of glycogen stores to form glucose for cell energy [1,3]. Additionally, gluconeogenesis, resulting in glucose synthesis via lipid and protein breakdown products increases [1,3]. Adipocytes release fatty acids and glycerol, whereas myocytes release amino acids such as alanine to help fuel these metabolic pathways. Ketone bodies and free fatty acids replace glucose as a major energy source in human starvation [1,3]. Once refeeding starts, a physiological shift from fat to carbohydrate metabolism takes place. This elicits insulin release resulting in cellular uptake of glucose, as well as phosphate, potassium, and magnesium ions thereby increasing the extracellular fluid volume and causing the serum levels of these ions to drop. Refeeding increases intracellular utilization of glucose and glycogen synthesis and subsequently leads to thiamine consumption as thiamine is an essential cofactor for various metabolic pathways such as the decarboxylation of 2-oxoacids, involved in the conversion of pyruvate to acetyl coenzyme-A [1,3]. Thiamine is also an essential cofactor for the transketolase enzyme in the pentose-phosphate pathway [1-3]. Because of these metabolic derangements patients with RFS manifest with dehydration, hypocalcaemia, hypophosphatemia hypomagnesemia, hypokalaemia, lactic acidosis and acute kidney injury [1,3] (Figure 1).

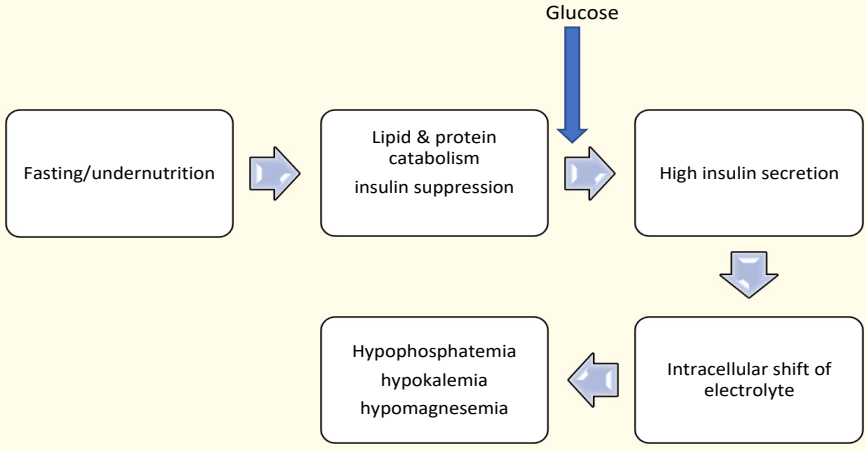

Figure 1: *Speculative mechanisms of intracellular plasma electrolyte depletion [2].*

Management of RFS

Refeeding syndrome may be readily missed in severely malnourished patients [4]. This is particularly concerning as RFS is a life-threatening condition, although it need not be so, and early recognition may reduce complications [1]. Identification of high risk patients is crucial and any patient with negligible food intake for more than five days is at risk of developing refeeding problems [5]. Management of RFS requires close monitoring of body weight, urine output, fluid balance, and vital functions. It is also essential to monitor plasma glucose, albumin, protein, calcium, the full blood count, and liver function tests because hepatic dysfunction can occur in RFS [1]. It is generally agreed that prevention and management of RFS includes identification of individuals at risk, thoroughly monitored nutritional intake, and careful electrolyte and fluid replacement by an experienced multidisciplinary team [1].

The NICE guidelines recommend that refeeding is started at no more than 50% of energy requirements and the rate can then be increased if no refeeding problems are detected on clinical and biochemical monitoring (Figure 2) [5,6]. For patients at high risk of developing refeeding syndrome, nutritional repletion of energy should be started slowly and should be tailored to each patient. It can then be increased to meet or exceed full needs over four to seven days. In patients who are very malnourished (body mass index ≤ 14 kg/m^2 or a negligible intake for two weeks or more), the NICE guidelines recommend that refeeding should start at a maximum of 0.021 MJ/kg/24

hours, with cardiac monitoring owing to the risk of cardiac arrhythmias. This explicit specification of the rate of refeeding in severely malnourished patients should help avoid complications arising from rapid refeeding and is an improvement on previous guidelines [5,6]. The NICE guidelines also state that correcting electrolyte and fluid imbalances before feeding is not necessary and that this should be done along with feeding [5,6]. All guidelines recommend that vitamin supplementation should be started immediately before and for the first 10 days of refeeding. Circulatory volume should also be restored. Oral, enteral, or intravenous supplements of the potassium, phosphate, calcium, and magnesium should be given unless blood levels are high before refeeding [5,6]

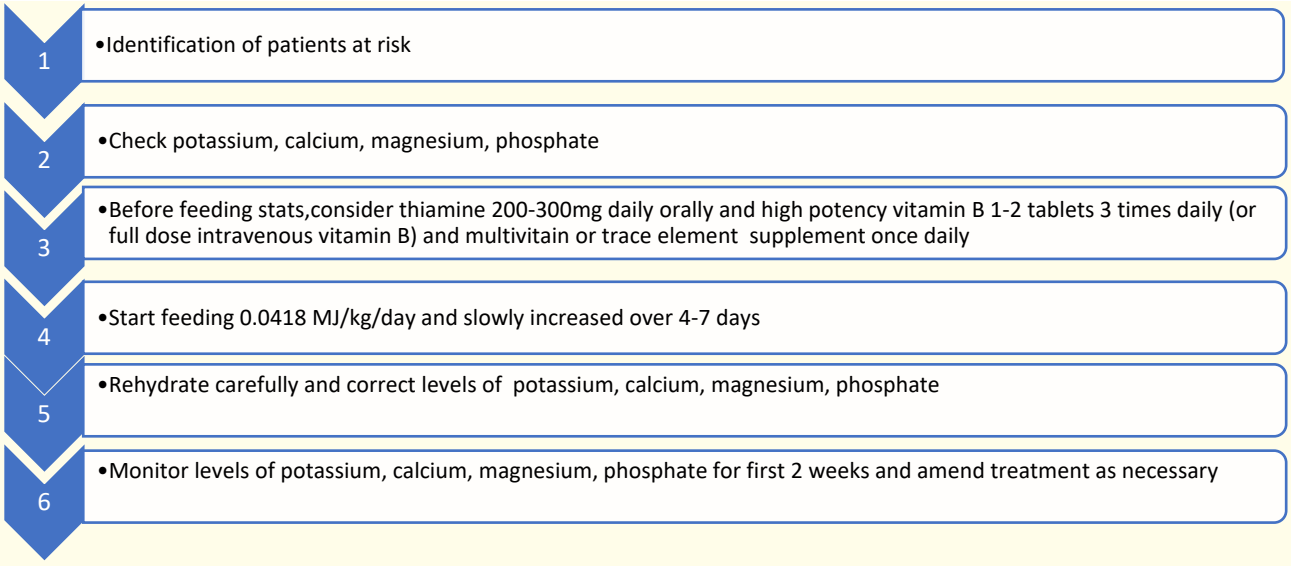

Figure 2: *NICE Guidelines for management [6].*

Conclusion

RFS is not uncommon especially in patients in our South African setting as many of them are admitted with malnutrition related to HIV and tuberculosis. Identification of such patients at risk of RFS is essential for its diagnosis. A retrospective study investigated the rates and outcomes of medical and surgical patients reviewed and identified by dietitians as at risk of RFS in a 350-bed acute care hospital between March 2012 and February 2013. They found that 9% of acute medical and surgical patients, majority of which were receiving nutrition orally were identified by dietitians as at risk of RFS in the first dietetic assessment [7]. RFS should therefore be considered in patients at risk and managed timeously and appropriately in order to avoid its severe and often life-threatening complications.

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