Case Study: Nutritional management of a patient at high risk of developing refeeding syndrome

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The following case study was discussed during the fourth-year dietetics evaluation process at North-West University, Potchefstroom Campus. It is a reflection of the opinion of the dietitians, students and lecturers involved, describes the actions taken during the nutritional management of the case, and is based on current literature and guidelines relevant to the topic.

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Introduction

Although there are various definitions and diagnoses for refeeding syndrome,[1,2] it is basically described as the occurrence of a shift in fluids and electrolytes when malnourished patients receive artificial refeeding (either enteral or parenteral).[3] Critically ill patients, such as oncology patients and those with chronic malnutrition, are often at risk of developing refeeding syndrome, which can be fatal.[3] Psychiatric, physiological, metabolic, surgical and neoplastic-related complications also contribute to the risk of the development of refeeding syndrome.[4]

Glycaemia leads to increased insulin production and decreased glycogenolysis during refeeding syndrome. Insulin stimulates glycogen, protein and fat synthesis which requires minerals, such as phosphate and magnesium, as well as co-factors, such as thiamin.[3] Based on this, those with refeeding syndrome often present with salt and water retention, hypokalaemia, hypophosphatemia, rapid thiamin depletion and hypomagnesaemia.[1]

Walmsley grouped patients as either having definite or possible refeeding syndrome.[1] Patients with definite refeeding syndrome are those who present with a fall in serum phosphate levels, as well as the accumulation of pathological extracellular fluid. On the other hand, possible refeeding syndrome is defined as a fall in either serum potassium and/or magnesium, with the accumulation of pathological extracellular fluid.[1]

It is not possible to accurately report on the incidence and prevalence of refeeding syndrome mostly owing to lack of an official definition.[1] Walmsley reviewed studies in which parenteral nutrition was examined in the UK and New Zealand, and reported an occurrence of refeeding syndrome of approximately 4-5%, based on a very loose definition thereof, in patients receiving parenteral nutrition.[1] Only 50% of these cases were identified before the initiation of feeds.[1]

Very few randomised controlled trials have been conducted for the purposes of providing treatment guidance to prevent the development of refeeding syndrome.[3] However, the National Institute for Health and Clinical Excellence (NICE) developed best practice guidelines for the identification (Table I), management and evaluation of patients at risk of developing refeeding syndrome.[5]

To prevent the development of refeeding syndrome, nutrition support, either via enteral or parenteral feeding, should be cautiously introduced.[5] Therefore, feeding should be initiated at 50% (10 kcal/kg/day) of the initial calculated energy (20 kcal/kg/day) and protein requirements. This should then be slowly increased during the ensuing 24-48 hours, based on individual metabolic and

Table I: National Institute for Health and Clinical Excellence criteria for identifying patients at risk of developing refeeding syndrome[5]

One or more of the following symptoms:		Two or more of the following symptoms:
Body mass index < 16 kg/m^2		Body mass index < 18.5 kg/m^2
Unintentional weight loss greater than 15% in the past 3-6 months	or	Unintentional weight loss greater than 10% in the past 3-6 months
Little or no nutritional intake for more than 10 days		Little or no nutritional intake for more than 5 days
Low levels of potassium, phosphate or magnesium before feeding		A history of alcohol misuse or drugs, including insulin, chemotherapy, antacids or diuretics

gastrointestinal tolerance. However, full fluid, electrolyte, vitamin and mineral requirements should be provided to the patient on the first day of feeding.[5]

Case study

A 69-year-old woman was admitted to the surgical ward in a hospital in North-West province on the first of June 2015 for the insertion of a percutaneous endoscopic gastrostomy (PEG) tube, after being referred from the oncology department where she was admitted two days previously. The patient was newly diagnosed with squamous cell carcinoma located behind the nasal cavity, and above the border of the soft palate. The carcinoma co-existed with an acid-fast *Mycobacterium tuberculosis* infection, for which she was treated. The medical history indicated that she was known to have pulmonary tuberculosis, and had already suffered from hearing loss, an ototoxic effect of the pulmonary tuberculosis medication, as well as blindness due to the carcinoma. She was also known to have hypertension, which was controlled with treatment. On admission, she presented with symptoms of nasal obstruction, a nodal posterior nasopharyngeal mass, cranial nerve palsies, tinnitus, chronic headaches and proptosis (the bulging of an eye due to a lesion). A detailed diet history could not be obtained, but a family member reported an extremely poor dietary intake due to dysphagia of solids and fluids in the previous two weeks.

Upon admission to the surgical ward, the patient's anthropometric measurements for height and weight were 1.62 m and 80.9 kg, respectively, with a body mass index of 30.8 kg/m^2. Her usual body weight was approximately 95 kg, with at least 15% unintentional weight loss over the previous four months.

Her urea, electrolyte and phosphate levels were measured daily to monitor tolerance of her administered feeds, and to detect the development of refeeding syndrome (Table II).

Discussion

After an initial assessment, during which the NICE guidelines were taken into account, the patient was identified as a patient at high risk of developing refeeding syndrome.[5] This was based on the presence of unintentional weight loss greater than 15% in the past four months, little or no nutritional intake during the past 14 days, and initial borderline low levels of phosphate and potassium.

Nutritional diagnosis

The patient presented with a high risk of refeeding syndrome relating to minimal nutritional intake for more than 10 days, as evidenced by unintentional weight loss (> 15% in four months), and a diet history.

She also presented with an inability to consume food orally, which related to the posterior nasopharyngeal mass, as evidenced by a nutritional and clinical assessment.

The patient further experienced unintentional weight loss, as evidenced by anthropometry-related minimal food intake and increased requirements due to the carcinoma.

Based on the nutritional diagnoses, the nutritional goals were identified as follow:

- Provide adequate nutrition to meet the patient's macro- and micronutrient requirements, in order to address the malnutrition and increased catabolism.
- Correct the patient's micronutrient deficiencies.
- Adjust the feeding protocol to prevent the development of refeeding syndrome.

Diet prescription

Energy and macronutrient distribution

O'Connor and Nicholls systematically reviewed the available research and found that malnutrition was a more important marker when identifying patients at risk of refeeding than total energy administration on the initiation of feeding.[6] Nevertheless, according to the available literature, feeding should be initiated at 50% of the calculated basal energy expenditure.[4] Universally, it is recommended that energy requirements be calculated at 10 kcal/kg at the start of feeding.[4-8]

It is recommended that a more conservative feeding approach should be followed with malnourished and critically ill patients (Table III). Initially, energy should be restricted to as little as 5 kcal/kg.[4,9] This should slowly be increased in the following seven days to the

Table II: The patient's biochemical values on admission and during her stay in the surgical ward

Biochemical parameters	Day 1	Day 3	Day 4	Day 5	Day 6	Day 7
Sodium (135.0-147.0 mmol/l)	120.3	130.1	135.5	129.9	131.2	139.1
Potassium (3.3-5.0 mmol/l)	3.2	3.5	3.4	3.8	4.1	4.0
Magnesium (0.6-1.1 mmol/l)	0.58	0.61	0.65	0.68	0.7	0.7
Urea (2.6-7.0 mmol/l)	9.1	7.0	6.4	6.1	5.9	6.0
Creatinine (60.0-120.0 mmol/l)	43.0	40.1	41.2	44.4	45.2	46.9
Phosphate (0.8-1.4 mmol/l)	0.79	0.80	0.88	0.85	0.91	0.95
Albumin (35.0-55.0 g/l)	25.0				22.5	
C-reactive protein (< 5.0 mg/l)	120.9		150.9		173.3	

Table III: Macronutrient requirements of patient during the first seven days

Macronutrient requirement	Reference	Recommendation	Actual macronutrient delivered to the patient
Energy	NICE[5]	*Initial:*10 kcal/kg *Day 4-7:* Meets or exceeds requirements	*Initial intake:* 10 kcal/kg/day Increased over 3 days to 20 kcal/kg/day
	Stanga et al[8]	*Day 1-3:* 10 kcal/kg/day *Day 4-6:* 15-20 kcal/kg/day *Day 7-10*: 20-30 kcal/kg/day	
	Boateng et al[4]	*Initial:* 5 kcal/kg/day *Day 10:* Intake of 15-20 kcal/kg	
	Viana et al[9]		
	Stanga et al[8]	Increase to 25-35 kcal/kg by day 7	
	Mc Clave et al[10]	Initiate nutrition support at 25% of the estimated goal	
Protein	Boateng et al[4]	20-30% of total energy	*Initial intake:* 0.8 g/kg (63 g) (31% total energy) *Increased to:* 1.0 g/kg/day (80.4 g) (20% of total energy)
	NICE[5]	15-20% total energy	
	Stanga et al[8]		
	McClave et al[10]	Initiate at 25% of actual requirement calculated	
	Crook[11]	1.2-1.5 g/kg/day	
Carbohydrates	NICE[5]	50- 60% total energy	*Initial intake:* 50% of total energy *Increased to:* 55% of total energy
	Stanga et al[8]		
	Crook[11]	40% of total energy	
Fat	Boateng et al[4]	15-40% total energy	*Initial intake:* 19% of total energy *Increased to:* 25% of total energy
	NICE[5]	30-40%	
	Stanga et al[8]		
	Crook[11]	3.8 g/kg/day	

NICE: National Institute for Health and Care Excellence

full requirement of 25-35 kcal/kg/day.[8] Boateng et al recommend a slow energy increase from days 4-10 to reach a total energy intake of 15-20 kcal/kg/day.[4] The decision to increase or decrease energy provision should be based on biochemical and symptomatic monitoring.[4]

In this case, feeding was initiated at 10 kcal/kg/day and slowly increased, as tolerated. The aim was to achieve 20 kcal/kg within the first 10 days. After the initial aim of 20 kcal/kg was reached, the goal was to further increase intake to 25-35 kcal/kg/day, as recommended to patients with head or neck cancer.[12] The patient's energy requirements were calculated using actual body weight (80 kg).

The calculated macronutrient distribution in the prevention of refeeding syndrome, as well as the actual macronutrients delivered to the patient, are detailed in Table III. Protein recommendations vary between the different literature sources. Stanga et al[13] recommends that it should comprise 20% of the total energy, and Boateng et al, 20-30%.[4]

It was decided to calculate the protein requirement at 20% of total energy for this patient. The goal was to reach a protein intake of 1.5 g/kg ideal body weight, as indicated by Viana et al.[9] The recommended fat and carbohydrate distribution also differs in the literature, ranging from 15-40% and 50-60%, respectively. Fat and carbohydrates were calculated at 28% and 51% of the total energy, respectively, for this patient.

Practical implementation

As a result of the size and position of the carcinoma, a nasogastric tube could not be passed. Furthermore, oral feeding was excluded due to dysphagia. As the tumour was inoperable, a long-term feeding solution was required. Therefore, a PEG tube was the most practical and effective feeding route. A PEG tube was inserted on the second day post admission to the surgery ward. Feeding was initiated within 24 hours post insertion, i.e. on the third day of admission of the patient to the surgical ward.

A semi-elemental feed high in whey peptides, containing fish oil and medium-chain triglycerides, was provided in combination with an enteral formula that was suitable for the purposes of delivering key nutrients, including glutamine, essential for gastrointestinal

Table IV: Causes of micronutrient inadequacy and the clinical consequences thereof

Micronutrient	Causes of micronutrient inadequacy	System where the inadequacy is presented	Clinical consequences of such inadequacy
Thiamin	Increased cellular utilisation	Neurological	Wernicke-Korsakoff syndrome (an inflammatory, haemorrhagic degenerative condition of the brain, in coexistence with amnesia)[14]
		Cardiovascular	Congestive heart failure, lactic acidosis and beriberi[14]
		Skeleton	Muscle weakness[14]
Phosphate	• Cellular phosphate redistribution[11] • Poor phosphate intake[11] • Renal tubular phosphate loss[11] • Liver disease[11] • Septicaemia[11]	Cardiovascular	Arrhythmia, heart failure, cardiomyopathy and shock[14]
		Renal	Metabolic acidosis and acute tubular necrosis[14]
		Skeleton	Rhabdomyolysis (breakdown of the skeletal muscle fibres), weakness, myalgia and diaphragm weakness[14]
		Neurological	Delirium, coma, seizures and tetany[14]
		Haematological	Haemolysis, thrombocytopenia and leukocyte dysfunction[14]
		Endocrine	Hyperglycaemia, insulin resistance and osteomalacia[14]
Potassium	• Redistribution of potassium ions[11] • Gastrointestinal loss of potassium[11] • Renal potassium loss[11] • Renal tubule mechanisms[11]	Cardiovascular	Hypotension, ventricular arrhythmias, cardiac arrest, bradycardia and tachycardia[14]
		Respiratory	Hypoventilation, respiratory distress and respiratory failure[14]
		Skeleton	Weakness, fatigue and muscle twitching[14]
		Gastrointestinal	Diarrhoea, nausea, vomiting, anorexia, paralytic ileus and constipation[14]
		Metabolic	Metabolic alkalosis[14]
Magnesium	• Cellular magnesium redistribution[11] • Drug interactions[11] • Increased renal loss of magnesium[11] • Poor magnesium intake[11] • Alcoholism[11] • Diabetes mellitus[11] • Hyperaldosteronism[11] • Hypercalcaemia[11] • Hyperthyroidism[11]	Cardiovascular	Paroxysmal atrial or ventricular arrhythmias[14]
		Respiratory	Hypoventilation, respiratory distress and respiratory failure[14]
		Neuromuscular	Weakness, fatigue, muscle cramps, ataxia, vertigo, paraesthaesia, hallucinations, depression and convulsions[14]
		Gastrointestinal	Abdominal pain, diarrhoea, vomiting, loss of appetite, and constipation[14]
		Other related consequences	Anaemia and hypocalcaemia[14]
Sodium	Serum osmolality changes in the central nervous system[15]	Cardiovascular	Heart failure and arrhythmia[14]
		Respiratory	Respiratory failure and pulmonary oedema[14]
		Renal	Renal failure[14]
		Skeleton	Muscle cramps, fatigue, fluid retention and oedema[14]

resuscitation, i.e. 0.37 g/kg/day glutamine. This combination of feeds was given for the first three days post initiation. On the first day post the PEG insertion, feeding was started at 40 ml/hour for 24 hours, and increased in increments of 5 ml/day until 50 ml/hour was reached on the third day post feeding initiation. This was decided on the basis that biochemical values do not indicate the presence of refeeding syndrome. The administration of specialised formula was terminated on the fourth day, and the semi-elemental feed continued at a rate of 50 ml/hour for 24 hours, as the composition of the feed met the nutritional requirements at this rate (20 kcal/hour). The aim was to start a polymeric feed on the fifth day (i.e. the seventh day post admission of the patient to the surgical ward). However, the patient was discharged to the oncology unit before this feed could be initiated.

Micronutrients and refeeding

The provision of phosphorous, potassium, vitamin B complex and magnesium were taken into special consideration during the development of the nutritional management to prevent refeeding syndrome. The clinical consequences of the inadequacy of each micronutrient are provided in Table IV, while a summary of the treatment options is provided in Table V.

Vitamin B complex

Thiamin deficiency is the most important vitamin to monitor during the prevention of refeeding syndrome since it is a co-enzyme in carbohydrate metabolism.[7] The recommended intake range is between 200 and 300 mg daily.[5] When repleting thiamin levels, it

Table V: A summary of the treatment options for micronutrient inadequacy

Micronutrient	Treatment options
Thiamin	IV 300 mg when the feed is initiated, and 100 mg per day as maintenance[4]
Phosphate	
Mild (2.3-3.0 mg/dl)	0.32 mmol/kg*[4,16]
	Increase dietary intake or oral phosphate containing a multivitamin[15]
Moderate (1.6-0.2 mg/dl)	0.64 mmol/kg[4,16]
	Oral supplementation: 2.5-3.5 g/day in divided doses, or 0.32-0.64 mmol/kg IV slowly over 6 hours[15]
Severe (1.5 mg/dl)	1 mmol/kg*[4,16]
	1 mmol/kg IV slowly over 8-12 hours[15]
Potassium	
Mild (4.0-3.7 mEq/l)	40 mEq oral or IV[16]
	Increase dietary intake and/or add salt substitutes[15]
	Oral supplementation: 40-100 mEq daily in divided doses, or 40 mEq IV x 1, or 10 mEq IV over 1 hour x 3-4 doses[15]
Moderate (3.6-3.4 mEq/l)	60 mEq oral or IV[16]
	20 mEq *per os* every 2 hours x 3 doses, or 10 mEq IV over 1 hour x 4 doses (recheck and repeat, if needed)[15]
Severe (< 3.3 mEq/l)	80 mEq oral or IV[16]
	40 mEq IV over 2-4 hours (recheck and repeat, as needed), or 40 mEq IV over 4 hours, as needed[15]
Magnesium	
Mild	Oral, increase daily intake, or oral supplement (magnesium lactate)[15]
Moderate	10-15 mmol oral magnesium oxide or citrate[4]
	IV 8-32 mEq (maximum 1.0 mEq/kg) slowly, with 8 mEq over 1-2 hours daily[15]
Severe	25 mmol/day parenteral magnesium[4]
	IV 32-64 mEq (maximum 1.5 mEq) slowly, with 8 mEq over 1-2 hours[15]
Sodium	
Mild	Oral
	Free water restriction[15]
Moderate	Consider free water restriction
	Provide half normal saline and/or saline corrected at a rate of 1-2 mEq/l/hour[15]
Severe	3% sodium chloride (correct at a rate of 1-2 mEq/l/hour)[15]

* Actual body weight (if < 130% of ideal body weight). If > 130% of ideal body weight, then adjust body weight, i.e. [ideal body weight + 0.25 (actual body weight – ideal body weight)][16]
IV: intravenous

is recommended that an intravenous dose of 300 mg is given when the feed is initiated (Table V). A maintenance dose of 100 mg per day should then be given.[4]

In this case study, thiamin was provided at an initial dose of 300 mg, followed by a daily maintenance dose of 100 mg. In addition to thiamin, vitamin B_6 (pyridoxine), vitamin B_{12} (cobalamin) and the patient's folate levels were also monitored.[4]

Phosphorous

Phosphorous is an intracellular mineral which is involved in the intracellular processes, together with the structural integrity of the cell membranes. It is necessary for the production of energy presented in the form of adenosine triphosphate. During the development of refeeding syndrome, the depletion of serum phosphorous occurs because of the increased phosphorylation of glucose.[1]

Hypophosphataemia can be classified into three groups of mild (0.75-1.00 mmol/l), moderate (0.50-0.74 mmol/l) and severe (< 0.50 mmol/l).[4]

Skipper conducted a systematic review of cases with patients presenting with refeeding syndrome, and indicated a prevalence of hypophosphataemia in up to 96% of patients.[2] Thus, it is advisable that serum phosphorous levels are closely monitored to prevent the development of refeeding syndrome.[4]

Phosphate requirements range between 0.3 and 0.6 mmol/kg/day.[4] If mild hypophosphateemia occurs, it should be treated with 0.32 mmol/kg/day of IV or oral *(per os)* potassium phosphate, while moderate depletion levels should be replaced with 0.64 mmol/kg/day of IV potassium phosphate (Table V).[4] On the other hand, severe hypophosphataemia should be treated with 1 mmol/kg/day of IV potassium phosphate (Table V).[4] However, it is important to continue monitoring phosphate levels to prevent neurological symptoms.[4]

The patient discussed in this case study had borderline low phosphate levels. Her phosphate levels were monitored daily, but the levels improved in the days that followed to such an extent that the phosphate supplementation was discontinued.

Potassium

Low potassium levels can lead to hypokalaemia (< 3.5 mmol/l), and thus salt and water retention.[13] This retention then results in oedema, and eventually heart failure.[13] It is recommended that patients' potassium levels are monitored daily,[4] and if high or low, an electrocardiogram should be considered to determine the presence of arrhythmia.[4] Patients should be provided with 1-4 mEq/kg/day of oral potassium in the form of either potassium chloride or other potassium formularies (Table V).[4] Severe deficiencies should be treated with IV supplementation, although this should be monitored closely to prevent hyperkalaemia (Table V).[4]

In this case study, the patient's potassium levels were borderline low; and although the potassium was not supplemented, it was monitored daily.

Magnesium

Hypomagnesaemia can lead to cardiac arrhythmia, abdominal discomfort and/or neuromuscular abnormalities (Table IV).[4] Mild to moderate hypomagnesaemia (0.5-0.7 mmol/l) should be treated with 10-15 mmol oral magnesium oxide or citrate (Table V).[4] Ideally, when severe symptomatic hypomagnesaemia (< 0.5 mmol/l) is present, it should be treated with 25 mmol/day parenteral magnesium.[4] However, this should be assessed every 8-12 hours.[4]

Conclusion

The patient in this case study was transferred to the oncology ward, where chemotherapy treatment was planned. Unfortunately, she aspirated and passed away owing to complications of aspiration pneumonia. The importance of a comprehensive nutritional assessment and monitoring are highlighted by this case study. Furthermore, as demonstrated by the biochemical profile of this case, cautious feeding is essential in the prevention of refeeding syndrome in a patient at high risk of developing this syndrome.

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