The Refeeding Syndrome: a neglected but potentially serious condition for inpatients. A narrative review

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The Refeeding Syndrome: a neglected but potentially serious condition for inpatients

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Author contributions

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Abstract

The Refeeding Syndrome (RFS) is a potentially serious but still overlooked condition, occurring in individuals who are rapidly fed after a period of severe undernourishment. RFS derives from an abnormal electrolyte and fluid shifts leading to many organ dysfunctions. Symptoms generally appear within 2-5 days of re-feeding and may be absent/mild or severe and life-threating, depending on the pre-existing degree of malnutrition and comorbidity. The lack of a standard definition and the non-specificity of the symptoms make both incidence estimate and diagnosis difficult. In 2020, the American Society for Parenteral and Enteral Nutrition (ASPEN) proposed a unifying definition for the RFS and its severity classification. The awareness of the condition is crucial for identifying patients at risk, preventing its occurrence, and improving the management.

The objectives of this review are to summarize the current knowledge and recommendations about the RFS and to provide useful tips to help physicians to recognise and prevent the syndrome.

Keywords

Hypophosphatemia; hypokalaemia; hypomagnesemia; malnutrition; refeeding syndrome; thiamine.

Introduction

Malnutrition is a frequent and often unrecognized condition among inpatients [1, 2]. Indeed, 20-50% of individuals are at risk of malnutrition or already malnourished at hospital admission, but malnutrition is diagnosed in 7% only [3]. Older age, low socio-economic status, lack of organisational support, chronic systemic or psychiatric diseases, polytherapy, poor diet, reduced absorption capacity, excessive nutrient losses are the most frequent conditions underlying malnutrition [4]. The management of malnourished inpatients can be difficult due to the risk of metabolic impairment after the start of nutrition [5]. The adverse outcomes of refeeding were firstly reported during the World War II in rapidly re-fed prisoners who had starved for five to six months [6]. People who have fasted for a long time, developed heart and/or respiratory failure, peripheral oedema, neurological symptoms, and death after the introduction of excessive or even appropriate calorie amount [6–8]. In the 80s, the term 'refeeding syndrome' (RFS) was introduced to describe severe hypophosphatemia and other electrolyte/metabolic abnormalities and the related cardiovascular and pulmonary manifestations leading to death occurring in two chronically malnourished patients who received aggressive dextrose-based parenteral nutrition (PN) [9]. Since then, many cases of RFS have been described as a rare but severe and potentially fatal complication related to re-feeding (either orally, enterally or parenterally) of individuals who have fasted or consumed very few calories over a long period of time [10, 11]. The switch from a catabolic to an anabolic state may be the cause of the clinical manifestations of the RFS, even though the pathophysiological mechanisms are still not fully understood [12]. Furthermore, the lack of a clear definition accounts for the difficulty of diagnosis and uncertainties in treatment [2, 13]. Therefore, the RFS is a potentially serious condition, often overlooked by many physicians [14]. This is of particular concern because of the high prevalence of hospital malnutrition often underestimated even in the internal medicine wards [15, 16].

The objectives of this review are to summarize the knowledge on the RFS and to focus on the most useful topics for the clinical practice.

Methods

The following databases were queried: PubMed (National Library of Medicine), the Cochrane Library, Excerpta Medica dataBASE (EMBASE), and the Cumulative Index to Nursing and Allied Health Literature (CINAHL). The search strategy was performed by using the following keywords: refeeding syndrome OR phosphate, potassium, magnesium AND anorexia nervosa, cancer, critically ill patients, elderly. The filters 'humans' and 'adults' were used. Hand-searching the references of the identified studies and reviews was carried out too.

Incidence rates for RFS

The lack of a universally recognized RFS definition makes it difficult to obtain precise estimates of its incidence [17]. Indeed, either hypophosphatemia only or multiple electrolyte abnormalities (with different cut-offs) with or without clinical manifestations have been considered in its definition [18, 19]. The reported incidence rates ranged between 0% and 80%, depending on the definition and the patient population studied [18]. RFS has been described in 48% of severely malnourished patients, in 34% of intensive care unit (ICU) patients, in 25% of cancer inpatients, and in 9.5% of patients hospitalized for malnutrition from gastrointestinal fistulae [10, 17, 20]. Many factors may lead to underestimation of RFS incidence rate, such as insufficient monitoring of the patients' electrolytes after nutrition starting, lack of consultation by experts in clinical nutrition, the non-specificity of the clinical manifestations of the syndrome in patients with multiple comorbidity, and the physician unawareness [11].

Population at risk for RFS

The first step to identify patients at risk for RFS is the diagnosis of malnutrition [21]. Distinguishing malnutrition from the other related conditions, such as starvation, cachexia, and sarcopenia, is important from a clinical point of view (**Table 1**). Nutritional status can be assessed through validated screening tools, such as the Malnutrition Universal Screening (MUST), the Mini Nutritional Assessment-short form (MNA-SF), the Nutritional Risk Screening 2002 (NRS-2002), the Short Nutritional Assessment Questionnaire (SNAQ), and the Subjective Global Assessment (SGA) [5, 17, 25, 26]. If an individual at malnutrition risk is identified, a nutritional assessment by an expert in nutrition is required for further investigation and diagnosis of malnutrition.

The following diseases or conditions predispose to malnutrition [12, 17, 18, 26–30]:

- psychiatric diseases (i.e. anorexia nervosa, depression, chronic alcohol, or drug abuse),
- chronic diseases leading to reduced intakes and/or increased energy expenditure and/or increased calorie loss (i.e. cancer, chronic inflammatory or infectious diseases, chronic heart, lung, kidney, liver diseases with organ dysfunction, uncontrolled diabetes mellitus, advanced neurologic impairment, and dysphagia),
- peri-operative/procedural prolonged fasting or any conditions determining nil by mouth for an extended period,
- gastrointestinal malabsorption (i.e. inflammatory bowel disease, short bowel syndrome, cystic fibrosis, chronic diarrhoea, protracted vomiting post-bariatric surgery),
- long-term poly-therapies (i.e. anti-acids, diuretics, angiotensin-converting enzyme inhibitors, biguanides, opioids, protease inhibitors, chemotherapeutic and cancer medication, antihistamine, antibiotics, and antivirals),
- adverse socio-economic conditions (i.e. homelessness, poor living conditions, living alone, refugees),
- frailty conditions (i.e. elderly, history of abuse or psychological trauma/stress, athletes, military recruits),

- fasting (<500 kcal/day) or severe caloric restriction (very low-caloric intakes) from days up to weeks (i.e. severe dieting, religious fasting, hunger strikers).

In the presence of severe underweight or weight loss, prolonged fasting period, and/or low electrolyte concentrations, the risk of RFS is particularly high [14].

In 2006, the National Institute for Health and Clinical Excellence (NICE) guidelines [31] reported the risk factors for RSF. Recently, the American Society for Parenteral and Enteral Nutrition (ASPEN) published updated consensus criteria for identifying adult patients at risk for RFS [17]. Those criteria are presented in **Table 2**.

Diagnosis of RFS

The difficulty in RFS diagnosing is due to the discrepancy between the onset of the symptoms and the occurring of metabolic shift (see below), and the non-specific nature of its clinical manifestations [29]. There is a great heterogeneity among the published definitions of RFS [18]. Only hypophosphatemia has been universally recognized as a feature of the syndrome [25]. Friedly et Coll. proposed diagnostic criteria for imminent or manifest RFS, based on electrolyte blood concentrations and clinical symptoms in order to standardise its prevention and treatment [28]. According to this definition, "imminent" RFS is present when a shift in electrolytes occurs within 72 h after the start of nutritional treatment (i.e. >30% decrease in blood phosphate from baseline or phosphate values <0.6 mmol/L or any two other electrolyte shifts below normal range) [28]. "Manifest" RFS is considered if any electrolyte shift occurs in conjunction with typical clinical symptoms (see below) [28].

More recently, the ASPEN proposed diagnostic criteria for distinguishing mild, moderate or severe RFS [17] (**Table 3**). The extent of the decrease in the serum levels of one or more electrolytes (among phosphate, potassium, or magnesium) defines RFS severity: 10%–20% (mild RFS), 20%–30% (moderate RFS), >30% and/or organ dysfunction and/or thiamine deficiency (severe RFS) [17]. Thus, either hypophosphatemia and/or hypokalaemia and/or hypomagnesemia qualify the presence of the RFS. The timing of onset is determinant for the diagnosis, since the RFS develops shortly (from hours up to 5 days) after having substantially increased the energy provision to individuals who have been undernourished [17].

Pathophysiology and clinical manifestation

The pathophysiology of the RFS is probably related to the shift from the catabolic to the anabolic metabolic pathways occurring after the re-start of feeding in undernourished subjects. During early starvation, blood glucose and insulin levels decline while glucagon concentrations increase stimulating glycogenolysis in the liver. When glycogen reserves become depleted, gluconeogenesis is stimulated in the liver, using amino acids derived from muscle breakdown [32]. During prolonged fasting, the body switches to use fats as the main sources of energy with a decrease in basal metabolic rate of 20–25% [33]. Increased lipolysis in fat reserves leads to the production of ketones that are used by the brain as preferred fuel during starvation [13, 32]. During prolonged fasting, several intracellular minerals become severely depleted, particularly phosphate, potassium, and magnesium. However, the concentrations of these minerals may remain within the normal range in the serum because there is a reduction in their renal excretion and because of the phosphate outflow from the cells into the blood, leading to normal blood phosphate levels despite depleted storages [28].

Rapid refeeding in a starved patient causes the metabolic and hormonal changes underlying the syndrome [34]. The provision of nutrients, above all carbohydrates, increases insulin secretion and promotes a sudden shift from fat to carbohydrates metabolism. Insulin stimulates the sodium potassium ATPase symporter, with magnesium as co-factor, which transports glucose and potassium into the cells and moves out sodium. Moreover, insulin release stimulates anabolic processes that require minerals (promoting cellular uptake of phosphate, potassium, and magnesium) and coenzymes such as thiamine [13]. The electrolyte shift, along with the depletion of the mineral pool, could lead to profound hypophosphatemia and low extracellular magnesium and potassium concentrations, but not necessarily to the depletion of all together.

The phosphate is predominantly an intracellular mineral that plays a key role in energy production and transfer (as a component of adenosine triphosphate (ATP) [35] and it is necessary for many enzymatic processes of cellular metabolic pathways [36]. During refeeding, the increased phosphate consumption due to enhanced production of phosphorylated intermediates results in reduced generation of ATP and 2,3-diphosphoglycerate with impaired cardiac and respiratory functions, and decreased oxygen release to the tissues (**Table 4**). Potassium is an intracellular mineral and it is crucial for the maintenance of the sodium-potassium membrane gradient; hypokalaemia causes imbalance in the electrochemical membrane potential and impaired transmission of electrical impulses resulting in arrhythmias, cardiac arrest, and neurologic symptoms [37–39]. Magnesium plays a role as a cofactor for the phosphorylation of ATP and it is important for the maintenance of neuromuscular and enzymatic functions. Its depletion results in increased renal losses of potassium, aggravating hypokalaemia with arrhythmias and ECG abnormalities, and in abdominal discomfort and neuromuscular symptoms [40]. Thiamine is another cofactor in ATP production. Its increased consumption during refeeding by the enhanced activity of enzymes implicated in the carbohydrate metabolism may lead to neurologic disorders (dry beriberi, Wernicke encephalopathy and Korsakoff's syndrome), cardiovascular disorders, and metabolic acidosis (due to the conversion of glucose into lactate) [41] (**Table 4**). Furthermore, insulin has an anti-natriuretic effect on renal tubules causing a decrease in urinary sodium and water excretion [34]. This determines a rapid fluid overload that can lead to congestive cardiac failure, arrhythmia, and pulmonary oedema.

Symptoms generally appear within 2-5 days of re-feeding and may range from absent/mild to a severe and life-threating clinical syndrome, depending on the pre-existing degree of malnutrition and comorbidity [10, 11, 27]. All the body organs may be involved, leading to cardiac, respiratory, haematologic, gastrointestinal, neurologic, and musculoskeletal manifestations, until death [10, 28, 35].

Prevention and treatment

The identification of patients at risk for RFS is the first step to prevent the onset of the syndrome, and to avoid an excessive nutritional replenishment in individuals with the above reported metabolic impairment [28, 42]. Risk factors should be carefully investigated before starting either oral, enteral, or parenteral nutrition, because every route of calorie administration is implicated in the occurrence of the RFS [17, 35]. Well-trained medical staff and specialized nutritional support teams, consisting of physicians, dieticians, nurses, and pharmacists, positively impact on the patient outcomes [31]. However, a multidisciplinary metabolic team is not available in all hospital settings, and often the evaluation of the risk for RFS is left to the clinician's critical sense at the time of starting nutritional support [11, 17, 20, 25, 43]. After defining the degree of RFS risk, the rate of fluid and nutrition administration, the correction of electrolyte imbalances, and the supplementation of vitamins and micronutrients (zinc, iron, selenium) can be determined [20]. If a prolonged nutritional support is required, adjustments over time in accordance with the patient clinical conditions might be necessary [35].

Several therapeutic approaches have been proposed to prevent or treat the RSF [10, 12, 20, 27–29, 31, 43, 44]. Since hypophosphatemia occurs after refeeding, according to the grade of RSF risk, phosphate may be administered preventively before the initiation of nutritional therapy, even if blood levels are in the low-normal range [28]. Similarly, thiamine is essential in carbohydrates metabolism and should be supplemented before restart feeding even in the case of normal blood levels [28]. An excessive administration of glucose by stimulating insulin production leads to the consumption of electrolytes (mainly phosphate) through the anabolic pathways. Starting re-feeding very gradually, independently of the route of administration, is therefore mandatory [35]. Due to the risk of fluid overload, sodium and hydration should be provided cautiously, until the patient is metabolically stable [25]. In case of overt symptoms, energy and fluid intakes should be reduced and adapted to the clinical conditions [14]. In **Table 5**, a day-to-day approach is described based on the RFS risk, assessed according to the ASPEN criteria. **Figure 1** describes the tips that should be keep in mind in the clinical practice to prevent and/or treat the syndrome.

Conclusions

The RFS is a frequent condition, often undiagnosed and overlooked by physicians, which can have serious consequences for the human health. Its knowledge is essential to avoid rapid and excessive nourishing of at-risk patients, thus preventing serious complications, long hospital stays and the increase in health costs.

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Table 1. Definition of malnutrition and other related conditions

Malnutrition [21]
At least 1 phenotypic criterion and 1 etiologic criterion should be present Phenotypic Criteria: - Non-volitional weight loss - Low Body Mass Index - Reduced Muscle Mass Etiologic criteria: - Reduced food intake or assimilation - Disease burden/inflammation condition
Starvation [22]
Reduction in both fat and fat-free mass due to protein-energy deficiency, which could be reversed solely by the provision of nutrients
Cachexia [23]
Severe weight loss (adults) or growth failure (children) due to loss of muscle +/- loss of fat mass associated with increased protein catabolism by underlying chronic illness
Sarcopenia [24]
Sarcopenia is a progressive and generalized skeletal muscle disorder that is associated with increased likelihood of adverse outcomes including falls, fractures, physical disability, and mortality. Sarcopenia is *probable* when low muscle strength is detected (handgrip strength < 27 kg for males and < 16 kg for females). A sarcopenia diagnosis is *confirmed* by the presence of low muscle quantity or quality (ASM/height^2 < 7.0 kg/m^2 for males and < 5.5 kg/m^2 for females). When low muscle strength, low muscle quantity/quality and low physical performance (low gait speed ≤ 0.8 m/s both for males and females) are all detected, sarcopenia is considered severe

BMI=body mass index; ASM=Appendicular Skeletal Muscle Mass

Table 2. Criteria for identifying adult patients at risk for RFS

	NICE		ASPEN 2020	
	High risk in the presence of		Moderate risk: 2 risk criteria needed	Significant risk: 1 risk criteria needed
	one or more of the following:	two or more of the following:		
BMI	<16 kg/m^2	< 18.5 kg/m^2	16–18.5 kg/m^2	<16 kg/m^2
Weight loss	>15% within the last 3–6 months	> 10% within the last 3–6 months	5% in 1 month	7.5% in 3 months or >10% in 6 months
Caloric intake	Little or no nutritional intake >10 days	Little or no nutritional intake >5 days	None or negligible oral intake for 5–6 days OR <75% of estimated energy requirement for >7 days during an acute illness or injury OR <75% of estimated energy requirement for >1 month	None or negligible oral intake for >7 days OR <50% of estimated energy requirement for >5 days during an acute illness or injury OR <50% of estimated energy requirement for >1 month
Prefeeding potassium, phosphate, or magnesium serum concentrations	Low levels		Minimally low levels or normal current levels and recent low levels necessitating minimal or single-dose supplementation	Moderately/ significantly low levels or minimally low or normal levels and recent low levels necessitating significant or multiple-dose supplementation
Loss of subcutaneous fat			Evidence of moderate loss	Evidence of severe loss
Loss of muscle mass			Evidence of mild or moderate loss	Evidence of severe loss
Higher-risk comorbidities*		A history of alcohol abuse or drugs including insulin, chemotherapy, antacids, or diuretics	Moderate disease	Severe disease

BMI=body mass index

* Acquired immunodeficiency syndrome; Advanced neurologic impairment or general inability to communicate needs; Cancer; Chronic alcohol or drug use disorder; Dysphagia and esophageal dysmotility; Eating disorders; Food insecurity and homelessness; Failure to thrive, including physical and sexual abuse and victims of neglect; Hyperemesis gravidarum or protracted vomiting; Major stressors or surgery without nutrition for prolonged periods of time; Malabsorptive states (e.g., short-bowel syndrome, Crohn's disease, cystic fibrosis, pyloric stenosis, maldigestion, pancreatic insufficiency); Post-bariatric surgery; Postoperative patients with complications; Prolonged fasting; Protein malnourishment; Refugees.

Table 3. Diagnostic criteria for RFS severity [17]

Severity of RFS	**Mild**	**Moderate**	**Severe**
Serum electrolytes*	10%–20% less	20%–30% less	>30% less and/or organ dysfunction**
Timing	From hours up to 5 days after increasing the energy provision in an individual at risk		

*decrease in any (one or more) of electrolyte serum levels, among phosphate, potassium, and/or magnesium

** resulting from the decrease in any electrolyte and/or from thiamine deficiency

Table 4. Physiopathology and main clinical features of the RFS

Pathophysiological mechanisms	**Clinical manifestations**
Hypophosphatemia	
Increased phosphate consumption due to enhanced production of phosphorylated intermediates for glycolysis, the Krebs cycle, and the electron transport chain to produce adenosine triphosphate and 2,3-diphosphoglycerate	Impaired cardiac and respiratory functions (i.e. tachycardia, tachypnoea) Neurologic symptoms (i.e. confusion, somnolence, lethargy, coma, paresthesia, seizures) Hematologic disorders (i.e. haemolysis, dysfunction of platelets and leukocytes, thrombocytopenia) Hypoxia (due to impaired oxygen release from 2,3-diphosphoglycerate) Muscular disorders (i.e. weakness, rhabdomyolysis, decreased cardiac contractility, myalgia)
Hypokalaemia	
Intracellular shift of potassium by insulin stimulation of the Na+/K+ ATPase Impairment of potassium reuptake in the nephron (role of hypomagnesemia)	Cardiac arrhythmias Neurologic symptoms (i.e. weakness, hyporeflexia, respiratory depression, and paralysis) due to impaired transmission of electrical impulses
Hypomagnesemia	
Not completely clear Intracellular shift of magnesium after carbohydrate feeding	Increased renal losses of potassium Cardiac arrhythmias (i.e. torsade de pointes, atrial fibrillation, ventricular arrhythmias) Electrocardiograph changes (i.e. prolonged QT and PR, widened QRS) Abdominal discomfort (i.e. anorexia, diarrhoea, nausea, vomiting) Neuromuscular symptoms (i.e. tremor, paresthesia, tetany, seizures, irritability, confusion, weakness, ataxia)
Thiamine deficiency	
Increased consumption of thiamine by glucose metabolism enzymes	Neurologic disorders or dry beriberi, Wernicke encephalopathy and Korsakoff's syndrome (i.e. ataxia, disturbance of consciousness, oculomotor abnormalities, symptoms of acute peripheral neuropathy, coma) Cardiovascular disorders or wet beriberi (i.e. peripheral oedema, heart failure) Metabolic acidosis (due to glucose conversion to lactate)
Sodium and fluid retention	
Renal sodium and fluid retention due to insulin anti-natriuretic properties (after carbohydrate feeding)	Peripheral oedema Pulmonary oedema and heart failure (due to increased vasoconstriction and peripheral resistance by sodium stimulation of noradrenaline and angiotensin II)
Hyperglycaemia	
Increased tissue resistance to endogenous glucose	Metabolic acidosis Hypercapnia, respiratory failure, and risk of fatty liver due to lipogenesis (stimulated by insulin)

ATP=adenosine triphosphate

Table 5. Prevention and treatment of the RFS according to the risk [25, 28]

Day	Treatment	Low risk	High risk	Very-high risk	Monitoring
1	Thiamine	200-300 mg	200-300 mg	200-300 mg	Body weight Vital signs Clin Exam Lab tests§
	Multivitamin*	yes	yes	Yes	
	Sodium restriction	no	<1 mmol/kg/day	<1 mmol/kg/day	
	Fluids	30-35 ml/kg/day	25-30 ml/kg/day	20-25 ml/kg/day	
	Nutritional support**	15-25 kcal/kg/day	10-15 kcal/kg/day	5-10 kcal/kg/day	
2	Thiamine	200-300 mg	200-300 mg	200-300 mg	Body weight Vital signs Clin Exam Lab tests§
	Multivitamin*	yes	Yes	Yes	
	Sodium restriction	no	<1 mmol/kg/day	<1 mmol/kg/day	
	Fluids	30-35 ml/kg/day	25-30 ml/kg/day	20-25 ml/kg/day	
	Nutritional support**	15-25 kcal/kg/day	10-15 kcal/kg/day	5-10 kcal/kg/day	
3	Thiamine	200-300 mg	200-300 mg	200-300 mg	Body weight Vital signs Clin Exam Lab tests§
	Multivitamin*	yes	Yes	Yes	
	Sodium restriction	no	<1 mmol/kg/day	<1 mmol/kg/day	
	Fluids	30-35 ml/kg/day	25-30 ml/kg/day	20-25 ml/kg/day	
	Nutritional support**	15-25 kcal/kg/day	10-15 kcal/kg/day	5-10 kcal/kg/day	
4	Thiamine	no	No	200-300 mg	Vital signs Clin Exam
	Multivitamin*	yes	Yes	Yes	
	Sodium restriction	no	<1 mmol/kg/day	<1 mmol/kg/day	
	Fluids	30-35 ml/kg/day	30-35 ml/kg/day	25-30 ml/kg/day	
	Nutritional support**	30 kcal/kg/day	15-25 kcal/kg/day	10-20 kcal/kg/day	
5	Thiamine	no	No	200-300 mg	Body weight Vital signs Clin Exam Lab tests§
	Multivitamin*	yes	Yes	Yes	
	Sodium restriction	no	<1 mmol/kg/day	<1 mmol/kg/day	
	Fluids	30-35 ml/kg/day	30-35 ml/kg/day	25-30 ml/kg/day	
	Nutritional support**	full requirements	15-25 kcal/kg/day	10-20 kcal/kg/day	
6	Multivitamin*	Yes	Yes	Yes	Vital signs Clin Exam
	Sodium restriction	No	<1 mmol/kg/day	<1 mmol/kg/day	
	Fluids	30-35 ml/kg/day	30-35 ml/kg/day	25-30 ml/kg/day	
	Nutritional support**	full requirements	25-30 kcal/kg/day	10-20 kcal/kg/day	
7	Multivitamin*	Yes	Yes	Yes	Vital signs Clin Exam
	Sodium restriction	No	<1 mmol/kg/day	<1 mmol/kg/day	
	Fluids	30-35 ml/kg/day	30-35 ml/kg/day	30-35 ml/kg/day	
	Nutritional support**	full requirements	full requirements	20-30 kcal/kg/day	
8	Multivitamin*	Yes	Yes	Yes	Vital signs Clin Exam
	Sodium restriction	No	No	<1 mmol/kg/day	
	Fluids	30-35 ml/kg/day	30-35 ml/kg/day	30-35 ml/kg/day	
	Nutritional support**	full requirements	full requirements	20-30 kcal/kg/day	
9	Multivitamin*	Yes	Yes	Yes	Body weight Vital signs Clin Exam Lab tests§
	Sodium restriction	No	No	<1 mmol/kg/day	
	Fluids	30-35 ml/kg/day	30-35 ml/kg/day	30-35 ml/kg/day	
	Nutritional support**	full requirements	full requirements	20-30 kcal/kg/day	
10	Multivitamin*	Yes	Yes	Yes	Vital signs Clin Exam
	Sodium restriction	No	No	<1 mmol/kg/day	
	Fluids	30-35 ml/kg/day	30-35 ml/kg/day	30-35 ml/kg/day	
	Nutritional support**	full requirements	full requirements	full requirements	

Clin Exam= clinical examination. *Vitamins should be supplemented to 200% and the trace elements to 100% of the recommended daily intakes; replace electrolyte according to the electrolyte serum levels and RFS severity: 1-1.5 mmol/Kg/day potassium, 0.2-0.4 mmol/Kg/day magnesium, 0.3-0.6 mmol/Kg/day phosphate. **Provide 15-20% proteins, 30-40% carbohydrates, 40-60% fats. §Laboratory tests include phosphate, sodium, potassium, magnesium, calcium, glucose, creatinine, urea.

Figure 1. Practical tips for the prevention and approach to the RFS