ISSN: 2469-4142

Gratis

Journal of Nutritional Biology

Review Article

Gastrointestinal Complications of Refeeding in Anorexia Nervosa

Trees N[1*], Beaty L[1], Cusimano C[1], Estry K[1], Koutsavlis A[1] and Mehler P[1,2,3]

[1]Eating Recovery Center, 1830 Franklin Street Denver, CO 80218, USA
[2]Department of Medicine, University of Colorado Health Sciences Center, USA
[3]ACUTE at Denver Health 777 Bannock Street, MC4000, Denver, CO 80204, USA

Received: Jan 01, 2016; Accepted: March 25, 2016; Published: April 01, 2016

Abstract

Anorexia nervosa (AN) is a complicated and life-threatening mental illness. Restoration of weight and nutrition rehabilitation are key elements for the treatment of AN. However, gastrointestinal (GI) complications develop due to eating disorder behaviors, concomitant malnutrition, and during the refeeding process. These problems may give rise to significant medical sequela and contribute to increased difficulties with the critically important refeeding and weight restoration. Thus, this review aims to describe complications that may occur when refeeding a patient with AN including delayed gastric emptying, constipation, gastric dilatation, superior mesenteric artery (SMA) syndrome, refeeding hepatitis, and refeeding syndrome. It will also provide medical practitioners with a better understanding of the current nutritional recommendations for refeeding a patient with AN. This knowledge is required for correct management, successful nutritional rehabilitation, and improved treatment outcomes of patients with AN.

Keywords: Anorexia nervosa; Refeeding; Gastrointestinal complications; Nutritional therapy; Weight restoration; Gastric motility

Abbreviations: AN: Anorexia Nervosa; BMI: Body Mass Index; RD: Registered Dietitian; GI: Gastrointestinal; mL: milliliter; TPN: Total Parenteral Nutrition; SMA: Superior Mesenteric Artery; CT: Computerized Tomography; NGT: Nasogastric Tube; NJT: Nasojejunal Tube; PEG-J: Gastrojejunostomy Tube; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; ATP: Adenosine-5-triphosphate; 2,3 DPG: 2, 3-diphosphoglycerate; EN: Enteral Nutrition; NICE: National Institute of Health and Clinical Excellence

Introduction

Anorexia nervosa (AN) is a serious psychiatric illness. The American Psychiatric Association (DSM-5) defines AN via three key components: 1) Restriction of energy intake relative to requirements, leading to significantly low body weight (weight less than minimally normal), 2) Intense fear of gaining weight or becoming fat, or persistent behavior that interferes with weight gain, 3) Disturbance in the way in which one's body weight or shape is experienced, undue influence of body

***Correspondence:** Trees N, Eating Recovery Center, Denver, CO 80218, USA, Tel: 720-258-4048; E-mail: Ntrees@eatingrecoverycenter.com

weight or shape on self-evaluation, or persistent lack of recognition of the seriousness of the current low body wt. [1]. AN is divided into two subtypes, restricting and binge/purge; it can also be defined in severity by an individual's body mass index (BMI) [1]. Effective medications geared specifically for the treatment of AN have yet to be defined. Overall, the evidence base for treatment therein remains weak [2]. Individuals with eating disorders, including AN, often have coexisting mental health concerns including mood, anxiety, impulse control, or substance abuse disorders. Eating disorders also have the highest rate of medical complications among all psychiatric disorders [3].

Several factors, such as childhood eating and gastrointestinal problems, increased body image concerns, negative self-evaluation and sexual abuse, have all been identified as possible etiologic factors in the development of AN [4]. While research on the genetic predisposition for developing eating disorders continues to progress, it is increasingly clear from twin studies that approximately 60% of the variance in risk for developing AN is due to genetic factors [5]. Genetics studies have also revealed that serotonin-associated genes have been related to an increase in AN [6]. Specific temperament traits have been associated with the development of AN, including a history of global childhood rigidity and increased persistence. Individuals with temperaments indicating increased harm-avoidance, less self-directedness, less reward-dependence, more persistence, and lower levels of novelty seeking, are more likely to develop AN [6]. In the end, the combination of genetics, biology, temperament, and environment all play a role in the development of AN [3].

In samples of mainly young women from the United States and Europe, the average point prevalence of AN has been found to be 0.3% [7] and the prevalence of AN among adult men is 0.1% [8]. From 1935-1999, a significant increase in the development of AN was observed, particularly in females ages 15-24 years of age [9]. The most common age of onset for AN is 15-19 years, however the incidence appears to be increasing in the pre-pubertal period and in older adults [2].

When compared to individuals with other eating disorders, those with AN have a greater incidence of relapse and a higher mortality rate [3]. Standardized mortality rates from AN are 12 times are higher than the annual death rate from all causes of death among females aged 15 to 24 years in the general population. Recovery rates for adolescents at 10-15 years of follow-up were much higher at 69-75.8%, as opposed to adults diagnosed later in life who had only a 30-50% chance of achieving full recovery [3].

AN patients present with psychological, medical, and nutrition concerns, which is why the approach of a multidisciplinary team is imperative for positive treatment outcomes [10]. The registered dietitian (RD) plays a crucial role as a part of the multidisciplinary treatment team, possessing unique skills to apply medical nutrition therapy and assist with medical monitoring, while also addressing food-related behaviors [3,11]. The RD is the member of the multidisciplinary team who often guides the weight restoration process by determining a starting kilocalorie point for the patient's meal plan and working with the patient to apply continuous increases in energy intake while monitoring patterns of weight gain as well as any medical side effects from the refeeding process [10,12]. Weight restoration has been shown to be absolutely essential in rehabilitation and recovery from AN, and has been associated with positive short and long-term outcomes, as well as an improvement in several psychological and medical complications [12].

Given the centrality of food in the treatment of patients with AN and the significance that weight restoration plays in the recovery from AN, it is important to understand the gastrointestinal complications, which often occur and may frustrate sustained weight gain. On a very rudimentary level, all of these complications are a direct result of prolonged starvation and weight loss, but they generally will resolve as the patient undergoes nutritional rehabilitation. The purpose of this paper is to explore the role that these complications, including delayed gastric emptying, constipation, gastric dilatation, superior mesenteric artery (SMA) syndrome, refeeding hepatitis, and refeeding syndrome, may play in the treatment of AN. The body of rigorous, eating disorder-specific literature on this topical area is not robust enough to perform a systematic review for the topics discussed as defined by PRISMA guidelines.

Therefore, a qualitative review of mostly medical literature was conducted.

Delayed Gastric Emptying

Symptoms of gastroparesis, i.e. delayed gastric emptying, are often described by patients with AN secondary to weight loss and restrictive food intake [13-15]. These include symptoms of fullness, early satiety and nausea. Research has shown that postprandial fullness and abdominal distention are reported early on in the refeeding process in over 90% of cases [13,16]. Diagnosis of gastroparesis can be objectively defined by finding delayed gastric emptying without gastric obstruction during a nuclear medicine gastric emptying study (scintigraphy) [17]. However, because research suggests a poor correlation between severity of reported symptoms and the diagnosis of impaired gastric motility; empiric diet modifications may be prudent to improve patient symptoms and their ability to obtain adequate nutrition, without the need of subjecting every patient to a definitive nuclear medicine study [15]. Nuclear medicine testing is likely only necessary if symptoms persist despite significant nutritional rehabilitation and in more refractory cases. In fact, as patients gain weight and BMI increases with nutrition and psychotherapy, reports of GI discomfort and early satiety have been shown to significantly improve [13,18].

Research has shown that various textures and nutritional content of meals can impact symptoms of delayed gastric emptying. This includes both higher calorie content of a meal, as well as smaller particle size of meal components [19]. Diet modification recommendations to achieve adequate nutrition in AN are based on known physiological processes of food and nutrient digestion, notwithstanding a paucity of controlled studies. Small particle size feeds have also been previously found to enhance the rate of gastric emptying [20,21]. Adjusting particle size may include blending foods, processing food in a food processor, or simply including easy to chew and mashed foods, while avoiding foods with peels, husks, stringy membranes, seeds, grains, compact foods, and foods known to be poorly digestible particles [20].

It is also appropriate to encourage adequate chewing of food, smaller and more frequent meals (4-6 meals per day), low fat meal content and low residue content of meals for delayed gastric emptying [21]. Utilizing liquid calories to help enhance the emptying process, including fat containing liquids, may improve symptoms [22]. Additional recommendations include avoiding carbonated beverages to prevent distention of the stomach and eliminating alcohol consumption to prevent further slowing of gastric emptying [23,24].

In cases where weight restoration goals are not achieved orally, the patient, doctor, and dietitian may assess that enteral nutrition is the appropriate means for nutrition. There are several options for placement of feeding tubes, including nasogastric, percutaneous gastrostomy, jejunostomy or a nasojejunal tube [25]. Enteral formula preparations of 1.0-1.5 calories per milliliter (mL), initiated at a slow infusion rate of 25-50 mL/hr and gradually increased by 10-25 mL/hr every 24-48 hours, are utilized to achieve 2-3 lbs of weight gain per week. In some cases, gastroparesis can also be associated with poor motility in the small bowel. Although considered a last resort, total parenteral nutrition (TPN) may be appropriated for the rare patient with a severe delay in motility [26].

Finally, medications may be deemed necessary to relieve symptoms of gastroparesis and hasten gastric emptying. Prokinetic medications such as low dose metoclopramide (2.5 mg), 30 minutes before meals or azithromycin (250 mg) given once daily may improve contraction of the gastrointestinal tract. The appropriateness of these medications is judiciously determined by the patient and doctor based on different individual treatment factors. Their ongoing need should be reevaluated within a few weeks of initiation, as delayed gastric emptying seems to resolve over time [25].

Constipation

Complaints of constipation are frequent in patients with AN and can be associated with weight loss. This is likely related to the misperception of stool frequency and quantity as a result of laxative abuse, which the patient may believe to help reduce calorie absorption [27]. Due to decreased caloric intake and decreased

motility of the GI tract, slowed GI transit times and reflex hypofunction of the colon are real phenomena in anorexia nervosa [28]. Weight restoration can improve colonic motility and prevent progressive constipation, in addition to diet modifications and medical therapy. Ensuring adequate fluid intake can often aid in symptom relief. Stimulant laxatives are not recommended, as not only can they also cause painful cramping, but also they can cause damage to colonic nerve cells [27]. The preferred treatment modalities are osmotic laxatives, such as polyethylene glycol powder and lactulose, dosed based on the frequency of defecation [27].

Gastric Dilatation

As previously explained, patients with AN have delayed gastric emptying and poor GI motility from their malnutrition, which in turn can increase the risk of rare, but severe, gastric dilatation during refeeding [29]. Reducing the chance of gastric dilatation requires an approach of carful monitoring of electrolytes to achieve normal serum levels and gradually incorporating increased calories and oral intake. Symptoms that should prompt a search for gastric dilatation include GI distention, left upper quadrant pain, bloating, nausea, vomiting, and hypoactive bowel sounds [29-31]. Monitoring for this by obtaining a plain abdominal radiograph can prevent more severe consequences including gastric perforation or superior mesenteric artery syndrome [31]. Treatment of acute gastric dilatation includes temporary cessation of oral food intake while nasogastric suction is initiated to remove stomach contents. Once decompression is completed, the tube is removed and the patient's diet is cautiously advanced to clear liquids, and then full liquids as tolerated before returning to a full diet [29-31].

Superior Mesenteric Artery (SMA) Syndrome

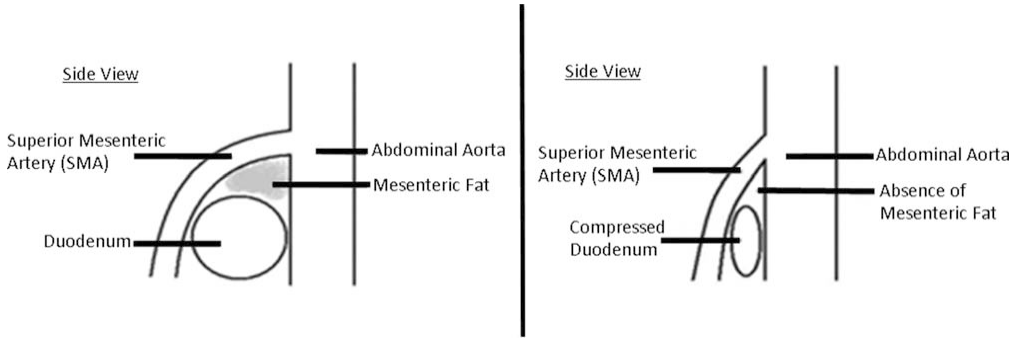
One additional mechanical complication, which can impede weight restoration, is known as the superior mesenteric artery (SMA) syndrome. While this has been described as a rare problem, this syndrome is observed in severe AN due to the significant weight loss. SMA syndrome impacts between 0.013% and 0.3% of the general population and is more commonly observed in females between 10 and 39 years of age [32]. Conditions such as trauma to the spine, wasting diseases like cancer and burns, and malnourished states, as a result of malabsorption and anorexia nervosa result in the loss of the mesenteric fat pad to cause SMA syndrome (Figure 1) [29]. Reduction of this fat pad, which lies between the duodenum and the spine allows the SMA to compress the duodenum against the vertebrae. In the absence of an appropriate fatty support, the angle at which the SMA leaves the aorta promotes more compression of the third portion of the duodenum [33].

SMA syndrome manifests with nonspecific symptoms of nausea, vomiting, early satiety, and postprandial epigastric pain due to a significant reduction in the luminal diameter of the duodenum [33]. The postprandial epigastric pain is a common symptom of SMA syndrome and usually begins 15-30 minutes following eating, lasts for 2-3 hours, and gradually subsides. In some rare instances, an abdominal bruit can be found on physical examination [34].

Radiologic diagnostic findings of SMA syndrome, by an upper GI barium series or abdominal contrast computerized tomography (CT), include an angle between the aorta and SMA of less than 25° and an aortic-mesenteric distance of less than 8 mm [35,36]. While the clinical manifestations of SMA syndrome are somewhat nonspecific, the diagnosis of SMA syndrome can be confidently confirmed through these radiology procedures.

The presentation of SMA syndrome in the setting of AN is uniquely challenging due to the overlapping signs and symptoms inherent to AN and SMA syndrome. Thus, the diagnosis is often delayed and this delay can exacerbate AN, as these symptoms inhibit the critically important caloric intake needed for weight restoration and resolution of SMA syndrome. Recognition of SMA syndrome in anorexia nervosa is vital to prevent worsening weight loss along with serious complications such as electrolyte imbalance, further malnutrition, gastric dilation, and even death [32].

The treatment for SMA syndrome is aimed at restoring



Normal State **SMA Syndrome**

Figure 1: Pictorial image of SMA syndrome showing loss of the mesenteric fat pad and narrowed angle between the SMA and the aorta. Loss of the fat pad ultimately causes a compressed duodenum and obstructed blood flow from the SMA to foregut structures.

the mesenteric fat pad and cushioning the mesenteric bundle [29]. This can generally be achieved through nutritional therapy. Surgical treatment is only very rarely indicated if conservative management fails or symptoms are unrelieved by weight gain and repletion of the mesenteric fat stores [36]. The most common surgical operation for SMA syndrome is duodenojejunostomy, in which the compressed portion of the duodenum is bypassed by constructing an anastomosis between the 2nd portion of the duodenum and proximal jejunum anterior to the superior mesenteric artery [37].

While SMA syndrome in the setting of AN has been recognized, little has been published regarding successful management and treatment [38]. Conservative treatment via weight restoration is almost always recommended for SMA syndrome in AN [39] due to the typically young age of this patient population and acute onset of symptoms. Thus, oral feeds should be initiated and advanced as tolerated. The feeds should consist of liquids and soft foods as small volume meals with provision of oral liquid supplements. This can be used to progressively increase caloric intake and enhance weight restoration. Postprandial positions such as knee-chest, assumption of the left lateral decubitus, or prone positions have been found to alleviate SMA syndrome symptoms. Promotility agents, such as metoclopramide, are generally not appropriate since increasing upper GI motility when a distal duodenal obstruction is present, increases the pain component. Antiemetics can be supportive [36,39]. Most importantly, symptoms of SMA syndrome will resolve fairly quickly with restoration of the lost weight. This in turn restores the fat pad, increases the aortomesenteric angle, relieves the extrinsic compression of the superior mesenteric artery on the underlying duodenum, and normal GI function is restored [40]. Recent data indicate that conservative, nutritional management is successful in 70-80% of cases [32]. However, enteral feeding with a nasojejunal tube (NJT) or surgically placed gastrojejunostomy tube (PEG-J) distal to the compression site is the next step after a trial of oral feeding has failed.

Refeeding Hepatitis

Mild abnormalities in liver function tests are frequently seen in patients with AN, with an increase in serum aminotransferase levels (AST, ALT) found in up to 60% of patients. As such, the 2006 practice guidelines of American Psychiatric Association recommend the systematic assessment of liver function tests [41]. The possible mechanism of liver damage in AN was studied by Rautou et al. [41], who showed an up-regulation of the homeostatic mechanism, in which autophagy and the resultant increased permeability of the hepatocyte plasma membrane, are responsible for the elevated aminotransferase levels when hepatocyte necrosis is not present.

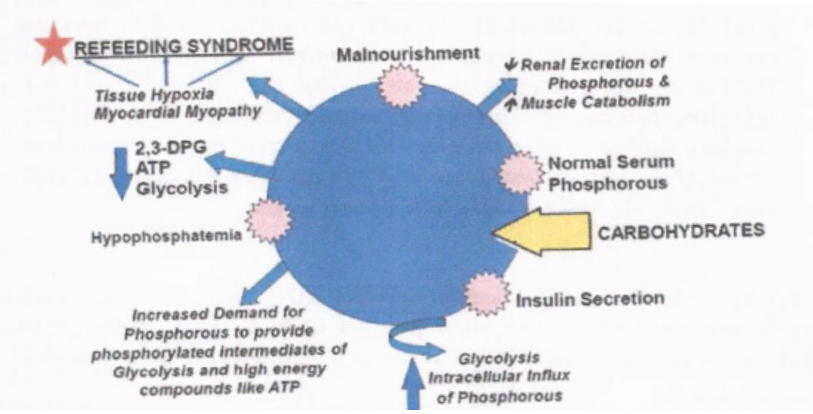


Figure 2: The Development of Refeeding Hypophosphatemia: Introducing carbohydrates in a state of malnutrition increases insulin secretion, which in turn causes an influx of phosphorus in the intracellular space. This leads decreased levels of serum phosphorus, 2,3 DPG, ATP, decreased glycolysis, and refeeding syndrome.

The inverse relationship between hypertransaminasemia and BMI is well described [41-45]. Hypertransaminasemia and refeeding steatosis can also occur soon after nutrition therapy has been initiated in AN [46]. While the link between transaminitis and steatosis has not been proven in AN, clinical experience suggests that it does occur across a wide acuity spectrum during the later refeeding stages when apoptosis is no longer relevant. When AST and ALT become elevated in these situations, they improve with a reduction in carbohydrate-derived calories, especially in those being fed enterally. Excessive dextrose calories or use of total parenteral nutrition have been implicated as potential causes of refeeding steatosis [47-49]. The medical nutrition therapy required if hypertransaminasemia is found in AN depends on the pathology of the liver enzyme elevation. A liver ultrasound may be useful when trying to determine the etiology of enzyme elevation. If the liver ultrasound shows a small shrunken liver with normal echo texture, the enzyme elevations can likely be attributed to starvation-induced abnormalities (autophagy) where the treatment is continued feeding. If, however, the ultrasound demonstrates a large fatty liver, it indicates refeeding steatosis where the treatment is rather a reduction in dextrose-based calories. In addition to the liver ultrasound, weight gain or the lack thereof may be an important distinguishing factor between refeeding liver function abnormalities and starvation-induced abnormalities [47].

Refeeding Syndrome

When refeeding a patient with anorexia nervosa (AN), medical practitioners must be cautious of the refeeding syndrome, a set of metabolic complications that can occur early on during the refeeding process. When it occurs, refeeding syndrome consists of medical complications and shifts in fluid and electrolytes in malnourished patients who are being fed orally, enterally, or parenterally [50]. Although refeeding syndrome is multi-faceted, hypophosphatemia (low serum phosphate level) is recognized as playing a major role in the onset of the syndrome. Phosphorus levels are depleted in starved patients, and this can be further exacerbated during the initial phase of refeeding. When the body begins to process carbohydrates, insulin is released, which causes glucose and phosphorus to move into the body's cells, thereby worsening the already present state of hypophosphatemia [50]. In turn, production of adenosine-5-triphosphate (ATP) and 2, 3-diphosphoglycerate (2,3 DPG) are reduced. Inadequate production of ATP and 2,3 DPG can result in organ dysfunction, cell death, acute respiratory and cardiac failure, tissue hypoxia, and hemolysis (Figure 2) [51].

In addition to hypophosphatemia, other electrolyte abnormalities may occur with the refeeding syndrome. These include decreases in serum potassium, magnesium, sodium, and thiamine levels, which can

Table 1: Clinical presentation of electrolyte abnormalities associated with refeeding syndrome.

Clinical presentation of electrolyte abnormalities associated with refeeding syndrome	
Phosphate	Hypophosphatemia presents as: **Cardiovascular:** heart failure, arrhythmia, hypotension, cardiomyopathy shock, death **Renal:** acute tubular necrosis, metabolic acidosis **Skeletal:** rhabdomyolysis, weakness, myalgia, diaphragm weakness **Neurologic:** delirium, coma, seizures, tetany **Endocrine:** hyperglycemia, insulin resistance, osteomalacia **Hematologic:** hemolysis, thrombocytopenia, leukocyte dysfunction
Potassium	Hypokalemia presents as: **Cardiovascular:** hypotension, ventricular arrhythmias, cardiac arrest, bradycardia **Respiratory:** hypoventilation, respiratory distress, respiratory failure **Skeletal:** weakness, fatigue, muscle twitching **Gastrointestinal:** nausea, vomiting, paralytic ileus, constipation **Metabolic:** metabolic alkalosis
Magnesium	Hypomagnesemia presents as: **Cardiovascular:** paroxysmal atrial or ventricular arrhythmias **Respiratory:** hypoventilation, respiratory distress, respiratory failure **Neuromuscular:** weakness, fatigue, muscle cramps, atazia, vertigo, paresthesia, hallucinations, depression, convulsions **Gastrointestinal:** abdominal pain, diarrhea, vomiting, loss of appetite, constipation **Other:** hypocalcemia (due to decreased release of parathyroid hormone)
Sodium	Hyponatremia presents as: **Cardiovascular:** heart failure, arrhythmia **Central nervous system:** delirium, seizures **Respiratory:** respiratory failure, pulmonary edema **Renal:** renal failure **Skeletal:** muscle cramps, fatigue, fluid retention, swelling
Vitamins	Deficiency of thiamine presents as: **Cardiovascular:** congestive heart failure, lactic acidosis, beriberi, **Skeletal:** muscle weakness **Neurological:** Wernicke-Korsakoff syndrome, Karsakoff's psychosis

further adversely impact the clinical stability of patients undergoing refeeding. Table 1 outlines the impact of electrolyte and vitamin deficiencies on various body systems [52-57].

In addition to electrolyte shifts, cardiac complications can also occur during the early refeeding process although these are rare. Patients with AN have diminished cardiac muscle mass as part of their overall weight loss, which can lead to difficulty tolerating the increased plasma volume that comes with refeeding. When a patient begins to take in nutrition, the cardiac system can become overwhelmed, leading to peripheral edema, arrhythmias, and although uncommon, heart failure [50,51].

Successful management of refeeding syndrome starts with prevention. If judiciously approached, this is almost always preventable. It has been identified that three components play a role in preventing the

Table 2: Strategies to Avoid Refeeding Syndrome.

Identify patients at risk (e.g. any patient who is chronically malnourished or who has note eaten for seven to ten days).
Measure serum electrolyte levels and correct abnormalities before refeeding.
Obtain serum chemistry values in phosphorus every other day for the first seven to ten days, then weekly during the remainder of refeeding.
Attempt to slowly increase daily caloric intake by 300 to 400 kcals every three to four days until level of caloric intake is adequate.
Monitor patient carefully for development of tachycardia and edema.

refeeding syndrome. These are: early identification of at risk patients, close monitoring during refeeding, and an appropriate refeeding regimen [58]. Patients with one or more of the following are said to be at high risk for refeeding syndrome: BMI <16 kg/m^2, unintentional weight loss of >15% in the past 3-6 months, little or no nutritional intake for >10 days, or low levels of potassium, phosphorus, or magnesium before refeeding. A patient with two or more of the following is also at high risk for refeeding syndrome: BMI < 18.5 kg/m^2, unintentional weight loss of >10% in the past 3-6 months, little or no nutritional intake from >5 days, and history of alcohol or drug misuse [59]. Patients should be screened for risk of refeeding syndrome by obtaining a detailed history, clinical examination, and laboratory testing. Early intervention with a nutrition support team is crucial. This team should include a RD to perform nutritional assessments and oversee the refeeding process. Clinical evaluation and monitoring plays a crucial role in avoiding refeeding syndrome (Table 2) [50].

The refeeding meal plan should be prescribed and managed by a RD. The amount of calories initiated in AN is certainly gathering more recent interest. However, the National Institute of Health and Clinical Excellence (NICE) criteria continue to mention initial lower rates of refeeding starting at 5-10 kcal/kg/day for patients who are at high risk for refeeding, and 25-30 kcal/kg/day for patients that are not at risk of refeeding [60]. Typically patients starting the refeeding process may start on a meal plan between 1400-1600 kcal per day, or about 20-40 kcal/kg of body weight [61,62]. Patients with AN binge/purge subtype may tolerate an initial meal plan that is higher than that for a patient with AN restrictive type. The RD will then increase the meal plan 300-400 kcal every 3-4 days to achieve 2-4 pounds of weight gain per week [59,60].

Electrolytes, phosphorus, and liver tests are closely monitored every 1-2 days during the first week or two of refeeding. If the patient develops abnormalities in phosphorus or other electrolytes, they would be aggressively repleted with oral supplements. On rare occasions, intravenous supplementation would be required when potassium is < 2.5 meq/L or phosphorus is < 2.1 meq/L [62]. In order to weight restore at an appropriate rate, patients may ultimately need a meal plan that contains 70-100 kcal/kg of body weight [61]. When patients become hypermetabolic or as they approach their ideal body weight range, they may need meal plans at the higher end of the 70-100 kcal/kg of body weight range [61]. Typically, macronutrient makeup of the refeeding meal plan should include: 50-55% carbohydrates, 30% dietary fat, and protein intake of 1.5-2 g/kg of body weight [61].

Ideally, patients should be fed orally in order to utilize and rehabilitate the GI tract. However, alternate modes of refeeding can be utilized if clinically indicated and judiciously deemed necessary by the clinical team, including the RD. Enteral nutrition (EN) therapy and very rarely total parenteral nutrition (TPN) may be indicated in patients who fail to gain weight on an oral meal plan, experience ongoing life-threatening weight loss, or who present with worsening psychological state even with standard intervention and treatment. However, due to the potential medical complications associated with these alternate modes, oral refeeding remains the

preferred method [59].

Conclusion

In summary, anorexia nervosa has a litany of serious medical complications, which if ignored can be fatal. Most commonly noted by the patient with AN are their gastrointestinal complications, such as gastroparesis or delayed gastric emptying, constipation, gastric dilatation, superior mesenteric artery syndrome, refeeding hepatitis, and refeeding syndrome, all of which can impede adequate caloric intake, weight restoration, and resolution of symptoms. Many of these complications can be difficult to distinguish from the somatic complaints that follow eating disorder patients; therefore, successful treatment requires a team to include a dietitian, physician, and psychiatrist. Multidisciplinary care can recognize and prevent most of these GI complications from becoming worse in order to achieve successful weight restoration and overall treatment outcome.

References

1. American Psychiatric Association (2013) Diagnostic and statistical manual of mental disorders: DSM-5, 5th edn. American Psychiatric Association, Washington, D.C.

2. Boraska V, Franklin CS, Floyd JA, Thornton LM, Huckins LM, et al. (2104) A genome-wide association study of anorexia-nervosa. Mol Psychiatry 19: 1085-1094.

3. Tholking MM, Mellowspring AC, Eberle SG, Lamb RP, Myers ES, et al. (2011) American Dietetic Association: Standards of practice and standards of professional performance for registered dietitians (competent, proficient, and expert) in disordered eating and eating disorders (DE an ED). J Am Diet Assoc 111: 1242-1249.

4. Wade TD, Gordon S, Medland S, Bulik CM, Heath AC, et al. (2013) Genetic variants associated with disordered eating. Int J Eat Disord 46: 594-608.

5. Bakalar JL, Shank LM, Vannucci A, Radin RM, Tanofsky-Kraff M (2015) Recent advances in developmental and risk factor research on eating disorders. Curr Psychiatry Rep 17: 42.

6. Hudson JI, Hiripi E, Pope HG Jr, Kessler RC (2007) The prevalence and correlates of eating disorders in the national comorbidity survey replication. Biol Psychiatry 61: 348-358.

7. Jacobi C, Hayward C, de Zwaan M, Kraemer HC, Agras WS (2004) Coming to terms with risk factors for eating disorders: Application of risk terminology and suggestions for a general taxonomy. Psycho Bull 130: 19-65.

8. Hoek HW (2006) Incidence, prevalence, and mortality of anorexia nervosa and other eating disorders. Curr Opin Psychiatry 19: 389-394.

9. Mittnacht AM, Bulik CM (2014) Best nutrition counseling practices for the treatment of anorexia nervosa: a Delphi study. Int J Eat Disord 48: 111-122.

10. Dejesse LD, Zelman DC (2013) Promoting optimal collaboration between mental health providers and nutritionists in the treatment of eating disorders. Eat Disord 21: 185-205.

11. Lund BC, Hernandez ER, Yates WR, Mitchell JR, McKee PA, et al. (2009) Rate of inpatient weight restoration predicts outcome in anorexia nervosa. Int J Eat Disord 42: 301-305.

12. Sato Y, Fukudo S (2015) Gastrointestinal symptoms and disorders in patients with eating disorders. Clin J Gastroenterol 8: 255-263.

13. Salvioli B, Pellicciari A, Iero L, Di Pietro E, Moscano F, et al. (2013) Audit of digestive complaints and psychopathological traits in patients with eating disorders: A prospective study. Dig Liver Dis 45: 639-644.

14. Chiarioni G, Bassotti G, Monsignori A, Menegotti M, Salandini L, et al. (2000) Anorectal dysfunction in constipated women with anorexia nervosa. Mayo Clin Proc 75: 1015-1019.

15. Benini L, Todesco T, Grave RD, Deiorio F, Salandini L, et al. (2004) Gastric emptying in patients with restricting and binge/purge subtypes of anorexia

nervosa. Am J Gastroenterol 99: 1448-1454.

16. Kamal N, Chami T, Andersen A, Rosell FA, Schuster MM, et al. (1991) Delayed gastrointestinal transit times in anorexia nervosa and bulimia nervosa. Gastroenterology 101: 1320-1324.

17. Abell TL, Camilleri M, Donohoe K, Hasler WL, Lin HC, et al. (2008) Consensus recommendations for gastric emptying scintigraphy: a joint report of the American neurogastroenterology and motility society and the society of nuclear medicine. J Nucl Med Technol 36: 44-54.

18. Riguad D, Bedig G, Merrouche M, Vulpillat M, Bonfils S, et al. (1988) Delayed gastric emptying in anorexia nervosa is improved by completion of renutrition a program. Dig Dis Sci 33: 919-925.

19. Marciani L, Gowland PA, Spiller RC, Manoj P, Moore RJ, et al. (2001) Effect of meal viscosity and nutrients on satiety, intragastric dilution, and emptying assessed by MRI. Am J Physiol Gastrointest Liver Physiol 280: G1227-G1233.

20. Olausson EA, Storsrud S, Grundin H, Isaksson M, Attvall S, et al. (2014) A small particle size diet reduces upper gastrointestinal symptoms in patients with diabetic gastroparesis: A randomized controlled trial. Am J Gastroenterol 109: 375-385.

21. Olausson EA, Alpsten M, Larsson A, Mattsson H, Andersson H, et al. (2008) Small particle size of a solid meal increases gastric emptying and late postprandial gylcaemic response in diabetic subjects with gastroparesis. Diabetes Res Clin Pract 80: 231-237.

22. McCallum RW, Brill BB, Lange R, Planky M, Glass EE, et al. (1985) Definition of a gastric emptying abnormality in patients with anorexia nervosa. Dig Dis Sci 30: 713-722.

23. Pfeiffer A, Hogl B, Kaess H (1992) Effect of ethanol and commonly ingested alcoholic beverages on gastric emptying and gastrointestinal transit. Clin Investig 70: 487-491.

24. Van Eatvelde E, Verfaillie L, Van De Winkel N, Hubloue I (2014) Acute gastric dilatation causing acute limb ischemia in an anorexia nervosa patient. J Emerg Med 46: e141-e143.

25. Camilleri M (1994) Appraisal of medium-and long-term treatment of gastro paresis and chronic intestinal dysmotility. Am J Gastroenterol 89: 1769-1774.

26. Mehler PS, Weiner KL (2007) Use of total parenteral nutrition in the refeeding of selected patients with severe anorexia nervosa. Int J Eat Disord 40: 225-287.

27. Mehler, PS, Krantz, MJ, Sachs, KV (2015) Treatment of medical complications of anorexia nervosa and bulimia nervosa. J Eat Disord 3: 15.

28. Chun AB, Sokol MS, Kaye WH, Hutson WR, Wald A (1997) Colonic and anorectal function in constipated patients with anorexia nervosa. Am J Gastroenterol 92: 1879-1883.

29. Mascolo M, Dee E, Townsend R, Brinton JT, Mehler PS (2015) Severe gastric dilatation due to superior mesenteric artery syndrome in anorexia nervosa. Int J Eat Disord 48: 532-534.

30. Barada KA, Azar CR, Al-Kutoubi AO, Harb RS, Hazimeh YM, et al. (2006) Massive gastric dilatation after a single binge in an anorectic woman. Int J Eat Disord 39: 166-169.

31. Tweed-kent AM, Fagenholz PJ, Alam HB (2010) Acute gastric dilatation in a patient with anorexia nervosa binge/purge subtype. J Emerg Trauma Shock 3: 403-405.

32. Chan DK, Mak KS, Cheah YL (2012) Successful nutritional therapy for superior mesenteric artery syndrome. Singapore Med J 53: e233-e236.

33. Anderson JR, Earnshaw PM, Fraser GM (1982) Extrinsic compression of the third part of the duodenum. Clin Radiol 33: 75-81.

34. Ikegaya H, Nakajima M, Shintani-Ishida K, Uemura K, Yoshida K (2006) Death due to duodenal obstruction in a patient with an eating disorder: A case report. Int J Eating Disorders 39: 350-352.

35. Mukherjee D, Cho L (2004) Mesenteric artery stenosis. In: Bhatt DL, editor. Guide to Peripheral

and Cerebrovascular Intervention.

36. Bowden DJ, Kilburn-Toppin F, Scoffings DJ (2013) Radiology of eating disorders: a pictorial review. Radiographics 33: 1171-1193.

37. Jia Y, Sosa O, McCallum R (2014) Superior Mesenteric Artery Syndrome. Practical Gastroenterology 12-19.

38. Ylinen P, Kinnunen J, Hockerstedt K (1989) Superior mesenteric artery syndrome. A follow-up study of 16 operated patients. J Clin Gastroenterol 4: 386-391.

39. Verhoef PA, Rampal A (2009) Unique challenges for appropriate management of a 16-year-old girl with superior mesenteric artery syndrome as a result of anorexia nervosa: A case report. Journal of Medical Case Reports 3: 127.

40. Dao TV, Beydoun T, Jorgensen S, Towbin AJ, Towbin R (2014) Pediatric Radiological Case: Superior mesenteric artery compression syndrome. Appl Radiol 64-66.

41. Rautou PE, Cazals-Hatem D, Moreau R, Francoz C, Feldmann G, et al. (2008) Acute Liver Cell Damage in Patients with Anorexia Nervosa: A Possible role of starvation-induced hepatocyte autophagy. Gastroenterology 135: 840-848.

42. Hanachi M, Melchior JC, Crenn P (2013) Hypertransaminasemia in severely malnourished adult anorexia nervosa patients: Risk factors and evolution under enteral nutrition. Clin Nutr 32: 391-395.

43. Tsukamoto M, Tanaka A, Arai M, Ishii N, Ohta D, et al. (2008) Hepatocellular injuries observed in patients with an eating disorder prior to nutritional treatment. Intern Med 47: 1447-1450.

44. Tomita K, Haga H, Ishii G, Katsumi T, Sato C, et al. (2013) Clinical manifestations of liver injury in patients with anorexia nervosa. Hepatol Res 44: E26-E31.

45. Mickley D, Greenfeld D, Quinlan DM, Roloff P, Zwas F (1996) Abnormal liver enyzmes in outpatients with eating disorders. Int J Eat Disord 20: 325-329.

46. Harris RH, Sasson G, Mehler PS (2013) Elevation of liver function tests in severe anorexia nervosa. Int J Eat Disord 46: 369-374.

47. Rosen E, Sabel AL, Brinton JT, Catanach B, Gaudiani JL, et al. (2015) Liver dysfunction in patients with severe anorexia nervosa. Int J Eat Disord 49: 153-160.

48. Narayanan V, Gaudiani JL, Harris RH, Mehler PS (2010) Liver function test abnormalities in anorexia nervosa--cause or effect. Int J Eat Disord 43: 378-381.

49. Sheldon GF, Peterson SR, Sanders R (1978) Hepatic dysfunction during hyperalimentation. Arch Surg; 113: 504-508.

50. Mehler PS, Crews CK (2001) Refeeding the patient with anorexia nervosa. Eat Disord 9: 167-171.

51. Brown CA, Sabel AL, Gaudiani JL, Mehler PS (2015) Predictors of hypophosphatemia during refeeding of patients with severe anorexia nervosa. Int J Eat Disord 48: 898-904.

52. Crook MA, Hally V, Panteli JV (2001) The importance of the refeeding syndrome. Nutrition 17: 632-637.

53. Stanga A, Brunner M, Leuenberger, Grimble RF, Shenkin A, et al. (2008) Nutrition in clinical practice-the refeeding syndrome: illustrative cases and guidelines for prevention and treatment. Eur J Clin Nutr 62: 687-694.

54. Mehanna H, Nankivel PC, Moledina J, Travis J (2009) Refeeding syndrome- awareness, prevention and management. Head Neck Oncol 1: 4.

55. Marik PE, Bedigian MK (1996) Refeeding hypophosphatemia in critically ill patients in an intensive care unit. A prospective study. Arch Surg 131: 1043-1047.

56. Mehanna HM, Moledina J, Travis J (2008) Refeeding syndrome: what it is, and how to prevent and treat it. BMJ 336: 1495-1498.

57. Hayek ME, Eisenberg (1989) Severe

ypophosphatemia following the institution of enteral feedings. Arch Surg 124: 1325-1328.

58. Tresley J, SheeanPM (2008) Refeeding syndrome: recognition is the key to prevention and management. J Am Diet Assoc 108: 2105-2108.

59. Mehler PS, Winkelman AB, Anderson DM, Gaudiani JL (2010) Nutritional rehabilitation: Practical guidelines for refeeding the anorectic patient. J Nutr Metabol 2010: 1-7.

60. National Institute for Health and Clinical Excellence (2006) Nutrition support in adults: Oral nutrition support, enteral tube feeding and parenteral nutrition.

61. Sachs K, Anderson D, Sommer J, Winkelman A, Mehler PS (2015) Avoiding medical complications during the refeeding of patients with anorexia nervosa. Eating Disorders 23: 411-421.

62. Arthur B, Strauss L, Mehler PS (2015) Refeeding the patient with anorexia nervosa: Perspectives of the dietitian, psychotherapist and medical physician. J Nutr Health 3: 29-34.