

Anorexia Nervosa and the Use of Total Parenteral Nutrition Refeeding

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Abstract: Anorexia nervosa is a chronic eating disorder which often has a poor prognosis. The likelihood of success in treating this disorder, which most commonly strikes females in their prime of life, is greatly enhanced by the attainment of ideal body weight during the refeeding-weight restoration process. For a select number of refractory, chronic, severe anorexic patients, in whom traditional modes of refeeding through oral or nasogastric routes has not been successful, total parenteral nutrition (TPN) may offer an alternative method of refeeding for this population. Judicious usage of TPN is critical in this markedly malnourished cadre of patients to avoid the morbid complications associated with the refeeding syndrome.

Keywords: Anorexia nervosa, total parenteral nutrition (TPN), refeeding syndrome, hypophosphatemia.

INTRODUCTION

The *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) defines anorexia nervosa as having an intense fear of gaining weight, putting undue emphasis on body shape, having a body weight that is less than 85% of the predicated weight, and missing three consecutive periods (Table 1) [1]. Anorexia nervosa is further divided into restricting and purging subtypes. Patients with the more common restricting subtype drastically limit their food intake, whereas patients with the purging subtype also engage in purging behaviors. In contrast to the bulimic patient, whose appearance is often unremarkable and whose disease may therefore initially go unrecognized in clinical settings [2], the cachectic appearance of the patient with severe anorexia is readily noticeable. Although the differential diagnosis for weight loss is extensive [3, 4], the young age of most patients with anorexia nervosa simplifies the evaluation. Malabsorption and catabolic states can easily be excluded with a careful history and physical examination and judicious laboratory testing, including tests for levels of thyroid-stimulating hormone and serum albumin.

No controlled trials have been performed to define when inpatient hospitalization is indicated. Commonly accepted indications include a weight that is more than 25% to 30% below ideal body weight, rapid and severe weight loss refractory to outpatient treatment, marked symptomatic hypotension or syncope, a pulse rate less than 35 to 40 beats/min, arrhythmias, or a prolonged QT interval (Table 2) [5]. A lower weight at referral is consistently associated with less frequent attainment of normal weight and a greater risk for chronic anorexia and death [6, 7].

Because severe anorexia nervosa is often chronic and very complicated, experts in dealing with patients who have eating disorders should handle psychiatric and refeeding management. The psychiatrist or psychologist usually leads a

Table 1. Criteria for Anorexia Nervosa

Intense fear of weight gain
Undue emphasis on body shape
Body weight <85% of predicted
Amenorrhea for 3 consecutive months

multidisciplinary team that includes representatives of the necessary clinical specialties, including an internist and a dietitian. This multidisciplinary approach is particularly relevant to patients with more severe disease or to patients who receive care at a specialty unit for eating disorders. The mental health professional must be able to intervene, achieve patient adherence, integrate and prioritize treatments, and effectively treat comorbid psychiatric illnesses. He or she must work with ancillary staff to educate and support patients so that the terror accompanying their fears of becoming fat are attenuated.

Table 2. Indications for Inpatient Treatment

Markedly abnormal vital signs (heart rate <35-40 beats/min, symptomatic hypotension)
Weight <70%-75% of ideal body weight
Rapid and severe weight loss unresponsive to outpatient treatment
Cardiac arrhythmias

EPIDEMIOLOGY

It is estimated that the average prevalence of anorexia nervosa among young women is approximately 0.3%. The highest rates appear to be in girls aged 15 to 19, with this group comprising 40% of all cases [8]. While the incidence of anorexia nervosa steadily increased through the 1970's, it appears to have reached a plateau. One recent Swiss study showed that the rates of anorexia nervosa between 1993 and 1995 in young women did not differ significantly from the

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same period ten years earlier [9]. The incidence of anorexia nervosa in young males, however, while still representing a small percentage of cases, may be increasing. Kjelsas et al found the prevalence of anorexia in their sample of young Norwegian males to be 0.2%, which was nearly a third of that of young women in the same study [10]. Previously, female anorexics had been felt to outnumber males by approximately 10:1.

Black women appear to be far less affected by anorexia nervosa than their white counterparts. A 10-year longitudinal self-reporting survey of over two thousand women showed that 1.5% of white women studied met criteria for anorexia nervosa, while none of the black women surveyed met criteria [11]. Similarly, a cohort study by Lindberg and Hjern found that while the cumulative incidence of anorexia nervosa was 0.22% for young women, those with a middle eastern heritage had an incidence of only 0.02%, and those of African ancestry had a 0.03% incidence [12].

Athletes also appear to be a population at higher risk for anorexia nervosa. Elite athletes were found in one study to be at nearly three times the risk for eating disorders as controls [13]. This risk does not appear to be limited to females, and affects recreational athletes as well, along with other professions for which body image is an integral part of the occupation such as dancers and models [14]. Other proposed risk factors are perfectionism and negative comments from others about body appearance [15]. In addition, new evidence has established a genetic basis for increased risk [16].

Overall, anorexia nervosa has a much less favorable outcome than bulimia with only about 50% of patients having a sustained recovery [17]. Anorexia nervosa is often a protracted illness with almost 20% of patients continuing to meet criteria for anorexia nervosa more than a decade before the initial diagnosis [18]. Medications do not play a major role in the success of weight restoration [19]. Therefore even with an experienced eating disorder treatment team, some patients with anorexia nervosa will have a tremendous amount of difficulty gaining weight. Similarly, despite a regimented refeeding program, defined by a progressive increase in oral caloric intake, some anorectic patients continue with their severe levels of malnutrition and remain markedly underweight. A lower body weight in anorexia nervosa is consistently associated with less frequent attainment of normal weight and a greater risk for chronic anorexia nervosa and death [20]. Moreover, many of the medical complications of anorexia nervosa are inherently more frequent at lower body weights. As an example, osteoporosis is often severe and irreversible in anorexia nervosa and is directly related to the duration and severity of the anorexia nervosa [21]. Similarly, many of the cardiac adverse sequelae from anorexia nervosa are more prevalent at lower body weights [22].

MEDICAL COMPLICATIONS

In addition on a more minor scale, brittle nails, lanugo hair growth, cold intolerance, constipation, amenorrhea and dry skin, are all inherent to anorexia nervosa. There are a litany of other medical complications associated with anorexia nervosa. The endocrine complications associated

with anorexia nervosa are widespread and profound. First and foremost is amenorrhea which is now one of the diagnostic criteria for anorexia nervosa. It is due in part to low levels of plasma luteinizing hormone (LH) and follicle-stimulating hormone (FSH), despite low estrogen levels [23]. Further, there is a lack of the normal variation in LH secretion. Instead there is reversion to prepubertal state characterized by a blunted response of LH to gonadotropin releasing hormone (GnRH) [24]. This type of secretory pattern is unable to properly maintain normal menstrual function resulting in amenorrhea.

It is clear that many of the endocrine changes of anorexia nervosa represent adaptive responses to malnutrition. The aforementioned reproductive changes observed in anorexia nervosa are indeed associated with the expected reduction in fertility during the severe stages of this illness. Changes in the ovary in the form of multiple small follicles instead of one dominant cyst may also contribute to the infertility, when combined with diminished uterine volumes and other atrophic changes [25]. One other issue to consider in this regard is that even if patients with anorexia nervosa do conceive, the outlook may still be grim. Low birth weight babies and an increased incidence of spontaneous abortions, congenital malformations, perinatal mortality, together with ineffective parenting have been described [26, 27].

In addition to the reproductive changes, there are other endocrine abnormalities which also suggest a global state of hypothalamic dysfunction in anorexia nervosa. Hypercortisolism, despite normal levels of adrenocorticotropic hormone, have been described [28]. This is due to decreased metabolic clearance of cortisol with increasing levels being associated with the degree of weight loss. This can be viewed, at least partly, as a protective mechanism ensuring the production of glucose from alternative sites [29]. Lack of suppression by dexamethane has likewise been described [30].

There are also abnormalities in thyroid function. The lowered triiodothyronine (T_3) levels, low thyroxin levels (T_4) and elevated reverse T_3 , characteristic of the euthyroid sick syndrome, are found in most anorexic patients [31]. Again, this may simply reflect a protective mechanism to conserve precious calories, and thus, thyroid hormone replacement is certainly not indicated.

Lastly, anorexia nervosa is associated with impaired release of vasopressin consistent with partial diabetes insipidus. It is due to a neurogenic type defect since anorexics do concentrate their urine when given vasopressin [32]. This increased urine output state affects 40% of anorexics and is reversible with weight gain.

In addition to the aforementioned hypothalamic endocrine disturbances another serious endocrine complication of anorexia nervosa is profound osteopenia [21]. This is especially disconcerting since the most common age of onset of anorexia corresponds to the time period wherein maximum skeletal growth and mineralization normally occur. The key clinical question is thus what are the long-term health consequences of developing anorexia nervosa during this critical period of bone formation. Although it was thought that the amenorrhea experienced by

most anorectics was devoid of adverse consequences, this thinking was radically changed with the demonstration of lower vertebral bone density in this population [33]. This important study reported that there was no significant change in cortical bone density during more than two years of follow-up even though many of the patients regained weight, took estrogen and calcium supplements, and exercised regularly. This was in contrast to earlier studies which had suggested that bone mass increases with recovery [34]. Additional studies on trabecular bone in women with anorexia nervosa again showed the persistence of osteopenia despite estrogen replacement [35]. Other studies have also highlighted this disparate relationship between cortical and trabecular bone in anorexia nervosa in that anorectic females seem more vulnerable to some degree of irreversible bone loss in trabecular regions despite improved overall status [36]. This pattern is in contrast to postmenopausal osteoporosis in which decreased bone mass is seen in both predominantly cortical as well as trabecular sites. One theory to explain this is that the traditionally active lifestyle of young anorectics attenuates bone loss at appendicular sites [37].

Another body system which is affected by anorexia nervosa is the gastrointestinal tract. As opposed to bulimics who vomit excessively or abuse laxatives, anorectics have less severe gastrointestinal problems. Gastrointestinal transit is known to be prolonged in patients with anorexia, affecting up to 80% of patients [38]. Alterations in antral motility and gastric atrophy are thought to be responsible for these problems. Symptoms such as postprandial gastric fullness and discomfort are frequently reported, and may lead to a viscous cycle by provoking vomiting to relieve the discomfort noted during refeeding. Rarely, disastrous consequences occur due to marked dilatation of the stomach and gastric rupture [39]. Small bowel transit time is also prolonged in patients with anorexia nervosa [40].

Other consequences of prolonged starvation include chronic constipation due to a lack of oral intake and reflex hypofunctioning of the colon [41]. Fecal impaction can also occur in anorectic patients with very poor oral intake [42]. Inattentiveness to these complaints on the part of the care provider may markedly interfere with nutritional rehabilitation due to lack of alleviation of their distress [43]. In general, these symptoms all abate with judicious nutritional rehabilitation, adequate fluid intake, minimal increases in dietary fiber and patience [44].

Medical complications of anorexia nervosa also involve the central nervous system. It has been noted that during the course of their illness, these patients demonstrate cerebral atrophy, coupled with loss of brain volume [45]. Recent studies provide clear evidence that nearly all patients with anorexia nervosa show significant reversibility toward normal brain volumes upon weight normalization [46]. Generalized muscle weakness is the most common neurologic complaint seen in anorexia nervosa patients [47].

Dermatologic associations of anorexia nervosa are common, benign, and completely reversible with weight gain. Dry scaly skin, brittle hair and nails, and an increased lanugo-like body hair on the back, arms, legs, and side of the face are commonly seen [48]. It is important to emphasize to

female anorectics that this hair growth is not a sign of virilization, but rather an adaptive mechanism to conserve body heat.

A frequently mentioned association with anorexia nervosa is that of elevated serum cholesterol levels. The larger body of evidence available for anorexia nervosa suggests that the hypercholesterolemia that occurs in this disorder is characterized by an increase in the low-density lipoprotein (LDL) fraction alone. However, many of these studies are rather old. Recent data suggests that much of the total elevation is due to high density lipoprotein (HDL) levels [49].

Lastly, there are significant hematological changes in anorexia nervosa. Serous fat atrophy of the bone marrow with pancytopenia has been reported in several patients with anorexia nervosa [50]. There is dramatic reversal following nutritional support. Isolated leukopenia, and anemia of the normocytic or macrocytic types, have also been commonly noted [51].

While reports regarding immune status in anorexia nervosa are inconsistent, these patients are known to underreport and conceal symptoms. Therefore, given the lack of traditional signs of infection, namely leukocytosis, a high sedimentation rate and fever, extra vigilance is necessary when evaluating anorectics for the possible presence of an infection. T-cell abnormalities, low complement levels and granulocyte functional abnormalities have also been reported [52]. However, cytofluorometric study of immune function did not show significant alterations or impairment of the immune system [53]. Older studies also failed to show an increased incidence of infection [54].

REFEEDING

Clearly, the standard of care when treating anorexia nervosa is to utilize a structured oral refeeding program for the vast majority of these patients during their recovery. This has often been referred to as staged oral refeeding, and entails a slow progressive increase in the daily oral intake of calories. Generally, changes in the caloric intake are made every 3-4 days to achieve a 2-3 pound weight gain per week while on an inpatient unit and 1-2 pounds as an outpatient. However, some patients find this to be too difficult. This may be attributable to the delayed gastric emptying seen in anorexia nervosa. Oral refeeding, especially in the early stages of a refeeding program, may cause gastric distention, abdominal pain and intense psychological distress and preclude weight restoration. Enteral (nasogastric) refeeding is occasionally utilized for more refractory cases but may be viewed as aversive and impractical. Although some programs may have successfully utilized supplemental nocturnal nasogastric refeeding to augment weight gain, even this intervention is felt to be aversive by some patients and is associated with minor complications [55]. Nasogastric refeeding may also be viewed as a form of forced feeding with all of its attendant complex legal and ethical issues. There is however a distinct paucity of solid data with regard to the role of nasogastric refeeding in anorexia nervosa. One retrospective self-report study demonstrated the whole gamut of sentiments in regard to this mode of refeeding from decidedly negative feelings to fairly positive [56]. There has

never been a randomized head to head comparison of parenteral versus enteral nutrition in patients with severe anorexia nervosa. Clinical outcome data are available in other medical illnesses wherein nutritional support is a key determinant of outcome such as in surgically-treated trauma patients [57]. Similarly, there are some data in acute pancreatitis. However the results have been mixed. A recent meta-analysis in acute pancreatitis favored enteral nutrition over parenteral nutrition [58]. However this may be more relevant to pancreatitis wherein the potential issues with immune function and infections have increased importance and thus TPN may be less desirable. In contrast in anorexia nervosa where these complications are less inherent, TPN may be well suited as a tool for weight restoration.

TPN

Thus, when it is clinically indicated, total parenteral nutrition (TPN) may offer a desperately needed mode of refeeding for a small segment of patients who are severely and chronically afflicted with anorexia nervosa. This may be of even greater importance since patients with severe anorexia nervosa whose weight on discharge from the hospital was more than 10% below ideal body weight have a more guarded prognosis. It is therefore worthwhile to be familiar with the specifics of TPN in regard to anorexia nervosa.

In general the use of TPN should not be considered for the very short-term. Rather, TPN is to be administered for a number of weeks, and even months, to achieve weight restoration. It will therefore be necessary to have a central line in place. There are two types of central venous catheters. One type is inserted percutaneously and has the advantages of relative ease of insertion, low risk of complications and good patient tolerance [59, 60]. Examples of this type of catheter are the peripherally inserted central catheter (PICC) and the Hohn catheter. The second type of central venous catheter is surgically tunneled under the skin. The tunneled catheters have a portion exiting the skin and a Dacron cuff just inside the exit site. These devices are more durable and can be used for longer periods than the percutaneous ones, even up to one year. In general, rates of infection with tunneled catheters are lower than those reported with the use on nontunneled catheters [61, 62]. Examples of tunneled catheters include the Hickman, Broviac, Groshong and Quinton catheters.

It is estimated that more than 15% of patients who receive central venous catheters have some form of complications from them. The most common types of complications associated with central venous catheters are infectious, which occur in 5 to 26% of patients, thrombotic in 2 to 26%, and mechanical in 5 to 19% [63-67]. Infectious complications can be divided into three basic types: catheter colonization, catheter-related bloodstream infection and exit-site infection. Although exit-site infections are often amenable to treatment with antibiotics, and do not absolutely necessitate catheter removal, most other catheter-related infections require removal of the central lines along with antibiotics to optimally treat. The recent development of anti-microbial impregnated catheters has been shown to lower the rate of catheter-related bloodstream infections [66,

68]. Thrombotic complications are fairly common and several studies have shown that subclavian venous catheterization as opposed to internal and external jugular vein catheterization, carries the lowest risk of catheter-related thrombosis [63, 69]. Often this also necessitates catheter removal. The use of lytics, such as urokinase, may be successful in reestablishing flow through these catheters and obviate the need for removal. The most common serious mechanical complications of central venous catheterizations are arterial puncture, hematoma and pneumothorax [70].

REFEEDING SYNDROME

From the outset once the decision has been judiciously made to utilize TPN, it must be initiated with cautious restraint at a rate which will give only 600-800 Kcal/day for the first few days. This is in order to avoid a serious condition known as the refeeding syndrome [71, 72]. It is now clear that this syndrome encompasses the ramifications of many different interactions and can occur in all malnourished people who are being refeed with either oral, enteral, or parenteral nutrition. The refeeding syndrome was first described in survivors of World War II concentration camps. After having survived years of horrific conditions, these people died of heart failure, and seizures within a few days of being liberated. Their deaths are attributed to being fed highly caloric foods by their well-intentioned liberators in quantities which overwhelmed their tenuous cardiac reserve.

The causes of this sobering syndrome are multifactorial. A main cause is the potentiation of starvation-induced hypophosphatemia after the ingestion of foods high in glucose content. The glucose load suppresses gluconeogenesis and increases insulin release which drives the uptake of glucose, phosphorous and potassium into cells. This in turn results in widespread abnormalities at the cellular level due to depletion of adenosine triphosphate (ATP). As a result thereof, decreased myocardial contractility and congestive heart failure occur [73]. Refeeding-induced hypophosphatemia can also result in respiratory failure. This is thought to be due to a reduction in available ATP, which is needed to enhance diaphragmatic contractility. Previously, it has been demonstrated that respiratory muscle function is severely depressed in patients with hypophosphatemia who are being mechanically ventilated [74]. Other sequelae of hypophosphatemia include red and white blood cell dysfunction, rhabdomyolysis, seizures, and muscle weakness.

Other factors involved in the refeeding syndrome are hypokalemia and hypomagnesemia. During nutritional restoration, these two electrolytes are deposited in newly synthesized cells, resulting in a concomitant fall in their serum levels. This can also cause cardiac arrhythmias and dysfunction, skeletal muscle weakness, seizures and acid-base disorders.

In addition to the electrolyte causes, there is also an independent cardiac abnormality that is involved in the evolution of this dangerous syndrome. In 1945, Keys demonstrated in a group of conscientious objectors, that there is a significant decrease in overall cardiac size with starvation and weight loss [75]. Similar studies in anorectics have shown diminished cardiac output in these patients due

to myofibrillar atrophy [76]. Given the above findings, it is readily understandable how injudicious and overly aggressive nutritional intake might strain the atrophic heart and result in congestive heart failure. It is worth noting that the diminution in heart size and cardiac output are generally reversible over the course of a few weeks while the patient is being refeed.

To prevent this syndrome from developing, blood chemistry values must be followed closely, especially during the first 2 weeks of nutrition repletion. It is prudent to assiduously check blood chemistry values, including magnesium, phosphorous, electrolytes, and serum hepatic enzymes, daily for the first 3 days of infusion. If everything remains stable, this may be reduced to twice per week and, after a few weeks of treatment, to a weekly schedule. Frequently, phosphorous supplements must be given to replenish phosphorous levels. If the phosphorous level is only mildly low (between 1.8 meq/L – 2.2 meq/L), it can be restored using 0.08 mmole/kg of a phosphorus preparation. If however the serum level is more severely low, the calculation is based on 0.16 mmole/kg. Both of these dosages should be given four times in twenty-four hours and then the serum level rechecked to guide the need for additional phosphorous [73].

Concomitantly, daily clinical assessments are imperative for the first week or so, with a gradual decrease in the frequency as the patient stabilizes. Specifically, pulse and respiratory rate should be followed for unexpected increases from baseline. Since anorectic patients are generally bradycardic [77-79], increases in the pulse rate even to levels that are not “tachycardic” may indicate a change in the clinical status. Checking for leg edema is also a crucial part of the treatment plan. The development thereof may be a harbinger of the refeeding syndrome and should result in a reduction in the rate of refeeding.

REFEEDING WITH TPN

There are some general guidelines to adhere to while refeeding refractory severe anorectics to prevent untoward side effects (Table 3). This is applicable for all forms of

nutrition. Initially, it is important to ascertain what the daily energy requirements are for the particular patient. This can be accomplished either by estimation using the Harris-Benedict equation or by more precise measurement through indirect calorimetry where resting energy expenditure is calculated from carbon dioxide production and oxygen consumption; studies in critically ill patients have shown that these methods are generally equally reliable [80]. The caloric value obtained must be multiplied by an “activity factor” to determine total daily energy requirements. Generally, this exceeds the basal energy expenditure (BEE) by 10% to 60%, depending on the degree of catabolism [81]. It should rarely ever exceed twice the BEE. Furthermore, the value obtained should not be a starting point, but rather a goal to attain within 2 weeks of initiating nutritional restoration. Often, clinicians should start at or below the BEE requirement for the first few days, and advance slowly by 250-300 Kcal increments every few days to achieve a consistent weight gain of 1-1.5 kg/week.

Weight gain during TPN therapy should not exceed 1-1.5 kg per week. Protein load should not exceed 1.5 to 2.0 g/kg per day, especially in the early stages of refeeding. Ultimately, there should be a maximum of 2 g of protein/kg per day to avoid problems with protein metabolism and renal and hepatic dysfunction. A rate less than one gram will not be sufficient for anabolism. Most TPN solutions contain a mixture of essential and nonessential amino acids in concentrations of 3.5 to 8.5% containing 35 to 85 g/L. There is also a 15% amino acid preparation which allows clinicians the liberty of escalating the number of grams of protein in fluid –restricted patients. Dextrose calories also need to be monitored closely. The general rule for patients being retreated with TPN is not to exceed 7.0 mg/kg per minute [82].

The danger in providing glucose calories in excess of energy requirements is that the body increases the nonoxidative disposal of glucose *via* hepatic lipogenesis. The result of this is the potential development of respiratory distress due to excessive carbon dioxide production and the subsequent need to increase minute ventilation to dispose of the carbon dioxide [83]. In patients with anorexia nervosa,

Table 3. Guidelines for TPN in Anorexia Nervosa

Do	DO NOTs
1. Do restrict usage to refractory patients	1. DO NOT exceed 7.5 mg/kg per minute for carbohydrates
2. DO agree on target weight <i>before</i> starting	2. DO NOT exceed 2.0 g/kg for protein
3. DO check serum chemistries, coagulation parameters, and blood cell count before starting TPN	3. DO NOT exceed 1.5-2.0 kg/wk of weight gain
4. DO initiate TPN at 25 mL/h	4. DO NOT use TPN in anorectics with a history of a recent suicide attempt
5. DO follow serum chemistries regularly	5. DO NOT allow the patient to refuse a daily oral meal plan
6. DO weigh the patient daily for 2 weeks and then biweekly	6. DO NOT insist upon inpatient hospitalization
7. DO require concomitant intensive psychotherapy	

who may have impaired cardiovascular and cardiopulmonary reserve, this can lead to respiratory difficulties. Therefore, a rate of 7 mg of carbohydrate per kilogram of body weight per minute should not be exceeded. Dextrose calories above this level offer no additional benefit to the patient. Dextrose and lipid preparations are the main source of energy substrate. Various concentrations are available in commercially prepared TPN formulas including a 10%, 20%, 50% or 70% concentration of dextrose. The 50% concentration provides 1,700 Kcal/L, whereas the 70% solution provides 2,380 Kcal/L.

Another way of ascertaining the amount of carbohydrate calories to provide is based on the energy to nitrogen ratio. Ideal ratios seem to be 80 to 200 Kcal of carbohydrates per gram of nitrogen [84]. If inadequate energy substrates are given, the patient utilizes amino acids as an energy source. This can also cause problems manifested by marked elevations of the blood urea nitrogen level. Alternatively, a general rule recommended by some nutritionists is to provide 10 to 40% of energy substrates as lipid, and the remaining 60 to 90% as glucose [85].

With regard to lipids, they are prepared as 10 to 20% emulsions providing 550 and 1,100 Kcal per 500 ml. Once again, approximately 10 to 40% of nonprotein calories should be derived from lipid emulsions. An alternative target to aim for is to ultimately give these patients between 60 and 70 non-protein Kcal/kg per day. Fatalities have been reported when amounts greater than 100 Kcal/kg per day were administered [86]. This seemingly high number of calories is necessary because anorectic patients who are regaining weight have abnormally high caloric requirements [87]. This is especially relevant during the later stages of refeeding where daily caloric intake may exceed 4500 Kcal/day to sustain ongoing weight gain.

Resting energy expenditure (REE) is consistently low in severely underweight anorexia nervosa patients compared with normal-weight controls. The decrease in REE is not explained entirely by the reduction in free-fat mass. However it increases substantially and in some instances dramatically with refeeding. Thus, the number of calories needed to gain weight progressively increases. There is even evidence that REE increased disproportionately to weight gain. This physiological finding corroborates the clinical reality that it is often very difficult to refeed patients with severe anorexia nervosa because these aforementioned very large amounts of calories are necessary to achieve sustained weight gain. TPN may thus have a beneficial role for this very specified segment of anorexic patients who are markedly underweight and have failed with the traditional modes of refeeding. It may avert a refractory state in this unfortunate predicament for the patient and their medical provider.

For the first 1-2 weeks after initiation of TPN daily accurate weights should guide the escalation of the TPN rate with changes every 3-4 days in the amount of 200-300 Kcal to result in the desired rate of weight gain. Weighing these patients can evoke intense fear and anxiety as well as attempts to mislead the treating team. It is necessary to have a protocol for this which includes who will do the weighing, when the weighing will occur and whether or not the patient will know their weight [88]. Given the fact that the usage of

TPN will be reserved for the most severe anorectic patients, this mode of refeeding should be initiated as an inpatient in a setting where cardiac monitoring and qualified medical oversight is available on a daily basis to guide weight restoration and to monitor for the development of side-effects. As the patient stabilizes, begins to consistently gain weight and their clinical and metabolic situation stabilizes, it is reasonable to transition the patient to a less medicalized treatment environment including home for continuation of TPN and ongoing intensive psychiatric care.

Although there is no definitive recommendation for the duration of TPN therapy, most would insist on recovery to between 90% to 100% of ideal body weight before cessation of the TPN. The eating disorder guidelines of the American Psychiatric Association certainly are consistent with this sentiment [89]. There are controlled studies which have demonstrated that less relapses occur if these goals are promoted and attained as opposed to discontinuing weight restoration at a weight below this target [90-93]. This seems especially applicable to the usage of TPN wherein the inherent risks and complications are higher.

In summary, anorexia nervosa has a guarded prognosis. Consistent risk factors for this less than desirable outcome include weight that is a larger percentage below ideal body weight and a longer duration of illness. The decision to utilize TPN for a very limited, well-defined segment of these patients may indeed be life saving and offers an alternative to anorectic patients who have repeatedly failed to overcome this dangerous chronic illness.

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