Clinical Medicine Insights: Case Reports

CASE REPORT

Metabolic and Nutritional Needs to Normalize Body Mass Index by Doubling the Admission Body Weight in Severe Anorexia Nervosa

Maria Gabriella Gentile, Chiara Lessa and Marina Cattaneo

Eating Disorders Unit, Niguarda Hospital, Milan Italy.
Corresponding author email: mariagabriella.gentile@ospedaleniguarda.it

Abstract: Anorexia nervosa exhibits one of the highest death rates among psychiatric patients and a relevant fraction of it is derived from undernutrition. Nutritional and medical treatment of extreme undernutrition present two very complex and conflicting tasks: (1) to avoid "refeeding syndrome" caused by a too fast correction of malnutrition; and (2) to avoid "underfeeding" caused by a too cautious refeeding. To obtain optimal treatment results, the caloric intake should be planned starting with indirect calorimetry measurements and electrolyte abnormalities accurately controlled and treated. This article reports the case of an anorexia nervosa young female affected by extreme undernutrition (BMI 9.6 kg/m^2) who doubled her admission body weight (from 22.5 kg to 44 kg) in a reasonable time with the use of enteral tube feeding for gradual correction of undernutrition. Refeeding syndrome was avoided through a specialized and flexible program according to clinical, laboratory, and physiological findings.

Keywords: extreme undernutrition, anorexia nervosa, hypophosphatemia, refeeding syndrome

Clinical Medicine Insights: Case Reports 2013:6 51–56

doi: 10.4137/CCRep.S11471

This article is available from http://www.la-press.com.

Introduction

Anorexia nervosa patients are affected by self imposed chronic starvation. According to the degree of malnutrition, the clinical findings reveal loss of subcutaneous fat and muscle, as well as marked changes in body spaces and in body masses and composition. If caloric deficiency is severe and prolonged, adults can lose up half of their body weight and body mass index could decrease to 13 kg/m^2 or less.

Severe undernutrition, even when inflammation is absent, affects every area of the body including cardiovascular, respiratory, nervous, digestive, and immune systems in addition to muscle, blood, and metabolism. As a consequence, the patients present hemodynamic instability, severe volume derangement, electrolytic disturbances, hypoglycemia, hypothermia, and bone marrow depression.[1–4]

During starvation the body tries to compensate for the lack of energy through changes in metabolism regulation with a reduction of basal metabolic rate. A shift from carbohydrate metabolism to fat and protein catabolism occurs to provide glucose and ketones for energy; there is therefore a loss of lean body mass, which affects major organs. There is also a marked loss of electrolytes, including phosphate, potassium, and magnesium primarily from intracellular compartments.

Moreover, the patient is put at risk of refeeding syndrome, ie, metabolic and clinical changes caused by a too fast and/or unbalanced nutritional restoration, with which the deranged bodily systems cannot cope. The main hallmarks of refeeding syndrome are: salt and water retention that may lead to edema and heart failure (possibly worsened by cardiac atrophy), hypophosphatemia, hypokalemia and hypomagnesaemia (due to profound derangement of cellular processes), and depletion of vitamins as B1, B6 etc, which can lead to neurologic damage and dysfunction.[5–8]

Nutritional support in a seriously undernourished patient has the 5 following main objectives: (1) to prevent heart and respiratory failure; (2) to contrast or avert metabolic complications; (3) to restore lean body mass; (4) to preserve or restore immune function; and (5) to attenuate oxidative cellular injury and metabolic response to stress or starvation.

Nearly always, refeeding of severely malnourished patients involves two very complex and conflicting tasks: (1) to avoid "refeeding syndrome" caused by a too fast correction of malnutrition; and (2) to avoid "underfeeding" caused by a too slow/cautious nutritional restoration.

The open question until now is how slowly these kinds of patients have to be refed and how many kcal/kg/day we are allowed to provide to them. There are still some disagreements among researchers. Some recommend small amounts such as 10 kcal/kg/day[5–10] or similar amounts[11] to prevent refeeding syndrome. Others believe that the "start low, advance low" strategy can be questioned.[12–14] The Marsipan's report, recently published by the Royal College of Physicians, states that this issue has not been settled.[15]

Here we describe the manner by which an anorexia nervosa patient with extreme malnutrition (BMI about 9.6 kg/m^2), admitted to our Eating Disorder Unit, doubled her body weight within a reasonable time frame without refeeding syndrome signs or complaints, following a specialized nutritional program.

Case Presentation

A 24 years old single female with extreme undernutrition caused by dietary restriction and over-exercise pursued over the 12 previous months, was referred to our inpatient Eating Disorder Unit. As the only daughter of two employees, she was attending a university course and, at age 23, she started to reduce food intake and to increase physical activity to lose body weight, developing an anorexia nervosa disease.

At time of admission (November 2011) examination showed weight of 22.5 Kg, height of 1.53 cm, and BMI of 9.6 kg/m^2. Her heart rate was 48 bpm, blood pressure was 75/40 mmHg, and oral temperature was 36.1 °C. She appeared well oriented in space and time, although nervous and tense as well. Modest ankle edema was present.

Initial laboratory investigations revealed an increased level of hepatic enzymes (aspartate aminotransferase 226 u/L, alanine aminotransferase 276 u/L, γ-glutamyl transferase 63 u/L), a light hypoproteinemia (serum protein 6.1 g/dL), a reduction of platelets (94 10^ g/L), and euthyroid sick syndrome, ie, abnormal findings of thyroid function tests in a setting of no thyroidal illness (FT3 0.9 pg/mL, FT4 6.9 pg/dL).

Serum electrolytes were normal: potassium 4.1 mg/dL, calcium 8.7 mg/dL, phosphate 3.7 mg/dL, magnesium 1.95 mg/dL, zinc 79 mg/dL.

Plasma glucose level was 82 mg/dL. EKG confirmed sinus bradycardia with prolonged QTc of 0.47 seconds. Because of her life-threatening condition, immediate medical support was started with: (a) oral Thiamine and vitamins B (double daily recommended intake); (b) intravenous fluid (10% glucose 20 mL/h); (c) enteral nutrition by nasogastric feeding at low rate (20 mL/hour); and (d) oral and IV phosphate supplements (see Table 1).

To avoid the risk of over feeding (ie, refeeding syndrome) and to avoid further nutritional and metabolic deterioration, the resting metabolic rate (REE) was measured upon admittance through indirect calorimetric measurement, to establish the caloric intake level (Fig. 1).

Her weight was monitored daily. Her bed rest was strictly organized and monitored. To avoid fluid overload and in order to reduce gastric discomfort, a commercially polymeric, lactose-free, gluten-free, high caloric (2 kcal/mL), high nitrogen (17% kcal intake) completely fluid formula was chosen. Oral fluids were restricted to 1000 mL/day for the first month, and progressively increased to 1500 mL/day.

Nasogastric tube feeding was continuously delivered over 24/h daily, using feeding pumps also to reduce gastric discomfort. The amount of caloric intake was gradually increased according to clinical results (starting from the increase of body weight) and according to the findings of REE's measures taken every month in the first 120 days (Fig. 1).

Our strategy was to improve REE by enteral nutrition (EN) feeding and to commit the duty of anabolic rebuilding increasing amounts of oral feeding. Nasogastric enteral feeding was stopped after 75 days of treatment. For the subsequent 45 days, oral diet was enhanced with oral liquid supplements. To prevent hypophosphatemia, it is not sufficient to evaluate the level of phosphate before starting nutritional restoration. It is also necessary to assess the serum level frequently.[16] For this reason, during the refeeding period, almost every day in the first weeks, her electrolytes, particularly plasma phosphate, were carefully checked and the amount of supplementation was modulated. During the first two weeks it was necessary to supplement approximately 5000–6000 mg/day of phosphate to prevent and/or contrast hypophosphatemia.

Dietitians encouraged, not forced, the patient to start eating and every meal was supervised by

Table 1. Nutritional treatment of an anorexia nervosa patient with extreme undernutrition.

Days		Proteins/g/d		Lipids/g/d		Carbohydrates/ g/d		Kcal/d			Phosphate/mg/d				Tot/ phosphate/d
From	To	OD	OD + EN	OD	OD + EN	OD	OD + EN	OD	EN	OD + EN	OD	EN	KPHOS	NaPhos	
0	1	21.8	41.8	9.0	28.5	24.8	86.3	261	486	747	366	360	1500	2920	5146
1	3	21.8	51.8	9.0	38.2	24.8	117.1	261	729	990	366	540	1500	2920	5326
3	12	45.0	82.8	44.3	73.7	59.8	145.0	803	735	1538	1007	540	1500	1460	4507
12	20	57.8	108.2	58.2	97.4	110.8	224.4	1170	980	2150	1324	720	1500	1095	4639
20	34	59.0	109.4	63.8	103.0	119.8	233.4	1259	980	2239	1394	720	1500	0	3614
34	64	61.5	106.5	88.8	132.3	212.9	319.9	1843	973	2816	1313	600	250	0	2163
64	77	65.8	110.8	91.1	134.6	227.8	334.8	1938	973	2911	1385	480	250	0	2115
77	96	77.0	104.0	89.2	115.3	293.5	357.7	2214	584	2798	1564	360	0	0	1924
96	113	82.7	100.7	97.8	115.2	329.2	372.0	2448	389	2837	1695	240	0	0	1935
113	223	90.0	90.0	106.3	106.3	338.6	338.6	2590	0	2590	1764	0	0	0	1764

Abbreviations: OD, oral diet; EN, enteral nutrition; d, day; KPHOS, oral phosphate supplement; NaPhos, intravenous phosphate supplement; Tot/phosphate/d, diet phosphate plus oral phosphate supplement plus intravenous phosphate supplement.

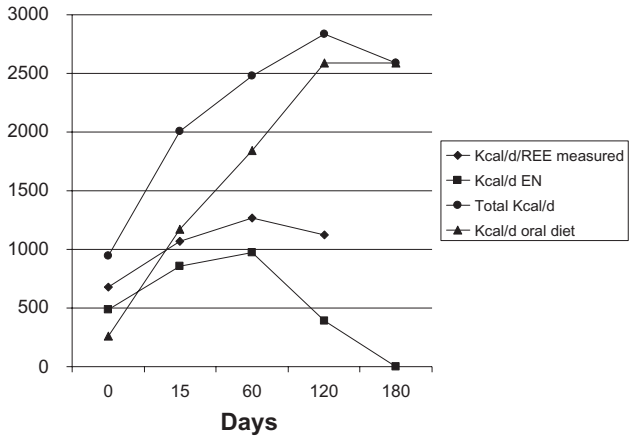

Figure 1. Amount of caloric intake and measured resting metabolic rate during the refeeding period.

dietitians and/or nurses. Oral caloric intake started at time = 0 with 260 kcal/day (protein gr. 22/day). After a week it was increased to 800 kcal/day (protein gr. 45/day), and after a month of care to 1260 kcal/day (protein gr. 59/day). At the end of the second month of treatment the oral caloric intake reached kcal 1850/day (protein gr. 61/day).

Psychotropic medications and psychotherapy helped the patient to control anxiety and obsessive-compulsive symptoms. The psychotropics drugs used were diazepam (starting from 1 mg/day to reach 3 mg/day) and aloperidol (starting from 1 mg/day arriving to 2 mg/day).

In approximately three months the patient's body weight doubled and BMI and all laboratory investigations normalized; to obtain this result the patient needed approximately 46,900 kcal (Fig. 2). We did not observe any major signs and symptoms of refeeding (heart failure, edema, rhabdomyolysis, and encephalopathy).

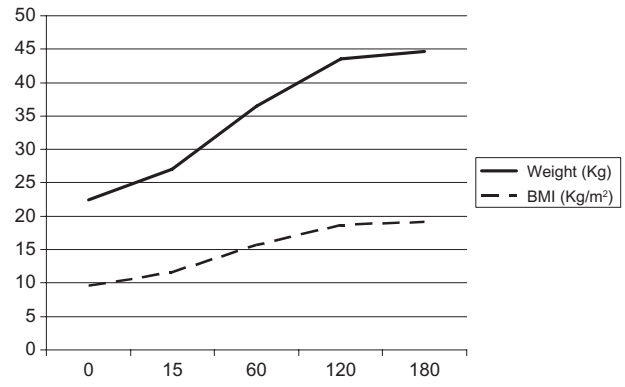

Figure 2. The modification of body weight and BMI during treatment period.

Pressure ulcers were prevented by changing the patient's position and using a special fluidized bed.

After inpatient treatment, the patient agreed to continue the follow up in our unit as day hospital patient. After six months from the beginning of care, the patient's menses resumed with full restoration of hypothalamic-pituitary-ovarian function and body weight was normal. In addition, we may hypothesize that brain abnormalities will be recovered with clinical improvements, however only indirect data in possessed.[17]

Discussion

Patients with anorexia nervosa can be viewed as one of the prototypical populations of refeeding syndrome. Many authors have reported clinical cases with this complication during nutritional rehabilitation, not only in past years, but also recently,[18–22] and some have reported death resulting from it.[11,22,23]

Refeeding syndrome is a potentially fatal complication of nutritional management of severely malnourished patients, but it is an entirely avoidable condition. In order to avoid it we should control: (1) electrolyte abnormalities; and (2) caloric intake. Therefore electrolyte blood levels and body weight modifications should be monitored very closely. In this complex syndrome, hypophosphatemia is characteristically present. This is because when a whole body with chronic depletion of phosphorus experiences a large increase in the uptake and utilization of phosphate in the cells, a deficit of intracellular and extracellular phosphorus can be experienced, with dangerous consequences for every physiological system. When we start to refeed severe malnourished patients, it is mandatory to supplement oral, enteral, and/or intravenous phosphate and other electrolytes such as potassium and magnesium, unless pre-feeding blood levels are high. To set the amount of phosphate, potassium, and magnesium needed, it is necessary to evaluate the serum level daily during the first period of refeeding.[23] We initially prescribed a caloric intake higher than recommended by the other authors, because we believe that such extremely undernourished patients need a supply no less than the measured REE, 30.2 kcal/kg/day in our patient.[14,25] If the amount still recently suggested by some authors,[22] 10 kcal/kg/day, had been started with some major and fatal complications of undernutrition would have very probably appeared.[26–28]

The refeeding syndrome occurs in significantly malnourished patients during the early phase of nutritional replenishment.[29–31] The caloric requirements for severe malnourished anorexic patients is more accurately estimated starting from basal energy expenditure (BEE) as the BEE value basically reflects the energy used when the patient is at rest. As metabolic requirements change during the process of weight restoration, we considered it useful to repeat the calorimetry measurements during refeeding period.

Conclusion

Our results seem to suggest that nutritional rehabilitation accurately performed may prevent the occurrence of refeeding syndrome, even in extremely malnourished patients. In order to succeed in this objective, however, it is necessary to treat high-risk patients in a specialized unit with a multi-disciplinary team, operating with a clearly defined and flexible plan.[9,15,32]

Acknowledgments

We acknowledge the support of the Foban (Obesity, Bulimia, Anorexia Nervosa and Nutrition Foundation), which supported the preparation of this manuscript.

Author Contributions

MGG developed the structure and argument of the paper. MGG and CL were involved in the clinical care of the patient. CL and MC analyzed the data contributed to the writing the manuscript, tables and figures. MGG wrote the draft of manuscript and took part in analysis and interpretation of data. CL and MC contributed to the writing of manuscript and analyzed the data. All authors reviewed and approved of the final manuscript.

Funding

Authors disclose no funding sources.

Competing Interests

Authors disclose no potential conflicts of interests.

Disclosures and Ethics

As a requirement of publication the authors have provided signed confirmation of their compliance with ethical and legal obligations including but not limited to compliance with ICMJE authorship and competing interests guidelines, that the article is neither under consideration for publication nor published elsewhere, of their compliance with legal and ethical guidelines concerning human and animal research participants (if applicable), and that permission has been obtained for reproduction of any copyrighted material. This article was subject to blind, independent, expert peer review. The reviewers reported no competing interests.

References

1. Norman K, Pichard C, Lochs H, Pirlich M. Prognostic impact of disease-related malnutrition. *Clin Nutr*. 2008;27(1):5–15.
2. Winter TA. Cardiac consequences of malnutrition–Ancel keys revisited! *Nutrition*. 2001;17(5):422–3.
3. Henry CI. Body mass index and the limits of human survival. *Eur J Clin Nutr*. 1990;44(4):329–35.
4. Winter TA, Lemmer ER, O'Keefe SJ, Ogden JM. The effect of severe undernutrition, and subsequent refeeding on digestive function in human patients. *Eur J Gastroenterol Hepatol*. 2000;12(2):191–6.
5. Stanga Z, Brunner A, Leuenberger M, et al. Nutrition in clinical practice e the refeeding syndrome: illustrative cases and guidelines for prevention and treatment. *Eur J Clin Nutr*. 2008;62(6):687–94.
6. Marinella MA. Refeeding syndrome and hypophosphatemia. *J Intensive Care Med*. 2005;20(3):155–9.
7. Hearing SD. Refeeding syndrome. *BMJ*. 2004;328(7445):908–9.
8. Mehanna HM, Moledina J, Travis J. Refeeding syndrome: what it is, and how to prevent and treat it. *BMJ*. 2008;336(7659):1495–8.
9. National Institute for Health and Clinical Excellence. Quiche reference guide: Nutrition support in adults. Clinical Guideline 32. *NHS*. 2006.
10. Byrnes MC, Stangenes J. Refeeding in the ICU: an adult and pediatric problem. *Curr Opin Clin Nutr Metab Care*. 2011;14(2):86–192.
11. Vignaud M, Constantin JM, Ruivard M, et al. Refeeding syndrome influences outcome of anorexia nervosa patients in intensive care unit: an observational study. *Crit Care*. 2010;14(5):R172.
12. Garber AK, Michihata N, Hetnal K, Shafer MA, Moscicki AB. A prospective examination of weight gain in hospitalized adolescents with anorexia nervosa on a recommended refeeding protocol. *J Adolesc Health*. 2012;50(1):24–9.
13. Katzman DK. Medical complications in adolescents with anorexia nervosa: A review of the literature. *Int J Eat Disord*. 2005;37 Suppl:S52–9.
14. Gentile MG, Pastorelli P, Ciceri R, et al. Specialized refeeding treatment for anorexia nervosa patients suffering from extreme undernutrition. *Clin Nut*. 2010;29(5):627–32.
15. MARSIPAM Group. MARSIPAN. Management of Really Sick Patients with Anorexia Nervosa. *Royal College of Psychiatrists and Royal College of Physicians*. London; 2010.
16. Gentile MG, Manna GM. Refeeding hypophosphataemia in malnutrition patients: prevention and treatment. *Clin Nutr*. Jun 2012;31(3):429.
17. Van den Eynde F, Suda M, Broadbent H, et al. Structural magnetic resonance imaging in eating disorders: a systematic review of voxel-based morphometry studies. *Eur Eat Disorders Rev*. 2012;20(2):94–105.
18. Leroy S, Gout A, Husson B, De Tournemire R, Tardieu M. Centropontine myelinolysis related to refeeding syndrome in an adolescent suffering from anorexia nervosa. *Neuropediatrics*. 2012;43(3):152–4.
19. Webb GJ, Smith K, Thursby-Pelham F, Smith T, Stroud MA, Da Silva AN. Complications of emergency refeeding in anorexia nervosa: case series and review. *Acute Med*. 2011;10(2):69–76.
20. Norris ML, Pinhas L, Nadeau PO, Katzman DK. Delirium and refeeding syndrome in anorexia nervosa. *Int J Eat Disord*. 2012;45(3):439–42.
21. Altinyazar V, Kiylioglu N, Salkin G. Anorexia nervosa and Wernicke Korsakoff's syndrome: atypical presentation by acute psychosis. *Int J Eat Disord*. 2010;43(8):766–9.

22. Kohn MR, Golden NH, Shenker IR. Cardiac arrest and delirium: presentations of the refeeding syndrome in severely malnourished adolescents with anorexia nervosa. *J Adolesc Health*. 1998;22(3):239–43.
23. Miller SJ. Death resulting from overzealous total parenteral nutrition: the refeeding syndrome revisited. *Nutr Clin Pract*. 2008;23(2): 166–71.
24. Ahmed S, Travis J, Mehanna H. Re-feeding syndrome in head and neck-prevention and management. *Oral Oncol*. 2011;47(9):792–6.
25. Gentile MG. Enteral nutrition for feeding severely underfed patients with anorexia nervosa. *Nutrients*. 2012;4(9):1293–303.
26. Li RL, Sherbet DP, Elsbernd BL, Goldstein JL, Brown MS, Zhao TJ. Profound hypoglycaemia in starved, ghrelin-deficient mice is caused by decreased gluconeogenesis and reversed by lactate or fatty acids. *J Biol Chem*. 2012;287(22):17942–50.
27. Gaudiani JL, Sabel AL, Mascolo M, Mehler PS. Severe anorexia nervosa: outcomes from a medical stabilization unit. *Int J Eat Disord*. 2012;45(1):85–92.
28. De Jager CM, Hoekstra M, Nijsten MW, Lansink AO, Ismael F. Metabolic and neurologic sequelae in a patient with long-stanting anorexia nervosa who presented with septic shock and deep hypoglycemia. *Int J Eat Disord*. 2011;44(8):756–9.
29. Mehler PS, Winkelman AB, Andersen DM, Gaudiani JL. Nutritional Rehabilitation: Practical Guidelines for Refeeding the Anorectic Patient. Hindawi Publishing Corporation Journal of Nutrition and Metabolism. *J Nutr Metab*. 2010;2010:625782.
30. Van Wymelbeke V, Brondel L, Marcel Brun J, Rigaud D. Factors associated with the increase in resting energy expenditure during refeeding in malnourished anorexia nervosa patients. *Am J Clin Nutr*. 2004;80(6):1469–77.
31. Forman-Hoffman VL, Ruffin T, Schultz SK. Basal metabolic rate in anorexia nervosa patients: using appropriate predictive equations during the refeeding process. *Ann Clin Psychiatry*. 2006;18(2):123–7.
32. Practice guideline for the treatment of patients with eating disorders (revision). American Psychiatric Association Work Group on Eating Disorders. *Am J Psychiatry*. Jul 2006;163(Suppl 7):4–54.