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Higher Caloric Intake in Hospitalized Adolescents With Anorexia Nervosa Is Associated With Reduced Length of Stay and No Increased Rate of Refeeding Syndrome

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A B S T R A C T

Purpose: To determine the effect of higher caloric intake on weight gain, length of stay (LOS), and incidence of hypophosphatemia, hypomagnesemia, and hypokalemia in adolescents hospitalized with anorexia nervosa.

Methods: Electronic medical records of all subjects 10–21 years of age with anorexia nervosa, first admitted to a tertiary children's hospital from Jan 2007 to Dec 2011, were retrospectively reviewed. Demographic factors, anthropometric measures, incidence of hypophosphatemia (≤3.0 mg/dL), hypomagnesemia (≤1.7 mg/dL), and hypokalemia (≤3.5 mEq/L), and daily change in percent median body mass index (BMI) (%mBMI) from baseline were recorded. Subjects started on higher-calorie diets (≥1,400 kcal/d) were compared with those started on lower-calorie diets (<1,400 kcal/d).

Results: A total of 310 subjects met eligibility criteria (age, 16.1 ± 2.3 years; 88.4% female, 78.5 ± 8.3 %mBMI), including 88 in the lower-calorie group (1,163 ± 107 kcal/d; range, 720–1,320 kcal/d) and 222 in the higher-calorie group (1,557 ± 265 kcal/d; range, 1,400–2,800 kcal/d). Neither group had initial weight loss. The %mBMI increased significantly ($p < .001$) from baseline by day 1 in the higher-calorie group and day 2 in the lower-calorie group. Compared with the lower-calorie group, the higher-calorie group had reduced LOS (13.0 ± 7.3 days versus 16.6 ± 9.0 days; $p < .0001$), but the groups did not differ in rate of change in %mBMI ($p = .50$) or rates of hypophosphatemia ($p = .49$), hypomagnesemia ($p = 1.0$), or hypokalemia ($p = .35$). Hypophosphatemia was associated with %mBMI on admission ($p = .004$) but not caloric intake ($p = .14$).

Conclusions: A higher caloric diet on admission is associated with reduced LOS, but not increased rate of weight gain or rates of hypophosphatemia, hypomagnesemia, or hypokalemia. Refeeding hypophosphatemia depends on the degree of malnutrition but not prescribed caloric intake, within the range studied.

IMPLICATIONS AND CONTRIBUTION

In adolescents hospitalized with anorexia nervosa, commencing refeeding with 1,400–2,000 kcal/d is associated with reduced length of stay and no increased rates of hypophosphatemia, hypomagnesemia, or hypokalemia, compared with starting on <1,400 kcal/d. Refeeding hypophosphatemia depends on the degree of malnutrition but not prescribed caloric intake. Concerns about refeeding syndrome should not limit amount of calories prescribed, within the range studied.

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Hospitalized adolescents with anorexia nervosa (AN) are frequently started on low-calorie diets, based on national and international guidelines, because of concerns about refeeding syndrome [1–3]. The refeeding syndrome is a life-threatening constellation of clinical and metabolic changes induced by refeeding a malnourished patient, and is most likely to occur during the first week of refeeding. Those <70% of expected body weight are at particular risk [4,5]. The clinical features of the refeeding syndrome reflect cardiovascular, hematologic, respiratory, and neuromuscular compromise including arrhythmias, cardiac failure, hemolytic anemia, acute respiratory failure, seizures, coma, and sudden death [6,7]. Multiple case reports have described refeeding syndrome in AN [4,8–15]. Hypophosphatemia is the biochemical hallmark of the syndrome [4,6,7], but hypomagnesemia and hypokalemia may also contribute to the clinical consequences. Early detection and correction of these electrolyte abnormalities can help avert the full clinical syndrome [5,16,17].

Weight gain is an important early component of the treatment of AN, and is necessary to reverse the medical complications and enable effective psychological intervention. Hypocaloric diets can be associated with initial weight loss and prolonged length of stay (LOS). Garber et al. [18] recently found that starting patients on a diet of 1,200 kcal/d was associated with initial weight loss in 83% of subjects and significant weight gain was achieved only after 8 days of hospitalization. They found that prescribing higher calories at baseline was significantly associated with faster weight gain and shorter hospitalization. By "starting low and going slow," both the amount and the rapidity of weight gain may be compromised.

Whereas initial weight loss during nutritional rehabilitation of malnourished patients is well known [19,20], the safety of more aggressive refeeding protocols has not been well studied. The risk of developing the refeeding syndrome needs to be balanced against the benefits of more rapid weight gain. Before national recommendations are revised, we need scientific evidence to demonstrate the safety and efficacy of more aggressive protocols. Such studies should include a large number of participants, and should specifically include subjects at highest risk for developing the refeeding syndrome: those <70% expected body weight.

The aim of the present study was to determine the effect of higher caloric intake on daily weight gain, LOS, and incidence of hypophosphatemia, hypomagnesemia, and hypokalemia in a large sample of hospitalized adolescents with AN, admitted to a tertiary children's hospital for medical instability. We hypothesized that higher caloric intake would increase rate of weight gain and reduce LOS, and would not be associated with increased incidence of hypophosphatemia, hypomagnesemia, or hypokalemia.

Methods

Study population

Eligible subjects were adolescents aged 10–21 years with AN admitted to Lucile Packard Children's Hospital inpatient eating disorders unit for medical stabilization, whose first admission occurred between January 2007 and December 2011. A child psychiatrist made the diagnosis of AN on presentation by according to the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition [21]. Criteria for admission to the unit include one or more of the following: severe malnutrition (<75% expected body weight), vital sign instability, (heart rate <50 beats/minute during the day or 45 beats/minute at night), hypotension <90/45 mm Hg, hypothermia <36.3°C, orthostatic changes in pulse and blood pressure, dehydration, electrocardiographic abnormalities, or electrolyte disturbances, according to published national guidelines [1,22,23]. Patients with bulimia nervosa or eating disorder not otherwise specified were excluded. For subjects who were readmitted during the study period, only the first admission was included, to ensure that the response to refeeding analyzed in this study would not reflect prior medical interventions. Subjects who were transferred from another facility after nutritional rehabilitation had already been initiated, those who signed out against medical advice before they were medically stable, and those requiring nasogastric feeding were excluded.

Study design

Electronic medical records of eligible subjects with AN were retrospectively reviewed. Duration of illness, rate of weight loss, demographic factors (age, race, and sex), anthropometric measures (height and daily weight), and the presence or absence of hypophosphatemia (≤3.0 mg/dL), hypomagnesemia (≤1.7 mg/dL), and hypokalemia (≤3.5mEq/L) were recorded. Duration of illness was ascertained from the history and physical performed by the admitting physician using a standardized template. One investigator (C.K.M.), a registered dietitian, reviewed the recorded 24-hour diet recall obtained by the unit dietitian in an interview with the patient within 24 hours of admission. Prescribed caloric intake on the first day of hospitalization and on the day of discharge were reviewed and recorded by C.K.M.

Body mass index (BMI) was calculated using the formula: BMI = weight in kilograms divided by the square of height in meters. Median BMI (mBMI), the 50th percentile BMI for exact age, was determined using the sex-specific 2000 Centers for Disease Control and Prevention BMI-for-age growth charts for children and adolescents aged 2–20 years (http://www.cdc.gov/growthcharts). Percent median BMI (%mBMI) was calculated by dividing daily BMI by median BMI × 100.

Baseline weight was defined as the weight obtained at 0600 hours on the first full day after admission. For each subject, change in %mBMI was calculated for each day of hospitalization from baseline. Length of stay was defined as the number of days from admission to discharge. Rate of change of %mBMI was calculated by dividing the total percent change in mBMI by the number of days hospitalized. Subjects started on a higher-calorie diet (≥1,400 kcal/d) were compared with those started on lower-calorie diets (<1,400 kcal/d). The reason for selecting this cutoff is that most protocols based on the belief that caloric content predisposes to refeeding syndrome will start patients on <1,400 kcal/d.

The Stanford University Human Subjects Research Committee reviewed the protocol. A waiver of informed consent and a Health Insurance Portability and Accountability Act–compliant waiver of individual authorization were granted. The Stanford University Institutional Review Board approved data collection protocols.

Protocol for refeeding and monitoring of daily weight and electrolytes on our unit

Weight is obtained daily at 0600 hours post-void in a hospital gown only. Three meals and two snacks are prescribed. All meals