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Basal Metabolic Rate in Anorexia Nervosa Patients: Using Appropriate Predictive Equations during the Refeeding Process

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Background. *The refeeding process is a particularly dangerous time for some anorexia nervosa (AN) patients. Great physiologicatress can occur from imposing a large caloric intake on a body dealing with the effects of long-term starvation. Accurate predictive equations of basal metabolic rate (BMR) are needed to ensure AN patients gain weight at a safe rate.*
Methods. *Patients with AN undergoing strictly controlled nutritional rehabilitation on an inpatient unit were examined for changes in BMR via indirect calorimetry. Seven female patients were assessed shortly after inpatient admission. Follow-up measures of weight and BMR were obtained after three weeks of refeeding treatment comprised of approximately 3500 kcal/day.*
Results. *Body mass index (BMI) increased in all subjects from a median 13.7 kg/m2 at baseline to 15.2 kg/m2. BMR also increased from a median of 1000 kcal/day to 1220 kcal/day. The Owens and Mifflin equations were moderately accurate (within 10%) of predicted BMR at baseline and 3-week follow-up, and the Harris-Benedict equation was very accurate (within 2%) at 3-week follow-up only.*
Conclusions. *These results may guide nutritional therapies for AN by demonstrating the suppression of metabolism induced by calorie restriction as well as its relatively prompt rebound to expected values with weight gain. Derivation of accurate predictive equations for use during the early refeeding period is needed.*

Keywords anorexia nervosa, basal metabolic rate, predictive equations, refeeding, eating disorder treatment, weight gain

INTRODUCTION

Anorexia Nervosa (AN) is a complex disorder associated with high rates of mortality and medical and psychiatric comorbidities. Despite extreme emaciation, an individual with AN continues to severely restrict food intake. Starvation is known to adaptively decrease the rate of metabolism as the body attempts to conserve the little energy it obtains, as demonstrated initially in the classic Minnesota starvation studies (1). As the basal metabolic rate (BMR) decreases, it becomes more and more difficult to lose additional weight. This conservation of energy can be overturned, however, with the reintroduction of food and increased energy intake. The refeeding process, however, is a particularly dangerous time for some AN patients due to the physiologic stress that large caloric intake may incur when there has been prolonged acclimation to very low intake.

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Basal metabolic rate (BMR) dictates the absolute calorie requirements of an individual under conditions of rest (normal body and ambient temperature without physical or psychological stress). Resting energy expenditure (REE) is defined less rigorously than BMR since it does not control for temperature or stress, although BMR and REE are used interchangeably. Total energy expenditure (TEE) is defined as the total amount of energy burned per day, and therefore is determined by activity level and resting metabolic rate. One way to estimate BMR and TEE is through indirect calorimetry methods, which are based on oxygen consumption and carbon dioxide production. When indirect calorimetry methods are not feasible or preferable, BMR can be predicted using proposed equations. These formulas typically include a calculation of BMR based on known determinants such as weight, height, and age. The most widely used equation, the Harris-Benedict (H-B) equation (2), calculates BMR for males and females separately due to differing physiologic characteristics and rate of calorie expenditure. Studies also have found that some equations are accurate for adolescent anorexics but not young adult women with AN (3).

Several studies have determined that BMR is significantly lower in anorectic patients as compared to weight-restored AN patients and healthy controls (4). Some hypothesize that the BMR is reduced in AN due to a decrease in lean body mass (LBM) (4), although others suggest that it is related to decreased levels of triiodothyronine (T3) or reduced norepinephrine secretion. Some studies, however, contradict these hypotheses. For example, a study by Obarzanek et al. (5) determined that BMR per kilogram is not significantly different from healthy volunteers on admission, during refeeding, or at target weight and there were not significant correlations between plasma norepinephrine and thryroid hormones and RMR (5). Furthermore, although REE increases during AN treatment, the REE per kg of lean body mass remains unchanged after weight restoration (6).

Previous studies have determined that the H-B equation greatly overestimates BMR in patients with AN prior to refeeding. In a study by Vaisman et al. (7), BMR was reduced to 49% to 91% of the values predicted by the H-B equation in AN patients in the acute phase of illness. During refeeding, however, BMR tends to increase, in part due to anxiety, abdominal pain, physical activity, and/or cigarette smoking (8). Research has determined BMR is lower than predicted by the H-B equations at the beginning of treatment for AN, and that BMR increases significantly during weight gain (6–7,9). In a study by Schebendach et al. (10), mean resting BMR increased significantly in the first two weeks of hospitalization from 72 (+/–11.7) to 83.2 (+/–12.6) percent of predicted value ($p < 0.001$). Krahn et al. (11) concluded that the H-B equation overestimated BMR during the first week of refeeding by 14%, and underestimated in subsequent weeks by 8%, 24%, and 23% (11). The increase in BMR, however, could not totally be explained by the additional body mass gained during treatment.

Accurate prediction of BMR and total energy expenditure in AN patients would be clinically useful in terms of determining the rate and amount of refeeding, particularly given their high risk of mortality. Schwartz and Thompson (12) studied anorexic patients for a mean of 5.3 years and determined a mortality rate of 6%. The mortality rate increases with longer follow-up periods, and has been estimated to be approximately 15–20% for a mean of 15 years (13). While some of these deaths are due to suicide, many are a result of cardiac complications. Refeeding is a vulnerable time for anorexics, as the refeeding syndrome is associated with dramatic aberrations in electrolyte and fluid balance which may incur a risk of adverse events such as cardiac arrhythmias in conjunction with the thermogenic effects of food (14).

Researchers have attempted to create equations that more accurately predict BMR in AN patients, given their special risks of cardiac complications as well as their decreased metabolic rate during starvation. The Schebendach equation was proposed after determining that predicted BMR was significantly lower than measured BMR in patients with acute AN. The Schebendach formula was created by studying 32 patients, all white females with eating disorders, aged 8.3 to 23.8 years. Scalfi et al. (15), however, found that the Schebendach (16) equation underestimated BMR by an average of 362 kJ/day in 86 young women (ages 18–30) with AN, prompting the creation of another set of equations to estimate BMR in AN patients undergoing refeeding. The equation by Owen et al. (17) was based on examining 36 healthy women from a community sample that excluded professional athletes. The equation by Mifflin et al. (18) was derived from 247 healthy, normal and obese females, aged 20–76 years. The purpose of our study is to determine which of the BMR estimation equations most accurately predicts BMR in AN patients prior and during refeeding.

METHODS

Subjects

Seven female patients admitted to the inpatient eating disorders program at the University of Iowa participated in the study. Each participant met DSM-IV diagnostic criteria for Anorexia Nervosa (AN) but no additional primary Axis I diagnosis of major mental illness. Participants ranged in age from 19 years old to 40 years old (mean = 24.3 +/– 7.1). At baseline (before refeeding), the mean BMI at for the sampled participants was 14.4 +/– 1.3 kg/m2 (mean height = 160.9 +/– 8.1 cm; mean weight = 37.3 +/– 3.5 kg). Approval to conduct this study was granted by the University of Iowa's Institutional Review Board. Informed consent was obtained from each study subject in accordance with the University of Iowa IRB standards.

Procedure

The height and weight were obtained by study nurses at baseline (pre-refeeding) and 3 weeks after beginning refeeding (follow-up). The refeeding period consisted of an upward titration of caloric intake as tolerated to a treatment goal of 3500 kcal/day. All participants complied with the program and reached the goal of 3500 kcal. The patients were not permitted to exercise during this time. BMI was calculated at each time point (baseline and follow-up) by dividing weight in kilograms by height in meters squared.

REE was measured by indirect calorimeter (Datex-Ohmeda; Deltatrac) using a computerized flow-through, canopy-gas analyzer system, which was calibrated with a precision gas mixture before each measurement. Samples of inspired and expired air were analyzed for the differences in oxygen concentration by using a paramagnetic differential oxygen sensor and the differences in carbon dioxide by using an infrared carbon dioxide analyzer. The computer processed signals from the gas analyzers; oxygen consumption (VO_2) and carbon dioxide production (VCO_2) were calculated once a minute for 20 minutes. The first 5 minutes were discarded and the mean value of the data for the remaining minutes was used in the calculations. The measurements were made with study subjects reclining in bed immediately upon awakening in the early morning and before any active movements. No oral intake or any physical activity was permitted prior to the metabolic measures. Each subject was asked to recline quietly to acclimate to the environment for 30 minutes prior to the measurements, then was asked to breathe quietly at a normal rate within the hood for 20 minutes.

Predicted BMR was calculated using 10 different equations previously created for estimating BMR in patients with AN. The Harris-Benedict, Schebendach, and Mifflin equations incorporate weight, height, and age into their BMR estimating equations. Three of the Scalfi equations incorporate weight and age into their BMR estimating equations, while the other three Scalfi and the Owen equations incorporate only weight into their BMR estimating equations.

1. Harris-Benedict equation:

$$\begin{aligned}\text{BMR(hb)} = 655 + (9.6 * \text{weight in kg}) + \\ (1.8 * \text{height in cm}) - (4.7 \times \text{age in yrs})\end{aligned}$$

2. Schebendach equation:

$$\begin{aligned}\text{BMR(s)} = (-1435 * 4.186) + \\ (1.84 * \text{Harris-Benedict predicted value})\end{aligned}$$

3. Scalfi equations:

All patients, intercept, weight only:

$$\text{BMR(scl)} = 148.3 + (91.5 * \text{weight})$$

All patients, intercept, both weight and age:

$$\text{BMR(sc2)} = -394.7 + (93.9 * \text{weight}) + (22.2 * \text{age})$$

Young adult patients, intercept, weight only:

$$\text{BMR(sc3)} = 297.7 + (88.7 * \text{weight})$$

All patients, no intercept, weight only:

$$\text{BMR(sc4)} = 95.3 * \text{weight}$$

All patients, no intercept, weight and age:

$$\text{BMR(sc5)} = (87.1 * \text{weight}) + (15.9 * \text{age})$$

Young adult patients, only weight:

$$\text{BMR(sc6)} = 96.3 * \text{weight}$$

4. Owen equation for healthy women:

$$\text{BMR(o)} = 795 + (7.18 * \text{weight})$$

5. Mifflin equation

$$\text{REE(m)} = -161 + (10 * \text{weight}) + (6.25 * \text{height}) - (5 * \text{age})$$

The predicted value resulting from each calculation was compared to the actual measured BMR using the difference between the predicted and measured values divided by the measured value

$$\begin{aligned}&\text{\% Above Actual (measured) BMR} = \\ &\text{BMR(predicted)} - \text{BMR(measured))/BMR (measured)}.\end{aligned}$$

Statistical Analyses

Data are expressed as medians and ranges, given the small sample size.

RESULTS

The BMI significantly increased between baseline (pre-refeeding, median = 13.7 kg/m2) and follow-up (after 3 weeks of refeeding, median = 15.2 kg/m2). The median change in BMI between baseline and 3-week follow-up was 1.7 kg/m2 (range = 1.4–2.3 kg/m2, Sign Test M = 3.5, p = 0.02). Median BMR at baseline (1000 kcal/day) was also significantly lower than median BMR at 3 weeks post refeeding (1220 kcal/day). The median change in BMR was 182 kcal/day (range = 62–334 kcal/day, Sign Test M = 3.5, p = 0.02).

At baseline, none of the 10 equations used to predict BMR closely replicated the BMR measured by indirect calorimetry (see Table 2). The most accurate equation was the Mifflin equation, which overestimated BMR by a median of 5.7%, followed by the Owen equation, which overestimated BMR by a median of 8.9%. The Harris-Benedict equation overestimated BMR by a median of 21.5%, while the Schebendach and Scalfi formulas underestimated BMR by a median ranging from 14.6% to 25.3%.

Table 1 Median Baseline % Above BMR as Predicted by Estimation Equations

Equation used for Estimate	Median % BMR	Minimum % BMR	Maximum % BMR
Harris-Benedict	21.5	0.4	28.7
Schebendach	–25.3	–35.9	–13.6
Owen	8.9	–11.5	15.7
Mifflin	5.7	–5.0	18.4
Scalfi-1	–16.0	–28.2	–3.5
Scalfi-2	–15.8	–27.0	–2.4
Scalfi-3	–14.6	–27.4	–2.7
Scalfi-4	–16.5	–28.3	–3.3
Scalfi-5	–15.0	–27.2	–3.0
Scalfi-6	–15.6	–27.5	–2.3

Table 2 Median Three-week Post Treatment % Above BMR as Predicted by Estimation Equations

Equation used for Estimate	Median % BMR	Minimum % BMR	Maximum % BMR
Harris-Benedict	1.8	–3.4	7.4
Schebendach	–32.0	–40.0	–20.2
Owen	–8.7	–13.6	–5.2
Mifflin	–6.1	–13.4	2.8
Scalfi-1	–18.9	–32.5	–12.8
Scalfi-2	–19.3	–32.3	–8.1
Scalfi-3	–18.2	–31.5	–12.4
Scalfi-4	–18.7	–32.7	–12.2
Scalfi-5	–19.4	–32.0	–11.2
Scalfi-6	–17.9	–32.0	–11.2

At 3 week follow-up, however, the Harris-Benedict equation nearly approximated the BMR measured by indirect calorimetry. Using the H-B equation only overestimated BMR by a median of 1.8%. The Scalfi and Schebendach formulas greatly underestimated post-refeeding BMR (by a median range of 17.9% to 32.0%).

DISCUSSION

This study supports a significant increase in metabolic rate during nutritional rehabilitation for AN. At baseline, the participants, who were patients in the acute phase of AN, had lower than normal BMR as measured using indirect calorimetry methods. Just three weeks subsequent to refeeding, however, the measured BMR of participants returned to near-normal levels.

Although none of the proposed BMR estimation equations accurately predict BMR in the acute phase of AN, the Harris-Benedict equation is reasonably accurate in predicting BMR three weeks following the beginning of the refeeding period. In terms of clinical utility, however, the Owens and Mifflin equations could be considered since both yielded BMR estimates within 10% accuracy of the median actual values for both baseline and follow-up assessment points. Future studies to develop an even more accurate BMR equation for patients with AN entering nutritional rehabilitation are necessary to calculate appropriate caloric requirements. Having an accurate equation to calculate BMR prior to and during refeeding will enable the patient to gain weight appropriately and safely. Even an overestimation of BMR of 21.5% (as was the case of using the Harris-Benedict equation at baseline) is clinically significant when dealing with medically compromised AN patients. Those who are refed too rapidly have a heightened risk of fluid and electrolyte imbalances that can lead to cardiac complications.

The study is not without limitations. The small sample size requires that a large-scale study be conducted to confirm the findings. Also, since the mean age of the sample (24.3 years) is also somewhat older than the mean age found in most treatment settings, the study should be replicated to determine if the findings are generalizable to younger samples. We also were not able to determine if variables (smoking, physical activity, abdominal pain, anxiety levels) recently identified as important predictors of energy expenditure (8) increase during refeeding influenced our outcome variable. More frequent assessments of BMR as well as a longer follow-up period would be beneficial to determine when, during the refeeding process, BMR starts to increase to near-normal levels in AN patients, and whether the increases persist over time. The precision of the measurements, however, and close monitoring of the study conditions lends credibility to our findings.

CONCLUSIONS

This study was motivated by the fact that “refeeding requires an understanding of both baseline requirements and metabolic changes that occur during nutritional rehabilitation” (16). These results may help guide nutritional therapies for anorexia nervosa by demonstrating the suppression of metabolism induced by calorie restriction as well as its relatively prompt rebound to expected values. Understanding the physiology of body processes during the refeeding period is critical in understanding the risks of cardiac-related problems, particularly due to the high potential for mortality during this period.

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