Intensive Care Med (1998) 24: 464–468
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Comparison of measured and predicted energy expenditure in mechanically ventilated children

Received: 27 June 1997
Accepted: 12 February 1998

Part of this work was presented on the 2nd World Congress on Pediatric Intensive Care, June 23–26, Rotterdam, The Netherlands

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Abstract *Objective:* To determine the energy requirements in mechanically ventilated pediatric patients using indirect calorimetry and to compare the results with the predicted metabolic rate.
Design: In 50 mechanically ventilated children with a moderate severity of illness, energy expenditure was measured by indirect calorimetry. Daily caloric intake was recorded for all patients. Total urinary nitrogen excretion was determined in 31 patients.
Results: Although there was a close correlation between the measured total energy expenditure (mTEE) and the predicted basal metabolic rate (pBMR) ($r = 0.93$, $p < 0.001$), Bland–Altman analysis showed lack of agreement between individual mTEE and pBMR values. The ratio of caloric intake/mTEE was significantly higher in the patients with a positive nitrogen balance (1.4 ± 0.07) compared with those with a negative nitrogen balance (0.8 ± 0.1; $p < 0.001$).
Conclusions: Standard prediction equations are not appropriate to calculate the energy needs of critically ill, mechanically ventilated children. Individual measurements of energy expenditure and respiratory quotient by means of indirect calorimetry in combination with nitrogen balance are necessary for matching adequate nutritional support.

Key words Energy expenditure · Indirect calorimetry · Mechanical ventilation · Critical illness · Nitrogen excretion

Introduction

Nutritional support is an essential management aspect of pediatric intensive care patients. Energy requirements of critically ill children were determined by calculation of basal metabolic rate with adjustment for degree of stress [1, 2]. Daily energy expenditure determination in the critical care setting can be performed by indirect calorimetry [3]. Indirect calorimetry is the method by which the metabolic rate is calculated from measurements of oxygen consumption and carbon dioxide production. Use of indirect calorimetry enables the clinician to assess more accurately the patient's caloric energy needs and the patient's ability to utilize nutrient substrates [4]. In this way appropriate feeding regimens for critically ill children can be designed.

Studies of nonventilated children have shown a wide variation of measured resting energy expenditure. It was recommended in these studies that measurement of resting energy expenditure (mREE) should be performed in individual patients instead of using a prediction equation for ensuring adequate nutrition [5, 6]. In only six studies with small numbers of mechanically ventilated children were results of energy expenditure using indirect calorimetry presented (Table 1) [2, 7–11]. In five of these six studies resting energy expenditure was measured, and in one study prolonged measurements of energy expenditure were performed. These studies all showed a wide variation in individual actual energy

Table 1 Study population characteristics (*MEE* measured energy expenditure, *TEE* total EE, *REE* resting EE, *pBMR* predicted basal metabolic rate)

[Reference]	Age group	*n*	Diagnosis	MEE/pBMR (mean ± SEM)	MEE (range)
[7]	5–17 years	9	Head injury	1.19 ± 0.07[a]	–
[8]	5 days–46 months	20	Wide range	1.02 ± 0.07[b]	100–343[b]
[2]	2–18 years	18	13 trauma; 5 other	1.48 ± 0.09[a]	130–336[a]
[9]	2 days–120 months	12	Wide range	–	125–236[a]
[10]	2 months–12 years	26	Open heart surgery	0.96 ± 0.03[a]	126–289[a]
[11]	3 months–10 years	18	Wide range	0.97 ± ?[a]	–
Present study	2 days–13 years	50	Wide range	1.04 ± 0.03[b]	85–270[b]

[a] mREE (kJ/kg per day)
[b] mTEE (kJ/kg per day)

requirements in different diseases and a wide range in the ratio of measured total energy expenditure (mTEE) or mREE to predicted basal metabolic rate (pBMR).

The purpose of this study was to perform measurements of energy expenditure which represent total daily energy expenditure in mechanically ventilated children, in order to get a better insight into actual energy requirements and to compare these measurements with the pBMR, energy intake, and nitrogen balance.

Materials and methods

Patient selection

Patients were eligible for the study when they met the following criteria. (1) Mechanical ventilation with a Servo Ventilator 300 (Siemens-Elema, Solna, Sweden) either with pressure-regulated volume control mode or with volume support mode. (2) A fractional inspired oxygen (FIO_2) of less than 0.60. (3) A tube leakage of less than 10% (considered not to influence the measurement significantly [12]). Tube leakage was determined by comparison of inspired and expired tidal volumes measured by the ventilator, assuming that there were no other leaks in the patient–ventilator circuit. (4) A hemodynamic stable condition indicated by a normal, stable blood pressure according to age within 2 SD [13], and normal renal function expressed by a normal serum creatinine concentration [14].

Severity of illness on the day of measurement was assessed by the Pediatric Risk of Mortality score (PRISM) [15] and Therapeutic Intervention Scoring System (TISS) [16]. The study was approved by the local Ethical Committee and informed consent was obtained from the parents.

Energy expenditure

Oxygen consumption ($\dot{V}O_2$), carbon dioxide production ($\dot{V}CO_2$) and respiratory quotient (RQ) were measured with a previously validated metabolic monitor (Deltatrac I MBM-100 and Deltatrac II MBM-200, Datex Division Instrumentarium, Finland) [17]. All gas measurements were standardized for temperature, barometric pressure, and humidity (STPD). The Deltatrac is an open system indirect calorimetry device. The difference between the inspired and expired oxygen fractions is measured with a fast-response, paramagnetic differential oxygen sensor (OM-101, Datex Instrumentation). The expired CO_2 fraction is measured with an infrared CO_2 sensor. Before each test, the calorimeter was calibrated with a reference gas mixture (95% O_2, 5% CO_2). The accuracy of the Deltatrac was assessed with a butane burner. The mean error of $\dot{V}O_2$ and $\dot{V}CO_2$ obtained in repeated tests was 2.7 ± 0.5 and 3.7 ± 0.6%, respectively. The mean RQ was 0.62 ± 0.01 (RQ of butane 0.615), with a mean error of 2.2 ± 0.4%. Studies were carried out for a period of at least 4 h with a maximum of 24 h. The mean coefficient of variation for measured energy expenditure was 4.6 ± 0.4%.

Measurement results of at least 4 h were considered to represent the total daily energy expenditure [18, 19]. Mean mTEE was calculated using the modified Weir formula [20]: mTEE = 4184 (5.5 $\dot{V}O_2$ + 1.76 $\dot{V}CO_2$); mTEE in kJ/day; $\dot{V}O_2$ in l/min; $\dot{V}CO_2$ in l/min. The respiratory quotient was calculated by dividing $\dot{V}CO_2$/$\dot{V}O_2$. The nonprotein RQ was calculated with the formula: ($\dot{V}CO_2$ – 4.84 N)/($\dot{V}O_2$ – 6.04 N). N is urinary urea nitrogen excretion in g/min. pBMR was calculated from each patient's weight, age, and sex using the appropriate Schofield equations [21].

Caloric intake

The patients were fed enterally and/or parenterally. Enteral feeding was given continuously via a nasoduodenal drip with standard soya-based formula (Nutrilon soya for children ≤ 6 months, Nutrilon soya plus for children 6–12 months, 75% Nutrison soya and 25% water and 4% Fantomalt added for children 1–4 years, 90% Nutrison soya and 10% water and 4% Fantomalt added for children 4–10 years, and Nutrison soya for children > 10 years of age; Nutricia, Zoetermeer, The Netherlands). Parenteral feeding was given either by peripheral infusion or by a central venous line (Intralipid 20%, Pharmacia Upjohn Holland and Aminovenös N-paed 10%, Fresenius, The Netherlands). Fluid and electrolyte intakes were adjusted to individual requirements. Daily caloric intake (subdivided into carbohydrate, protein, and fat) was recorded for all patients. Caloric intake was corrected for extra protein calories from plasma infusions and/or albumin infusions on the day of measurement.

Urinary nitrogen excretion

In 31 patients, urine was collected on the day of measurement and analyzed for urinary urea nitrogen. In the remaining 19 patients, urine was not collected because of logistical problems. In 18/31 pa-

Table 2 Clinical diagnosis of study patients

Diagnosis	Number of patients
Congenital heart defect	15
Sepsis	9
Pneumonia	6
(RS) Bronchiolitis	5
Resection subglottic stenosis	4
Upper airway obstruction	3
Near drowning	2
Leigh's syndrome	1
Pediatric AIDS	1
Cardiomyopathy	1
Status asthmaticus	1
Post-pylorotomy	1
Status epilepticus	1
Total	50

Table 3 Patient characteristics and results of measurements

Patients (n = 50)	Mean ± SEM	Range
Age	25 ± 6 months	2 days–13 years
PRISM	6 ± 1	0–13
TISS	18 ± 1	10–32
Intake (kJ/kg per day)	243 ± 17	22–520
mTEE (kJ/day)	1987 ± 238	640–8678
mTEE (kJ/kg per day)	212 ± 5	85–270
pBMR (kJ/day)	2029 ± 212	590–6903
pBMR (kJ/kg per day)	213 ± 6	98–298
RQ	0.89 ± 0.01	0.77–1.02
TUN (n = 31) (mg/kg per day)	249 ± 22	68–493
N balance (n = 31) (mg/kg per day)	– 4 ± 38	– 471–335

tients, a urinary bladder catheter was in place and urine was collected over a 24-h period. In 13/31 patients, however, a pediatric urine collector was used and urine was collected over a shorter period but over 1 of at least 6 h. This can be used to estimate a 24-h period, but the inconsistency has to be taken into account when interpreting the results.

Total urinary nitrogen excretion (TUN) was defined as 1.25 × urinary urea nitrogen, in order to adjust for the 20% of urinary nitrogen loss as ammonia, creatinine, and uric and amino acids [22]. No correction was made for nitrogen losses through stools, skin, wounds, nasogastric suction, or blood sampling. Nitrogen balance was calculated with the following formula:

Nitrogen balance (mg/kg per day) = (protein intake/6.25) – (urinary urea nitrogen × 1.25).

Statistical analysis

Statistical analyses were performed with a software program (SPSS 7.0 for WINDOWS 95, SPSS Software, Chicago, IL, USA). Results are expressed as mean ± SEM, unless otherwise indicated. For comparisons between groups, the independent samples t-test was used. A p value of 0.05 or less was defined as statistically significant. Pearson's correlation coefficient *(r)* and a Bland–Altman plot were used to evaluate the relationship between mTEE and pBMR [23].

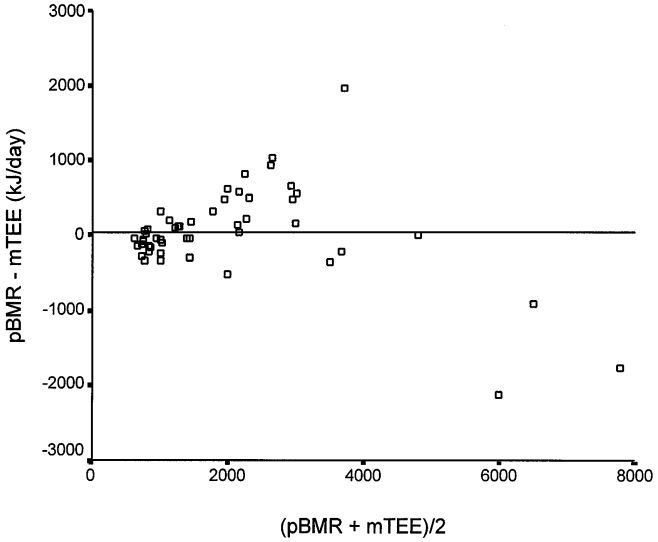

Fig. 1 Bland–Altman plot for mTEE and pBMR

Results

From among the 80 patients who were admitted consecutively from September 1995 to May 1996 to our pediatric intensive care unit (PICU), 30 patients were excluded because they did not fulfill the inclusion criteria. The study group consisted of 50 patients, 28 boys and 22 girls, with a wide range of clinical characteristics (Table 2). The median age was 7 months (2 days–13 years). Median PRISM score was 6 (0–13) and median TISS score was 17 (10–32) (Table 3). All patients were sedated with midazolam and/or morphine and 4 patients with pharmacological muscle paralysis. Five patients received inotropic drugs. There were no known pathological gastrointestinal absorption disturbances. The mean day of measurement after intubation was 5 ± 4 days. Ventilatory characteristics were as follows: mean FIO_2 was 0.35 ± 0.018 and mean tube leakage was 6 ± 1%; 24 patients were on pressure-regulated volume control, 25 on volume support, and 1 was on continuous positive airway pressure. The results of the energy expenditure measurements are shown in Table 3. The correlation coefficient between mTEE and pBMR was $r = 0.93$ ($p < 0.001$). A Bland–Altman plot for mTEE and pBMR shows a wide scatter around the mean (difference from the mean: – 2120 to 1970 kJ/day) (Fig. 1).

Thirty-five patients received enteral nutrition (EN), 7 received only glucose infusion, 6 received total parenteral nutrition (TPN), and 2 received a mixture of EN and TPN. Mean caloric intake was 243 ± 17 kJ/kg per day.

TUN was determined in 31 patients (Table 3). Mean TUN was 249 ± 22 mg/kg per day. The nitrogen balance was positive in 19 patients and negative in 12 patients. The ratio of caloric intake/mTEE was significantly high-

Table 4 Nitrogen balance in relation to ratio of intake/mTEE and nonprotein RQ

	N balance > 0	N balance < 0	*p* value
Patients	19	12	
Intake/mTEE	1.4 ± 0.1	0.8 ± 0.1	< 0.001
Nonprotein RQ	0.90 ± 0.02	0.87 ± 0.02	0.3

er in the patients with a positive nitrogen balance (1.4 ± 0.1 mg/kg per day) compared with those with a negative nitrogen balance (0.8 ± 0.1 mg/kg per day; $p < 0.001$) (Table 4). The actual caloric intake in patients with a positive nitrogen balance was 318 ± 21 versus 163 ± 29 kJ/kg per day for patients with a negative nitrogen balance ($p < 0.001$). There was no significant difference in nonprotein RQ between patients with a positive or negative nitrogen balance. In 6 patients the nonprotein RQ was > 1.0. The carbohydrate intake in 4 of them was 9–10 mg/kg per min, and in the other 2 patients, 4.2 and 7.5 mg/kg per min, respectively.

Discussion

We determined the metabolic and nutritional state of a heterogeneous group of mechanically ventilated PICU patients with different clinical diagnoses. Because of methodological problems (tube leakage, FIO_2 above 0.60, unstable hemodynamics), we were only able to perform energy expenditure measurements on 50 of the 80 mechanically ventilated patients admitted to our PICU in the study period.

As a consequence of these limitations, only patients with a moderate severity of illness in the beginning of disease or patients recovering from a severe illness could be included for indirect calorimetric studies, as indicated by the low PRISM and TISS scores of our patient population.

Total energy expenditure consists mainly of basal metabolic rate, growth, heat loss, and mechanical work. Growth can account for a substantial-proportion of the energy expenditure in children (30–35 %), especially in the first year of life [24]. However, in critically ill, mechanically ventilated children, counter-regulatory hormones could diminish and even stop growth, and mechanical ventilation will reduce the work of breathing [8]. As a result, the total energy which is needed will be lower and resemble basal metabolic rate. So far, there have been only six previous studies on mechanically ventilated children in which TEE or REE was measured by means of indirect calorimetry [2, 7–11]. In five of these studies, there was a correlation between mTEE or mREE and pBMR. These correlations are misleading because of the wide variation in individual measurements. In our study, we also found a wide range of individual measurements. From the wide scatter of the Bland–Altman plot, it becomes obvious that the use of predicted energy expenditure is inappropriate for clinical purposes. Our study showed that the mean coefficient of variation for measured energy expenditure was 4.6 ± 0.4 % compared with a coefficient of variation of 19.4 % for prediction of mREE for an individual as stated by Schofield. This also advocates the use of measured energy expenditure instead of using prediction equations.

Prolonged measurements of energy expenditure, like we did in our study, give a better reflection of total daily energy expenditure. The calorie intake should be based on these measurements rather than on the basal or resting energy expenditure. These prolonged measurements are only possible in clinically stable, sedated patients. To determine resting energy expenditure a shorter period can be used (20–30 min with a steady state of 5 min during which average $\dot{V}O_2$ and $\dot{V}CO_2$ change by less than 10 % and average RQ changes by less than 5 %) [25].

In order to provide an appropriate number of calories, caloric intake should be individualized using mTEE and RQ. In our study, we showed that feeding according to the mTEE could be a guideline because the ratio of caloric intake/mTEE was significantly higher in patients with a positive nitrogen balance (1.4 ± 0.07) compared to those with a negative nitrogen balance (0.8 ± 0.1) ($p < 0.001$). Feeding higher than mTEE is necessary for growth and tissue repair. In our patients with a positive nitrogen balance, the caloric intake exceeded the mTEE by 40 %. However, in the case of enteral feeding, not all of the administered calories will be absorbed; the loss of energy in stools can account for 10–20 % of the total caloric intake [26].

The RQ is the ratio of $\dot{V}CO_2$ to $\dot{V}O_2$ and reflects the percent substrate utilization of fat and carbohydrate in the body. By excluding protein, the nonprotein RQ provides a range of substrate utilization from 0.70 (100 % fat utilization) to 1.0 (100 % glucose utilization). Alcohol or ketone metabolism may reduce the nonprotein RQ below this range to 0.67. Overfeeding with lipogenesis may increase it above this range to 1.3. In our study, 4 patients with a carbohydrate intake of 9–10 mg/kg per min showed an RQ > 1.0, suggesting excessive carbohydrate intake resulting in lipogenesis. A lower carbohydrate intake, however, can also lead to an RQ > 1.0, as was shown in 2 of our patients with a carbohydrate intake of 4.2 and 7.5 mg/kg per min, respectively. There seems to be a maximum carbohydrate oxidation rate and thus a maximal capacity to use carbohydrate as a source of calories in the stressed patient. Beyond this oxidation maximum carbohydrate administration will lead to hyperglycemia, excess of CO_2 (RQ > 1.0) and hepatic steatosis [27, 28]. An excessive amount of carbohydrate will not always lead to an RQ > 1.0, because in the hypermetabolic patient there is still ongoing oxida-

tion of fat for energy, resulting in an RQ < 1.0 [29]. This was the case in 2 of our patients with a carbohydrate intake of 9.8 and 11.4 mg/kg per min and an RQ < 1.0 (0.78 and 0.95, respectively). Thus, the RQ can be used to detect overfeeding, but one should be cautious in using it as such.

In summary, this study shows that in critically ill, mechanically ventilated pediatric patients, although mTEE seemed to resemble pBMR, there was a wide range in the ratio of mTEE to pBMR and lack of agreement. Therefore, it seems not to be appropriate to use a standard prediction equation but to perform individual measurements of energy expenditure and RQ with indirect calorimetry in combination with nitrogen balance for matching adequate nutritional support. Outcome-based studies could give more insight into how optimal nutritional support could be given to mechanically ventilated children in the intensive care setting.

Acknowledgment The authors would like to thank Professor P. J. J. Sauer for his critique on this manuscript.

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