Testing a Novel Method for Measuring Sleeping Metabolic Rate in Neonates

Suzanne S Summer MSc RD, Jesse M Pratt MSc MA, Elizabeth A Koch RRT RPFT, and Jeffrey B Anderson MD MPH

BACKGROUND: Sleeping metabolic rate (SMR) is used as a proxy for basal metabolic rate in infants, when measurement while awake is not practical. Measuring SMR via indirect calorimetry (IC) can be useful for assessing feeding adequacy especially in compromised neonates. Standard IC equipment, including a hood placed over the head, is not designed for the smallest of patients. Our aim was to determine whether a nonstandard smaller hood measures SMR in neonates similarly compared with a standard large hood. METHODS: SMR was measured in healthy neonates (controls) and those born with single-ventricle congenital heart disease (cases). Two measurements were performed: SMR using a standard large hood and SMR using a smaller hood. Time-to-steady state, minute ventilation ($\dot{V}_E$), and fraction of exhaled carbon dioxide ($F_{\bar{E}CO_2}$; an indicator of data quality) were also measured. Primary outcome was SMR using both hoods. Results are stated as median (interquartile range). Spearman's correlations measured association between the small and large hoods. RESULTS: We studied 9 controls and 7 cases. SMR in controls was not different between the small and large hoods (35.7 [15.14] vs 37.8 [7.41] kcal/kg/d, respectively). In cases, SMR with the small hood was significantly greater than that with the large hood (45.5 [4.63] vs 34.2 [8] kcal/kg/d, $P < .02$). $F_{\bar{E}CO_2}$ was significantly higher with the small hood versus the large hood in both groups, and $\dot{V}_E$ was significantly lower with the small hood versus the large hood in controls only. The SMRs with the small and large hoods were significantly correlated in the control group (r = 0.80, $P < .01$). Time-to-steady state was similar in both groups regardless of hood size. CONCLUSIONS: SMR measured with a small hood yields results similar to those measured with a large hood in healthy neonates without affecting testing time or other aspects of the IC procedure. Furthermore, results in compromised infants suggest that a smaller hood may facilitate SMR testing in this population. *Key words: indirect calorimetry; basal metabolic rate; infant; newborn; energy metabolism.*
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Introduction

Meeting the nutritional energy needs of newborns and infants is crucial for optimal growth. Healthy infants require ~110 kcal/kg of body weight in the first month of life to promote normal growth and development.[1,2] Meanwhile, specific energy needs in compromised infants are not defined, yet are higher than those of their healthy

counterparts to fight illness or recover from treatment while still achieving nutritional goals for catch-up growth.[3,4]

While the adequacy of infant feeding can be determined prospectively by regular measurements of length, weight, and head circumference, understanding the energy needs of an individual infant would allow targeted treatment, particularly for those at risk of failure to thrive. Total energy needs for infants are the sum of the basal metabolic rate (BMR), thermic effect of food, and physical activity expenditure, plus energy needed for growth.[1] The BMR, energy required by the human body at rest, is the largest component of the total energy equation.[2] BMR is measured via indirect calorimetry (IC), in which a hood placed over the head of the patient collects and measures respiratory gases (inspired oxygen and expired carbon dioxide) to derive metabolic rate.[5] Standard practice for measuring BMR is to do so while the patient is awake but resting supine. When metabolic rate is measured in infants, sleeping metabolic rate (SMR) has been used as a proxy for BMR because measurement while awake is not typically practical.[6,7] Although metabolic rate has been routinely measured via IC in older children and adults,[8-11] there are limited data in infants and neonates, and devices used to collect respiratory gas exchange can affect results.[12] Today's commercially available IC equipment, including a hood placed over the head for testing, is not designed to capture respiratory gas exchange in very small, very young infants.

The purpose of this study was to evaluate the use of a smaller hood to measure SMR in neonates and to compare metabolic results using small and large hoods to determine whether use of one hood is preferable over the other when measuring SMR in both healthy and compromised infants.

Methods

Design

This was a crossover study using a within-subject design to compare measurement outcomes. This project was part of a larger case-control study investigating energy needs and growth in infants born with complex congenital heart disease (CHD). The study was approved by the Institutional Review Board of Cincinnati Children's Hospital Medical Center.

Subjects

Cases were infants born with hypoplastic left heart syndrome or another variant of single-ventricle CHD. Patients who met inclusion criteria were recruited during their neonatal hospital admission for cardiac evaluation and surgical palliation. Controls were healthy neonates with no known medical problems. Recruitment of controls was

QUICK LOOK

Current knowledge

Indirect calorimetry allows the measurement of caloric requirements to guide nutritional support in at-risk patients. Neonates are a particular challenge for metabolic measurements owing to the lack of specialized equipment and small patient size.

What this paper contributes to our knowledge

The use of an open circuit dilutional system with a modified hood of reduced size and volume was comparable to that with a standard hood. In compromised infants, the smaller hood facilitated testing.

done via advertisement within our hospital and at local private pediatric practices. Informed consent for cases and controls was obtained from parents or legal guardians. All subjects were enrolled in the study and underwent the procedures described here between May and November of 2011.

Test Preparation

Infant controls and at least one parent arrived at the Clinical Translational Research Center of Cincinnati Children's Hospital for their scheduled study visit. Upon arrival, the infant was fed his or her normal meal (formula or breast milk) for that time of day. Next, the infant was kept awake and active for as long as possible after feeding, up to 1 h. The 1-h fasting time was used to allow adequate digestion time for the meal consumed plus time for SMR testing while not encroaching upon the next feeding time. Similar preparations were applied to cases, except these infants were already staying in the hospital for treatment of their heart condition, and testing was done in their hospital room. All cases were under cardiorespiratory monitoring throughout the test period, and a cardiology nurse was available if needed.

Measurement of Sleeping Metabolic Rate

Testing was initiated 1-h post-feeding. SMR was measured via IC using the Vmax Encore indirect calorimeter (CareFusion, San Diego, California). This method uses a ventilated hood placed over the head of the subject to measure oxygen consumption ($\dot{V}_{O_2}$) and carbon dioxide production ($\dot{V}_{CO_2}$), and the Weir equation is used to calculate SMR from these values.[13] The Vmax system uses a dilution pump to control the speed at which these respiratory gases flow into and out of the hood. In adult testing,

Fig. 1. Infant when being tested under both the small hood (left) and the large hood (right). Photographs published with parental permission.

the standard pump flow is 30 L/min, and the lowest flow is 15 L/min. For this study, the system was modified by the inclusion of special software allowing the dilution pump to reach a very low speed (3 L/min), which was necessary for capturing the gases in the tiny breaths of infants. Prior to the start of testing, the Vmax flow sensor and gas analyzer were calibrated. The flow sensor was calibrated using a 3-L syringe, providing a known volume of air at various flows. The analyzer was calibrated against two standard gas mixtures: one containing 16% oxygen ($\pm 0.02\%$) and 4% carbon dioxide ($\pm 0.02\%$) and the other containing 26% oxygen ($\pm 0.02\%$). These calibrations are required to ensure accurate measurements of $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$.

IC was performed two times on each subject using either the standard adult (large) hood or a smaller hood (Superdome, Maxtec, Salt Lake City, Utah) typically used for infant oxygen therapy. The volume of the standard hood is 11.25 L, whereas the small hood holds just 4.8 L. The small hood was not equipped with a drape to block out room air, so we fixed blankets and hand towels snugly around the hood to cover openings. Figure 1 shows the same infant under each hood for size and set-up comparison. $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ were measured for up to 30 min (or until the infant awoke if before 30 min) with each hood. Room environment (lighting, noise, others present) was manipulated to allow the infant to remain asleep as long as possible. Testing with both hoods was usually done back-to-back, except in one case, where the infant did not remain asleep after the first test. In this instance, the two hoods were tested on the infant within the same day following the fasting guidelines described previously each time.

The final SMR for each test was determined from an average of values collected while the infant was in steady state, defined as a minimum of 5 min during which the average $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ both change by $< 10\%$, and the respiratory quotient changes by $< 5\%$.[14] Data from the first 5 min of each test were excluded, as the metabolic rate during this initial phase has been shown to be higher than the rate measured during subsequent minutes.[15]

In addition to SMR, we recorded average steady-state values of the fraction of exhaled carbon dioxide ($F_{\bar{E}CO_2}$).

$F_{\bar{E}CO_2}$ is an indicator of the quality of the data collected during testing and helps determine the speed of the dilution pump. During testing, $F_{\bar{E}CO_2}$ should be maintained between 0.5 and 1.0% (ideally, within the optimal range of 0.7–0.8%); this range allows the proper calculation of the equations for $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ that are used to determine SMR. If $F_{\bar{E}CO_2}$ is low, this could indicate that the breath sample is too diluted under the hood, possibly due to shallow breathing in the infant or the dilution pump flow being too high. If $F_{\bar{E}CO_2}$ is high, this could mean that either the breath sample is not diluted enough or the pump flow is too low and may stimulate increased respirations in the infant. We also measured minute ventilation ($\dot{V}_E$), the volume of gas exhaled per minute, as an indicator of breathing frequency. Finally, time-to-reach steady state was recorded to determine if there is a difference between hoods in this respect.

Data Methods

Data were assessed for normality, and since this assumption was violated, medians and interquartile ranges were computed for time-to-steady state (min), SMR (kcal/kg/d), $F_{\bar{E}CO_2}$ (%), and $\dot{V}_E$ (L/min). For both cases and controls, the Wilcoxon signed rank test was used to test for a difference between the small and large hoods. Spearman's correlations were used to measure the association between the SMRs of the small and large hoods in both cases and controls. A P of $< .05$ indicated a statistically significant result. All analyses were performed using SAS 9.3 (SAS Institute, Cary, North Carolina).

Results

Subjects

Data from the first 20 subjects in the larger cohort study were analyzed. The SMR measurement was successfully obtained using both hoods on 16 subjects (9 controls, 7 cases), and their data were used for our final analysis. Four subjects (3 controls, 1 case) were excluded due to time constraints of the family (2 controls), subject waking up during testing in at least one of the hoods (1 control), and subject going on supplemental oxygen between hoods (1 case).

Sleeping Metabolic Rate, $F_{\bar{E}CO_2}$, and $\dot{V}_E$

Data are presented as median (interquartile range). In healthy controls, SMR was not significantly different between the measurement with the small hood and the large hood (35.7 [15.14] vs 37.8 [7.41] kcal/kg/d, respectively). However, in cases, SMR using the small hood was significantly greater than SMR measured using the large hood

Table 1.   Controls: Median and Individual Results for Age, Weight, and Metabolic Measures

	Age (d)	Weight (kg)	SMR (kcal/kg)		P	$F_{\bar{E}CO_2}$ (%)		P
			Small Hood	Large Hood		Small Hood	Large Hood	
Median (IQR)	26 (14)	4.14 (0.56)	35.7 (15.14)	37.8 (7.41)	.57	0.72 (0.10)	0.65 (0.15)	.01
Control*								
1	22	4.1	50.24	37.80		0.72	0.58	
2	29	2.8	53.93	51.43		0.71	0.55	
3	24	3.98	39.20	45.98		0.83	0.74	
4	25	4.54	35.68	37.22		0.81	0.71	
5	30	4.14	44.44	39.13		0.83	0.76	
6	18	2.95	30.51	41.36		0.65	0.62	
7	35	5.23	18.93	26.77		0.56	0.53	
8	26	4.3	29.30	33.95		0.71	0.73	
9	30	4.7	26.81	28.30		0.81	0.65	

* Results for individual control subjects (1–9)
SMR = sleeping metabolic rate
$F_{\bar{E}CO_2}$ = fraction of exhaled carbon dioxide
IQR = interquartile range

Table 2.   Cases: Median and Individual Results for Age, Weight, and Metabolic Measures

	Age (d)	Weight (kg)	SMR (kcal/kg)		P	$F_{\bar{E}CO_2}$ (%)		P
			Small Hood	Large Hood		Small Hood	Large Hood	
Median (IQR)	17 (14)	3.30 (1.1)	45.5 (4.63)	34.2 (8)	.02	0.69 (0.12)	0.50 (0.23)	.03
Case*								
1	24	3.5	50.00	47.14		0.70	0.63	
2	15	4.0	45.50	29.50		0.79	0.57	
3	39	4.9	45.31	36.33		0.68	0.70	
4	18	3.3	48.79	34.24		0.77	0.47	
5	7	2.9	48.28	30.00		0.65	0.39	
6	17	2.4	44.17	37.50		0.53	0.40	
7	10	3.2	39.38	27.19		0.69	0.50	

* Results for individual case subjects (1–7)
SMR = sleeping metabolic rate
$F_{\bar{E}CO_2}$ = fraction of exhaled carbon dioxide
IQR = interquartile range

(45.5 [4.63] vs 34.2 [8] kcal/kg/d, $P < .02$]. $F_{\bar{E}CO_2}$ was significantly higher, although still within the recommended range, with the small hood versus the large hood in both controls and cases. Time-to-steady state was similar in both groups regardless of hood size. Individual and median results for these measures are given in Tables 1 (controls) and 2 (cases). Spearman's rank correlation indicates that the SMRs for the small and large hoods were significantly correlated in the control group (r = 0.80, $P < .01$); however, there was not enough evidence to conclude that they were correlated in the case group (r = 0.43, $P = .34$). Finally, $\dot{V}_E$ measured during steady state was significantly lower with the small hood versus the large hood in controls (3.8 [0.1] vs 4.5 [0.1] L/min, $P < .01$). Similar values were found for $\dot{V}_E$ when comparing small and large hoods in cases (3.7 [0.1] vs 4.5 [0.1] L/min, respectively), but these were not statistically significant.

Discussion

This is the first study to test the use of a smaller hood to measure SMR in both healthy and compromised neonates. In controls, but not in cases, results for SMR were similar for both hoods. This may be explained by the fact that the controls were slightly older (26 vs 17 d) and weighed more (4.1 vs 3.3 kg) than the cases, and therefore, because of their size and health status, they were able to produce adequate respiratory gas exchange under either hood. This finding supports our conclusion that the small hood is an acceptable substitute for the standard adult (large) hood

when performing IC in healthy neonates. Time-to-steady state was also similar in both hoods, and median $F_{\bar{E}CO_2}$ values in cases and controls were within the acceptable range of 0.5–1.0 for both hoods, providing further evidence that viable measurements can be obtained with both hoods in a healthy population. Interestingly, $F_{\bar{E}CO_2}$ values using the small hood were at or near the optimal range (0.7–0.8) to capture respiratory gas exchange and were significantly greater with the large hood in both groups, indicating better gas mixing and less dilution under the small hood. Meanwhile, $F_{\bar{E}CO_2}$ with the large hood was below optimal in both groups, and several cases exhibited $F_{\bar{E}CO_2}$ values below the minimum acceptable value of 0.5. One explanation for this is that the space inside the hood may be too large, resulting in overdilution of the breath sample; in other words, the large hood may not be capturing sufficient respiratory gas exchange in these compromised infants to provide a useful measurement. Bauer et al[12] performed IC in infants using three breath-sampling devices: a face mask, head hood, and canopy, each with progressively larger volume around the infant's nose and mouth. They found that more accurate results were obtained with the face mask, in part because of its minimal open space around the head. However, the mask is not practical for measuring SMR because affixing it to the infant may cause discomfort and wake the subject during testing. The higher F_{ETCO_2} with the small hood compared with the large hood could produce stimulated respiration, altering the energy expenditure. However, the F_{ETCO_2} values were still within the optimal range for data collection, and our $\dot{V}_E$ results confirm normal respiration. Interestingly, we found a higher $\dot{V}_E$ with the large hood, which could indicate a greater respiratory demand (increased ventilation) on the infant or overdilution of the exhaled sample, resulting in more variability in the data obtained with this hood.

Most published studies that have measured energy metabolism in an infant population have done so in the sleep state.[6,16] Although it is known to lower the metabolic rate,[1] sleep is necessary in infants to achieve the still rested state required for the measurement. Bines and Truby[6] compared the metabolism measurement in infants while sleeping (SMR) with the measurement while awake (BMR). They found that the SMR was 75% of the BMR and that there was a significant correlation between the two, with the SMR consistently lower than the BMR.

The values for SMR measured in this study are similar to or slightly lower than those reported in the literature. The SMR of a normal healthy infant ranges from 43 to 60 kcal/kg/d, and total energy requirements are 107–113 kcal/kg/d[1]; therefore, SMR makes up between 40 and 55% of total energy needs. The SMR measured in our cases with the small hood is 24% greater than that measured with the large hood. Based on SMR representing 40–55% of total needs, the small hood results indicate that the subject needs 84–115 kcal/kg/d, and the large hood results indicate that the subject needs 62–85 kcal/kg/d. If we apply these results to a typical infant weighing 4 kg, the difference could be as much as 120 kcal/d, a clinically important amount for a growing child. Thus, there is the risk that an infant would be underfed if following the large hood results, affecting potential for growth and increasing the risk of failure to thrive.

The ability to measure SMR in infants at risk for growth failure could help target nutritional interventions. Infants with complex CHD are one population where this methodology may be very helpful. The measured SMRs in our cases with the small hood are higher than those in the healthy controls. It is hypothesized that infants with complex CHD have higher than normal resting metabolic rates, and this question is being addressed by the larger study in which these cases were also enrolled. Adequate growth and nutrition are critically important in these compromised infants. Poor growth and nutrition are common in infants with CHD, and malnutrition in this population has been estimated to be as high as 53%.[17] Poor nutrition in children with complex CHD has been shown to be associated with infection risk, increased hospital stay, and mortality after cardiac surgery.[18-20] The methods described here may support nutritional interventions in other chronic conditions known or suspected to increase the risk for growth failure in infancy, such as cystic fibrosis,[21] immune disorders,[22] and inflammatory bowel disease.[23] Similarly, babies born prematurely have increased nutritional needs that vary based on gestational age and birth weight.[24] They also could benefit from this method, which allows SMR to be determined in smaller infants.

This was a pilot study that was part of a larger cohort study. To fully understand the use of this new method and to determine its generalizability to different populations, a larger cohort of subjects with a diverse group of medical conditions should be studied.

Conclusions

The use of a small size-appropriate hood when measuring metabolic rate in neonates yields results similar to those with the standard large hood while not affecting testing time or other aspects of the IC procedure. Furthermore, the outcomes of metabolic parameters such as $F_{\bar{E}CO_2}$ in compromised neonates suggest that using a smaller hood may facilitate SMR testing in this population. A method that accurately measures metabolic rate in high-risk infants would be extremely useful in predicting energy needs and establishing appropriate caloric intake goals for improved outcomes.

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