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STUDIES IN HUMANS

Nutritional status, metabolic state and nutrient intake in children with bronchiolitis

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ABSTRACT
Nutrition has a coadjuvant role in the management of children with acute diseases. We aimed to examine nutritional status, macronutrient requirements and actual macronutrient delivery in bronchiolitis. The nutritional status was classified according to WHO criteria and resting energy expenditure (MREE) was measured using an indirect calorimeter. Bland–Altman analysis was used to examine the agreement between MREE and estimated energy expenditure (EEE) with standard equations. Based on the ratio MREE/EEE in relation to Schofield equation on admission, we defined the subjects' metabolic status. A total of 35 patients were enrolled and 46% were malnourished on admission, and 25.8% were hypermetabolic, 37.1% hypometabolic and 37.1% normometabolic. We performed a 24-h recall in 10 children and 80% were overfed (AEI: MREE >120%). Mean bias (limits of agreement) with MREE was 8.9 (−73.9 to 91.8%) for Schofield; 61.0 (−41 to 163%) for Harris–Benedict; and 9.9 (−74.4 to 94.2%) for FAO-WHO equation. Metabolism of infants with bronchiolitis is not accurately estimated by equations.

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Indirect calorimetry; nutrition; energy expenditure; metabolism; malnutrition

Introduction

Bronchiolitis secondary to respiratory syncytial viral infections (RSV) is a predominant cause of respiratory insufficiency and hospitalization in infants during the first year of their life (Pinnington et al. 2000; Papadopoulos et al. 2002; Merril and Owens 2007). Reduced fluid and nutrient intake secondary to respiratory distress and the need for supplemental oxygen are the main factors necessitating hospitalization in this cohort. Optimal nutrient intake during bronchiolitis is an important goal, but it is impeded due to the respiratory issues. Suboptimal nutrition may negatively impact recovery time and therefore, nasogastric feeding is used to supplement poor oral intake (SIGN 2006; Campanozzi et al. 2009). Energy prescriptions based on standard equations may be inaccurate and result in unintended underfeeding or overfeeding in sick infants (Miles 2006; Mehta et al. 2009). Optimal protein delivery has been shown to improve nitrogen balance and prevent lean body mass deterioration in infants with bronchiolitis (de Betue et al. 2011).

We aimed to describe the nutritional status, metabolic state and the accuracy of equations used to estimate resting energy expenditure in infants hospitalized with bronchiolitis.

Methods and statistical analysis

In this prospective observational study, we enrolled infants less than 2 years of age with a clinical diagnosis of acute viral bronchiolitis (Baraldi 2014) admitted to the Pediatric Department between October 2014 and March 2015. Patients needing supplemental oxygen were not eligible for the study, because of technical difficulties in performing indirect calorimetry. The study was approved by the local Ethics Committee and informed consent was obtained.

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Assuming a mean resting energy expenditure (±SD) of 346 ± 85 kcal/die, the estimated minimum sample size was 19 per group to achieve $\alpha = 0.05$ and $\beta = 80\%$.

A multidisciplinary team completed the nutritional assessment and the anthropometric measurements on admission and prior to hospital discharge. Weight (using a gram scale, accurate to 0.1 kg) and length (using the 417 SECA stadiometer ® SECA Medical Measuring Systems and scales, Birmingham, UK, or a flexible but nonstretchable tape measure) were measured (Khoshoo 1997; Papadopoulos et al. 2002). Z-scores for weight for age (WFA), BMI, weight for length (WFL) and length for age (LFA) were calculated using the WHO Anthro Plus® software, and the WHO reference charts (Pinnington et al. 2000; World Health Organization 2007). Malnutrition was diagnosed according to WHO criteria if WFL *z*-score was < -2. Resting energy expenditure (REE) was measured in thermoneutral conditions after 4-h fasting, using an open-circuit indirect calorimeter (Vmax 29®, Sensor Medics, Yorba Linda, CA) and a transparent canopy. Minute-to-minute VO_2 and VCO_2 were measured during steady state and were reported in ml per kg of body weight (Haugen et al. 2007). Data from patients who did not meet steady state or had a respiratory quotient <0.67 or >1.3 were excluded.

Energy expenditure was estimated using the Harris–Benedict, the Schofield and the FAO-WHO equations (Koletzko et al. 2005; SIGN 2006). Based on the ratio of measured resting energy expenditure (MREE) and the estimated energy expenditure (EEE) by Schofield equation, individual patients were classified as, (a) normometabolic (MREE:EEE =0.9–1.1), (b) hypermetabolic (MREE:EEE >1.1) and (c) hypometabolic (MREE:EEE <0.9) (de Betue et al. 2011; Mehta et al., 2011).

A 24-h food recall was used to determine daily nutrient intake. We classified the feeding status of patients based on the ratio of actual energy intake (AEI) and measured resting energy expenditure, as underfed (AEI:MREE <0.8), overfed (AEI:MREE >1.2) or normally fed (AEI:MREE = 0.8–1.2). Biochemical characteristics, including albumin and prealbumin, were measured on admission, with methods standardized in the central laboratory of the hospital. Data are presented as median ± interquartile range (IQR). We used the Bland–Altman analysis to determine mean bias and limits (95% confidence intervals) of agreement between MREE and each of the estimated EEE. Differences between groups were assessed with Wilcoxon signed rank test and analysis of variance (ANOVA), as appropriate. Statistical significance was defined at $p < .05$.

Table 1. Demographic, anthropometric data and nutritional status on admission in children admitted to the hospital with bronchiolitis.

	Median (IQR 1,3)
Age, months	5.4 (2.7–11.7)
Weight, kg	6.9 (4.8–8.5)
Length, m	0.6 (0.6–0.7)
BMI, kg/m^2	15.4 (14.6–16.6)
Weight for length *z* score	−0.5 (−0.9–0.8)
Undernourished	7.0 (20.0)
Overweight/obese	9.0 (25.7)
BMI, *z* score	−0.5 (−1.6–0.6)
Weight for age *z* score	−0.4 (−1.9–0.09)
Length for age *z* score	−1.0 (−1.8–0.5)
Respiratory rate breaths/min	50.0 (28.0–80.0)
Cardiac rate bpm	140.0 (98.0–180.0)
O_2 saturation %	95.0 (85.0–100.0)
Temperature °C	36.2 (35.5–38.0)
Albumin[a], g/L	0.043 (0.041–0.045)
Prealbumin[b], g/L	0.120 (0.092–0.177)
Etiological agent bronchiolitis	%
RSV	51
Rhinovirus	14
hMPV	6
Coronavirus	3
Mixed	26

Data are presented as median (1°–3° quartile) and *N* and % when appropriate.
[a]Data available for only 34 patents.
[b]Data available for only 26 patients.

Results

We enrolled 35 consecutive eligible patients (27 Caucasians, four Africans, three Hispanics, one Asiatic and 19 boys, 54%) aged 2.7–11.7 months, during the study period. Table 1 shows the demographic, anthropometric and clinical characteristics of children on admission. Globally, 45.7% of children were malnourished, overweight (25.7%) or undernourished (20%). Gas exchange, metabolic status and macronutrient intake both at admission and at discharge are reported in Table 2. One indirect calorimetry measurement did not reach the steady state and was excluded from the analysis. At admission, 63% of the patients were either hypermetabolic (25.8%) or hypometabolic (37.1%). There were no significant differences in the WFL-z scores between admission and discharge. Bland–Altman plots showing the agreement between measured resting energy expenditure by indirect calorimetry and estimated energy expenditure by three different predictive equations are depicted in Figure 1. The mean bias (limits of agreement) for Harris–Benedict was 61.0 (−41 to 163%); for FAO-WHO was 9.9 (−74.4 to 94.2%) and for Schofield was 8.9 (−73.9 to 91.8%). The median daily protein and actual energy intake for the cohort was 3 g/kg and

Table 2. Gas exchange, metabolic status and macronutrient intake at admission and at discharge.

	Admission		Discharge		
	N	Median (IQR 1,3)	*N*	Median (IQR 1,3)	*p* Value
VO2 mL/kg/min	34	12.2 (10.0–17.6)	21	9.1 (5.5–11.1)	NS
VCO2 mL/kg/min	34	10.4 (8.5–14.9)	21	7.3 (4.8–9.3)	NS
RQ	34	0.8 (0.8–0.9)	21	0.8 (0.8–0.9)	NS
MREE, kcal/d	34	346.5 (172.5–478.3)	21	424 (288.0–617.0)	NS
EEE by Harris–Benedict equation, kcal/d	35	626.1 (487.2–824.3)	21	789.1 (475.2–848.8)	NS
EEE by Schofield equation, kcal/d	35	360.0 (248.0–515.6)	21	366.0 (251.2–564.6)	NS
EEE by FAO-WHO equation, kcal/d	35	372.9 (241.9–462.1)	21	421.7 (251.1–516.3)	<.05
MREE/HB	34	0.5 (0.4–0.7)	21	0.6 (0.5–0.9)	NS
MREE/Schofield	34	1.1 (0.7–1.4)	21	1.3 (0.8–1.5)	NS
MREE/FAO-WHO	34	1.0 (0.7–1.2)	21	1.2 (0.8–1.4)	NS
Protein intake, g/kg	10	2.9	7	2.4	NS
Protein intake, %	10	9.7 (7.5–14.9)	7	7.4 (7.1–17.0)	NS
Lipid intake, g	10	30.2 (26.9–32.1)	7	47.9 (36.1–47.3)	NS
Lipid intake, %	10	47.9 (36.9–49.9)	7	45.1 (39.1–50.7)	NS
CHO intake, g	10	67.3 (62.1–88.5)	7	91.6 (76.6–110.0)	NS
CHO intake, %	10	43.3 (42.6–48.2)	7	42.5 (41.7–49.7)	NS
Metabolic status (MREE:EEE Schofield)					
Normometabolic, *N* and %	34	13 (37.1)	21	4.0 (19.0)	
Hypermetabolic, *N* and %	34	8 (25.8)	21	10.0 (48.0)	
Hypometabolic, *N* and %	34	13 (37.1)	21	7.0 (33.0)	
Feeding status					
Daily actual energy intake, kcal/kg	10	94.1 (74.9–127.6)	7	116.8 (91.2–150.9)	
Actual energy intake/REE	10	1.83 (1.5–2.0)	7	2.6 (1.5–3.5)	
Normal fed, *N* and %		2.0 (20.0)		1.0 (14.3)	
Underfed, *N* and %		0		1.0 (14.3)	
Overfed, *N* and %		8.0 (80.0)		5.0 (71.4)	

Data are presented as median (1°–3° quartile) and *N* and % when appropriate.
N = number of patients where the stated characteristic was assessed.
Respiratory quotient (RQ); Measured resting energy expenditure (MREE); Estimated energy expenditure (EEE).

94.1/kg, respectively, and 80% of the cohort in which we performed the 24-h recall was overfed (AEI:MREE >120%) and none of the children were underfed.

Discussion

Our results provide some insights into the nutrient needs and challenges to nutrient delivery in children hospitalized with bronchiolitis. Malnutrition was recorded in a majority of patients on admission. In particular, this cohort had a high prevalence of overweight/obesity. The hospital stay was short, average 7 days, and both nutritional and metabolic states did not change significantly during this period. Accurate data related to daily caloric intake were available in a small subgroup of patients. In this subgroup, we identified eight children who were overfed and none was underfed. We found only 13 children who were normometabolic, while the majority of them were either hypometabolic or hypermetabolic.

Other studies show that patients did not change their weight during hospitalization in agreement with our data (Miles 2006; Halvorson et al. 2013), but high percentages of undernutrition and risk of malnutrition are noteworthy, 21.7% and 17.5%, respectively (Bosa et al. 2008). While a preexisting malnutrition status is a strong predictor of mortality from acute lower respiratory tract infection in preschool-aged children (Johnson et al. 1992; Halvorson et al. 2013) and a marker of further nutritional and clinical deterioration, attention should be paid to the prevalence of obesity, too. We decided to use WHO growth charts, because only 51% of children in the study population were Italian, the others were Caucasians-not Italian and other ethnicities and the obesity prevalence was comparable to that described in northern Italian children (Turchetta et al. 2012).

Our results do not support the notion that low caloric intake is common among infants with bronchiolitis. In previous report, suboptimal nutrient delivery in children hospitalized with bronchiolitis has been associated with prolonged length of stay, low early hospital caloric intake and a slow rate of improvement (Weisgerber et al. 2013). In our subgroup, descriptive statistics revealed that the median caloric intake of infants at admission was ∼94 kcal/kg, while median protein intake was 2.9 g/kg, a value higher than recommended intakes (EFSA 2015). Providing both protein and energy intakes above-recommended intakes (Mehta et al. 2015) may promote protein anabolism in critically ill infants (de Betue et al. 2011).

Many equations have been developed as surrogate methods to predict REE, but they are not always

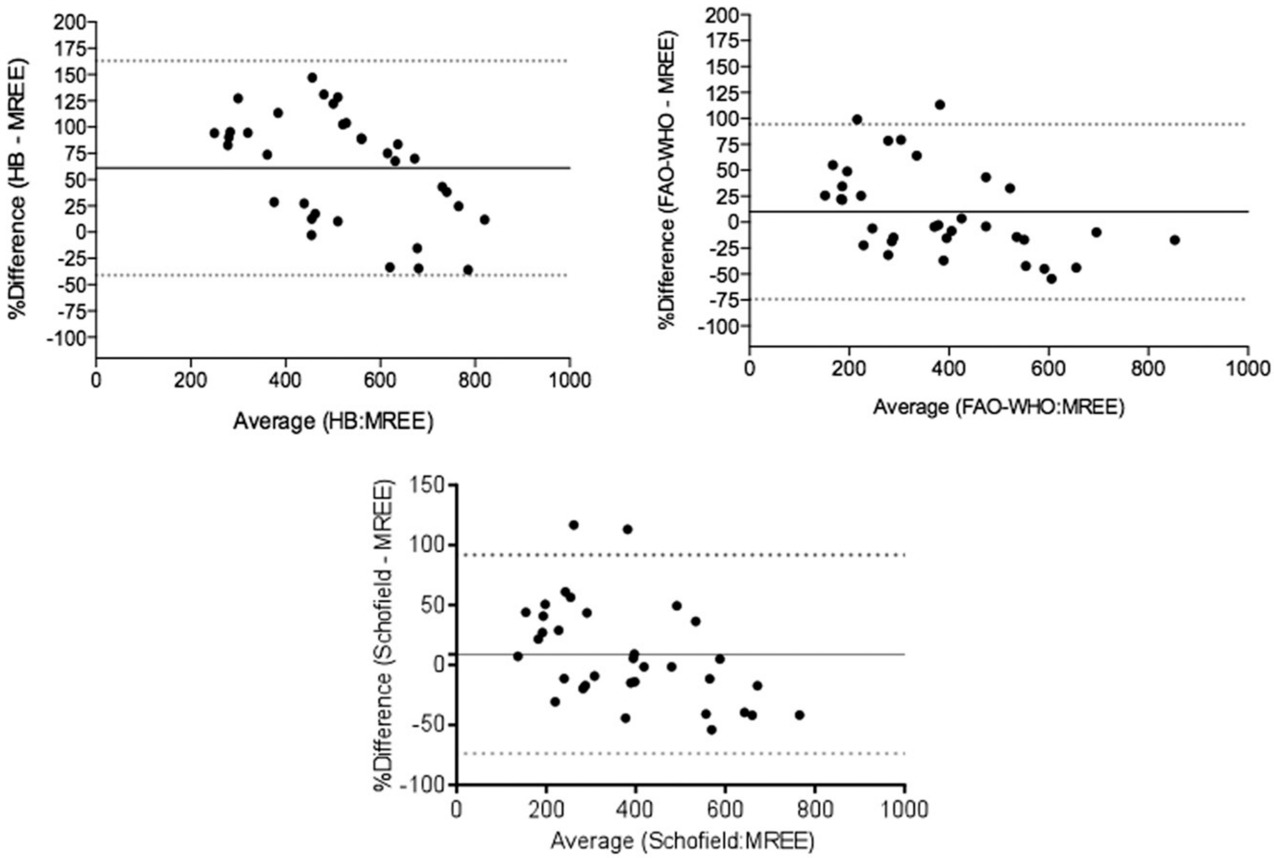

Figure 1. Resting energy expenditure in children with bronchiolitis on hospital admission. Agreement between indirect calorimetry and three different predictive equations. The *x*-axis shows the average measured energy expenditure by the two methods (kcal/d). The *y*-axis shows the % difference in measured energy expenditure between the two methods (kcal/d). If the two methods of measurement had good agreement, the points should be centered on the "0" *y*-axis, regardless of the average measured resting energy expenditure. In the population study, the higher the average MREE, the more likely the predictive equation is to underestimate MREE (negative difference), and the lower the average MREE, the more likely the predictive equation is to overestimate the MREE (positive difference on *y*-axis).

accurate to carefully monitor the energy needed to support growth and metabolic requests in disease conditions and they assume a lack of heterogeneity among individuals through ages in both genders (Battezzati & Viganò 2001). In the current study, measured energy expenditure and energy expenditure assessments with equations were not in agreement. The limits of agreement were wide and individual values of estimated energy expenditure must be interpreted with caution for these patients. Furthermore, looking at the slope of the three Bland–Altman Plots, in younger infants with lower mean energy expenditure (kcal/kg) the estimated energy expenditure overestimated measured energy expenditure; on the contrary in older patients, the equations underpredicted the measured energy expenditure.

Limitations

There are a number of limitations of the current study, beyond those already mentioned. Few patients were enrolled during the epidemic season and some data at discharge were lost (40%). Dietary intake data compared to resting energy expenditure were available in a very limited number of patients at admission and discharge, respectively, 10 versus 7. Nevertheless, the results suggest that an individualized metabolic and nutritional assessment in patients with bronchiolitis might be useful. This should be further elucidated in larger studies. Since our study was performed in a single Italian center, multicentric studies could more easily respond to open questions with a more meaningful statistical power. Accurate measurement of energy expenditure requires the achievement of oxygen and carbon dioxide exchange at a steady state. Certain procedures in the inpatient setting may affect the oxygen dynamics and accuracy of the examination; for this reason, we excluded one measure.

Finally, the role of the different viruses in establishing different metabolic expenses, and therefore, needs, in bronchiolitis, may be matter of further research.

For this aim, the current sample size was insufficient. Beyond RSV and rhinovirus, also the metabolic challenges in coinfection (ranging widely among studies from 6% to more than 30%) should be evaluated (Agostoni et al. 2014).

In children in whom we performed the 24-h recall, we identified eight who were overfed and none was underfed. These results represent the comparison between measured energy expenditure and intake and do not take into account the energy burden from diet induced thermogenesis, activity and growth. Nevertheless, hospitalized infants are generally quite sick and spend most of their time in bed. Furthermore, they are spending most of their energy to fight the acute infection, so that the energy spent for growth is likely negligible during this short period of time.

Conclusion

Infants with acute bronchiolitis present with a high prevalence of malnutrition and altered metabolic state, which is not accurately estimated by standard equations. Heterogeneity in metabolic state suggests the need for an individualized approach to nutrition (Dornelles et al. 2007). It would be desirable to focus on providing optimal nutrition and perform targeted indirect calorimetry on high-risk patients, to prevent cumulative excesses, deficits in energy balance and reduce length of stay (Mehta et al. 2009). A suboptimal nutritional status may persist also after the acute illness, so that a global health follow-up may be indicated to evaluate the growth of the child after the episode.

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Disclosure statement

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