Total energy expenditure in small for gestational age infants

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Abstract

Objective—To measure total energy expenditure and body composition in small for gestational age (SGA) infants, to investigate hypermetabolism.

Methods—A cross-sectional study was performed in 52 small for gestational age (SGA) measured at 5 weeks of age, using existing data from appropriate for gestational age (AGA) infants as controls. The doubly-labelled water technique was used to assess both total energy expenditure and body composition in both cohorts of infants.

Results—Multiple regression analysis revealed that expressing energy expenditure per kg fat free mass adjusts for body composition in infants of this age. Regression analysis also showed that the relation between total energy expenditure and fat free mass differed between the two groups. **Conclusion**—These data indicate that for a given fat free mass, the total energy expenditure of SGA infants is greater than that of AGA infants. Such data should be taken into account when energy requirements for SGA infants are being considered.

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It has long been suggested that small for gestational age (SGA) infants have a higher metabolic rate than appropriate for gestational age (AGA) infants,¹⁻⁵ leading to the concept of relative hypermetabolism in SGA infants. Understanding the pathophysiology of energy metabolism in growth retarded and undernourished infants is of considerable importance in nutritional management and may have implications for long term outcome. However, it is also known that body composition is altered in SGA infants, with a reduction in fat stores.⁶⁻⁷ Differences in body composition can produce artificial differences in metabolic rate when this is expressed as kJ/kg body weight or as oxygen consumption in ml/kg body weight.⁸⁻¹⁰ Metabolic variables are better expressed relative to fat free mass (FFM), which at least partly negates the effect of body size and body composition.¹¹⁻¹³

In the past it has been difficult to measure both total energy expenditure (TEE) and body composition in infants, but the doubly-labelled water technique now makes such measurements possible.¹⁴⁻¹⁵ Thus we have assessed the

relation between total energy expenditure and fat free mass in a cohort of SGA infants and AGA infants at 5 weeks of age, in order to investigate potential differences in energy metabolism between the two groups.

Methods

All infants were recruited from the Rosie Maternity Hospital, Cambridge. A total of 52 AGA infants and 54 SGA infants were recruited when the infants were less than 4 days old. Infants were classified as SGA if their birthweight was below the 10th centile for gestation, using Gairdner and Pearson charts.¹⁶

The SGA infants were initially recruited for a randomised, placebo controlled study to test the hypothesis that L-carnitine supplementation in term SGA infants would improve catchup growth. Infants were randomly allocated to receive daily carnitine or placebo for the first 12 weeks of life, and were stratified by diet and sex. The assessment of total energy expenditure in SGA infants, reported here, was an additional planned outcome of the study.

At about 5 weeks of age, TEE was measured using the doubly-labelled water technique over a seven day period. The technique, described elsewhere in detail,¹¹⁻¹⁴ involves an oral administration of two stable isotopes (²H and ¹⁸O) and the subsequent collection of spot urine samples for seven days. Isotopic enrichment in the pre-dosing sample and post-dose samples were analysed using isotope-ratio mass spectrometry. The multipoint approach was used with an assumed respiratory quotient over the seven days of 0.855.

Fat free mass (FFM) was calculated from the measurement of total body water inherent in the doubly-labelled water technique. Reference values¹⁷ were used for the proportion of water in FFM in the calculation. Body weight, length, and head circumference were also recorded.

STATISTICAL ANALYSIS

The relation between TEE and FFM in the AGA and SGA groups was modelled by multiple regression, with TEE as the dependent variable. Both TEE and FFM were analysed after logarithmic transformation, to test for a power relation and to adjust for heteroscedasticity. The difference between groups was modelled by a dummy variable (1/0) identifying the SGA group, and an interaction between the SGA babies and FFM was also tested for.

Results

Measurements of total energy expenditure were obtained in 89 (49 AGA; 40 SGA)

Table 1 Some physical characteristics of the infants at birth and at age 5 weeks

	AGA Mean (SD)	SGA Mean (SD)
Gestation (weeks)	39.8 (1.4)	39.2 (1.3)
Birthweight (kg)	3.42 (0.45)	2.60 (0.24)
Weight (kg)	4.42 (0.48)	3.71 (0.35)
Length (cm)	54.7 (1.8)	52.2 (1.9)
Head circumference (cm)	38.0 (1.2)	36.6 (1.05)
Total energy expenditure (kcal)	305 (91)	311 (96)
Fat free mass (kg)	3.73 (0.33)	3.23 (0.36)
Fat mass (kg)	0.81 (0.32)	0.47 (0.26)
% Fat	17.5 (5.9)	12.5 (6.7)

infants. Of the other 17 initial recruits, one of the SGA infants died before the age of 5 weeks, and four families withdrew from the study before measurement. Reasons for other loss of data included poor parental compliance and the infant possetting or vomiting during or soon after dosing. There was no significant difference in TEE between those infants receiving carnitine or placebo and so the data have been combined.

Some physical characteristics of the two groups at 5 weeks of age of infants are shown in table 1. The SGA infants differed significantly from the AGA infants in that they had a lower body weight ($t = 8.9$; $P < 0.001$), were shorter ($t = 6.35$; $P < 0.001$) and less body fat ($t = 3.72$; $P < 0.001$). Total energy expenditure did not differ significantly ($t = 0.34$). Data on the AGA infants have been reported before.¹¹ The relation between TEE and FFM in both the AGA and SGA infants are shown in fig 1.

The results of the multiple regression analysis shown in table 2 revealed that the appropriate power for FFM in the model—that is, 1.21—was not significantly different from 1, showing that the ratio TEE:FFM adjusts for FFM in this age group of infants. Furthermore, regression analysis showed that the relation between FFM and TEE differed between the two groups of infants, with the intercept of the regression lines differing significantly ($t = 2.65$; $P < 0.1$); the slopes were not significantly different ($t = 0.25$; $P = 0.803$). This indicates that for a given fat free mass, the total energy expenditure of SGA infants is greater than that of AGA infants.

Figure 1 Relation between total energy expenditure (TEE) and fat free mass (FFM) in SGA and AGA infants.

Table 2 Result of multiple regression analysis, with TEE being dependent variable

Predictor	Coefficient	Standard deviation	t Ratio	P value
Constant	4.09	0.39	10.42	<0.001
FFM	1.21	0.30	4.07	<0.001
Dummy variable (SGA vs AGA)	0.19	0.07	2.65	<0.01

Discussion

As would be expected at 5 weeks of age, the SGA infants were lighter, shorter, and had a smaller head circumference than AGA infants. Moreover, body composition differed: the SGA infants had a significantly lower percentage body fat. The definition of SGA below the 10th centile will clearly produce a heterogeneous group of infants and the reasons for their relative smallness may be varied. Nevertheless, the definition is a standard one and the differences we found in the relation between FFM and TEE might not have been so profound if the smallness of the babies was produced by a vast array of causes.

Total energy expenditure differs in SGA compared with AGA infants when the FFM of the infants is taken into account. Further measures of energy metabolism, such as sleeping metabolic rate, the energy cost of growth, and thermogenesis would be required to evaluate which components of total energy expenditure are raised in SGA infants. Nevertheless, existing data in slightly older infants suggest that the largest components of TEE are basal metabolic rate and the energy cost of activity.^{18,19} It should be remembered that while the energy cost of growth is very high at 5 weeks of age, this cost is primarily energy stored and this will not be measured by the doubly labelled water technique as energy expended.

There is little evidence to suggest that the energy cost of activity is greater in SGA infants, and in fact, several studies have reported similar levels of activity, when compared with AGA infants.^{3,5} Therefore, it is more likely that basal metabolic rate is greater per kilogram of FFM in SGA infants. The two compartment body composition model—that is, dividing the body into fat and fat free masses—is the simplest of a number of multicompartamental models that now exist. It would be naive to consider that the composition of the FFM is consistent between individual babies, in terms of either tissue types or organ sizes. Abdulrazzaq and Brooke⁵ suggested that the increased energy expenditure in SGA infants is explained, at least in part, by the relatively large brain in comparison with AGA infants. In this study the SGA infants had a significantly smaller mean head circumference than the AGA infants. Nevertheless, head size, and by inference, brain size, should be related to FFM in order to test this hypothesis. However, head circumference was not a significant factor in determining the TEE of the SGA infants, after adjusting for FFM.

While head circumference is, of course, only a proxy to brain size, this finding casts doubt on the often quoted perception, that a high TEE in SGA infants is due to a relatively large

brain size. The sizes of other organs that contribute significantly to metabolic rate in neonates (liver, heart, kidney, etc) could not be evaluated in this study and thus the combined effect of organ size relative to the remainder of the FFM cannot be evaluated. It is possible that a reduction in cell mass mainly affects muscle mass, a relatively low energy expending tissue, with other more metabolically active organs, such as the liver, being spared from a similar reduction in cell mass.

This study shows that total energy expenditure is significantly higher in SGA infants when FFM has been adjusted for. If energy requirements of SGA babies are based, therefore, on body weight alone, using national or international recommendations the energy requirement will be underestimated. Such data should be taken into account when energy requirements for SGA infants are being considered.

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