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Feasibility of using ultrasound to measure preterm body composition and to assess macronutrient influences on tissue accretion rates

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ABSTRACT

Background and aims: To assess ultrasound as a method for (i) measuring body composition (BC) of preterm infants and for (ii) assessing the influence of macronutrient intakes on tissue accretion rates.

Methods: Preterm ultrasound studies of four anatomical sites were performed approximately every three weeks from birth to corrected-term age. Preterm measurements were compared to foetal reference data. Duplicate scans at each site were taken on a subset of infants to test the reproducibility of the method, assessed as the coefficient of variation (CV). The influence of measured macronutrient intakes on preterm BC was assessed by regression analysis.

Results: Median (range) gestation and birth weight of 40 preterm infants were 27 (23–29) weeks and 1022 (480–1475) g, respectively. Accretion rates of adipose and muscle tissues were not uniform across the four sites. Relative to the foetus, preterm adipose tissue thickness was reduced at an equivalent (corrected) gestation, but towards term, a faster accretion rate of subcutaneous abdominal adipose and limb muscle tissue was evident. Timing of fortification ($p = 0.012$), enteral carbohydrate intake ($p = 0.008$) and the protein energy ratio of intakes ($p = 0.038$) moderated the ratio of adipose to muscle tissue accretion over the four sites by −0.004, −0.048 and −0.042, respectively.

Conclusions: Ultrasound provides a non-invasive, portable method of assessing changes in subcutaneous adipose tissue and muscle accretion and appears sufficiently sensitive to detect influences of macronutrient intakes on accretion rates from birth. The method warrants further investigation as a bedside tool for measuring BC of preterm infants.

1. Introduction

Early body composition (BC) measurements of preterm infants are difficult to obtain but are important for assessing growth and development, which is influenced among other things, by the amount of energy consumed and the macronutrient composition of the diet [1–3]. A variety of methods, including densitometry, dual energy X-ray absorptiometry (DXA) and magnetic resonance imaging (MRI) are used for BC measurement. Since many were originally designed to measure the BC of adults and have only recently been adapted to the measurement of infants and children, none is appropriately validated for measuring the BC of preterm infants. Commonly, BC measurements are based on derived algorithms and mathematical models that vary in both assumptions and reference data, making it difficult to accurately compare and interpret data from the past and emerging preterm BC data.

Few methods employed to measure BC are able to assess adipose tissue (AT) distribution. Calliper skin folds represent the cheapest, most portable means by which to assess distribution of subcutaneous AT. However, the pressure exerted by the calliper often causes preterm infants discomfort and may bruise and damage their often translucent, very fragile skin. Further, the accuracy of a skin fold measurement is influenced by the variability in skin thickness and the compressibility of the skin fold at different body sites [4]. In preterm infants, this method has produced inaccurate and biased estimates of total fast mass as assessed by total body water dilution [5]. Other methods, such as computed tomography and DXA, expose the infant to radiation and, together with MRI, are expensive and lack portability, making them unsuitable for bedside use in a neonatal nursery which is required for the very preterm infant.

Ultrasound has been used recently in adults to measure intra-abdominal AT [6,7] and is emerging as an alternative method for assessing BC of the foetus [8,9] and young infants [10]. Larciprete et al. [8] used ultrasound to measure the area of foetal adipose and muscle tissue at the mid-arm and mid-thigh and the depth of AT at the abdominal and the subscapular sites. These authors found

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significantly greater area and depth of AT in the foetus of mothers with gestational diabetes compared with those of healthy mothers [8], particularly in late gestation. Subsequently, they were able to show that subcutaneous abdominal, subscapular and mid-arm adipose as well as mid-arm muscle tissue were sensitive to metabolic impairment, but mid-thigh adipose and muscle tissue were spared in growth-restricted foetuses [9].

Ultrasound has the advantages of applying either little or no tissue compression on the infant, is non-invasive, relatively inexpensive and is routinely used as a diagnostic tool in the neonatal setting and therefore has the possibility of being refined as a portable method of assessing infant BC.

The primary aim of the study was to measure early changes in BC of a cohort of hospitalised preterm infants with ultrasound imaging, by applying the method of Larciprete et al. [8] and compare the patterns of change to the measurements made by Larciprete et al. [8] of the foetus in the second half of gestation [6,7]. The secondary aim was to determine if the ultrasound method was sensitive enough to detect the influence of postnatal nutrition on the BC of preterm infants.

2. Method

2.1. Subjects

Infants were recruited from a randomised study investigating the efficacy of targeting human milk fortification, using measured milk analysis, to achieve reference growth outcomes [11]. Infants were born <30 weeks gestation and admitted to the neonatal intensive care unit at King Edward Memorial Hospital (KEMH) in Perth, Western Australia. Inclusion criteria were absence of congenital abnormalities, maternal intention to feed human milk and an ability to attend three-weekly assessments until term corrected age (CA). Informed written consent was obtained and the ethics committees of both KEMH and The University of Western Australia reviewed and approved the study protocol.

All infants, from either singleton ($n = 24$) or twin ($n = 16$) births were randomised as individuals to receive milk, either fortified on measured milk composition or on assumed composition. As macronutrient intakes were similar for both groups they were combined for statistical analysis.

2.2. Body composition

Ultrasound studies of four sites, according to the method described by Larciprete et al. [8], were performed approximately every three weeks from birth to term CA using the TITAN (Sonosite, Bothell, WA, USA) machine. A high-resolution (5–10 MHz) linear array transducer (L38) was employed and the small-parts setting used to attain the highest resolution. The average gain setting was 61 dB and adjustments were made depending on the weight of the infant to provide optimal ultrasound images. Sterile, water-based gel was placed between the probe and the infant's skin to facilitate penetration of the ultrasound beam and often to act as a ‘stand off’ to minimise tissue compression and enhance imaging in the superficial region. Measurements were taken on the left side of the body.

Mid-arm and mid-thigh AT area (outer area minus inner area, cm^2) and mid-arm and mid-thigh muscle tissue area (MT) (inner area, cm^2), anterior and posterior arm and thigh AT thickness (mm), and abdominal and subscapular AT and MT thickness (mm) were measured from the images obtained using a Universal desktop ruler (v3.3.3268, 2002–2009, AVPSoft.com) (Fig. 1). The coefficients of variation (CV) between pairs ($n = 32$–34 pairs) of 12 different measurements obtained from ultrasound images of four anatomical sites were calculated to assess intra-observer agreement on a subset of 34 infants. Measurements were log transformed and the percentage CV was calculated using the formula $\%CV = 100 * (x(\exp(s) - 1))$, where s is the SD of the difference in log transformed measurements divided by the square root of two.

2.3. Anthropometry

In accordance with the nursery's measurement policy, weight, either taken in the infant's incubator or with digital scales (g; SECA, Germany 10/20 kg; $d = 5/10$ g), crown–heel length and occipital–frontal head circumference were measured at birth and discharge and again at the term CA follow-up appointment (if infants were discharged before term). Whilst in intensive care, infants were weighed daily and when in the special care nursery, infants were weighed twice weekly, with daily weight derived by interpolation between each of the time-points.

2.4. Statistical analysis

Descriptive statistics for continuous data were summarised using means and standard deviations or medians, interquartile ranges and ranges. Categorical data were summarised using frequency distributions. Univariate comparisons of limb subcutaneous adipose tissue measurements were conducted using the paired t-tests.

Corrected gestational age-specific 90% reference ranges were constructed for each subcutaneous tissue thickness (SCTT) parameter, according to the method described by Royston [12]. Logarithmic transformations of SCTT parameters were made to correct skewness and heteroscedasticity. Polynomial time-based curves were fitted to the SCTT parameters using regression analysis with data weighted according to the number of ultrasound measurements taken. Normality and homoscedasticity of residual errors within tertiles for each parameter were assessed visually and statistically according to Royston's method. Reference ranges were constructed from 23 weeks gestation to term corrected gestational age (cGA) in three-week intervals and illustrated alongside reference ranges for foetal SCTT parameters in a healthy pregnant group [8].

Linear mixed models analysis was conducted to produce a growth curve model for BC. Macronutrient intakes and clinical variables were assessed for their effects on BC ratios of adipose to muscle tissue across the four anatomical sites. Adjustment was made for cGA, chronological age and weight at time of measurement. SAS 9.1 of the SAS System for Windows. Copyright © 2002–2012 SAS Institute Inc., Cary, NC, USA and PASW® 17 statistical software (SPSS Inc., Chicago, IL) were used for data analysis. All tests were two-tailed and p-values < 0.05 were considered statistically significant.

3. Results

3.1. Subject demographics

Infants ($n = 40$) were born at a mean (SD) gestation and birth weight of 27 (1.9) weeks and 1010 (289) g, respectively. The infants were mostly Australian Caucasian ($n = 36$) (Australian Aboriginal $n = 2$, Asian $n = 1$, Other $n = 1$). With the exception of two infants whose birth weights fell on the 6th percentile, all had birth weights appropriate for gestational age. The infants had achieved a mean weight of 2736 (565) g when the term CA ultrasound measurements (37–42 weeks) were obtained. Fifty percent of infants ($n = 20$) weighed <10th percentile at term. The clinical characteristics of the infants are described in Table 1.

3.2. Body composition

The SCTT parameters of the infants obtained with ultrasound are shown in Table 2. Initial measurements for 85% of infants ($n = 34$) were taken in the first week post-partum and by day 15 for the remaining infants ($n = 6$). Subsequent measurements were taken at ~three-week intervals until near term CA. The coefficient of