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Assessment of total body water using bioelectrical impedance analysis in neonates receiving intensive care

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***Aims*—To determine the most suitable anthropometric and impedance measures and current frequency for the application of bioelectrical impedance to neonates receiving intensive care; and to derive predictive models for the estimation of total body water.**

***Methods*—Twenty eight babies (median gestational age 30.5 weeks, range 24–38; median birthweight 1.388 kg, range 0.690–3.510) were each studied once during the first week after birth. Total body water was first measured by the method of dilution of isotopic water ($H_2{}^{18}O$). Bioelectrical measurements were made using the tetrapolar surface electrode method from four main distal limb positions (right hand–right foot; right hand–left foot; left hand–left foot; left hand–right foot), the left upper arm–left thigh position and the left scapula–right buttock position, and using six frequencies ((500, 250, 100, 50, 10 and 5 kHz). Regression models, to predict total body water, which were both independent and dependent of body weight on the day of study, were derived.**

***Results*—Resistance readings at 50 kHz obtained from the distal limb positions performed best. There was no difference between the distal limb positions. There was no difference in the goodness of fit of the models when using each of three indices of conductor length, foot, spine and sternum. The model total body water (litres) (TBW) = 0.016 + 0.674 bodyweight(kg)−0.038 wt^2 + 3.84 foot length (cm)^2/resistance (50 kHz in OHMS) performed best, accounting for 99.5% of the variation in TBW, with a 95% prediction interval of 165 ml. The model TBW = 0.144 + 15.518 foot length (cm)^2/resistance (50 kHz in ohms) accounted for 96.4% of the variation and had a 95% prediction interval of 420 ml.**

***Conclusions*—Bioelectrical impedance analysis is a simple, non-invasive method of estimating total body water in neonates receiving intensive care. It can be applied to both the assessment of changes in body water and body composition.**

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Keywords: total body water; body composition; bioelectrical impedance; intensive care

Assessments of fluid balance and body composition are highly desirable in neonatal intensive care and a simple, non-invasive, repeatable method would be invaluable.

Bioelectrical impedance analysis is a non-invasive technique which can be used to assess total body water.[1] The basis of the method is that only water can conduct electricity within the body. Fat is relatively anhydrous, restricts the flow of current to lean body mass. At any given frequency and configuration, the impedance of a simple geometric system is a function of conductor length and cross sectional area. The theoretical relation was developed by Nyboer[2] as follows:

$$V \alpha L^2/Z$$

where V is volume of body water in the subject, Z is impedance, L is subject length.

In biological tissues impedance to the flow of current is a function of resistance (R) and reactance (X_c). Cell membranes act as small capacitors and therefore offer a reactive resistance (reactance) to the flow of current. Electrical theory suggests that the current at higher frequencies passes through both extracellular and intracellular fluid and thus provides an index of total body water.

This study aimed to develop and evaluate the use of bioelectrical impedance analysis for the estimation of total body water in neonates receiving intensive care. We wished to determine the most appropriate site for electrode placement, current frequency and index of conductor length. We also aimed to determine if the estimation was improved by the use of the resistance component of impedance as opposed to total impedance or by segmental body measurements.

Methods

Babies admitted to the neonatal intensive care unit at Queen Charlotte's and Chelsea Hospital in whom intra-arterial access was in place for clinical indications, were eligible for study. The project was approved by the Hammersmith and Queen Charlotte's Special Health Authority and Royal Postgraduate Medical School research ethics committee. Written parental consent was obtained.

Measurements were made of spinal length, sternal length, foot length, head circumference and body weight. Crown–heel length was not measured because to do so accurately requires additional patient handling which was not considered justifiable given the clinical condition

Table 1 Univariate correlation coefficients of impedance, resistance, and reactance with total body water, at each frequency (kHz), obtained at left upper arm-left thigh (LALT), left scapula-right buttock (LSRB), and average of all four distal limb electrode positions (average)

Frequency	*Impedance*	*Resistance*	*Reactance*
Average:			
5	−0.601	−0.602	−0.296
10	−0.604	−0.616	−0.274
50	−0.651	−0.674	−0.056
100	−0.686		
250	−0.705		
500	−0.712		
LALT:			
5	−0.245	−0.409	−0.123
10	−0.379	−0.510	−0.309
50	−0.578	−0.599	−0.118
100	−0.601		
250	−0.637		
500	−0.663		
LSRB:			
5	−0.224	0.041	0.306
10	−0.163	−0.018	−0.118
50	−0.047	0.010	−0.004
100	−0.050		
250	−0.132		
500	−0.302		

of the subjects. Electronic scales accurate to 1 g were used to weigh babies. Net body weight was obtained by subtracting the weights of any attachments. All measurements were made by a single investigator (WT).

Total body water was assessed using the classic method of $H_2{}^{18}O$ dilution space, developed for application to neonates, as described before.[3] Two blood samples were collected for determination of basal ^{18}O concentration and a dose of 0.1g/kg of isotopic water administered by nasogastric tube. This was rinsed with 1.0 ml of sterile water. Blood samples were then obtained 3 and 6 hours after the dose. The analytical error for $H_2{}^{18}O$ was 0.6 ppm, with a precision within 0.8%–1.6% in the analysed enrichment range. This method has a mean difference of 5.3 ml/kg from the double exponential curve fit technique, requiring multiple sampling (limits of agreement, −67.4, 77.9).[3]

Bioelectrical measurements were made over a range of frequencies from 5–500 kHz, using the tetrapolar surface electrode method, with equipment specifically built for this study. Briefly, six frequencies are generated from a 4 MHz oscillator and logic circuit (500, 250, 100, 50, 10 and 5 kHz). The required frequency is switched to a tuned inductor–capacitor circuit, the output of which is a sine wave. This is then passed to a voltage to current generator and the output applied to the subject via two surface electrodes. The amplitude of the applied current is calibrated before application (0.8 mA rms). The voltage produced by applying this current is detected by a separate pair of surface electrodes. The received signal is passed through processing circuitry to give an impedance output for all six frequencies, as well as resistive and reactive components for the lower frequencies (5, 10, and 50 kHz). At higher frequencies reactance readings are unreliable, a problem widely acknowledged when using a constant current source over a wide frequency range.[4]

Table 2 Correlation coefficients from univariate analysis of anthropometric and bioelectrical variables as predictors of total body water

Body weight (on day of study)	0.995
Birthweight	0.990
Gestational age	0.886
Foot length	0.955
Spinal length	0.964
Sternal length	0.935
Head circumference	0.934
Foot length^2/impedance (500 kHz)	0.974
Foot length^2/impedance (50 kHz)	0.979
Foot length^2/resistance (50 kHz)	0.983
Foot length^2/reactance (50 kHz)	0.365

Table 3 Regression models for predicting total body water

Model prediction equation	*Adjusted R^2*	*Residual SD*	*95% prediction interval*
M1 TBW = 0.011 + 0.858 wt − 0.043 wt^2	99.2	0.047	200
M2 TBW = 0.144 + 15.518 L^2/R	96.4	0.099	420
M3 TBW = 0.016 + 0.674 wt − 0.038 wt^2 + 3.84 L^2/R	99.5	0.037	165
M4 TBW = 0.0125 + 0.868 wt − 0.0437 wt^2 + 0.00035 L^2	99.2	0.048	210

TBW: total body water in litres; wt: body weight on study day in kg; L: foot length in cm; R: resistance at 50 kHz in ohms.

Measurements were made using electrodes cut to 1 cm diameter (ClinicAid Ltd., University Innovation Centre, Swansea, UK) and repeated at each of six positions. These were four distal limb positions (right hand–right foot, right hand–left foot, left hand–left foot, left hand–right foot), the left upper arm–left thigh position and the left scapula–right buttock position. Babies were placed in a prone position with slight pelvic elevation, legs bearing weight through the anterior knee and hips flexed by 30°. The knees were flexed to 30° and ankles dorsiflexed to 70°. The arms were placed lying comfortably forward with the forearms parallel to the long axis of the body. Arms were adducted by 45°, elbows flexed by 45°, and the hands comfortably extended. For the distal limb positions, the voltage electrodes were placed so that the lower edge of the electrode overlapped the proximal skin crease on the dorsal aspect of the wrist and ankle, at the level of the styloid process and medial malleolus, respectively. The current electrodes were positioned distal to the voltage electrodes, at a centre to centre distance of 2 cm and 3 cm, for hand and foot, respectively, and 3 cm for the scapula–buttock and arm–thigh positions.

Preliminary data screening was performed by correlating anthropometric and bioelectrical variables, over the range of frequencies and electrode sites, with TBW, using univariate analysis. For each of the bioelectrical measurements, comparisons were made between the readings from the four main distal limb positions (right hand–right foot; right hand–left foot; left hand–left foot; left hand–right foot) and the six frequencies, using ANOVA. The residuals from the ANOVA were checked for non-normality using the Shapiro-Francia W' test. The equal variances assumption was checked using Bartlett's test. A reliability coefficient (intra-class correlation coefficient) was calculated to measure the agreement between the four main limb positions for each frequency.

Stepwise regression analysis was then used to develop predictive models using these variables. Regression analysis was carried out mostly in a forward selection mode, although other selection procedures were also used. Residual analysis was performed on each of the models considered. Models containing transformed variables were also considered. The residuals from the regression of total body water on body weight on the day of study indicated a slight curvature in the data. As this violates one of the assumptions of the regression analysis, an extra term, wt^2, was incorporated into the model to allow for this. This curvature seems intuitively reasonable as, in larger babies, total body water would not necessarily be expected to be linearly related to body weight in view of the progressive increase in anhydrous adipose tissue. Residual analysis conformed with the assumptions of the regression. Nested models were compared in the standard way using an F test.

Models to predict total body water were developed, which either incorporated or excluded body weight on the day of study.

Results

Twenty eight babies (15 boys and 13 girls) were each studied once during the first week after birth. The babies were clinically stable with intra-arterial access in place for clinical indications at the time of study. Thirteen babies were receiving positive pressure ventilation. The following values are presented as median and range: gestational age 30.5 weeks (24–38); birthweight, 1.388 kg (0.690–3.510); postnatal age 2 days (1–7); $H_2^{18}O$ dilution volume 1.085 l (0.577–2.354); $H_2^{18}O$ dilution volume (TBW), as a percentage of body weight, 79.6 (71–92). There was a negative correlation between percentage TBW and birthweight ($r = -0.75$).

The reliability coefficients (intraclass correlation coefficients) for measurements made at the four distal limb positions, at each frequency, ranged from 0.88–0.98. This showed that there was very good agreement between the four readings and therefore the average of the four distal limb readings at each frequency was used for subsequent analyses.

Table 1 shows the univariate correlations of impedance, resistance, and reactance readings, at each frequency, for the average of the four distal limb positions, the left upper arm–left thigh position and the left scapula–right buttock position, with TBW. The distal limb electrode position performed best. Bioelectrical measurements made at the left scapula–right buttock electrode position showed a very weak correlation with TBW at all frequencies and readings made at this position were therefore excluded in subsequent analyses. The results of the ANOVA showed that there were significant differences in readings between frequencies, as predicted. No interaction was detected in the readings from individual babies between limb position and frequencies, nor was a significant difference found between the limb positions for any of the bioelectrical measurements.

Table 2 shows the correlation coefficients from the univariate analysis of anthropometric and bioelectrical variables as predictors of total body water. Body weight on the day of study and birthweight were the best single predictors of total body water. When L^2 (as foot length^2) was divided by bioelectrical impedance measure, the best correlation with total body water was obtained using resistance readings at 50 kHz. There was poor correlation between total body water and L^2 divided by reactance. Resistance readings at 50 kHz were therefore used for subsequent analyses, as electrical theory suggests that total body water is best represented by the resistive component of total impedance.

Models to predict total body water, which were both independent and dependent of body weight on the day of study, were derived. There was no evidence of a difference in the goodness of fit of the models when using each of the three indices of body (conductor) length (foot, spine, and sternum). Foot length was therefore used for all subsequent analysis as it is the easiest to measure.

The best fit models are shown in table 3. These show the prediction of total body water from equations incorporating body weight (model M1), L^2/R (resistance measured at 50 kHz) (model M2), and both body weight and L^2/R (model M3). In view of the possibility, given the strong correlation between foot length and weight and total body water, that the incorporation of $1/R$ would not make a significant improvement to the prediction, a further model (M4), which excluded $1/R$, was derived. However, the addition of length as L^2 to the model containing just weight, produced no significant improvement to the fit ($P=0.9$).

Model M3, with a prediction interval of 165 ml, performed best and significantly better than model M1 which had a prediction interval of 200 ml ($P<0.001$) and model M2, which had a prediction interval of 420 ml ($P<0.001$). The 95% prediction interval of model M4 was 210 ml.

Table 4 Published regression models predicting total body water in neonates

Reference	*n =*	*Age (days)*	*Weight (kg)*	*Equation*	*R^2*	*Residual SD*
Mayfield *et al*[7] 1991	15	1	< 2.5	TBW (ml) = $523 + 217.6\ wt\ H^2/R$	95.3*	
	17	4-7	< 2.5	TBW (ml) = $567 + 235.8\ wt\ H^2/R$	91.6*	
Kushner *et al*[10] 1992	175	See text	See text	TBW†‡ (kg) = $0.04 + 0.065\ wt + 0.593\ H^2/R$		0.13
				$= -0.32 + 0.7\ H^2/R$		0.15
Novak *et al*[9] 1992	32	6-10yr	—	TBW‡ (kg) = $0.158 + 0.662\ H^2/X_c$		
Wilson *et al*[8] 1993	17	21-71	0.871-1.919	TBW‡ (kg) = $0.55\ L^2/I + 0.09$	92.0*	
Present study	28	< 7	0.690-3.510	TBW (l) = $0.135 + 0.516\ wt + 4.074\ L^2/R$	99.4	0.042
				$= 0.144 + 15.518\ L^2/R$	96.4	0.099

* Calculated from published data; † Included subjects from Mayfield *et al*[7]; ‡ Repeated measures. All readings made at 50 kHz; H: height in cm; L: foot length in cm; R: resistance; X_c: reactance; wt: weight in kg.

For the weight dependent models (M1 and M3), the segmental readings from the left upper arm–left thigh electrode position performed as well as the average of readings obtained from the four distal limb positions. For the others, the averaged limb readings were better. The averaged limb readings were therefore used in each of models 1–4.

Discussion

The management of fluid balance and nutrition is an important part of neonatal intensive care. Standard clinical assessment of alterations in fluid balance and growth in sick newborn babies is imprecise. Monitoring changes in weight alone will not provide information about the relative contribution of changes in body water and body solids. A non-invasive repeatable method to estimate total body water would therefore be invaluable.

The use of bioelectrical impedance analysis to estimate total body water began with the work of Hoffer[5] in 1969 and was followed by that of other investigators, reviewed by Van Loan.[6] It has also been applied to children and there have been a few reports specifically addressing its application to newborn babies.[7–10] Mayfield *et al*[7] made 32 measurements in 22 babies in the first week after birth. Wilson *et al*[8] also performed 17 measurements in eight babies during the first 73 days after birth. Novak *et al*[10] studied 16 children, aged 6 days to 10 years, after cardiac surgery, of whom four were less than 1 month old. Using measurements of $H_2{}^{18}O$ or deuterium dilution space, regression equations were developed to predict total body water from bioelectrical resistance. Although these authors concluded that the technique is applicable to population studies of neonates, different statistical techniques and impedance methodology make comparison with our data difficult (table 4). Furthermore, in two of these studies data obtained on separate occasions from the same baby were combined in the regression models, a questionable analysis as the measures are not independent.

Kushner *et al*[10] concluded that the index L^2/resistance is a significant predictor of total body water, and that the addition of body weight improved the prediction. Our study confirms the correlation of L^2/R with total body water and shows that $1/R$ is a significant additive factor to L^2 in the prediction.

Our data performed best with resistance measurements obtained at 50 kHz, although there was little difference when compared with total impedance at 500 kHz. It was not technically possible to assess prediction of total body water using resistance measurements at frequencies higher than 50 kHz. If this is possible in future, it may further improve the technique, as in theory, impedance to the flow of current offered by cell membranes is reduced at higher frequencies.

It has been said of bioelectrical impedance analysis that: “the technique should be judged primarily on its ability to predict total body water.”[1] Our study confirms that bioelectrical impedance analysis is a simple non-invasive method to estimate total body water in newborn babies receiving intensive care. It should prove to be a useful tool both for the assessment of changes in body water and body composition.

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