Prediction of outcome following hypoxia/ischaemia in the human infant using cerebral impedance

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ABSTRACT

Objective: Changes in cerebral impedance in the newborn piglet are able to discriminate, within 1–2 h of acute hypoxia, between animals which will have a good neurological outcome, and those who have suffered more severe hypoxia resulting in poor outcome. The aim of this study was to determine if cerebral impedance could be used to identify those human infants with an encephalopathy following acute hypoxia who subsequently have a poor neurological outcome. It is these infants who may benefit most from neural rescue treatment.

Methods: Twenty-four newborn term infants with evidence of severe acute intrapartum hypoxia and encephalopathy were studied. Bioimpedance spectroscopy was commenced as soon as possible after birth and repeated every 30 min until the infant was 12 h old. Neurodevelopmental outcome was assessed at 12 months of age.

Results: Although cerebral impedance was different to control values, there was no significant difference in cerebral impedance between hypoxic babies with normal and those with abnormal development.

Conclusion: Cerebral impedance was increased in hypoxic babies, as predicted from animal data, but the method was not suitable for discrimination of outcome.

Significance: Cerebral impedance is not useful for early identification of infants who subsequently have a poor outcome after acute intrapartum hypoxia and who may benefit from neural rescue treatment.

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1. Introduction

Severe perinatal asphyxia occurs in about 1 in every 500 births carrying with it a high risk of death or neurological disability throughout life. A small window of opportunity exists (within 6–12 h of hypoxia) to implement neural rescue strategies to prevent or reduce neuronal injury. However, potential treatments may involve risks such as delayed neural development, and metabolic and cardiovascular complications. Consequently, these treatments should only be used in neonates for whom the potential benefits of treatment outweigh the risks (Gunn et al., 1998). There is currently no technique available that can accurately identify these infants either before birth or within the short period after birth when neuroprotective treatments

may be effective (du Plessis and Johnston, 1997; Gunn et al., 1998). Although aEEG may be useful it is altered by medications commonly used in these infants and can be difficult to interpret accurately with 6–12 h of birth (de Vries and Toet, 2006; Hellström-Westas and Rosén, 2006).

One of the early events that occurs following reduced oxygen supply to the brain is the movement of fluid from the extracellular to the intracellular compartment, resulting in cerebral oedema (Klatzo, 1994). The degree and duration of this oedema is related to the degree of damage to the brain (Klein et al., 1993; Lupton et al., 1988; Vannucci et al., 1993; Williams et al., 1991). Thus a methodology which is able to measure the severity of cerebral oedema would be useful for early prediction of neurological outcome following hypoxia-ischemia.

Bio-impedance spectroscopy (BIS, formerly known as multiple frequency bio-electrical impedance analysis) is a rapid, safe, non-invasive and inexpensive technology which can be used to obtain estimates of total body water and extracellular water. We have shown that cerebral BIS can be used to detect cerebral edema following hypoxia-ischemia in the newborn piglet (Lingwood et al., 2002). In addition, our studies in the piglet have

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shown that BIS can discriminate, as early as 1–2 h after an hypoxic insult, between those animals that will have a good neurological outcome, and those who have a poor neurological outcome (Lingwood et al., 2003). Changes in impedance variables associated with alterations in brain water (Grasso et al., 2002), alterations in morphology of the extra-cellular spaces (Ivorra et al., 2005), and disturbances of fluid balance associated with critical illness (Itobi et al., 2006) have also been shown. The feasibility of measuring whole-body and cerebral impedance in human neonates has been demonstrated (Healy and Lingwood, 2006; Lingwood et al., 2000). If cerebral impedance changes in the human infant are related to neurological outcome then these measurements may make it possible to identify at an early stage those infants who have suffered a significant acute hypoxic insult and may benefit from neural rescue treatments.

The aim of this study was to determine if cerebral impedance can identify those infants who have suffered an acute intrapartum hypoxic event and will have a poor neurological outcome. The study uses a set of inclusion criteria which were not designed to unequivocally identify only babies who would benefit from neural rescue treatment, but to identify those for whom the question: “Would this baby benefit from neural rescue treatment?” might be posed. After early measurement of cerebral impedance, the study then uses more specific criteria to separate retrospectively those who would have benefited from treatment, from those who would not have benefited because:

- they would have had a good outcome without treatment,
- they suffered from chronic or antepartum hypoxia/ischaemia and neural rescue treatment would be too late to be effective, or
- their encephalopathy was not caused by hypoxic/ischaemic injury.

2. Methods

The study was approved by the Human Ethics Committees of the Royal Brisbane and Women’s Hospital, the Mater Mothers’ Hospital, Brisbane, The Canberra Hospital and the University of Queensland. Written informed consent was obtained from at least one parent of each study subject.

2.1. Study subjects

Term and near term (gestation ≥ 35 weeks) newborns were recruited from the neonatal intensive care units of Royal Brisbane and Women’s Hospital, the Mater Mothers’ Hospital, Brisbane and The Canberra Hospital.

Inclusion criteria were:

- <12 h after birth and
- 5 min Apgar score <6 or
- cord arterial or early arterial pH more than 2SD below the mean (i.e. <7.12) (Helwig et al., 1996) or arterial base excess <–12 mEq/L (Gray et al., 1993; Low, 1997) and
- encephalopathy (altered level of consciousness, abnormal tone or reflexes, or the presence of seizures).

Both inborn and outborn infants were considered. Infants with major congenital malformations were excluded as were infants with evidence of chronic antepartum hypoxia as indicated by birthweight below the 10th percentile. Body temperature will influence impedance values and also has the potential to alter outcome, and thus babies where the body temperature was excessively low (<36.2 °C) or high (>37.5 °C) data were excluded from the study.

2.2. Impedance measurements

BIS measurements were made using a bioimpedance spectrometer (SFB3 model 3.3, Impedimed-SEAC, Brisbane, Australia) as previously described (Healy and Lingwood, 2006). Cerebral impedance measurements were made in triplicate using an automated data collection system consisting of a PC and custom-produced software. BIS measurements were commenced as soon as convenient after birth and continued at 30-min intervals until the infant was 12 h old. In order to account for the possible impact of overall disturbances in fluid balance on cerebral impedance, whole body impedance measurements were made at the same times by placing gel electrodes in standard positions on one arm and one leg (Lingwood et al., 2000).

Software supplied with the impedance analyser (Impedimed Ltd., Brisbane, Australia) was used to extract impedance parameters from the measured data using the Cole–Cole model (Cole and Cole, 1941). We have previously shown that the resistance at zero frequency (R_0) is predictive of outcome after hypoxia/ischaemia in the neonatal piglet (Lingwood et al., 2003). In addition to this parameter impedance, resistance, reactance and phase at the characteristic frequency (frequency at which the reactance is maximum), and at 5 and 50 kHz, as well as the co-ordinates of the centre of the Cole–Cole plot were calculated. The y-coordinate of the centre of the plot (X_{centre}) is proportional to the α parameter, reported to provide a measure of the integrity of the morphology of the extracellular spaces (Ivorra et al., 2005). A number of other parameters reported to be measures of alterations in brain water or critical illness were also calculated. Grasso et al. (2002) calculated a predictor of total brain water using the expression: [cranial circumference]²/resistance. Itobi et al. (2006) report the ratio of impedance at 200 kHz to that at 5 kHz to be predictive of disturbances in fluid distribution and the development of critical illness. Data were examined for consistent time trends. As no such trends were apparent data are presented as the mean of each variable for the time periods corresponding to 0–8 h old and 8–12 h old.

2.3. Acute intrapartum hypoxic event

The occurrence of an acute, intrapartum hypoxic event was determined from patient history and clinical course, by the presence of one or more of the following criteria used by MacLennan (1999) to establish timing of an insult, in addition to initial inclusion criteria:

- a sentinel hypoxic event occurring immediately before or during labour eg placental abruption, cord prolapse, ruptured uterus, fetal/maternal haemorrhage;
- a sudden, rapid and sustained deterioration of the fetal heart rate pattern where the pattern was previously normal. Cardiotocographic recordings were assessed by an experienced midwife blinded to impedance results and other clinical data;
- early evidence of multi-organ hypoxic/ischaemic injury such as urine flow <1.0 ml/kg/h for more than 24 h, or serum creatinine above 0.12 mmol/L for more than 24 h, or presence of red blood cells in the urine, or mean arterial pressure <35 mmHg;
- imaging evidence of acute cerebral abnormality consistent with generalized cerebral oedema prior to 4 days of age.

The occurrence of an acute, intrapartum hypoxic event was assigned by an observer who was unaware of cerebral impedance results.

2.4. Assessment of neurodevelopmental outcome

Outcome was determined at 12 months of age when infants were seen for follow-up at the neurodevelopmental clinic of the

Royal Brisbane and Women's Hospital, the Mater Mothers' Hospital or the Canberra Hospital. At that time, a neurological assessment was made by a specialist pediatrician, and a Bayley assessment (Bayley Scales of Infant Development II, Bayley, 1993) made by a psychologist. Vision and hearing were also assessed by the appropriate specialists. A poor outcome was defined as death, or Bayley score >2SD below the mean, or Bayley score not testable due to motor or visual impairment. Neurodevelopmental outcome result was assigned by an observer who was unaware of cerebral impedance results.

2.5. Other clinical data

Information on a range of other clinical variables that may impact on cerebral or whole body impedance was collected. These included birth weight, gestational age, gender, mode of delivery, head circumference (at commencement of the study), temperature and serum sodium levels.

2.6. Data analysis

Infants were retrospectively divided into two groups based on the presence of an acute intrapartum hypoxic event and on neurodevelopmental outcome. Group A includes those infants having both evidence of an acute intrapartum hypoxic event and a poor outcome. Group B includes all other infants (Table 1). Variables were also compared with data from a control group of babies previously described (Healy and Lingwood, 2006). ANOVA, with *post hoc* tests (LSD) where a significant difference was found, was used to test for differences between groups A and B, and control data for continuous variables. Pearson's Chi-square was used to test for group differences between categorical variables. Pearson's correlation was used to measure the strength of association between cerebral and whole body impedance variables, and between impedance parameters and sodium concentrations. All analyses were conducted using SPSS version 13.

3. Results

Impedance measurements were performed on 24 babies although measurements taken prior to 8 h after birth were only available in 18 babies. Of these 24 babies a total of 17 satisfied the criteria for acute hypoxia and 11 were assessed as having a poor outcome (including six deaths). There were 10 babies with both acute hypoxia and a poor outcome (group A), leaving 14 babies in group B (Table 1).

The demographic and clinical data for groups A and B, and data from a group of control babies previously described (Healy and Lingwood, 2006), are shown in Table 2. There were no statistical differences between groups A and B in any variable. Babies in group B were slightly heavier than the control group and babies in both groups A and B had a larger head circumference than the control group.

The cerebral impedance data for groups A and B are shown in Table 3 for variables considered most likely to be predictive of outcome, based on theoretical principles or previously published observations. There were no significant differences between

groups A and B in any cerebral impedance variable (including those not listed in Table 3), measured or calculated, except for X_{centre} at 0–8 h. Data for cerebral R_0 and X_{centre} are depicted graphically in Fig. 1. There were significant differences in cerebral impedance between group A and previously published control data (Healy and Lingwood, 2006) for R_0 at 0–8 h, Z_c at both time-points and X_{centre} at 8–12 h, and between group B and controls for R_0 at 8–12 h, Z_c at both time-points and X_{centre} at both time-points (Table 3). For all cerebral impedance variables there was no significant difference between group A and a subgroup of group B ($n = 7$) which included only those babies having evidence of acute hypoxia and a good outcome.

There was a significant difference between groups A and B for the whole body impedance variable Z_c at 8–12 h but not in any other variable (Table 4) (including those not listed in the table). There was no correlation between cerebral and whole body values for any impedance variables. For whole body impedance there were significant differences between group A and previously published control data (Healy and Lingwood, 2006) for R_0 , Z_c and X_{centre} at 8–12 h, and between group B and controls for R_0 at 8–12 h and X_{centre} at both time-points (Table 4).

Serum sodium can be quite variable in this population due to the effects of hypoxia on renal function. The relationship between cerebral or whole body impedance and serum sodium concentration was assessed to determine possible confounding effects of serum sodium concentration on impedance measurements. There was no significant correlation between either cerebral or whole body impedance variables, and serum sodium concentrations.

4. Discussion

Although our previous data have demonstrated that the cerebral impedance variable R_0 is effective for early prediction of outcome following hypoxia in the newborn piglet (Lingwood et al., 2003), we have been unable to confirm this in the human infant. There were no differences between group A and group B babies for any of the cerebral impedance parameters measured except for X_{centre} , or for any of the calculated variables previously reported as being useful for prediction of outcome.

The inability to show a significant difference between groups A and B may be due to the low numbers of babies in this study. However, Fig. 1 indicates that there is considerable overlap between groups A and B in both R_0 and X_{centre} . Thus even if greater numbers

Table 2

Demographic data for group A (acute hypoxia with poor outcome) and group B (others). Data from a group of control babies previously described (Healy and Lingwood, 2006) is included for comparison of some variables.

Variable	Group A (N = 10)	Group B (N = 14)	Control (N = 75) (0–8 h N = 43)
Birth weight (g)	3698 (677)	3852 (869)*	3506 (472)
Gestational age (weeks)	39.5 (1.9)	39.2 (1.9)	39.7 (1.4)
Percentage of male (n)	50.0 (5)	46.2 (6) ^a	44.0 (33)
Percentage of spontaneous vaginal delivery (n)	40.0 (4)	78.5 (11)	91.7 (69)
Head circumference (cm)	35.6 (1.4)*	35.4 (2.1)*	34.4 (1.5)
Temperature (°C)	36.4 (0.4)	36.4 (0.3)	N/A
Serum sodium (mmol/L)	136.3 (4.9)	136.0 (3.7)	N/A
5 min Apgar: median (range)	3.0 (0–5)	2.0 (0–7)	9 (8–10)
Cord pH ^b	6.94 (0.19)	6.92 (0.28)	N/A
Cord ABE ^b (mmol/L)	−21.6 (6.4)	−18.8 (5.0)	N/A
Percentage of outborn (n)	60.0 (6)	61.5 (8)	0
Age at first measurement (h)	6.9 (2.6)	5.7 (1.9)	7.7 (2.0)

Values expressed as mean (SD) unless otherwise indicated.

^a Gender not recorded in two babies.

^b Cord pH and ABE were not measured in all babies.

* $p < 0.05$ compared to control.

Table 1

Subjects were allocated to group A or group B based on both outcome and the presence of an acute intrapartum hypoxic event.

	Acute intra partum hy ox ic event	No acute intra partum hy ox ic event
Poor outcome	Group A (N = 10)	Group B (N = 1)
Good outcome	Group B (N = 7)	Group B (N = 6)

Table 3

Cerebral impedance data for the 0–8 and 8–12 h time periods in group A (acute hypoxia with poor outcome) and group B (others). Data from a group of control babies previously described (Healy and Lingwood, 2006) is included for comparison of some variables. Data are expressed as mean (SD).

Impedance variable	Group A N = 10 (0–8 h N = 7)	Group B N = 14 (0–8 h N = 11)	Control N = 75 (0–8 h N = 43)
R_0 (Ω)			
0–8 h	55.4 (7.2)*	49.0 (8.3)	46.4 (6.1)
8–12 h	49.7 (6.0)	50.5 (9.9)*	45.2 (6.0)
Z_c (Ω)			
0–8 h	45.4 (4.5)*	44.4 (5.5)*	39.9 (5.1)
8–12 h	43.2 (5.6)*	45.4 (7.3)*	38.4 (4.5)
Z_{50} (Ω)			
0–8 h	50.1 (6.8)	46.2 (6.4)	
8–12 h	45.8 (6.3)	47.4 (7.6)	
X_{50} (Ω)			
0–8 h	5.33 (1.91)	5.31 (2.06)	
8–12 h	5.73 (1.94)	6.14 (3.22)	
Ph_{50} ($^\circ$)			
0–8 h	6.23 (2.51)	6.58 (2.71)	
8–12 h	7.23 (2.59)	7.53 (3.23)	
X_{centre} (Ω)			
0–8 h	–5.95 (5.17)**	–0.38 (2.80)*	–3.40 (3.33)
8–12 h	–0.20 (1.60)*	0.31 (3.18)*	–4.18 (3.77)
Z_5/Z_{200}			
0–8 h	1.10 (0.20)	1.12 (0.06)	
8–12 h	1.14 (0.23)	1.36 (0.92)	
HC^2/R_0			
0–8 h	23.2 (3.6)	26.3 (4.1)	
8–12 h	26.1 (2.8)	25.6 (3.9)	
HC^2/R_{50}			
0–8 h	25.8 (3.9)	27.9 (3.9)	
8–12 h	27.0 (3.2)	27.5 (3.4)	

R_0 , resistance at zero frequency; Z_c , impedance at the characteristic frequency; Z_{50} , impedance at 50 kHz; X_{50} , reactance at 50 kHz; Ph_{50} , phase at 50 kHz; X_{centre} , y (reactance) co-ordinate of the centre of the circle; Z_5 , impedance at 5 kHz; Z_{200} , impedance at 200 kHz; HC, head circumference.

* $p < 0.05$ compared to control.

** $p < 0.05$ compared to group B.

were studied, and a significant difference found between the groups, the clinical utility of a test based on cerebral impedance for identification of acute hypoxia resulting in a poor neurodevelopmental outcome would be limited by low sensitivity and specificity values.

We have shown that in group A R_0 at 0–8 h and Z_c at 0–8 h and 8–12 h are significantly different to values obtained in a control population. This observation is consistent with the data obtained in the piglet and demonstrates that cerebral impedance in the human infant increases in the same way as in the piglet. However, mean cerebral impedance in group B is also elevated above that in control babies, and thus it is not possible to use these variables

Table 4

Whole body impedance data for the 0–8 and 8–12 h time periods in group A (acute hypoxia with poor outcome) and group B (others). Data from a group of control babies previously described (Healy and Lingwood, 2006) is included for comparison of some variables. Mean (SD).

Impedance variable	Group A (N = 10) (0–8 h N = 7)	Group B (N = 14) (0–8 h N = 11)	Control (N = 75) (0–8 h N = 43)
R_0 (Ω)			
0–8 h	659 (126)	633 (98)	683 (70)
8–12 h	609 (68)*	651 (94)*	722 (73)
Z_c (Ω)			
0–8 h	533 (83)	553 (71)	562 (64)
8–12 h	516 (71)***	570 (68)	589 (56)
Z_{50} (Ω)			
0–8 h	583 (112)	581 (63)	
8–12 h	553 (63)	602 (80)	
X_{50} (Ω)			
0–8 h	50.2 (45.5)	58.9 (46.6)	
8–12 h	44.9 (19.7)	77.0 (75.7)	
Ph_{50} ($^\circ$)			
0–8 h	4.71 (4.32)	7.52 (5.65)	
8–12 h	4.83 (2.52)	7.10 (6.02)	
X_{centre} (Ω)			
0–8 h	–93.2 (52.5)	–58.5 (65.7)*	–103.0 (43.0)
8–12 h	–64.0 (25.9)*	–31.7 (37.0)*	–105.1 (35.4)
Z_5/Z_{200}			
0–8 h	1.25 (0.58)	1.18 (0.08)	
8–12 h	1.26 (0.19)	1.14 (0.22)	

R_0 , resistance at zero frequency; Z_c , impedance at the characteristic frequency; Z_{50} , impedance at 50 kHz; X_{50} , reactance at 50 kHz; Ph_{50} , phase at 50 kHz; X_{centre} , y (reactance) co-ordinate of the centre of the circle; Z_5 , impedance at 5 kHz; Z_{200} , impedance at 200 kHz; HC, head circumference.

* $p < 0.05$ compared to control.

** $p < 0.05$ compared to group B.

clinically to distinguish those infants who have suffered acute hypoxia leading to a poor neurodevelopmental outcome from other infants who might also be considered for neural rescue treatment but would be unlikely to benefit from such treatment.

It is unclear why those babies in group B also have elevated cerebral impedance. Babies in both groups A and B had a larger head circumference than the control group perhaps reflecting the presence of cerebral oedema in group A. In group B the larger head circumference may solely reflect the larger average size of babies in group B, but it is possible that some babies in this group may have had mild cerebral oedema which contributed to the elevated cerebral impedance. Some may also have had pre-existing brain abnormalities from antepartum injury or altered brain development. It is unknown how these changes might affect cerebral impedance. The babies in group B (all those who were not classified as having acute hypoxia and a poor outcome) were not a homogenous group. This group included babies with evidence of

Fig. 1. Values of cerebral R_0 and X_{centre} for individual babies and the mean in group A (acute hypoxia with poor outcome) and group B (others) in the first 8 h after birth.

an acute intrapartum hypoxic event but having a good outcome, as well as those without acute intrapartum hypoxia but having a poor outcome. This may explain why the standard deviation of BIS variables in this group is slightly higher than in the babies with acute hypoxia and a poor outcome (group A). However, when babies in group A were compared with the subgroup that had evidence of acute hypoxia and a good outcome there was still no significant difference in impedance between the groups. There was only one baby with a poor outcome and no evidence of acute hypoxia and so this subgroup contributed little to the heterogeneity of the group. The inability to identify those with acute hypoxia leading to a poor outcome is not the result of the heterogeneity of group B (other babies).

An alternative explanation for the inability to show a difference in cerebral R_0 between groups A and B could be the misclassification of a number of babies because of the difficulty of being certain about the presence of acute hypoxia. However, the babies in group B with the four highest values of R_0 all had a good outcome and thus, even if they were wrongly classified in relation to the presence of acute hypoxia, they would remain in group B. The babies in group A with the two lowest values of R_0 both clearly satisfied two or more of the required criteria and thus had good evidence for acute hypoxia. The misclassification of babies is unlikely to account for the lack of difference between group A and group B in cerebral impedance.

We have previously shown that cerebral impedance is not affected by head circumference at least within a small range of circumferences (Healy and Lingwood, 2006). Likewise in this study, there is no relationship between head circumference and any cerebral impedance variable. There was also no relationship between cerebral or whole body impedance and serum sodium levels. Thus it is unlikely that inability to demonstrate a difference between groups A and B is the result of variations in head circumference or serum sodium.

The observation that cerebral X_{centre} is significantly more negative in group A than is group B is consistent with the results of Ivorra et al. (2005) who reported changes in the α parameter in association with tissue structural alterations. However, Fig. 1 indicates that this significant decrease may be the result of a single extreme point in group A. Even if this difference is real, once again the overlap between the two groups means that the parameter is not useful as a sensitive and specific identifier of those babies who are most likely to benefit from neural rescue treatment. Further research looking at combinations of multiple impedance parameters may yield a useful predictor of outcome.

In the piglet study it was possible to obtain impedance measurements prior to exposure to hypoxia and prediction of outcome was based on the change in cerebral impedance from the animal's own baseline value. For the human infant who has suffered intrapartum hypoxia, it is not possible to obtain baseline readings of impedance, and thus it is not possible to predict outcome using the amount of change that has occurred in that individual – only by comparing the absolute post-hypoxia values. This may contribute to the inability to discriminate those who have suffered acute hypoxia resulting in a poor neurodevelopmental outcome from all other babies who might also be considered for neural rescue treatment.

Cerebral oedema following hypoxia/ischaemia occurs in two stages (Klatzo, 1994). The first stage, cytotoxic oedema, results from the movement of water from the extracellular space to the intracellular space. This phase persists for 3–8 h (Klatzo, 1994) and corresponds to a decrease in extracellular volume. This is followed by vasogenic oedema which is characterized by an expansion of the extracellular space. Our piglet studies were all conducted within 6 h of hypoxia, i.e. within the cytotoxic oedema phase. Although the babies in this group were assessed within 8 h of birth, we do not know precisely when the hypoxic insult oc-

curred. Few babies had an obvious event that would enable us to accurately determine the time interval between hypoxia and the assessment of cerebral impedance. Thus some of these babies may have already entered the vasogenic oedema phase. The effects of vasogenic oedema on cerebral impedance are unknown. This factor may have impacted on our ability to identify those infants who would have benefited from neural rescue treatment.

Although not useful for prediction of outcome, the alterations in whole body impedance in these babies are of interest, particularly when compared with control values. In the first 8 h of life whole body impedance is not different to that in control babies indicating that fluid balance in these babies is not significantly altered at birth. However, by 8–12 h after birth whole body impedance is slightly increased in control babies and babies in group B, probably reflecting the normal loss of extracellular fluid which occurs in the first days of life. In contrast, whole body impedance in group A babies falls over the same time period and thus is significantly different to both control and group B babies in the 8–12 h period. This may be due to an overall increase in extracellular volume resulting from both administration of fluid and a reduced ability to excrete fluid in those babies who have experienced acute hypoxia with some resultant renal failure. Whilst these changes are interesting, the considerable overlap in impedance between groups A and B means that this parameter is also not useful for identification of those babies who may benefit from neural rescue treatment.

In conclusion, we have demonstrated that cerebral impedance, as applied in this study, in the human infant who has experienced acute hypoxia resulting in a poor neurological outcome increases in the same way as in the newborn piglet. However, similar increases also occur in other babies who may also be considered for neural rescue treatment but will not benefit because their outcome will be good without treatment, or they have not experienced acute hypoxia. Thus the technique is not useful for early identification of infants most likely to benefit from neural rescue treatment.

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