47 PROGNOSTIC VALUE OF CEREBRO-VASCULAR CO2-REACTIVITY IN PREMATURE INFANTS

Annalies E. Lipp, Cleopatra G. Morales, Gabriel Duc - Division of Neonatology, University Children's Hospital, CH-8032 Zürich, Switzerland

Studies in animals and human adults have shown that ischemic brain lesions are associated with dysregulation of cerebral blood flow (CBF) and loss of pCO2-reactivity. We measured CBF by means of the iv Xe-133 method in 60 premature babies at days 1,3 and 7, and asked whether (i) changes in arterial pCO2 might influence CBF, and (ii) whether periventricular leukomalacia (PVL) might impair CO2-reactivity. Patients: birthweight 1072 ± 156 g, gestational age 29.1± 2.1 wk. US was normal in 17 (28%), 14 (23%) had subependymal (SEH), and 11 (18%) intraventricular (IVH) hemorrhage; 10 (17%) had increased parenchymal echodensities (IPE), and 8 (13%) cystic PVL. In normal babies and those with SEH/IVH only, a positive correlation between pCO2 and CBF was found on day 3 ($r = 0.49$, $p<0.01$, $n=29$); multiple regression showed that the influence of pCO2 was significant and independent of Hkt, MABP and [HbF] at all days. The CO2-reactivity (Δ %CBF/ΔmmHg pCO2) was measured in 12 infants of this US-group. Mean: +3.47%/mmHg. In infants with IPE/PVL, CBF was not correlated with pCO2 and mean CO2-reactivity significantly reduced to -0.85% ($p < 0.0001$). Thus, normal babies and those with SEH/IVH only, have a CO2-reactivity comparable to normal adults. Infants with IPE/PVL show dysregulation of CBF with loss of CO2-reactivity before brain lesions can be visualized by means of US. Supp: NF 3.894.

48 NEONATAL ULTRASOUND BRAIN SCAN FINDINGS PREDICT NEUROLOGICAL AND COGNITIVE OUTCOME AT EIGHT YEARS IN VERY PRETERM INFANTS.

J Baudin, SC Roth, J Townsend, DC McCormick, AD Edwards, EOR Reynolds, AL Stewart. *Department of Paediatrics, University College and Middlesex School of Medicine, London. UK.*

We have previously reported the prediction of neurodevelopmental outcome at one and 4 years from neonatal ultrasound brain scan findings in a cohort of very preterm (<33 weeks) infants (1). To investigate prediction of outcome at school age 95% of the cohort were re-examined at a mean age of 98 (SD ±4) months with clinical and neurological examinations, tests of hearing, vision, visuo-motor integration (Beery), cognitive functioning (WISC-R, K-ABC) and school achievement (K-ABC). The main results were:

Neonatal Ultrasound	n	Eight years Impairment Major	Minor	Special School	Normal + help	WISC IQ±SD	Achieve. Score
Normal	92	5(5%)	12(12%)	4(4%)	6(6%)	105±15	99±13
Uncomplicated PVH	39	1(3%)	6(15%)	1(3%)	2(5%)	102±14	98±15
Ventricular dilat	16	4(25%)	4(25%)	5(31%)	1(6%)	92±21	90±23
Hydroceph/atrophy	15	7(47%)	3(20%)	4(27%)	4(27%)	88±16	87±9

Multiple regression analysis confirmed: 1. Hydrocephalus/cerebral atrophy and ventricular dilatation were highly significant independent predictors of neurodevelopmental impairment, IQ and school performance at 8 years in very preterm infants ($p<0.001$) 2. Neither uncomplicated PVH nor normal scans were significant predictors of outcome at 8.

1. Costello et al., Dev Med Child Neurol 1988;30:711-722.

49 NEUROLOGICAL IMPAIRMENT AT ONE YEAR PREDICTS NEUROLOGICAL AND COGNITIVE OUTCOME AT EIGHT YEARS IN VERY PRETERM INFANTS.

SC Roth, J Baudin, J Townsend, DC McCormick, AD Edwards, EOR Reynolds, AL Stewart. *Department of Paediatrics, University College and Middlesex School of Medicine, London. UK.*

We have previously reported the prediction of neurodevelopmental outcome at 4 years from the results of neurodevelopmental assessment at one year in a cohort of very preterm (<33 weeks) infants (1). At one year infants were classified by the presence of neurological impairment (major, with disability; minor, without disability) and the results of developmental testing (DQ). To investigate prediction at 8 years, 95% of the cohort were re-examined at a mean age of 98 (SD ±4) months with clinical and neurological examinations, tests of hearing, vision, visuo-motor integration (Beery), cognitive functioning (WISC-R, K-ABC) and school achievement (K-ABC). The main results were:

One year Classif.	n	DQ	Eight years Impairment Major	Minor	Special School	Normal + help	WISC IQ±SD	Achieve. Score
Normal	131	103±9	1(1%)	21(16%)	2(2%)	8(6%)	105±14	99±14
Minor	14	105±6	1(7%)	2(14%)	0	3(21%)	96±17	91±14
Major	17	79±17	15(88%)	2(12%)	12(70%)	2(12%)	76±14	83±18

Multiple regression analysis showed that neurological impairment at one year was a highly significant independent predictor of outcome at 8 years ($p<0.001$) whereas DQ at one year was not.

1. Stewart et al., Dev Med Child Neurol. 1988;30:53-63

50 LBWIs (BW ≤ 2500g) IN A KENYAN RURAL HOSPITAL

Donzelli G.P., Tomasini B., Zani S., Rapisardi C., Profeti C.,Moroni M. Department of Pediatrics, NICU, University of Florence, Italy

During their post at the Department of Obstetrics and Gynaecology at Consolata Hospital NKUBU, a rural hospital in Meru District, 230km NE highlands from Nairobi,Kenya, two members of our Department collected data, through a card system, on delivered women and their babies, from Jan 1987 to Dec 1988. The total number of deliveries was 10861. The prevalence of LBWIs (bw ≤ 2500g) was 11.5% of the total population (9.5% SGA term and 2% preterm infants). LBWIs (n=1240) significantly differed from NBWIs (bw > 2500g; n=9621) for maternal age, parity, fetal mortality rate, presence of major malformations ($p < 0.0001$), but not for previous abortions, sex or dystocic deliveries. Preterm LBW infants differed from term SGA infants for fetal mortality rate and multiparity ($p<0.01$), but not for maternal age, parity, previous abortions, dystocic deliveries, sex, major malformations and provenance area (data on provenance area were available only for LBWIs). The single most important factor in the prediction of bw (a stepwise multiple regression was computed in which maternal age, parity, previous abortion, sex and major malformations were entered),.was maternal age ($r^2=.027$). A highly significant relationship was found between maternal age and weight, with younger and older mother delivering the lightest babies, which was best expressed by a second order polynomial regression ($r=.20$, $p < 0.0001$).Parity was strictly associated with maternal age and it was not associated with bw when the independent variable 'maternal age' was controlled.

51 EFFECT OF NORDIHYDROGUAIARETIC ACID(NDGA) ON CEREBRAL RESPONSE TO HYPOXIA IN NEWBORN PIGLETS.

Jane E. DiGiacomo, Om P. Mishra, and Maria Delivoria-Papadopoulos. Dept of Physiology, Univ of Penna Sch of Med, Phila.

Cerebral hypoxia reduces brain cell membrane Na^+, K^+-ATPase activity (ATPase) and increases membrane lipid peroxidation (conjugated dienes, CD, and fluorescent compounds, FC). To test the hypothesis that NDGA, an inhibitor of lipoxygenase, modifies hypoxia-induced membrane changes, we measured ATPase, CD, and FC in 8 ventilated newborn piglets. Five received 3 mg/kg NDGA IV 15 min before reducing FiO_2 (HX). Cerebral hypoxia was confirmed with 31P-NMR spectroscopy as a decrease in PCr/Pi and maintained for 45 min. Three piglets were kept normoxic for 45 min after NDGA (NX). Direct effects were assessed in vitro by exposing normoxic brain cell membranes to 0.1 mM NDGA. ATPase (μmole Pi/mg protein/hr) in vivo was 44.1±7, 39.9±4.9, and 45.5±5 in HX, NX, and untreated controls (C), respectively (p=NS). FC (μg quinine sulfate/g brain) increased to 0.26±0.05 in HX ($p<0.05$ vs C of 0.18) but were not elevated in NX. CD were not significantly higher than C in HX or NX. In vitro, NDGA reduced ATPase 95% vs activity before exposure. Thus in vivo, NDGA reduces hypoxia-induced brain cell membrane changes. However, our in vitro data, as well as reports by others that NDGA reduces cellular O_2 consumption ($\dot{V}O_2$), suggest that NDGA has a direct action on cellular metabolism. Therefore the mechanism of its effect during hypoxia may be reduction of Na^+, K^+-ATPase activity and total cell metabolism rather than inhibition of lipoxygenase. By decreasing cellular ATP utilization and $\dot{V}O_2$, NDGA would eliminate the mismatch between O_2 supply and demand during hypoxia, preserving membrane function.

52 MODIFICATION OF BRAIN CELL MEMBRANE Na^+,K^+-ATPASE FOLLOWING RECOVERY FROM SEVERE ISCHEMIC AND HYPERCAPNIC INJURY IN NEWBORN PIGLETS.

Roy Schneiderman, O.P. Mishra, Johanna Kubin, and Maria Delivoria-Papadopoulos. University of Pennsylvania School of Medicine, Dept. of Physiology, Philadelphia, PA

The present study tests the hypothesis that changes in the brain cell membrane Na^+,K^+-ATPase are reflected in the kinetic characteristics of the enzyme molecule and are specific to the active sites for ATP, Na^+, K^+ and strophanthidin. Studies were performed in 7 normoxemic piglets hyperventilated to $PaCO_2$ of 8±1 mmHg for 1 hr and allowed to recover for 6 hrs (ischemic injury) and 8 normoxemic piglets with administration of 7% CO_2 for 90 min ($PaCO_2$ 84±7 mmHg) followed by 2 hrs recovery (hypercapnic injury). Brain cell membranes were prepared and the affinities of the Na^+,K^+-ATPase for ATP, K^+,Na^+(Km in mM) and strophanthidin (IC50 in mM) were determined in the hypo- and hypercapnic states, and their respective recoveries and compared to control. For ATP, Km decreases from 0.78±0.15 in controls to 0.62±0.11 during hypocapnia and 0.61±0.12 during hypercapnia; for K^+ the Km changes from 2.36±0.56 in controls to 4.06±0.37 during hypocapnia and 1.13±0.09 during hypercapnia, and for Na^+ the Km increases from 5.43±0.57 in controls to 8.33±0.72 during hypocapnia and 6.97±0.41 during hypercapnia. The IC50 for strophanthidin decreases from $1x10^{-6}$M in controls to $6x10^{-7}$M during hypocapnia and $7x10^{-7}$M during hypercapnia. The recovery phases yielded affinities which were not statistically different from the experimental conditions. These results indicate that the active sites of Na^+, K^+-ATPase are modified during hypo- and hypercapnia. The differential alteration of the affinity for K^+ suggests that during ischemia, dephosphorylation and therefore energy release are decreased, while hypercapnia favors enzyme dephosphorylation. We suggest that the K^+ site is the critical regulatory site for enzyme function in brain cell membranes of newborn piglets.