50

VERTICAL HCV TRANSMISSION IN HIV-HCV COINFECTED MOTHERS IS INFLUENCED BY NEVIRAPINE.

S. GIANNUZZO[1], F. BONSANTE[1], S. IACOBELLI[2], J.R. FIORE[3], M. CHIRONNA[4], F. INGRASSIA[4], A. MAUTONE[1], M.M. MANZIONNA[1] [1]DEPARTEMENT OF PEDIATRICS, NEONATOLOGY SECTION, UNIVERSITY OF BARI , [2]NICU AND NEONATOLOGY SECTION, MIULLI HOSPITAL, [3]CLINIC OF INFECTIOUS DISEASE, UNIVERSITY OF FOGGIA, [4]DEPARTEMENT OF INTERNAL MEDICINE AND PUBLIC HEALTH - HYGIENE SECTION, UNIVERSITY OF BARI (ITALY)

INTRODUCTION Vertical transmission of hepatitis C virus (HCV) is greater in infants from pregnant women HCV-HIV (human immunodeficiency virus) coinfected when compared with infants from HCV infected HIV negative mothers. The mechanism of this greater rate of transmission remains unclear. Highly active antiretroviral therapy immune restoration has been implicated in potential adverse effects such as severe presentation of HCV disease.

OBJECTIVE To determine the HCV vertical transmission rate from HCV-HIV coinfected mothers, in correlation with antiretroviral treatment.

METHODS 18 coinfected pregnant women and their infants were studied. HIV status (viral load, CD4, CD8), antiretroviral treatment, HCV-RNA viral load were analysed in the mothers early in pregnancy and closest to delivery. HCV-RNA viral load was determined in the newborns at birth, 15 days, 1, 2, 5 and 8 months. Vertical transmission was defined as two positive determinations in the newborn.

RESULTS During the pregnancy we found a significant decrease of HIV viral load ($p<0.01$) and increase of CD4 ($p<0.05$) and HCV viral load ($p<0.05$). HCV vertical transmission rate was 22%. It was not related to mother's age, coinfection duration, gestational age and birth weight neither to CD4, CD8, HIV and HCV viral load during the pregnancy.

Different treatment protocols were used: NRTI (AZT, 3TC, D4T, DDC, DDI), NRTI + IP (RTV), NRTI + NNRTI (NVP). Vertical transmission was not influenced by the number of drugs, neither by NRTI or IP treatment. Only mothers treated with NVP transmitted HCV (transmission rate 50 % ($p< 0.05$). All the infants HCV infected had HCV viral load negative at birth and at 15 days of life.

CONCLUSION Nevirapine strongly influenced the vertical transmission of HCV from coinfected mothers. Vertical transmission was not related to maternal HCV viral load. All infected infants were negative at birth, suggesting the presence of a virus reservoir.

51

HIPPOCAMPAL DEVELOPMENT, POST-NATAL GROWTH AND NEURODEVELOPMENTAL OUTCOME OF PREMATURE NEWBORNS FOLLOWING IUGR

C BORRADORI-TOLSA[1], G LODYGENSKY[1], M FRESCHI[1], F LAZEYRAS[2], P HÜPPI[1] [1]PEDIATRICS, CHILDREN'S HOSPITAL , [2]RADIOLOGY, UNIVERSITY HOSPITAL (SWITZERLAND)

Background: Severe placental insufficiency with fetal IUGR is generally associated with a decreased growth potential and a compromised neurodevelopmental outcome with learning difficulties and memory deficit. A recent study documented adverse effects of prematurity and IUGR on structural brain development (Borradori-Tolsa C et al. Ped Res 2004; 56:132–36). Hippocampus, in particular, has been shown to be affected by prematurity (Isaacs EB et al.Ped Res 2000; 47:713–20).

Aims: 1) to investigate the effects of IUGR following placental insufficiency in preterm infants on postnatal growth and 2) to study the impact of IUGR on the hippocampal development and the correlation between hippocampal volumes and neurodevelopmental outcome at 18 months corrected age.

Methods: 17 preterm infants born with IUGR following placental insufficiency (GA: 32.1±2.4 wks, BW < 10th percentile) were compared with 17 control infants matched for GA (GA: 31.8±2.2 wks) with normal BW. 3D-MRI to measure brain tissue volumes was performed at 40 wks PCA. We used a specially developed 3D rendering software, 3D Slicer that allows visualization of T2 weighted images in coronal , sagittal and axial plane in order to manually segment the hippocampus. Growth parameters were measured and neurodevelopmental outcome was assessed with the Bayley scales of infant development (MDI/PDI) at 18 months.

Results: At term, infants born with IUGR had a marked reduction in cortical gray matter (CGM) volume and a smaller hippocampal volume compared to control infants. By age of 18 months, body weight, height, and head circumference (HC) were significantly lower ($p<0.01$) in the IUGR group. Mean MDI showed a trend to lower scores in children born with IUGR. PDI scores were not different in the 2 groups. However, within the total group we observed a significant positive correlation between hippocampal volume at term and MDI scores at 18 months ($p<0.01$).

	IUGR (mean±SD)	Control (mean±SD)	p
CCGM (cc)	159±28	187.3±33.4	.003
Total hippocampal volume (cc)	1.9±0.2	2.1±0.1	.012
Weight 18 (kg)	9.7±1.4	11.2±1.3	.01
Height 18 (cm)	77.1±3.7	79.9±2.4	.01
HC 18 (cm)	46.5±1.6	48.1±1.4	.01
MDI 18	75.2±12.9	82.5±10.9	.077

Conclusion: These findings suggest a particular vulnerability of the hippocampus to structural changes after placental insufficiency with IUGR which may be responsible for cognitive impairment in this population. In IUGR children catch-up growth at 18 months of age was not achieved for all three growth parameters.

52

LONGITUDINAL NEURODEVELOPMENTAL OUTCOME AT 18 MONTHS AND 5 YEARS IN INFANTS BORN <32 WEEKS OF GA

C BORRADORI-TOLSA, T HASLER, A SANCHO-ROSSIGNOLI, PS HUPPI [1]CHILD DEVELOPMENT UNIT, DEPT. OF PEDIATRICS, CHILDREN'S HOSPITAL (SWITZERLAND)

Background: Children born preterm have a high prevalence of neurologic and developmental disabilities in the first two years of live. Their predictibility for developmental problems at 5 years of age is unclear. **Aims**: 1)to assess the neurological and developmental outcome at 18 months and 5 years of age in a regionally defined cohort of preterm infants born less than 32 weeks GA. 2)To investigate the effects of prematurity and growth impairment on later motor and cognitive development.

Methods: Perinatal data were collected retrospectively on a cohort from January 1996 through December 1996. Growth, neurological examination and development were evaluated at 18 months and 5 years of age. Psychomotor development at corrected age 18 months was assessed using the Bayley Scales of Infant Development (MDI/PDI). At 5 years, cognitive function was assessed with the Kaufman Assessment Battery for Children (K-ABC).

Results: Of 54 surviving children, 45 (83%) underwent neurological and developmental assessment by age 18 months. The rates of CP, minor neurological impairment, hearing impairment, visual impairment were 7%, 20%, 7%, 2% respectively. The mean MDI and PDI scores were 94.5±24.2 and 87.8±21.2 respectively. The neonatal factors significantly associated with neurodevelopmental disability at 18 months of age were BPD ($p<0.01$) and neonatal infection ($p<0.05$). Severe cranial ultrasounds abnormalities (PVL, IVH grade 3/4) were present only in one infant. Children with MDI<85 had significantly smaller had circumference at birth and still at 18 months of corrected age (both $p<0.05$). At 5 years of age, the followed 38 children born in 1996 (70% of survivors), scored within the normal range on all subscales of the K-ABC, but children with BW < 1000g exhibited lower general cognitive ability (MCP: 82.1±12.9,vs 95.2±14.8, $p=0.05$) and scored significantly below the norm in the sequential processing scale (SP: 82.4±6.1,vs 97.9±12.9, $p<0.01$). Neonatal factors like a smaller head circumference at birth, a higher incidence of neonatal infection and poor post-natal growth correlated negatively with cognitive development ($p<0.01$, $p<0.05$, $p<0.05$ respectively). Children with MCP<85 had already significantly lower MDI scores at 18 months than children who scored within the normal limits (83±20.9 vs 102±19.5, $p<0.05$)

Conclusion: This study provides outcome data for a geographically defined cohort. BPD and neonatal infection were associated with neurodevelopmental disability at 18 months of age. Poor postnatal growth and delayed development at the age of 18 months were predictive of cognitive impairment at 5 years of age.

53

EFFECTS OF INTRAUTERINE GROWTH RESTRICTION (IUGR) AND POSTNATAL CATCH-UP GROWTH ON ARTERIAL BLOOD PRESSURE (BP), GLUCOSE TOLERANCE (GT) AND RENAL FUNC

F BOUBRED[1,2], C BUFFAT[2], JM FEUERSTEIN[2], A DESOBRY[2], M LELIÉVRE-PÉGORIER[3], M TSIMARATOS[2], C OLIVER[2], U SIMEONI[1,2] [1]DPARTMENT OF NEONATOLOGY, HOSPITAL UNIVERSITY LA CONCEPTION AP-HM, [2]FACULTY OF MEDECINE, UNIVERSITY OF MEDITERRANEAN, UPRES EA 2193, [3]LABORATORY OF MEDICAL BIOLOGY LES CORDELIERS INSERM U356 (FRANCE)

Introduction: Epidemiological and experimental studies demonstrate that low birth weight is associated with increased risk of arterial hypertension and metabolic diseases in adulthood. Rapid postnatal catch-up growth may constitute an additional risk factor.

Aim: To investigate the long term effects of early postnatal overfeeding (OF) after IUGR, on arterial systolic blood pressure (SBP), GT, and renal function in 12 month old, adult rats.

Methods: 4 groups of animals were investigated from birth to 12 months: group I, controls: offspring of dams fed normal diet (NP, casein 22 %); group II: offspring of dams fed isocaloric low-protein diet (LP, casein 9 %); group III: postnatal OF (obtained by reduction of litter size); group IV: LP rats exposed to postnatal OF. SBP was measured at 1, 2, 8 and 12 months, glomerular number was determined in newborn pups and renal function (creatinine clearance (CrCl), was assessed at 4 and 12 months. Intraperitoneal glucose tolerance test was performed in 12 months old animals. Data were analyzed by Kruskall-Wallis and Mann-Withney tests.

Results: (mean +/- SEM). LP rats offspring had a 20 % birth weight and 38 % glomerular number reduction ($p < 0.01$). Postnatally OF rats had the higher growth rate during suckling period ($p <0.005$). Although smaller at birth, LP+OF rats caught up the weight of control offspring within the first postnatal month. Catch-up growth was associated with an elevated SBP from the age of 4 weeks (110 +/-3; 117 +/- 2; 116 +/- 3; 127 +/- 2 mmHg in groups NP, LP, OF, LP+OF rats respectively; $p < 0.05$), which remained higher in 12 months old LP+OF rats. LP and OF rats displayed a significantly elevated SBP from the age of 2 months in comparison with controls (144 +/- 3; 146 +/-1.6; 130 +/- 3 mmHg, respectively; $p < 0.05$). But the difference in SBP between LP and controls rats disappeared at the age of 12 months. CrCl decreased with age in LP+OF rats but reached statistical significance in males at 12 months (3.34 +/- 0.2; 4.26 +/-0.3; 4.61+/-1.6; 5.48 +/-1.6 ml/min/kg in LP+OF, LP, OF, controls respectively). At the age of 12 months, fasting glycaemia was significantly elevated in LP+OF rats compared to controls (6.4 vs 5.1 mmol/l). After challenge with a glucose load OF and LP+OF rats had significantly higher 30 min blood glucose levels compared with controls (24+/-1.9; 19+/-1.8; 17 +/-1.2;17+/-0.8 mmol/l in LP+OF, OF, LP, controls respectively; $p<0.05$).

Conclusion: Early catch-up growth in IUGR rats enhances alteration of SBP, glucose tolerance and renal function in adulthood. Long term alteration of renal function seems influenced by gender. Early postnatal overfeeding may amplify single nephron hyperfiltration, and insulin-resistance associated with IUGR, resulting in cardiovascular and metabolic diseases at adulthood.

54

EFFECTS OF INTRAUTERINE GROWTH RESTRICTION AND CATCH-UP GROWTH ON ARTERIAL BLOOD PRESSURE, GLUCOSE TOLERANCE AND RENAL FUNCTION IN ADULT RATS

F BOUBRED[1,2], C BUFFAT[1], JM FEUERSTEIN[1], A DESOBRY[1], M LELIÉVRE-PÉGORIER[3], M TSIMARATOS[1], C OLIVER[1], U SIMEONI[1,2] [1]FACULTÉ DE MÉDECINE, UNIVERSITÉ DE LA MÉDITERRANÉE, EA2193 , [2]SERVICE DE NÉONATOLOGIE, HÔPITAL DE LA CONCEPTION, AP-HM, [3]INSERM U356 (FRANCE)

Introduction: Low birth weight is associated with increased risk of arterial hypertension and metabolic diseases in adulthood. Rapid postnatal catch-up growth may constitute an additional risk factor.

Aim: To investigate the effects of postnatal overfeeding (OF) after intrauterine growth restriction (IUGR) in 12 month old, adult rats.

Methods: 4 groups of animals were investigated: group I, controls: offspring of dams fed normal diet (NP, casein 22 %); group II: offspring of dams fed isocaloric low-protein diet (LP, casein 9 %); group III: postnatal OF (obtained by reduction of litter size); group IV: LP rats exposed to postnatal OF. Systolic blood pressure (SBP), glomerular number, renal function, fasting glycaemia and intraperitoneal glucose tolerance test were obtained

Results: (mean +/- SEM). Offspring of dams fed LP diet had a 20 % birth weight and 38 % glomerular number reduction ($p < 0.01$). Catch-up growth was associated with an elevated SBP from the age of 4 weeks (110 +/-3; 117 +/- 2; 116 +/- 3; 127 +/- 2 mmHg in groups NP, LP, OF, LP+OF rats respectively; $p < 0.05$). But the difference in SBP between LP and controls rats disappeared at the age of 12 months. Creatinine clearance decreased with age in LP+OF rats but reached statistical significance in males at 12 months (3.34 +/- 0.2; 4.26 +/-0.3; 4.61+/-1.6; 5.48 +/-1.6 ml/min/kg in LP+OF, LP, OF, controls respectively). Proteinuria was significantly higher in LP+OF rats than in controls at 4 months . At the age of 12 months, glucose tolerance was significantly altered in OF and LP+OF rats.

Conclusion: Early catch-up growth in IUGR rats enhances alteration of SBP, glucose tolerance and renal function in adulthood. Early postnatal overfeeding may amplify single nephron hyperfiltration, and insulin-resistance associated with IUGR, resulting in cardiovascular and metabolic diseases at adulthood.