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MAGNETIC RESONANCE SPECTROSCOPY IN GALACTOSEMIA

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Purpose: In vivo magnetic resonance spectroscopy (MRS) was applyed to further clarify the pathogenesis of neurological abnormalities in galactosemia. Possible mechanisms, by which galactose (Gal) and/or its metabolites may lead to neurological symptoms include (1) toxic edema due to enhanced brain galactitol (Gal-*OH*) concentrations, (2) changes within the second messenger pathway, and (3) changes of the energy state of the brain. Methods: Six patients, aged 18 – 29 years, with classical galactosemia under dietary treatment underwent localized brain MRS (^1H and ^{31}P) and magnetic resonance imaging (MRI). IQ ranged over 45 – 97, dysarthria, a mild resting and intention tremor were present in two patients. Gal-1-phosphate (Gal-1-P) levels in erythrocytes were 1.1 – 3.7 mg/dl, plasma concentrations of Gal-*OH* were 8.4 – 14.2 μmol/l. Results: MRI revealed abnormal peripheral myelination in five and enlargement of side ventricles in two patients. Brain Gal-*OH* was below detectability (<1 mmol/l). Concentrations of inositol plus inositol phospohates were within the normal range. No changes in free inorganic phosphate plus Gal-1-P, phosphocreatine, and ATP and no indications for elevated lactate, i.e. no changes of the energy state of the brain were obtained. Conclusion: Brain spectra indicated normal metabolite concentrations as compared to healthy controls.

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PORTAL VEIN THROMBOSIS IN NEWBORN DUE TO PROTEIN C DEFICIENCY

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Protein C deficiency is one of the most important cause of thrombosis during early infancy and may have different ways of presentation. We have collected 11 patients, 10 with portal vein thrombosis, 1 with thrombosis of both right and left jugular vein after a Broviac catheter insertion. As far as the time and the trigger event are concerned, we suppose that the thrombosis took place in 9 patients during the neonatal period. Seven out of the nine patients with portal vein thrombosis had umbilical catheterization during neo-natal period (4 due to hyperbilirubinemia and 3 due to prematurity), one patient received surgery in the first day of life because anorectal malformation, whereas we have no information about the last patient. The early symptoms of thrombosis started within the first year of life in 5 patients and within the forth year in 4. In 9 patients the symptoms were, in sequence: splenomegaly, esophageal varices and hypersplenism. The diagnosis of protein C deficiency has been made from 6th month to 14th year after the trigger event. Protein C biological activity values was X = 47% ±9.03 (n.v. 65-128%) and Protein C antigen was X = 51% ±14 (n.v. 68-110%). Antithrombin III (ATIII) was slightly decreased in 7 patients, protein S in 2, factor V below the normal in 3, whereas FII was in the normal range. Four of these patients received Protein C concentrate (Immuno - Vienna), together with heparin treatment during vascular surgery (spleen, renal vein, shunt). In conclusion we can say that all our patients had a more or less marked first type Protein C congenital deficiency. From the pathogenetic point of view we can speculate that the mechanical and chemical action on the vessell wall due to the catheter and the fluid, associated with the prematurity related disorders, can trigger the thrombotic mechanism.

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ARTERIAL THROMBOLYSIS IN THE NEONATE BY RECOMBINANT TISSUE PLASMINOGEN ACTIVATOR (rtPA)

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As arterial thrombosis can be life threatening for the neonate, it requires a rapid diagnosis and location and indicates thrombolysis.

In two neonates, aortic thrombosis induced by arterial catheter was located in abdominal aorta extended to the right renal artery; one induced right leg cyanosis and the other was identified by echo control of aortic catheter. In the third neonate, left atrial thrombosis was induced by the tip of a wire positioned in left atria during aortic valvuloplasty and showed by post catheterism 2D echo control. The fourth neonate showed asystole related to myocardial ischemia after flushing a catheter inadvertently positioned in ascending aorta. In this case rtPA was immediately infused into the catheter which was then withdrawn. The three other neonates received a bolus rtPA 0.1 mg/kg/10 min followed by 0.9 mg/kg/3 hours then heparin 100 UI/kg/h.

Aortic thrombosis were relieved and echo control showed total disappearance of aortic thrombus. Blood pressure and renal urography control were normal two months latter. Lysis of left atrial thrombosis was successful after a second injection of rTPA after failure of the first dose. In the fourth case rtPA did not avoid infarct, cardiac hypokinetic state and heart failure. However three months later cardiac function and EKG were normal. Except in the third case where minor bleedings were present after the second dose, there was not adverse effect during rtPA therapy.

This short series demonstrated a very safe and rapid efficient action of rtPA in the treatment of severe neonatal systemic thrombosis.

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DO TROPHOBLASTIC RECEPTORS FOR INSULIN, IGF-I, AND IGF-II PLAY A ROLE IN FETAL OVERGROWTH IN DIABETIC PREGNANCY ?

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Fetal overgrowth in diabetic pregnancy (DP) is popularly attributed to hyperinsulinism. However, the roles of other growth-promoting peptides in the mother and the fetus and of their receptors in the placenta remain unclear. We measured at term, concentration and affinity of placental trophoblastic membrane receptors (TR) for insulin (I), IGF-I and IGF-II in 8 DP's (White Class B, I-dependent) and 8 non-DP's and correlated these with maternal and cord serum IGF-I and IGF-II levels, infant and placenta weights, and maternal body mass index (BMI). DP and non-DP differed significantly in infant weight (g), 4248±114 (M±SEM) vs 3555±119 (P<.0001); placental weight (g), 765±51 vs 575±24 (P<.005); cord IGF-I (ng/ml), 137±15 vs 86±12 (P<.025); and maternal BMI, 33±4 vs 21±1 (P<.02). No significant differences existed in cord IGF-II, maternal IGF-I and -II, and concentration and affinity of TR for I, IGF-I and IGF-II. ANOVA revealed an interaction between placenta weight and infant weight (P<.01), cord IGF-I (P<.02) and maternal IGF-I (P<.025); there was no significant interaction between BMI and infant weight. We conclude that in DP: placental overgrowth is concomitant with fetal somatic overgrowth; fetal and maternal IGF-I may contribute to fetal overgrowth; concentration and affinity of TR for I, IGF-I, and IGF-II play no roles in fetal overgrowth.

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MEASUREMENT OF 1,25 DIHYDROXYVITAMIN D RECEPTORS (VDR) IN TERM BABIES CORD PERIPHERAL MONONUCLEAR CELLS (PMN).

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Genomic actions of vitamin D are mediated by VDR. Because the placental and fetal production of 1,25D, receptors should play its binding role, but little is known about their concentration in the newborn. In the rat peripheral mononuclear cell receptors for 1,25D (p VDR) reflect changes of VDR in target tissues (M.M. Ped Res 32:629, 1992).

We studied (m±SD) 13 healthy mothers well nourished (pre-pregnant P/T^2: 23.7±3.2); aged 24.9±3.7 y and with normal bone mineral content (0.859±0.1 g/cm) at delivery which took place in Dec/January. Newborn babies, were all healthy term and appropriate for gestational age. Once cord was clamped the artery was isolated, and blood was drawn for analysis of vitamin D polar metabolites and pVDR. VDR concentration was measured after 72 hours culture of PHA activated cells, by Scatchard analysis after 3H 1,25D binding. Results. 32 normal adults give values of pVDR in venous blood of 71.3±21.7 fmol/mg p. Cord blood showed normal figures for calcium, magnesium, phosphate and alk p-ase. Levels of 25D were 9.5±3.7 ng/mL; 1,25D 89.8±26.5 pg/mL and pVDR 87.9±20.2 fmol/mg p. The Kd values were of 4.7-7.1 E-10 M. A weak correlation (r = 0.38) was found between pVDR and 1,25D. In conclusion in term babies pVDR are binding adequately 1,25D and its concentration are moderately higher than in normal adults control.

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LUNG HISTOPATHOLOGY IN NEONATES RECEIVING LOW-DOSE INHALED NITRIC OXIDE (NO)

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The use of inhaled NO for severe respiratory failure with refractory hypoxemia is rapidly being extended to sick premature neonates. However, the potential for NO and its oxidation product nitrogen dioxide (NO_2) to induce pulmonary toxicity in injured lungs with ongoing oxidant injury or in newborn lungs with altered oxidant defences is not known. Post-mortem lung tissue from 5 infants (26-36 weeks gestation) who died from a variety of causes including severe respiratory failure for which inhaled NO had been administered was examined under light microscopy for evidence of additional lung injury (accumulation of cellular debris, inflammatory cells, extravasation of erythrocytes into the alveolar space compartment, desquamation of mucosa and tissue disruption). Blocks of lung tissue were prepared and stained with haematoxylin and eosin by conventional methods. NO was administered at doses of 5-40 ppm (mean 10ppm). The duration of continuous NO inhalation was 2-31 days with the chronological age of the infants at death being 3-70 days. The NO_2 level in inspired gas was <1ppm and methaemoglobin levels were <2%. The pathological findings in all cases were consistent with the expected observations in each infant at the time of death. No consistent or additional pathological alterations were observed as determined by light microscopy. Our preliminary results suggest that inhaled NO does not cause obvious or marked additional histopathological alterations consistent with acute lung injury in sick newborns when inhaled at low doses. Further studies including electron microscopy are required before we can be more reassured.

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