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ADIPOSE TISSUE QUANTITY AND DISTRIBUTION IN HEALTHY TERM INFANTS USING MAGNETIC RESONANCE IMAGING

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Until recently lean mass and adipose tissue mass in infants and adults have been estimated by indirect methods. The use of magnetic resonance imaging has allowed direct measurement of these two components. There are no published data on normal values of adipose tissue and lean body mass in healthy term infants at birth using this technique. We carried out whole body adipose tissue (AT) magnetic resonance imaging. Individual volumes of subcutaneous, intra-abdominal and other internal adipose tissue were quantified and these summated to derive total AT. We converted total AT volume to adipose tissue mass and subtracted this from the body weight to derive the lean body mass. We expressed lean mass as a ratio of adipose tissue mass. Total adipose tissue mass is expressed as a percentage of body weight (%ATM) and the individual compartments of adipose tissue as a percentage of total adipose tissue volume. The local research ethics committee approved the study and written parental consent was sought. Results are expressed as mean (sd). 20 healthy appropriately grown Caucasian infants were studied within a week of birth. Their gestational age at birth was 39.9 (1.4) weeks. The %ATM in this group was 17.7 (2.6). Of the total adipose tissue, 91.9 (1.2) % was in the subcutaneous compartment and 3.1 (0.5) % was deposited intra abdominally. The lean to adipose tissue mass ratio was 4.8 (0.9). No significant differences were noted between male and female babies in any of the results. Normative data on body composition in the term infant has relied on data obtained either by whole body chemical analysis carried or derived from indirect measures of lean mass and fat mass. We have presented data from normal healthy term infants of similar ethnic origin using a novel technique to study body composition.

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PRETERM INFANTS AT TERM SHOW INCREASED INTRAHEPATOCELLULAR LIPID CONTENT ON PROTON MAGNETIC RESONANCE SPECTROSCOPY

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Proton magnetic resonance spectroscopy (1H MRS) offers a non-invasive means to quantify intrahepatocellular (IHCL) lipid content which until recently was only possible using liver biopsy. Non alcoholic fatty liver disease is a spectrum varying from fatty infiltration to cirrhosis. The prevalence of this condition is increasing worldwide and is increasingly being reported in younger populations. Increased IHCL is associated with obesity, particularly intra-abdominal adiposity, insulin resistance and type II diabetes. We have shown that adipose tissue (AT) distribution is altered in the preterm infant at term, with increased intra-abdominal AT. The aim of this study was to establish the feasibility of investigating IHCL deposition in infants using 1H MRS. Whole body MR AT imaging was performed as previously described on a 1.5T Eclipse system. Preterm infants were studied at term and term infants in the first week. Hepatic 1H MR spectra were obtained using a PRESS sequence (TR 1500ms, TE 135ms). We employed one way analysis of variance. The study was approved by the local research ethics committee. To date we have studied 9 infants, 5 preterm (gestational age 29 - 31 weeks) and 4 healthy term infants. These were compared with 5 healthy control adults. Although adults had a significantly increased content of total AT ($p=0.008$) with an increased ratio of intra-abdominal to subcutaneous AT ($p=0.028$), the preterm infants had significantly elevated IHCL compared with term infants and adults (Kruskal Wallis, $p=0.016$). We have demonstrated the feasibility of obtaining hepatic 1H MR spectra for quantification of IHCL in infants. The clinical relevance of increased hepatic lipid in preterm infants is as yet unknown. It may be transient and represent recovery from previous nutrient deprivation. Alternatively persisting increase in IHCL might underlie the observed abnormalities in insulin sensitivity in adolescence in children born preterm.

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OUTCOME AT 18 MONTHS OF AGE AFTER SILDENAFIL THERAPY FOR REFRACTORY NEONATAL HYPOXEMIA

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Background: There is still no sufficient evidence for the use of oral sildenafil for severe Pulmonary Hypertension of the Newborn, where there is no Nítric Oxide, High frequency Ventilation and/or ECMO. Despite only one proof of concept trial a few anecdotal reports and no report on safety, it is being offered in several regions as compassionate use. We performed detailed follow at 18 months of age to asses for adverse effects in the newborns who were treated with oral sildenafil in a randomized trial

Objective: To analyze the outcome of term newborns who were treated with oral sildenafil for neonatal PPH in a region where iNO is unavailable.

Design/Methods: Of the seven term newborns that were treated with oral Sildenafil during the study, five were alive at one year of age and four were followed up to 18 months. Anthropomorphic measurements, neurodevelopment assessment (Gesell developmental scale), magnetic resonance imaging (MRI), electroencephalogram (EEG), and otoacustic emissions (OAE) were done in all children.

Results: The mean of height (77.5 cm.) weight (11.02 Kg.), head circumference (46.5 cm) and neurodevelopment evaluation on Gesell scales (102.7) were within normal limits. The neuro-imaging (MRI) and neurophysiologic studies (EEG and OAE) also were normal.

Conclusions: From these results we cannot definitely conclude that oral sildenafil does not have a negative side effect. However, it is encouraging that this small group of infants did not have neurological sequelae that would prevent them from normal neurodevelopment, despite exposure to severe hipoxemia for periods greater than 12 hours.

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ORAL SILDENAFIL TREATMENT AS AN ALTERNATIVE TO INHALED NO THERAPY FOR PERSISTENT PULMONARY HYPERTENSION OF THE NEWBORN

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Background: Inhaled nitric oxide (iNO) has been successfully used in infants with severe persistent pulmonary hypertension (PPHN). This therapy, however, is expensive and complex and may not be available n developing countries. Sildenafil, a phosphodiesterase inhibitor (PDI) type V, has been shown to selectively reduce pulmonary vascular resistance in both animal models and patients. Weather Sildenafil could be effective as an alternative to iNO therapy in PPHN, is not known.

Objective: To compare the efficacy of oral Sildenafil therapy and conventional therapy in neonates with PPHN diagnosis, prospectively. DESIGN/METHODS: Term neonates with PPHN diagnosis and oxygenation index (OI) >25 were randomly assigned to placebo (n=11) or to Sildenafil at 2 mg/kg by orogastric tube every 6 h (n=13). Arterial blood gases, OI, mean airway pressure (MAWP) and mean blood pressure (BP) were periodically recorded at least up to 72 hours. Clinical management included IMV, inotropes, but no iNO.

Results: Oxygenation Index was gradually and significantly decreased in both placebo and Sildenafil groups (repeated measures of ANOVA followed by Dunnett multiple comparisons test). These changes in OI were significantly ($p<0.01$) lower in the Sildenafil-treated patients, starting with the first hour after its administration (ANOVA followed by Bonferroni correction for multiple comparisons). In both groups, PaO2 was also gradually and significantly increase and became significantly more pronounced at 72 hours with Sildenafil treatment ($p<0.01$). MAWP was significantly lower in the Sildenafil-traeted patients, starting 6 hours after its administration. No significant differences in PaCO2 or BP were observed.The ventilatory days were significantly lower in the Sildenafil group ($p<0.01$; unpaired t-test). All patients in the Sildenafil-treated patients survived, as compared to 8/11 patients in the placebo group

Conclusions: Oral Sildenafil in term infants with severe PPHN improves oxygenation indices (OI; PaO2; MAWP) without decreasing systemic blood pressure.

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VIRAL INFECTIONS AND NEONATAL DISEASE, THE VIND-STUDY.

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Introduction Viruses can cause serious neonatal infections. The incidence of viral infections in the NICU is not known. New diagnostics (PCR) and antiviral therapy make insight in incidence of viral infections possible and warranted.

Objective To study the incidence of viral infections in neonates admitted to the NICU, suspected of having infection (pneumonia, sepsis, meningitis) and to study the value of PCR compared to culture and direct immunofluorescence.

Methods Neonates on the ventilator and suspected of infection were included. Tracheal aspirate (TA), cerebrospinal fluid (CSF) and feces were tested for viral agents. TA: by viral culture; by Multiplex PCR on adenovirus, enterovirus, influenza A en B, parainfluenza 1 and 3, rhinovirus, RSV and chlamydia pneumoniae; by direct immunofluorescence for RSV, influenza A and B virus, parainfluenza virus, adenovirus, chlamydia pneumoniae and enterovirus. CSF: by PCR on enterovirus. Feces: by culture on enterovirus and adenovirus. The study period was 2 years to cover all seasons twice.

Results In 2003–2004 72 patients were included in whom 86 episodes of infection occurred. Multiplex PCR of TA was positive in 5 episodes (rhinovirus 3, enterovirus 1, adenovirus 1). In the enterovirus positive patient PCR of CSF and culture of TA showed also enterovirus (echovirus type 6). In the rhinovirus positive episodes culture was positive for rhinovirus in only 1 episode. In 1 episode CMV was detected by culture. The overall incidence of viral infections was 7% (6/86). Bacterial bloodstream infections were the cause in 51% (44/86, 64% Coagulase Negative Staphylococcus). In 13% (11/86) only TA contained bacteria. In 1,1% (1/86) only urine contained bacteria. In 28% (24/86) no agent was found.

Conclusion Viruses rarely cause infections in ventilated neonates admitted to the neonatal ward. No conclusions can be drawn about the value of PCR in comparison to conventional testing on viral agents.

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ANEMIA AND ELEVATED C-REACTIVE PROTEIN IN PREMATURE LOW BIRTH WEIGHT INFANTS AS PREDICTORS OF POSITIVE BLOOD CULTURES

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Background Infection remains a significant cause of morbidity in neonatal intensive care. Differentiation between sepsis and clinical deterioration from other causes is difficult. It would be of great value if quick and simple laboratory data support evidence of septic disease. Aim Commonly available laboratory data (Hemoglobin (Hb), white blood cell count (WBC) and C-Reactive Protein (CRP) were analysed for their reliability in predicting disease of infectious origin in newborns admitted to a neonatal intensive care unit (NICU).

Results 102 hospitalised newborns were analysed during a 3-months' study period. 81 newborns had one or more episodes of suspected sepsis and antibiotics were started 105 times. In 17 (20%) out of 85 obtained bloodcultures an organism was isolated. Newborns with lower birth weight and gestational age were more likely to have a positive bloodculture (1430 g vs 2070 g and 30 weeks vs 32.5 weeks, both $p<0.01$). Hb was significantly lower (7.9 vs 9.6 mmol/L, $p<0.01$), and the CRP higher (26 vs 8 mg/L, $p<0.001$) in newborns with a positive blood culture. WBC was similar in both groups. A CRP > 20 mg/l was 94% specific for a positive blood culture. In combination with a low Hb (< 8 mmol/L) or low WBC (< 8), specificity increased to 98% and 100%. Corresponding sensitivities were low (35%). Subset analysis in newborns with late onset sepsis showed no significant differences in CRP, Hb or WBC due to the small number of patients (n=13 and n=15). The specificity of CRP > 20 mg/l persisted (93%) and increased to 100% in combination low WBC. Low Hb had no more additive effect (specificity stayed 93%).

Conclusion A low Hb and/or low WBC with an elevated CRP are highly specific for a positive blood culture in premature low birth weight infants. In case of late onset sepsis the Hb is not discriminating.