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RISK FACTORS OF EXTRAUTERINE GROWTH RESTRICTION OF VERY PRETERM NEWBORNS. RESULTS FROM THE EPIPAGE NORD PAS DE CALAIS COHORT

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Background: Postnatal growth of very preterm neonates should approximate that of a normal fetus of the same postconceptional age. Extrauterine Growth Restriction (EUGR) is a major clinical problem especially in critically ill preterm neonates. Objective : to study growth of very preterm newborns (less than 33 weeks gestational age) during hospital stay and determine risk factors of postnatal growth restriction. **Design/Methods:** Every livebirths born before 33 weeks of GA in 1997 in 9 French areas (covering one third of French births) were prospectively included in the EPIPAGE study. Data are from one area (Nord-pas-de-Calais). From the appropriate for gestational age (AGA) population, EUGR was defined by weight at hospital discharge less than 2 standard deviations (Usher and Mc Lean). Birthweight was studied by class of 500g. Z score was assessed at day 14, at day 28, at hospital discharge. Risk factors for EUGR were studied by logistic regression.

Results: 486 newborns were AGA at birth. Rate of EUGR was 25% with a mean z score of -1.25(+/- 0.37) at day 28 and -0.67(+/-0.49) at hospital discharge . Factors independently associated with EUGR were : low class of birthweight (OR 5.3 [2.8–10.0]), respiratory distress syndrom (OR 1.7 [1.0–3.1]), necrotizing enterocolitis (OR 4.1 [1.4–11.9]), parenteral nutrition for more than ten days (OR 2.7 [1.3–5.8]) and hypertension during pregnancy (OR 1.9 [1.1–3.7]). High gestational age and no oxygen at day 28 reduced risk (OR 0.4[0.2–0.7] and OR 0.5[0.2–0.8] respectively).

Conclusions: EUGR rate was high in AGA very preterm newborns. Pregnancy hypertension appeared as a risk factor. Neonatal disease and nutritional status as well. This could lead to identify population at risk of EUGR for further prevention and follow-up.

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RETROSPECTIVE STUDY OF ROUTINE LUMBAR PUNCTURE IN THE EVALUATION OF NEONATAL SEPSIS

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Background: Lumbar puncture (LP) to exclude meningitis is part of an infection screen in many neonatal units. For best outcome, meningitis requires early initiation of treatment. Results of cerebrospinal fluid (CSF) microscopy may guide management before culture results are available. LP is, however, an invasive procedure that can be technically difficult in small infants. Blood staining of CSF is common making interpretation of microscopy impossible.

Aim: To examine the value of LP in evaluation of suspected sepsis.

Methods: Medical notes of infants having LPs between January 1999 and October 2001 were reviewed retrospectively. Data were collected for number of attempts to obtain CSF, procedural complications, results of CSF microscopy and culture and antibiotic treatment given.

Results: 630 LPs were carried out in 527 infants. Median (range) gestational age and weight at birth were 36(23–42) weeks and 2580(500–5430) grams respectively. The median (range) age at time of LP was 2(1–96) days. Multiple attempts to obtain CSF were documented in 67 cases; 29 required ≥3 attempts. 314(50%) of the records reviewed contained no information about occurrence of associated complications. 280(44%) stated that no complications were seen. Adverse events such as apnoea, desaturation or bradycardia were noted in 36(5%) cases. In 7, these led to the procedure being abandoned. CSF was obtained at LP in 605(96%) cases. Of these, 431(71%) were suitable for cell count by microscopy. 169 samples (28% of those obtained) were too heavily bloodstained to determine a white blood cell count. Results of CSF culture were available for 616 LPs. 590(95%) samples yielded no growth. 26 samples from 24 babies were positive. 12 infants were treated for bacterial (9) or viral (3) meningitis. CSF microscopy aided diagnosis in only 5 cases. All those with bacterial disease had positive blood cultures. The other 12 infants did not display clinical evidence of meningitis and the samples were presumed contaminated. Positive and negative predictive values for CSF culture and microscopy in diagnosis are 35% and 99% respectively.

Conclusion: In this group of infants, LP was often unhelpful. Many samples were unsuitable for microscopy and did not contribute to early exclusion or confirmation of meningitis. Multiple attempts and complications were common and may be underestimated in retrospective reviews. More selective identification of neonates at high risk of meningitis for investigation with lumbar puncture may avoid unnecessary intervention.

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Background: Lumbar puncture (LP) for the exclusion of meningitis is included as part of routine clinical investigation of suspected sepsis in many neonatal units. A retrospective review of medical records in our unit suggested that attempts to obtain cerebrospinal fluid (CSF) were often unsuccessful and associated with complications such as apnoea, desaturation or bradycardia. The results aided diagnosis or exclusion of meningitis in only a small number of infants. This prospective study aimed to further examine the value of lumbar puncture in the routine evaluation of suspected neonatal sepsis.

Methods: Data were obtained for all lumbar punctures performed over a period of 4.5 months. Information about number of attempts to obtain CSF, procedural complications and results of microscopy and culture was collected at the time of investigation.

Results: 99 lumbar punctures were performed in 86 infants. Median (range) gestational age and weight at birth were 36(24–42) weeks and 2740(640–4510) grams respectively. The median age at the time of investigation was 2 (1–91) days. Multiple attempts were required in 54 cases with 21 of these needing ≥3 attempts. Complications were documented on 21 occasions. 20 of these were episodes of apnoea, bradycardia or desaturation and 1 infant vomited during the procedure. 4 infants required intervention with respiratory support. In 8 cases, no CSF was obtained and in a further 3, there was insufficient for microscopy. Of the remaining 62 samples, 26(42%) were too heavily blood stained to allow determination of a white cell count. Results of CSF culture were available for 79 samples. 74 yielded no growth. CSF culture was positive in 5 infants (4 bacterial, 1 viral). Treatment for meningitis was initiated in 4 infants, of whom 2 had negative CSF cultures. 3 infants with cultures positive for coagulase negative staphylococcus were not treated; the organism was presumed to be a contaminant. Positive and negative predictive values for CSF microscopy and culture in this group of infants are 40% and 97% respectively.

Conclusion: The results of this prospective study confirm that LP frequently does not contribute to the early management of infants with suspected sepsis. Complication rates for the procedure are high given the low number of positive diagnoses made. The large number of failed LPs suggests that training in the technique may be an important issue for junior doctors. However, careful clinical judgement may allow more selective use of LP as a diagnostic tool.

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METABOLIC ADAPTATION IN INFANTS BORN SMALL FOR GESTATIONAL AGE

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Background: After birth the newborn infant must produce its own glucose until breastfeeding is established. Infants born small for gestational age (SGA) are at risk for neonatal hypoglycemia and development of metabolic syndrome in adulthood. The aim of this study was to investigate glucose production and lipolysis in newborn infants born SGA.

Methods: Thirteen infants were studied at a mean age of 23±6-h, following fast for 4±0.3-h. Mean gestational age was 35±2.5 weeks and mean birth weight 1.8±0.42 kg (< - 2 SD). Six of the infants obtained glucose infusion to avoid hypoglycemia. Rates of glucose production (GPR) and lipolysis were quantitated by use of [6,6–2H2]-glucose and [2–13C]-glycerol.

Results: Plasma levels of glucose and glycerol were 4.1±1.1 mmol . L-1 and 217±64 imol.L-1, respectively. For all infants the rate of glucose appearance (glucose Ra) averaged 30.7±8.3 and that of GPR 22.1±6 imol. kg-1 . min-1. GPR for infants obtaining additional glucose was 19.0±6.8 imol. kg-1 . min-1 whereas those without glucose infusion produced 24.2±4.4 imol. kg-1 . min-1. The rate of glycerol production, reflecting lipolysis, was 6.0±1.3 imol. kg-1. min-1 (corresponding values in the groups with and without glucose infusion were 5.1±1.7 and 6.6±0.9 imol. kg-1. min-1). Lipolysis correlated strongly to birth weight (r=0.86, p<0.001). Of the glycerol produced, 50±20 % was converted to glucose, representing 7.5±3 % of GPR. Concentrations of insulin (n=11) and glucagon (n=11) measured during steady state were 7.2±4 mU . L-1 and 78±31 pmol . L-1.

Conclusion: Our results show that SGA-infants have capacity for glucose production and lipolysis as well as for gluconeogenesis during their first day of life. In comparison with reported results from AGA-infants the present data is in the lower normal range. The correlation between glycerol production and birth weight indicates that lipolysis is dependent on the amount of depot fat. Although SGA-infants have a functioning hormonal regulation and enzymatic capacity for production of energy substrates, the small energy stores in this group of newborns may explain the increased risk of hypoglycemia. There are earlier reports of neonatal hyperinsulinemia in infants born SGA. However, all infants examined had normal insulin levels during the study period, contradicting early onset of insulin resistance.

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NF-EB ACTIVATION IN TRANSGENIC REPORTER MICE IS INCREASED AFTER RE-SUSCITATION WITH PURE OXYGEN IN CONTRAST TO ROOM AIR

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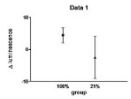
Background: Oxidative stress may induce apoptosis and influence cell growth and development. NF-êB is a transcription factor probably playing a key role in these processes. How resuscitation with 100% O2 influences these processes are not known. We have established an in vivo model to study the inflammatory process after hypoxia and reoxygenation using transgenic mice that express luciferase under the control of transcription factor NF-êB, enabling real-time in vivo imaging of NF-êB activity in intact animals. **Objective:** To study NF-êB in transgenic hypoxic mice reoxygenated using pure oxygen or room air.

Methods: Hypoxic, 4–7 weeks old transgenic NF-êB reporter mice were compared with a control mouse from the same cage, building couples where the two mice have the same parents, the same age, and are submitted to the same environment. All animal experiments were performed according to national guidelines for animal welfare. Hypoxia was induced by breathing 8, 6, 5, or 4% O2 in N2 for 2 hours. The animals were then randomly resuscitated with 21% or 100% O2 for 30 min. NF-êB activity was quantified by an imaging system delivered by Xenogen Corporation, counting the photons emitted from the animal in a complete dark environment. The value is proportional to the NF-êB activity. Luminescence was measured twice from the dorsal side of the head, first basal measurements two days prior to hypoxia, then three hours after reoxygenation.

Results: Hypoxia with 8% and 6% oxygen did not seem to affect the mice and 5% only slightly. However, in 4% oxygen all the mice were affected, acid base balance was gravely disturbed (n=13), and the mortality was 20% (N=62). An increase in luminescence was detected especially in the brain where the increase was significantly higher when 100% oxygen (n=13) was used for reoxygenation compared with room air (n=17) where no increase was detected (P=0.03) See figure.

Conclusion: Two hours of hypoxia with 4% oxygen followed by reoxygenation with pure oxygen induced an increase in NF-êB activity measured in transgenic luciferase mice. No increase was detected in mice resuscitated with 21% O2.



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FECAL CALPROTECTIN: AN INDICATOR OF NEC IN VLBW INFANTS?

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Background: Calprotectin is a calcium binding protein, abundant in neutrophils and stable in faeces. The aims of this study were to assess faecal calprotectin concentrations (f-calprotectin) in very low birth weight (VLBW, <1500 g) infants and to study possible differences in f-calprotectin between infants who develop severe abdominal disease and controls.

Methods: Serial faecal samples were collected from 22 VLBW infants (4 cases of severe abdominal disease and 18 controls) and analysed for calprotectin.

Results: Mean (SD) f-calprotectin in controls was 414 (417) ig/g faeces. In one case of necrotising enterocolitis (NEC) (stage III A) and one case of volvulus, f-calprotectin was increased to a maximum concentration of 22513 ig/g and 9228 ig/g, respectively. In two cases of isolated intestinal perforation, f-calprotectin never exceeded the range of controls.

Conclusions: The observed f-calprotectin in VLBW infants is similar to that seen in full term infants. In one case of NEC, f-calprotectin was markedly increased and should our ongoing study support the findings of this interim analysis, f-calprotectin might be a useful marker of NEC.