107 AMINO ACID METABOLISM IN CHRONIC VALPROATE TREATMENT AT TWO LEVELS OF CARNITINE INTAKE

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While valproate (VPA) is known to cause changes of nitrogen containing metabolites, the amino acid (AA) metabolism and its alterations during carnitine (C) therapy have not been studied. Ten VPA treated C deficient children equimolar C were given over a 14 days period. Before C treatment the fasting plasma levels of ammonia, taurine, aspartate, hydroxyproline, glutamate, proline, glycine, alanine, methionine were elevated, the levels of leucine and ornithine were depressed in VPA treated children as compared to controls ($p<0.05$), their levels remained unchanged after C therapy. The elevated ammonia and glutamate with normal glutamine levels show impaired glutamate-glutamine cycle. After a standard meal the plasma levels of AA exhibited different elevation before and after C treatment. The urinary output of AA was lower in the VPA treated group, output of 8 individual AA increased after the C treatment, showing that the C may influence the AA metabolism, yet most changes are C independent and are caused probably by the VPA per se.

108 EFFECT OF INDOMETHACIN ON CEREBRAL OXYGENATION AND HAEMODYNAMICS IN PRETERM INFANTS INVESTIGATED BY NEAR INFRARED SPECTROSCOPY (NIRS)

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NIRS was used to quantify the effect of indomethacin on cerebral blood flow (CBF), cerebral oxygen delivery (COD), cerebral blood volume (CBV), and the response of CBV to changes in arterial carbon dioxide tension (CVR). 8 infants born at 25-29 weeks gestation were studied on day 10-14 for 35-173 (median 50) minutes before and 43-240 (median 65) minutes after bolus intravenous injection of indomethacin (0.1-0.2 mg/kg) for treatment of a patent ductus arteriosus.

Results:	pre- median (range)	post-indomethacin median (range)
CBF($ml.100g^{-1}.min^{-1}$)	23 (12-37)	9 (5-20)*
COD($ml.100g^{-1}.min^{-1}$)	2.4 (1.7-4.0)	1.1 (0.6-2.1)*
CBV($ml.100g^{-1}$)	2.3 (1.1-3.2)	1.3 (0.6-2.0)*
CVR($ml.100g^{-1}.kPa^{-1}$)	0.32(0.16-0.60)	0.09(0-0.16)*

* = $p<0.05$ by paired Wilcoxon rank sum test

Conclusion:
Bolus injection of indomethacin caused significant reductions in all the indices studied.

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109 TIN-PROTOPORPHYRIN (Sn-pP) EFFECT ON HYPERBILIRUBINEMIA DUE TO CRIGLER-NAJJAR DISEASE (CND) TYPE I.

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CND is a rare disorder characterized by severe unconjugated hyperbilirubinemia appearing in the first days of life and persisting throughout life. We tried to control the hyperbilirubinemia in an infant with CND by parenteral administration of Sn-Pp, a strong inhibitor of heme-oxygenase. The dose administered was 0.5 uMol/kg b.w. Mild transient erythema appeared when the infant was exposed to sunlight after injection, but not during phototherapy. The serum clearance of Sn-Pp was found to be biphasic: over 90% of the Sn-Pp present in the serum 5 h after injection is eliminated within 48 h; the remaining Sn-Pp undergoes very slow clearance which is virtually complete after 7 days. Different treatment schedules have been tried; however, in no case was it possible to discontinue phototherapy. A suitable combination of phototherapy and Sn-Pp administration apepars to yield the most promising results. In particular, it is possible to maintain the serum bilirubin concentration below 14-15 mg/dl combining one injection of Sn-Pp every 7-10 days with 5 hrs of phototherapy per night.

110 PHENYTOIN REDUCES FREQUENCY AND DURATION OF NEONATAL SEIZURES IN THE NEWBORN: A RANDOMISED TRIAL OF FOUR ANTICONVULSANTS

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Ninety-one newborn babies had a continuous record of the electroencephalogram (EEG) while receiving intensive care. Seizures occured in 50% and after parental consent 40 entered a randomised trial of 4 anticonvulsants. The loading doses were: phenobarbitone 20mgs/kg, phenytoin 30mgs/kg, clonazepam 0.25mgs, sodium valproate 10mgs/kg. A polygraphic record of physiological variables was made during the infusion and for the next 24 hours. The continuous EEG was maintained for 5 days after treatment. The groups were similar for birthweight and gestational age. Frequency and duration of seizure was decreased by all drugs but phenytoin was the most effective. The median time to control seizures ranged from 18.8 hr (phenytoin) to 120 hr (phenobarbitone and clonazepam). Heart rate, blood pressure and intracranial pressure varied widely after all 4 drugs. Cardiac depression was particularly noticed in asphyxiated babies with myocardial ischaemia. These data suggest that the potentially adverse effects of high doses of anti-convulsants must be balanced against the benefits of early effective control.

111 OPIATE INFUSIONS FOR PRETERM CHILDREN?

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Despite recent calls for the administration of opiates to ventilated newborn infants, there is a paucity of data to support their use. Single dose studies during surgery suggest that commonly used drugs have a marked reduction in clearance. This study evaluates the use of a short acting synthetic opiod, alfentanil.

22 ventilated, paralysed preterm infants with hyaline membrane disease (median BW:1348g (r:690-4084g); median GA:30 weeks (r:25-36w)) were given 20 micrograms/Kg alfentanil by slow intravenous injection over two minutes. Peak serum concentration (med(r)) was 67ng/ml (13-606), clearance 0.9ml/min/kg (0.6-9.62) and elimination half life 321 mins (64-1251). Transient depression of BP and heart rate was noted. Using these data in six children satisfactory serum levels of alfentanil were achieved using 20 micrograms/Kg over 30 mins followed by 5micrograms/Kg/hour with no cardiorespiratory effects.

Further studies are necessary to establish the efficacy of such treatment.

112 EFFECTS OF PARENTERAL CALCIUM TREATMENT ON BLOOD PRESSURE, HEART RATE, STROKE VOLUME AND CARDIAC OUTPUT IN PREMATURE AND MATURE NEWBORNS.

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Recent animal experiments demonstrated that the contractility of the immature myocardium is supported largely by the influx of calcium across the sarcolemma and only when myocardium matures intracellular calcium uptake and release by the sarcoplasmic reticulum plays an increasingly important role in the development of myocardial contractility. The purpose of this study was therefore to delineate the acute hemodynamic effects of parenteral calcium treatment in critically ill and hypocalcemic premature and mature newborns.

Methods: The hemodynamically unstable and hypocalciemic newborns (Ca^{++} < 1,0 mmol/l) received a calcium chloride ($CaCl_2$) infusion (4mg/kg of elemental Ca^{++}) over a period of two min.

Results: After administration of $CaCl_2$ stroke volume (SV), cardiac output (CO, pulse conture technique) and blood pressure (BP) increased significantly, whereas heart rate (HR) remained unchanged and systemic vascular resistance decreased. The changes of these parameters are distinctly pronounced in the immature newborns and seem to be inversely proportional to the initial Ca^{++}-level.

Conclusions: Intravenous administration of calcium to hemodynamically unstable and hypocalcemic newborns leads to an increase in BP, SV and CO. Since HR is nearly unchanged this means an energetically favorable improvement of myocardial function. The pronounced increase of SV, CO, and BP in the immature newborn and the dependency of these changes on the initial serum calcium level are in agreement with the above mentioned animal experiments.

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