

ABSTRACTS

1 INDOMETHACIN AS AN INHIBITOR OF PREMATURE LABOUR: THE EFFECT ON RENAL FUNCTION POSTNATALLY. Heijden v.d. AJ, Sauer PJJ, Grose WFA, Oranje WA, Wolff ED, Department Paediatrics, Erasmus University and University Hospital Rotterdam/Sophia Children's Hospital, The Netherlands.

Indomethacin (ID) which is used with increasing frequency to stop preterm labor, impairs renal function in the preterm infant, when given postnatally. We studied serum ID levels and renal function in premature infants born despite ID therapy during pregnancy. Ten preterm infants, mean gestational age 29.5 wk (range 27.5 to 31 wk), were studied (group I). We used the continuous inuline infusion technique for measuring glomerular filtration rate (GFR). GFR, serum creatinine (Screat), osmolar clearance (Cosm), free H₂O clearance (C_{H₂O}) and fractional sodium excretion (FeNa) were measured on day 2, 3 and 4. Six preterm infants whose mother did not receive ID served as controls (group II). Serum ID levels measured directly after birth varied from 1.9 ng/ml to 0.1 ng/ml in group I. For renal function parameters (±SD) see table.

	GFR ml/min/kg	S creat umol/l	Cosm ml/min/kg	CH ₂ O ml/min/kg	FeNa %
group I	0,60±0,12	104±24	0,029±0,014	0,008±0,017	4,1±1,9
group II	0,82±0,14	89±20	0,047±0,023	0,039±0,031	2,2±1,2
	<0,05	ns	ns	<0,05	ns

Urine production returned to normal as did Screat within the first weeks of life. **Conclusions:** 1) ID given during pregnancy impairs renal function after birth. 2) Fluid intake should be reduced in these infants 3) ID levels found in our patients were comparable to levels found by ID administration for closure of the Ductus Botalli. 4) The effect on renal function is temporary.

2 PERCUTANEOUS ABSORPTION AT VARIOUS AGES IN PRETERM INFANTS. DP WEST, DR HARVEY, JM HALKETT, R WITHERSTONE, D HIBBERT, J HADGRAFT, LM SOLOMON, JI HARPER. Queen Charlotte's Maternity Hospital and Westminster Hospital, London; UWIST, Cardiff; University of Illinois, Chicago.

Percutaneous absorption at various ages in preterm infants was studied by using a transdermal stable isotope-labelled compound of (13C6) benzoic acid (BA). GC MS was used to analyze hydrolyzed BA recovered from urine at four 6h intervals after application of 1.8mg to 6 infants (31wk gestational age) and 1 infant (25wk gestational age) on d1 and d21 of life. Respectively, mean BA:urine creatinine=10.69 and 18.73 on d1; and 1.33 and 1.47 on d21. The 25wk baby was also evaluated on d2, d7 and d14 and=13.25, 7.14 and 4.27, respectively. A kinetic model was designed to evaluate excretion kinetics in these infants. The cumulative % dose appearing in the urine at time t is given by $\% = 100(1 + (k_4 \exp(-k_2 t) - k_2 \exp(-k_4 t)) / (k_2 - k_4))$, where k₂ relates to transport across viable epidermis to blood and k₄ characterizes elimination rate of chemical from blood to urine. Agreement between model and infant data is reasonable and the model is a credible approximation of the processes involved. The data indicated that percutaneous absorption was enhanced shortly after birth but gradually declined over 3 weeks to that expected of a full term infant. Further, the developed kinetic model may have value in predicting plasma and urine kinetics in pre-term infants.

3 Correction of selenium depletion: organic versus inorganic selenium (se) supplementation. M.van Caillie-Bertrand, A.Deschuytere, H.Deelstra, D.Vandenberghe, R.Clara. Antwerp Children's Hospital, Department of Pharmacology and Microbiology, University of Antwerp, Belgium.

The use of purified amino acid mixtures in children with inborn errors of metabolism on protein restricted diets has led to a reduction of the intake of most essential micronutrients. As an integral part of glutathione peroxidase (GSH-Px), se is considered to be essential: it should thus be provided in adequate amounts as a biologically active compound as to prevent selenium deficiency. We proceeded to supplement 1 child with lysinuric protein intolerance, born 3.1.81, whom se intake was 1.6 and 0.7 ug/day (safe and adequate intake: 10-30 ug/day) either with yeast-se, either with selenite (2 ug/kg day) during a period of 4 weeks each, at one year interval. Se was measured weekly with atomic absorption spectroscopy in plasma, RBC, urine, faeces and feeds. Weekly balances were calculated. GSH-Px activity was measured with butyl peroxide as substrate. During yeast-se supplementation, se retention approximated +98% (25 ug se/day). Plasma se rose (from 9 to 32 ug/l) as did GSH-Px activity. There was no changes in se levels (+20 ug/l, N:50 ±12 ug/l), neither in GSH-Px activity during and after the selenite study. Se faeces loss: 25%. During this period the child showed also diarrhea, vomiting, weight loss. In children on long term protein restricted diets, there is a need for se supplementation. Se has to be provided under a biologically active form. From this preliminary data we had to conclude that selenite was not available for metabolic processes.

4 HIGH IRON INTAKE DOES NOT NEGATIVELY AFFECT ZINC AND COPPER NUTRITIONAL STATUS OF TERM INFANTS. Haschke, F., Pietschnig, B., Vanura, H., Heil, M., Steffan, I., Schuster, E., Schilling, R.; University of Vienna, Austria.

Studies in animals and metabolic balance studies in infants showed that iron negatively interacts with zinc and copper at the site of absorption. Most infants receive formulas fortified with iron up to a level of 2mg/100kcal. Therefore we studied iron, zinc and copper intake and nutritional status of healthy, term infants receiving an iron fortified (1.6mgFe/100kcal; group Fe; n=15) or a non fortified (0.05mgFe/100kcal; group non Fe; n=13) cows milk formula (Beba[®], Nestle) from 122 through 365 days of age in a randomized, prospective study. Iron intake at 183, 274 and 365 days of age (from 3 day food record) was significantly higher in the group Fe (p<0.0001) but zinc and copper intake was similar. Body iron stores estimated from serum ferritin concentration (RIA) were better filled in the Fe group at 365 days of age (p<0.05). We found no difference in serum zinc and serum copper concentrations (ICP) between the two groups from 122 through 365 days of age. Moreover, the copper binding protein ceruloplasmin and the zinc binding proteins a-2 macroglobulin, albumin, prealbumin, retinol-binding protein and transferrin (all determined by radial immunodiffusion) were similar. We conclude that iron intakes in the range of the present infant feeding recommendations (ESPGAN) did not affect zinc and copper nutritional status.

5 THE EVALUATION OF TREATMENT IN WILSON'S DISEASE. Bouquet J, Cossack ZT*, Sinaasappel M, v. Caillie M, Degenhart HJ. Department Paediatrics, Erasmus University and University Hospital Rotterdam/Sophia Children's Hospital, The Netherlands, *Institute of Physiology, Odense University, Denmark.

Copper toxicity in liver, brain and kidney due to a congenital failure of the copper excretory mechanism in the liver is the main problem in patients with M. Wilson. Oral zinc sulphate as only treatment for this disease has successfully been used for several years as alternative therapy for D-Penicillamin which has several serious side effects. Quantitative balance studies comparing both forms of treatment were done in 2 sets of children. During the balance study a standardized hospital diet was used and identical food portions frozen for analysis of each patient. All fecal and urinary excretions were sampled each day for a seven day period.

Results:

Patients	Treatment	Balance (% of intake)		Plasma levels (ug/dl)	
		copper	zinc	copper	zinc
1	zinc	-13,5	+0,5	11,7	209
2	zinc	-14,2	+1,9	3,4	215
3	D-Penicillamin	-20,3	-1,6	7,5	110
4	D-Penicillamin	-45,4	-4,7	5,1	81

Additionally normal liverfunction tests and absence of clinical symptoms were found in both groups. Oral challenge with a high dose of D-Penicillamin in one day showed a significant rise in copper excretion in both groups, indicating still incomplete decoppering. Liver biopsy copper content confirmed this finding.

6 HOW TO DIAGNOSE ZINC-DEFICIENCY? Van Wouwe, J.P. and Van den Hamer C.J.A. Department of Pediatrics, University Hospital Leiden and Department of Radiochemistry, Interuniversity Reactor Institute Delft, the Netherlands.

Zinc-deficiency occurs in well-nourished children and is mostly of dietary origin. Vulnerability to infection, diarrhea, anorexia and growth retardation is its consequence. Easy reliable techniques to diagnose Zn-deficiency are not available. We have studied for this purpose: -1. salivary-Zn (0.08±0.03), urinary-Zn (480±135 ppm/day) and plasma-Zn (0.86±0.15 ppm steady decreasing for 6 hr after 100 mg egg) in volunteers (in one person no plasma decrease). -2. erythrocyte-Zn and in vitro uptake of 65-Zn in Zn-deficient rats (dietary-Zn v uptake r=0.99). -3. the behaviour of tracer Zn in mice (65-Zn, biological T_{1/2}, excretion and distribution), and humans (69m-Zn fig1). For pediatric use we have developed a stable-Zn loading test (68-Zn fig2). We expect the in vitro 65-Zn uptake by erythrocytes becomes a routine test to reliably diagnose Zn-deficiency.

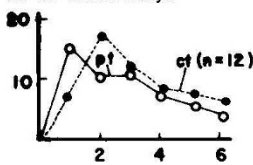


Fig 1: 69m-Zn in plasma (fr. dose/ml x 10⁶)

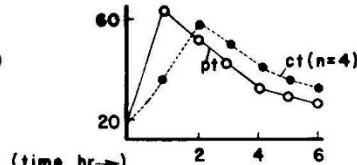


Fig 2: 68-Zn in plasma (% normalized).