83 THYROXIN (T_4) AFFECTS THE INTESTINAL TRANSPORT OF ELECTROLYTES

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Altered states of thyroidism are associated to alterations in stool patterns. The aim of our study was to see whether T_4 has a role in intestinal handling of electrolyte and water transport. In the first set of experiments, adult rats were divided into 3 groups (G-1,2,3) and either untreated (G-1), treated with Tapazole+ T_4 (G-2) or with Tapazole alone (G-3) for 4 wks. Transepithelial bidirectional fluxes of Na and Cl were measured (and J^Rnet calculated) across ileal mucosa mounted in Ussing chambers. Serum T_4 in G-1 (5.0±1.3µg/dl; mean+SD) and G-2 (5.2±2.2) did not differ but both differed from G-3 (2.7±0.5; p<0.001). Net ileal Cl flux (absorption "+"; secretion "-") did not differ between G-1 (-1.2±2.4 µEq/cm^{2}hr) and G-2 (-.2±1;6) but both differed from G-3 (+3.1±1.3; p<0.001). T_4 correlated with Cl net transport (r=.61;p<0.025), and the latter with J^Rnet (assumed to be HCO_3 net flux) (r=.65;p<0.005). In the 2nd set of experiments, rats were given orally T_4 for 4 wks. They were then divided in 3 groups, according to serum T_4 levels: G-4, T_4 ranging 6.0-7.5 µg/dl (controls), G-5, T_4 7.6-9.5 and G-6, T_4 >9.6. G-5 rats showed, when compared to G-4, marked shift toward secretion in J^{Cl}net (G-5: Cl= -4.5±1.2 vs G-4: Cl= +2.36±.92, p<0.01. Again, serum T_4 correlated (r= -.52,p<0.05) with Cl net transport. On the contrary, G-6 rats differed from G-5 in that they paradoxically showed higher rates of absorption for both Na and Cl.

We conclude that serum T_4 affects intestinal net transport of Cl by shifting it toward secretion, while it affects in the opposite manner the net transport of J^R. These effects, no longer seen at the highest T_4 serum levels, are consistent with a direct effect of T_4 on the Cl/HCO_3 exchange mechanism, and may explain the alterations in stool patterns seen in dysthyroid states.

84 THE EFFECTS OF VITAMIN E DEFICIENCY ON SMALL INTESTINAL TRANSPORT FUNCTION

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The gastrointestinal mucosa is vulnerable to damage by lipid peroxidation. Vitamin E (E) is a powerful membrane bound antioxidant present in high concentration in enterocytes. We have studied the effects of E deficiency on mucosal function. 20 day old male Wistar rats were placed on a diet either deficient in E or one to which E (100mg/kg) had been added. Brush border membrane vesicles of small intestine were prepared by a Ca^{++}precipitation method and glucose and sodium uptake measured. Na^+K^+ATPase, cAMP and cGMP were determined in mucosal homogenates. Na^+ stimulated glucose uptake was rapid with an 'overshoot' in both groups but after 9 months of E deficiency maximal glucose uptake was significantly impaired (757±116 vs 1152±324 pmol/hr/mg protein; mean±1SD; n=5; p<0.05). H^+ stimulated Na^+ uptake was similarly reduced (380±148 vs 743±181, p<0.02). In the absence of a Na^+ or H^+ gradient, uptake of glucose and Na^+ was not affected by E deficiency. No significant differences in Na^+K^+ATPase activity or cyclic nucleotide concentrations were observed. These data show that intestinal transport is disturbed in E deficiency and suggest that this is due to an effect on apical membrane transporters rather than on passive permeability or the enterocyte Na^+ pump. We speculate that E deficiency may contribute to the malabsorption seen in some states of malnutrition.

85 Symptomatic Selenium Deficiency in a child on home parenteral nutrition (HPN).

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A 2½ year old girl on long term HPN for microvillous atrophy presented with distal limb myalgia with normal power, reflexes & tone, & progressive inability to bear weight. Normal full blood count, electrolytes, creatine kinase and transaminases. Serum concentrations of Vitamins A, E & B_{12}, folate zinc and copper were normal. Plasma selenium was very low at < 0.05 µmol/l (reference range (RR) 0.8-2.0 µmol/l); RBC glutathione peroxidase was undetectable at < 1µ/g Hb) and plasma glutathione peroxidase was 6µ/l (RR 90-35µ/l). RBC enzymes showed normal vitamins B_1,B_2,B_6 status. Electromyogram was mildly abnormal. Muscle biopsy demonstrated atrophy of type II fibres & muscle selenium was 0.23µg/g dry weight (adult RR: 0.6-0.97 µg/g). Full cardiological evaluation was normal. Sodium selenite 15 µg/day was added to IV nutrition. Within 3 days muscle pain had improved; she began to crawl again & by 6 weeks she was walking normally. At 3 months, plasma selenium was 0.53 µmol/l. RBC glutathione peroxidase was 15 µ/g Hb. Sodium selenite supplements were reduced. Although biochemical evidence of selenium depletion is common in adults & children on HPN, associated clinical symptoms have rarely been reported. This is the youngest reported. Relationship between biochemical depletion & clinical symptoms is poorly understood, the dramatic response to selenium suggests that deficiency was the cause.

86 REDUCTION IN NEONATAL HYPERPHENYLALANINAEMIA WITH A LOW PHENYLALANINE AMINO ACID SOURCE

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We have recently drawn attention to the worrying incidence of hyperphenylalaninaemia in parenterally fed neonates (1), and have therefore compared Vamin 9 Glucose (KabiVitrum; 5.5 g/l phenylalanine) with Vaminolac (KabiVitrum; 2.7 g/l phenylalanine), a modified amino acid solution based upon the composition of human breast milk. Neonatal surgical patients requiring total parenteral nutrition were randomly allocated to receive either Vamin or Vaminolac as the amino acid source. 13 patients (4 gastroschisis, 4 small bowel atresia, 3 necrotising enterocolitis, 2 tracheo-oesophageal fistula) were given Vamin and 6 (4 NEC, 1 gastroschisis, 1 jejunal volvulus) received Vaminolac. Amino acid intake was stabilised at 2.5g/kg/day for a minimum of 3 days prior to plasma amino acid analysis, performed twice weekly for one week, then at weekly intervals. The median plasma phenylalanine concentration in the Vamin group was 200umol/l (range 49-983umol/l, n=32) compared with only 68umol/l (range 47-154umol/l, n=13; p < 0.00003) even though patients receiving Vamin were of significantly greater post-conceptual age at the time of sampling (median 38 weeks, range 31-53 weeks) than Vaminolac patients (median 38 weeks, range 31-41 weeks; p < 0.00003). No patients had grossly elevated plasma tyrosine concentrations or evidence of liver dysfunction. Three of the neonates given Vamin were found to have plasma phenylalanine concentrations above the commonly accepted neuro-toxic level of 600umol/l. The use of Vaminolac compared with Vamin 9 Glucose is therefore associated with a significant reduction in potentially toxic plasma phenylalanine concentrations.

(1) Puntis JWL et al., Lancet 2:1105-1106 (1986).

87 BONE MINERALIZATION OF PREMATURE INFANTS DEPENDS ON CALCIUM AND PHOSPHORUS INTAKE AND NOT ON THE DOSE OF VITAMIN D SUPPLEMENTATION.

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We have compared vitamin D (vit D) metabolite, calcium (Ca), phosphorus (P) and alkaline phosphatase (AP) blood values in permature infants fed human milk (mean birth weight 1478, range 645-1970, mean gestational age 31 weeks) receiving vit D 500 IU/d or 1000 IU/d with and without Ca (108 mg/kg/d) and P (53 mg/kg/d) supplementation. At 3 months of age the bone mineral content (BMC) of radius was measured by direct photon absorptiometry (125 I). In infants receiving 500 IU/d of vit D the mean 25(OH)D was 55.7 ng/ml (n=18, SD 33.8) and 1,25(OH)2D 94.0 pg/ml (n=17,SD 44.8) at 3 months of age. The values for those with 1000 IU/d were 56.2 ng/ml (n=20, SD 32.1) and 120.0 pg/ml (n=18, SD 72.2), respectively (ns). Ca, P and AP values were followed up every two weeks and were equal in the two groups. No differences were seen in BMC between the groups with different vit D dose (115±35 mg /cm, n=6 vs. 113±39 mg/cm, n=5). On the other hand in infants without Ca and P supplementation BMC was significantly lower (67±6 mg/cm, n=3) than in those receiving supplementation (132±27 mg/cm, n=8) (p=0.005). Hypophosphataemia was common in the very low birth weight infants not receiving Ca and P supplementation. We conclude that 500 IU/d of vit D is enough for premature infants if Ca and P supplementation is taken care of. There is no advantage of a higher vit D dose for bone mineralization.

88 NONINVASIVE ASSESSMENT OF WHOLE-BODY METABOLIC RATES IN RATS, PRETERM INFANTS AND ADULTS USING RNA CATABOLITES IN URINE

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For assessing the efficiency of nutritional supply, determination of whole-body metabolic activity, exemplified by measurements of protein turnover, are becoming more and more important. However, both technique and interpretation of protein turnover measurements with ^{15}N-amino acids are complex and time-consuming. As we have shown, RNA turnover is coupled to protein turnover (1) and can easily by estimated by measuring urinary excretion of modified RNA catabolites: N^2,N^2-dimethylguanosine (m_2^2G) or N^6-threoninocarbonyladenosine (t^6A) can be used to calculate tRNA turnover, similarly pseudouridine (Ψ) gives rRNA turnover and 7-methylguanine (m^7Gua) mRNA turnover. The relation between tRNA, rRNA, mRNA and protein turnover is constant irrespective of age, preterm infants and adults displaying only minor differences (1). Thus any one of the three RNA classes can be taken as representative. We have compared tRNA turnover rates in 320-g rats (pooled urine from 10 animals; 2.45 µmol $kg^{-1}d^{-1}$), 1.9-kg preterm infants (n = 21; 1.69 ± 0.39 µmol $kg^{-1}d^{-1}$) and adults (n = 32; 0.50 ± 0.12 µmol $kg^{-1}d^{-1}$). The relation between tRNA turnover rates in rats, preterm infants and adults (4.9 : 3.4 : 1) corresponds closely to the one observed by others for whole-body protein turnover (about 5 : 3.5 : 1 (2)) and to a lesser degree also to basal metabolic rates (about 4 : 2.5 : 1 (2)). (1) Sander G, Hülsemann J, Topp H, Heller-Schöch G, Schöch G (1986) Ann Nutr Metab 30: 137-142; 2. Waterlow JC (1984) Q J Exp Physiol 69: 409-439.