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T.M.Strom*, J.Weil*, A. Timnic*, D.Knorr, F.Bidlingmaier
Depart. of Paediatrics, University of Munich and Institute of Clinical Biochemistry, University of Bonn (FRG)

BINDING SITES FOR ATRIAL NATRIURETIC PEPTIDE (ANP) ON PLATELETS IN PATIENTS WITH HIGH PLASMA ANP LEVELS.

In our first study we found binding sites for ANP on human platelets. Binding studies on these easily accessible cells could be a useful model to investigate receptor-status in patients with elevated ANP plasma levels. We reported high ANP levels in neonates and in patients with heartfailure. Therefore we studied the number of binding sites on platelets in venous umbilical blood of term infants (n = 10), in adults (n = 15) with heartfailure and in controlsubjects (n = 18). For the binding studies 40 x 10^6 platelets were incubated with 10.000 cpm ^{125}J-ANP and increasing concentrations of unlabeled ANP. Time of incubation was 120' at room temperature. Separation of bound and free tracer was performed by filtration through Whatman CF/G filters.
In neonates we found 18-32 and in patients with heart failure 8-30 binding sites/platelet. In comparsion with control subjects (15-30 binding sites/platelet) there was only in patients with heartfailure a trend for reduction of binding sites ($p < 0.1$). The Kd (14 ± 8 pM) was similiar in all subjects studied.
In our results there was no convincing evidence of "receptor down regulation" in the presence of high ANP levels as described in in-vitro experiments.

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T.Kaethner*, C.Emmerich*, S.Gajowski*, °V.Duda*, °°K.Ehlenz*, °°°W.Rascher*,M.Brandis (Introd.by H. Helge)
Dept.of Pediatrics, °Obstetrics and °° Internal Med., Philipps -University ,355 Marburg/L. ,FRG
°°°Dept.of Pediatrics, Univ.of Heidelberg, FRG

LEVELS OF ALDOSTERONE AND VASOPRESSIN IN THE AMNIOTIC FLUID AND IN THE URINE OF NEWBORNS:

Recently we reported about a highly stimulated renin-angiotensin-aldosterone-system (RAAS) in newborns without elevation of vasopressin (ADH) levels. In the following study we examined aldosterone (ALDO) ,ADH, electrolytes, creatinine and osmolality in 53 amniotic fluid samples and in urines of premature and mature newborns.
Results: In all amniotic fluid samples ALDO and ADH were detectable.ADH levels were in the same range in amniotic fluids as in urines collected at the first day of life. (17 pg/ml vs. 10 pg/ml) In contrast ALDO levels in the amniotic fluid were 40 times lower than levels in urines. (37ng% vs.1280 ng%). Hormone concentrations were not correlated to fetal age,electrolytes, creatinine and osmolality in amniotic fluid.
Conclusion: In the 17th week of gestation the human fetus is able to produce ADH in a similiar amount as in the early postnatal life. But Aldo levels in the amniotic fluid are significantly lower than in the urines of newborns. This may reflect the onset of stimulation of RAAS in the early postnatal life.

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JW Honour,MJ Dillon, JM Cowen, HB Valman
Cobbold Laboratory,Middlesex Hospital, London, England: Institute of Child Health, London, England and Northwick Park Hospital, Harrow, England

THE AETIOLOGY OF ALDOSTERONE SECRETION AND SODIUM HOMEOSTASIS IN PRETERM INFANTS

Late hyponatraemia with negative sodium balance was previously seen in preterm infants in our hospital (Honour et al;1979;Acta Paed Scand 63:813). Contributory factors were a low salt intake and renal insensitivity to the high aldosterone production (APR) which followed 2-3 weeks with low APR. By increasing sodium intakes we maintained sodium balance in 15 preterm infants. We found plasma renin activity 20920 ± 5650 ng/l/h around day 7 falling to 6472 ± 4500 ng/l/h around day 33. Corresponding plasma aldosterone concentrations were 4893 ± 2483 pmol/l and 3960 ± 3135 pmol/l. In 15 infants of 27 - 35, mean 31.3 weeks gestation tetrahydroaldosterone (THAldo) excretion rates were normal at 29.2 ± 24 µg/24h. The ratio of urinary 18-hydroxy-THA (principal metabolite of 18-hydroxycorticosterone) to THAldo was 0.35 ± 0.22. These data (1)exclude a defect in aldosterone biosynthesis (2) show PRA does not relate to sodium balance and (3) the adrenal zona glomerulosa response to angiotensin in the neonatal period may be inhibited by other factors such as atrial natriuretic peptide.

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C.G.D.Brook, M.A.Livesey*
The Middlesex Hospital, Mortimer Street, London W1.

GROWTH AND GROWTH HORMONE (GH) TREATMENT FOLLOWING RADIOTHERAPY OF BRAIN TUMOURS.

Of a cohort of 132 children alive and well following treatment of brain tumours remote from the hypothalamus or pituitary with radiotherapy, 96% had evidence of GH abnormality. 32 had completed their growth. 14 who had received craniospinal irradiation, had final height SDS -2.03 (range, -3.7 to +0.09), sitting height (SH) SDS -3.22 and subischial leg length (SILL) SDS -0.61. 18 treated with cranial irradiation alone had final height SDS -0.93 (range, -2.8 to +2.07), SH SDS -1.24 and SILL SDS -0.53. Thus the effect of spinal irradiation on final height was considerable.

40 children were treated with GH for periods of 1-4 years. 32 had received craniospinal irradiation and 8 cranial irradiation alone. 17 children who had received craniospinal irradiation were treated with GH when prepubertal. Over the first 12 months of treatment mean height velocity SDS increased +2.52 (range -0.9 to +4.84). Mean height SDS for CA increased +0.27 (range -0.3 to +1.55) and height SDS for BA +0.09 (-0.89 to +0.99). Mean SILL SDS increased +0.33 (-0.41 to +1.13) but SH SDS was not improved. GH given to 23 children in puberty was without significant effect on growth.

We conclude: 1. Spinal irradiation adversely affected spinal growth and this did not respond to GH in the doses used. 2. After craniospinal irradiation, GH could only normalise leg growth and must therefore be instituted before puberty. 3. After cranial irradiation alone GH maintained height SDS. 4. Delay in instituting GH treatment leads to an irrevesible loss of final height prognosis.

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R. Brauner, F. Malandry*, R. Rappaport, JM. Zucker*, C. Kalifa*, A. Pierre-Kahn*, P. Bataini*, JL. Dufier*, A. Tar*.
Department of Pediatric Endocrinology and Diabetes and INSERM U30 Hôpital des Enfants-Malades, Paris, France.

SEQUENTIAL OCCURRENCE OF ENDOCRINE DISTURBANCES IN CHILDREN TREATED FOR OPTIC GLIOMAS (OG).

Children with OG are at major risk for short final stature because of the combined effects of GH deficiency (GHD) and central precocious puberty (PP). In order to better establish our therapeutic strategy, the course of the endocrine disturbances was reevaluated in 48 cases (28 boys, 20 girls), before and after cranial irradiation. 25 of them had neurofibromatosis. All received cranial irradiation at the dose of 50-55 Gy over 5-6 w at mean age of 6.2 ±0.5 yr (m± sem). Before irradiation GHD, with GH peaks< 8 ng/ml after AITT, was found in 4 cut of 26 cases tested. PP with growth acceleration was present in 22/48 patients. After irradiation 1) GHD occurred in all patients within 2 yr (peak < 5 ng/ml in 54% of them, 2) only 2 patients developped PP, 3) partial or complete gonadotropin deficiency occurred in 6 patients, of whom 3 had already PP, with a mean follow up of 4.8 ± 0.6 yr, 4) growth, as expressed by SD changes over the 1st two yr was -1.3 ± 0.2 SD in prepubertal patients (n= 9) and -0.1 ± 0.1 SD in pubertal patients (n= 9, $p<0.001$) with a parallel BA progression of 3.4 ± 0.45 yr in the 2d group, 5) final height reached in 16 cases was - 2.2 SD.

In conclusion: 1) radiation dose administered in OG invariably produced GHD, 2) such GHD induced a decreased growth rate in prepubertal children, 3) children with PP maintained a sufficient growth rate although BA progressed excessively, 4) this radiation dose induced gonadotropin deficiency.

This study provides usefull guidlines for the hormonal treatment of these patients using GH alone or in combination with LHRH analogue/or sex steroids according to the course of the endocrine disturbances.

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M. Fontoura*, R. Brauner, R. Rappaport, A. Fischer*, E. Quintana*, JM. Zucker*, F. Bernaudin*, E. Vilmer*, A. Devergie*.
Department of Pediatric Endocrinology and Diabetes and INSERM U30 Hôpital des Enfants-Malades, Paris, France.

GROWTH AND ENDOCRINE FUNCTION AFTER BONE MARROW TRANSPLANTATION (BMT) WITH OR WITHOUT TOTAL BODY IRRADIATION (TBI).

TBI preparing to BMT is frequently followed by growth retardation. As GH deficiency (GHD) is a well known complication of cranial irradiation, the purpose of this study was to evaluate the risk of GHD after TBI and its possible relationship to this failure of growth. 20 children received BMT for ALL (n= 8), immunodeficiency (n= 6) or other disease (n= 6). 15 of them (group I) had TBI at 9-12 Gy doses after conditionning by chemotherapy. They were compared to 5 children (group II) who had only chemotherapy. None of the children received additional cranial irradiation. Results were as follows (median - range) :

GROUP	AGE AT TBI (yr)	FOLLOW-UP (yr)	HEIGHT CHANGE (SD)	GH-AITT (< 8ng/ml)
I (15)	5.6 (1.5-12.7)	3.5 (1- 6.5)	-1 (1- -3)	1
II (5)	2.2 (0.6-2.8)	2.2 (1.6-4)	0 (1.5- -1)	0

Growth retardation was significantly superior in group I than in group II ($p<0.05$). In group I, out of 5 patients with growth failure (>1SD) one had GHD and the 4 others had normal GH secretion as shown by plasma Sm-C and 12 hr GH nocturnal profile. No significant growth retardation occured in group II. Elevated TSH was found in 5 cases of group I with T4 normal (3) or moderatly decreased (2).

In conclusion, after a mean interval time of 3.5 yr GHD does not appear as a major complication of TBI. Thyroid deficiency is more frequent. Growth retardation often severe, is probably more frequently the consequence of the cartilage irradiation. A more prolonged follow-up of these patients is still necessary.