89

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Blood pressure (BP) and metabolic control in IDDM.

We studied BP patterns and the Renin-Angiotensin-Aldosterone axis (RAA) of 97 IDDM children (3-15 yrs old) in relation to the auxological data,the metabolic control and duration of diabetes (1-13 yrs).We analysed a total of 712 BP measurements. RESULTS. Mean systolic BP levels for age groups were at the 50th percentile of the general population,while the mean diastolic BP were at the 75th in both sexes.Systolic and diastolic BP levels were directly and significantly related to age, weight,height,Quetelet index,duration of disease and HbA1. Plasma Renin Activity (PRA) levels,all within normal limits, were related neither to age,Natruria and Kaliuria (contrary to normal children) nor to the parameters of metabolic control. CONCLUSIONS. BP levels were not grossly altered but were under the influence of metabolic control. The absence of a correlation between PRA and age or electrolytes excretion suggest an early disturbance of RAA, probably caused by concomitant metabolic alterations.

90

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Simultaneous determination of prostanoid plasma concentration by GC-negative ion chemical ionisation MS.

For the measurement of prostaglandins several techniques, e.g. bioassay, RIA, HPLC, GC and GC-MS are used. Of these, GC-MS provides the most sensitive and specific methodology. Misinterpretation of data or confusion with other compounds is highly unlikely. Negative ion chemical ionisation mass spectra of methoxime (MO), trimethylsilyl (TMS), pentafluorobenzyl (PFB) derivatives of prostaglandins with CH_4 as reagent gas show a fragment ion at m/z $(m\text{-}PFB)^-$, which accounts for most of the total ion current. Sensitivity is about a hundred times as high as of electron impact MS. Blood is collected in tubes containing a sodium citrate-indomethacin solution. The plasma is separated and acidified after addition of ^2H and ^3H standards. Extraction is carried out using a reversed phase Sep-Pak. HPLC separation results in two peaks, the first containing PGE_2, TxB_2 and 6-k-$PGF_{1\alpha}$, the second $PGF_{2\alpha}$. Recovery after HPLC is about 50%. PGE_2, TxB_2 and 6-k-$PGF_{1\alpha}$ are converted to PFB, MO, TMS derivatives, $PGF_{2\alpha}$ to PFB, TMS derivative. The three MO's are determined in one capillary GC-MS run. Multiple ion detection is carried out by first using the fragment ions m/z 524 and 528 for PGE_2, then switching to m/z 614 and 618 for the TxB_2 and 6-k-$PGF_{1\alpha}$ fragment ions. Plasma concentrations of 5 healthy volunteers are: $PGF_{2\alpha}$ 3-15, PGE_2 2-12, TxB_2 7-20 and 6-k-$PGF_{1\alpha}$ 0.5-4 pg/ml. The method is already applied in various experimental and clinical investigations. -Supported by the DFG (Se 263-7).

91

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Prostaglandin(PG)-mediated hypokalemic renal tubular disorders in childhood.

The best described endocrinological form of hypokalemia in adults is Bartter's syndrome. Increased renal PG-synthesis secondary to decreased tubular reabsorption of chloride are thought to be involved in the pathogenesis of this syndrome. Systematic investigations of renal and systemic PG-production in chronic hypokalemia associated with various forms of renal tubular disorders in childhood are lacking. In 9 patients in the age of 3 m to 11 y (median:3 y) with these disorders urinary excretion (24h-urine) of PGE_2 and $PGF_{2\alpha}$ were determined as an index of renal PG-synthesis and of PGE-M and 6-k-$PGF_{1\alpha}$ as an index of systemic PGE_2 and PGI_2 production. The normal range (10th-90th percentile) of PG-excretion rates in healthy infants (n=30) of the same age were as following (mass spectrometric(MS)-analysis): PGE_2 2.7-13.0 (median: 7.2), $PGF_{2\alpha}$ 11.6-47.3 (median:29.7), PGE-M 106-519 (median:269) and 6-k-$PGF_{1\alpha}$ 3.9-24.7 (median:8.1) ng/h/1.73m². In all 9 hypokalemic patients PGE_2 excretion was elevated 3- to 19-fold when compared with the median of the control group; in 6 out of 8 patients PGE-M excretion was 3- to 18-fold elevated; no significant changes were observed in urinary $PGF_{2\alpha}$ and 6-k-$PGF_{1\alpha}$ levels. Considering that 8 out of the 9 patients depended on indomethacin treatment, it is proposed that MS determinations of PGE_2 and PGE-M excretion provide a sensitive indicator for PG-mediated hypokalemia in childhood. - Supported by the DFG (Se 263-7)

92

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Endocrine Studies in Male Pseudohermaphroditism. Muellerian structures and breast development are distinctive marks of androgen insensivity and gonadal dysgenesis.Clinical features of both conditions were found in thepresented case.A 17yrs.old 46,xy girl presented with amenorrhea,clitoral enlargement(4cm),well developed breasts(Tanner stage5),hirsutism,normal vagina and portio,and rudimentary uterus.The gonadotropins were elevated(LH7.6-9.1,FSH9.3-12.4µg/l),the rise in Gn-RH-test(60µg/m²)was increased(LH39.6,FSH41.1µg/l).Urinary gonadotropins were moderately elevated(9HMG-E/d).E_2ranged between 18-32 pg/ml(infantile values), T levels were stimulated(380-640pg/ml). Stimulation of the gonads with HMG(5x300E)revealed no E_2response (10-22pg/ml),but HCG(5x2000E)caused a distinct rise of T (740-2400pg/ml).Urinary estrogens were within the normal male range(15 µg/d)and urinary T was intermediate(20µg/d).Prolactin,17-OHP,ACTH, cortisol,17-OHCS,17-KS,pregnantriol,SMA12,bone age,and blood pressure were normal.After gonadectomy,the histologic examination revealed immature testicular tissue with fetal tubules,sertolicells, and interstitial complexes of leydig cells.A structure which appeared like a uterine tube was histologically undifferentiated epididymal tissue.The right gonad revealed malignant overgrowth by a germ cell tumor.While well developed breasts are features of androgen insensivity,all the other findings are consistent with partial testicular failure,probably due to a treatment with ethinylnortestosteron in early pregnancy.The breast development may be accounted for by estrogenic activity of the germ cell tumor or it may be interpretated as a considerable pubertal gynecomastia.

93

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Bartter's sydnrome in a 13.5-year-old girl: Growth characteristics and failure of Aspirin therapy.

A 13.5-year-old girl was referred for evaluation of hypokalaemia and growth retardation. She had felt fatigued for 2 years with polyuria, nocturia and episodic muscle cramps. Her apetite was poor and school performance declining. Physical examination revealed thin (26.5 kg), short (142.5 cm), normotensive (14/7.5 kPa) girl with delayed skeletal maturation (12 years). The serum K was 1.8, Na 135 and Co2 content 29 mmol/l, with mild hypomagnesemia (0.55 mmol/l). Polyuria was Pitressine resistant. Diagnosis of Bartter's syndrome was confirmed by increased reninemia (PRA 10.7 ng/ml) and urinary aldosterone elimination (15 ug/day), with juxtaglomerular cell hyperplasia in kidney tissue obtained at biopsy. She started treatment with potassium supplements (80 mmol/day), spironolactone (4 mg/kg/day) and propranolol (0.5 mg/kg/day). Response was satisfactory: hypokalemia was corrected, general condition improved, her appetite and linear growth increased (catch-up growth). Menarche occured at 16 years. Then we introduced Aspirin in a dose of 100 mg/kg/day. The girl remained hypokaliemic and adverse effects appeared: gastrointestinal upset and defect in coagulation mechanisms with epistaxis. Therefore Aspirin therapy was discontinued and conventional therapy reintroduced, with the same excellent results.

94

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Screening for congenital hypothyroidism - a pilot study in Belgrade.

A pilot study in Belgrade was carried out in order to establish optimal conditions for a nation-wide programme in Serbia. We measured TSH on PKU filter paper blood samples by Biodata's neonatal RIA kits. During the first 12 months, beginning in January 1983, 19.972 newborns were screened (97,5% of all live born infants in Belgrade area) and 3 cases confirmed giving an preliminary incidence of 1:6.657. Sixty one infants (0,3%) were recalled for another filter paper sample, but later with cut-off level of TSH above 30 mIU/l recallrate was 0,07%. Diagnosis was confirmed by Tc99 scan (one infant with aplasia, two with sublingual ectopia of thyroid), and therapy begun at 10-13 days of life. All three female patients had A Rh positive blood group. In the three groups of sick preterm infants with different mean gestational ages (31,0;34,8 and 37,7 weeks, respectively) there were no correlations with TSH values (7,4; 6,7 and 6,2 mIU/l). Neither in healthy term, nor in sick preterm newborns cases of transitory hypothyroidism were found, probably partly because of an efficient iodine prophylaxis of our population.