Acta Paediatrica Academiae Scientiarum Hungaricae, Vol. 21 (2—3), pp. 153—157 (1980)

Function of the renin-angiotensin-aldosterone system in relation to electrolyte balance in the small-for-date neonate

by

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Received 15th February, 1980

To assess the influence of intrauterine growth retardation on the electrolyte status and the activity of renin-angiotensin-aldosterone system of newborn infants, sodium and potassium balance, as well as plasma renin activity, plasma aldosterone concentration and urinary aldosterone excretion were determined simultaneously in a group of healthy growth retarded and healthy normally grown neonates.

It was observed that intake, urinary excretion and retention rate of sodium and potassium as well as the plasma sodium and potassium levels were essentially the same in the two groups. Similarly, no significant difference was found in plasma renin activity, plasma aldosterone level and urinary aldosterone excretion between the neonates whose birth weight was small or appropriate for gestational age.

It is concluded that intrauterine growth retardation has no significant influence on the electrolyte status and the activity of the renin—angiotensin—aldosterone system, suggesting that in the regulation of these functions gestational factors are mainly involved.

It has been reported previously that the activity of the renin-angiotensin-aldosterone system (RAAS) is highly elevated during the neonatal period [3, 4, 5, 8, 9, 14, 15, 17, 18, 21]. Although several factors have been suspected to be responsible for the increased activity of RAAS, the reason for the increase is not clear. In addition to perinatal stress imposed by labour and delivery [4, 8, 9, 16, 17], low systemic blood pressure [4, 5, 6] and renal tubular unresponsiveness to aldosterone [11, 25], postnatal changes in electrolyte balance were assumed to be of great importance in producing hyperactivity of RAAS in the neonate [27, 28]. Furthermore, we could demonstrate a developmental pattern of neonatal RAAS with advancing gestational age [27].

The question remained open whether the development of RAAS was similar in normal and small-for-date newborn infants.

In an effort to provide information concerning the effect on the activity of RAAS of intrauterine growth retardation, a study was designed to compare plasma renin activity (PRA),

plasma aldosterone concentration (PA), urinary aldosterone excretion (UAE) and electrolyte status in normally grown and growth retarded neonates.

Material and Methods

The subjects of the study were 12 small-for-date and 12 appropriate-for-date healthy male newborn infants with a mean birth weight of 2210 g (range, 1680—2650 g) and 3100 g (range, 2710—3640 g), respectively. Their mean gestational age was essentially the same, 38.6 weeks (range, 36—41 weeks), for both groups.

All infants were born after uncomplicated pregnancy and normal vaginal delivery with a one minute Apgar score of 7—10. The mothers were on a normal diet without diuretic therapy. All infants remained well during the whole period of study.

Intrauterine growth rate was estimated by using a local standard. Infants less than the 10th percentile of weight for gestational age were regarded as small-for-dates, while those between the 10th and 90th percentiles as appropriate-for-dates infants. The infants were fed cow's milk formula. Food intake was gradually increased to attain a daily fluid intake of 150—180 ml/kg by the end of the first week. The plasma level, the intake and the urinary excretion of sodium and potassium as well as PRA, PA and UAE were determined on the 7th day.

Urine was collected fractionally over a period of 24 hours. The specimens were refrigerated, pooled and stored at —20 °C until analysed. Blood samples were obtained from a scalp vein at 9.00 a.m. at least 2 hours after the last feeding. The infants were kept supine for a period of 1—3 hours before blood samplings. PRA was measured radioimmunologically according to the method of Haber et al [13] using SORIN-CEA-IRE-RENK kits. PA and urinary aldosterone concentration measurement was also made by radioimmunoassay [30] using SORIN-CEA-IRE-ALDOK kits [27, 28, 29]. Plasma, formula and urinary sodium and potassium were measured by flame photometry. Statistical evaluation was done by using Student's t test.

Results

Data on intake, urinary excretion and retention rate of sodium and potassium, as well as plasma sodium and potassium levels are summarized in Table I. It can be seen that sodium intake, urinary sodium excretion and sodium balance were essentially the same in the two groups, and no difference was noted in the plasma sodium level, either. Similarly, the intake, the excreted and the retained amount of potassium remained at about the same level irrespective of intrauterine growth rate. Small-for-date infants, however, had a slightly higher plasma potassium level than those grown normally.

The results of hormone determinations are given in Table II. No significant difference in hormone levels could be observed between the two groups. Still, PRA and UAE tended to be higher in the small-for-dates than in the infants with a normal rate of intrauterine growth.

Discussion

During the last years, evidences have been provided to indicate the increased activity of RAAS in the neonatal period [3, 4, 5, 8, 9, 14, 15, 16, 17, 18, 21]. Furthermore, it has

TABLE I

Electrolyte status of normally grown and growth retarded neonates at one week of age

		Sodium				Potassium			
		intake	urinary excretion	balance	plasma level mEq/l	intake	urinary excretion	balance	plasma level mEq/l
		mEq/kg/day				mEq/kg/day			
Normally	mean	1.80	1.11	0.69	146.0	3.00	0.36	2.64	5.20
Grown	n	12	12	12	12	12	12	12	12
	SE ±	0.18	0.32	0.25	2.44	0.14	0.14	0.54	0.20
Growth	mean	1.82	1.13	0.70	145.0	2.97	0.49	2.47	5.80
Retarded	n	12	12	12	12	12	12	12	12
	SE ±	0.12	0.28	0.22	1.81	0.16	0.10	0.48	0.26

TABLE II

Plasma renin activity, plasma aldosterone concentration and urinary aldosterone excretion of normally grown and growth retarded neonates at one week of age

		Plasma renin activity ng/ml/hr	Plasma aldosterone concentration ng/ml	Urinary aldosterone excretion ng/day
Normally	mean	13.41	1.44	6.65
Grown	n	12	12	12
	SE ±	3.41	0.72	1.28
Growth	mean	18.14	1.55	9.63
Retarded	n	12	12	12
	SE	4.21	0.30	2.99

been demonstrated, that the components of RAAS in healthy premature infants differed significantly from those of full-term newborn infants [5, 19, 27]. Namely, PRA [19, 27] and plasma angiotensin II concentration [5] was found to be higher, and UAE lower [27] in preterm infants than in their full-term matches. With increasing maturity each of these hormone levels gradually approached the values characteristic of full-term infants [27]. At the same time, PA appeared to be uniformly high and remained unchanged irrespective of gestational age [27].

The results of the present study showing no significant difference in the activity of RAAS in infants differing in birth weight but of the same gestational and postnatal age, are fairly consistent with the above-mentioned findings.

The fact that intrauterine malnutrition did not considerably influence the function of RAAS could be inter-

preted as indicating the prime importance of gestational age in establishing the activity of RAAS in the neonate.

It is, however, important to note that the developmental pattern of RAAS may be ascribed, at least in part, to the maturity-related alterations in electrolyte balance taking place in the early postnatal period [10, 27, 28]. For this reason, in addition to hormones, the parameters of sodium and potassium homeostasis were also measured. In agreement with other studies [1, 2, 20, 22, 26], renal sodium handling has been found to be governed by gestational factors and no discernible difference could be demonstrated in urinary sodium excretion, sodium balance and plasma sodium concentration between the normally grown and growth retarded neonates of the same gestational age. With respect to the significant volume expansion of extracellular fluid compartments [7], however, a higher rate of urinary sodium excretion could have been expected in the growth retarded group. In potassium homeostasis there was no considerable difference between the two groups except for a slightly increased plasma potassium level in the small-for-date infants which might have resulted from chronic fetal distress [12].

The increased potassium level might account for the somewhat higher UAE in the small-for-date newborns because potassium chloride has been shown to enhance aldosterone secretion by the neonatal adrenal [23, 24].

The main conclusion to be drawn from the above data is that electrolyte status and the function of RAAS in small-for-date newborns do not differ significantly from those of normally grown infants of the same gestational age, suggesting that mainly gestational factors are involved in regulating these functions.

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