AGE-DEPENDENT CHANGES OF PLASMA RENIN CONCENTRATION IN HUMANS

K. HAYDUK, D. K. KRAUSE, W. KAUFMANN, R. HUENGES, U. SCHILLMÖLLER AND V. UNBEHAUN

Department of Internal Medicine, Department of Pediatrics, and Department of Gynaecology and Obstetrics, University of Tübingen, Tübingen, West Germany

SUMMARY

1. Plasma renin concentration (PRC) in newborns greatly exceeded PRC in children and adults. PRC in cord plasma of newborns was higher than peripheral venous PRC in their mothers. PRC in the newborns increased further in the first 48 h post partum and then gradually decreased.

2. The mean PRC of healthy children and adults on free sodium intake decreased with age by an exponential function.

3. The absolute increase of PRC in response to upright posture (PRC_{upright} - PRC_{recumbent}) decreased with age. The relative increase of PRC in response to upright posture (PRC_{upright}/PRC_{recumbent}) remained unchanged with age, the PRC in upright posture being about twice the basal PRC in all age groups.

Key words: age-dependent renin, renin in childhood, plasma renin concentration.

ZUSAMMENFASSUNG


2. Der altersabhängige Abfall der PRC gesunder Kinder und Erwachsener während freier Nahrungsaufnahme folgte einer Exponentialfunktion.

3. Der absolute Anstieg der PRC nach aktiver Orthostase (PRC_{Orthostase} - PRC_{Ruhe}) verminderte sich mit zunehmendem Alter. Der relative Anstieg (PRC_{Orthostase}/PRC_{Ruhe}) war unabhängig vom Alter; die PRC nach Orthostase betrug etwa das Doppelte des Ruhewertes in allen Altersgruppen.

Correspondence: Dr Karl Hayduk, Medizinische Universitätsklinik, 74 Tübingen, Otfried-Müller-Strasse, West Germany.

273s
Numerous studies have been done on plasma renin concentration and plasma renin activity in adults in various physiopathological conditions, but there are only a few data in the literature concerning these parameters in the neonatal period and in childhood (Godard, Riondel, Veyrat, Mégevand & Muller, 1968; Imai, Igarashi & Sokabe, 1968; Amsterdam, Albers, Christlieb, Morgan, Nadas & Hickler, 1969; Arant, Brackett, Young & Still, 1970; Londe, Bourgoignie, Robson & Goldring, 1971; Vouëte, van der Meer & Staugaard-Klosterziel, 1971; Kotchen, Strickland, Rice & Walters, 1972; Krause, Schillmölë & Hayduk, 1972; Hayduk, Krause, Huenges & Unbehaun, 1972); however, at the present time there is no information available on age-dependence of plasma renin activity and plasma renin concentration.

MATERIAL AND METHODS

Plasma renin concentration (PRC) was measured with a micromethod (Krause, Hayduk, Meurer, Ganten, Boucher, Kaufmann & Genest, 1972) based on Boucher's method (Boucher, Veyrat, de Champlain & Genest, 1964; Boucher, Ménard & Genest, 1967): 0.1-1.0 ml of plasma was incubated with 150 mg of sheep angiotensinogen dissolved in 2.0 ml of trisphosphate buffer (containing EDTA and NaN₃) for 15 h at pH 7.0. The determination of renal renin concentration (RRC) was done analogically. Renin concentration is expressed in ng of angiotensin/ml of plasma or mg of renal tissue/h incubation (mean ± SEM). PRC was measured in healthy subjects on free diet.

(1) Newborns: in cord plasma (n = 24); post partum: 3-48 h (n = 17), the newborns received no food in the first 24 h post partum; 3-4 days (n = 9); 5-10 days (n = 13).

(1b) In the corresponding mothers after a normal pregnancy during uncomplicated vaginal delivery before administration of any oxytocic agent (n = 24); in nine of them PRC was measured for the second time 6 days post partum during resting conditions.

(2) Infants: 3-24 months of age (n = 46).

(3) Children: 3-12 years of age (n = 29).

(4) Adults: 20-35 years of age (n = 21).

(5) Adults: 49-76 years of age (n = 37).

In addition, PRC and RRC were determined before and after unilateral nephrectomy in a 6-year-old girl with renovascular hypertension.

With exception of groups 1 and 2 in all subjects PRC was measured after night rest in the recumbent position (‘recumbent’) and again after being 3 h in upright posture, or in children after a normal morning of playing (‘upright’). Statistical evaluation was done using Student's t-test for paired and unpaired measurements.

RESULTS

(1) PRC in cord plasma (12.5±1.8) was higher than in peripheral venous plasma of their mothers (6.3±0.7; P<0.0005). In the mothers PRC had dropped 6 days after delivery (2.4±0.7; P<0.0025). In the newborns PRC increased in the first 48 h post partum (23.0±2.5; P<0.0025) and had already fallen 3-4 days after delivery to 16.3±3.4 (P<0.0025) and 5-10 days post partum to 4.6±0.9 (P<0.0005).

(2) PRC in infants (3.4±0.5) was higher than in infants 5-10 days post partum, but without
Age-dependence of plasma renin concentration. (a) PRC in recumbent position; (b) PRC in upright position.
being significant. A comparison with the older children was not possible as in the infants the position (recumbent or upright) cannot be judged.

(3)-(5) PRC in children between 3 and 12 years (recumbent: 2.2±0.2; upright: 4.4±0.4) was significantly higher ($P<0.0005$) than in younger adults (recumbent: 0.98±0.12; upright: 2.12±0.22). PRC in this group of younger adults was higher than in the group of older adults (recumbent: 0.55±0.06; upright: 1.06±0.12; $P<0.0005$). The decrease of PRC was correlated to age by an exponential function (Fig. 1).

In the 6-year-old girl with renovascular hypertension the peripheral PRC was 15.8 before the operation, had dropped to 0.9 one day after removal of the affected kidney and increased to 3.9 one week after nephrectomy. In the removed kidney RRC was very low in four portions of the outer cortex and in three portions of the juxtamedullary cortex (2 resp. 1 ng mg$^{-1}$ h$^{-1}$; controls 100 resp. 50 ng mg$^{-1}$ h$^{-1}$). In another part of the juxtamedullary cortex RRC was 398 ng mg$^{-1}$ h$^{-1}$. The microscopical evaluation of the kidney showed circumspect hyperplasia of the juxtaglomerular apparatus (P. Schöningh, K. Hayduk, D. K. Krause & B. Meyer, unpublished work).

**DISCUSSION**

The finding of a higher PRC in cord plasma than in maternal plasma is in agreement with previous results (Brown, Davies, Doak, Lever, Robertson & Tree, 1964; Wernze & Seki, 1972; Hayduk et al., 1972). However, other investigators did not find significant differences between maternal and foetal plasma renin activity (Geelhoed & Vander, 1968; Kokot & Cekański, 1970) or PRC and plasma renin activity (Skinner, Lumbers & Symonds, 1972). The observation of a higher PRC in cord plasma and the further increase of PRC in the first 48 h postpartum is consistent with the hypothesis that PRC in cord plasma derives from the foetus. However, we cannot exclude that part of PRC in cord plasma derives from the uterus or intrauterine structures rich in renin (Skinner, Lumbers & Symonds, 1968). The high PRC in the neonatal period might be caused by the immaturity of the kidney with a relatively larger perfusion of the juxtamedullary portion than of the outer cortex (Jose, Logan, Slotkoff, Lilienfeld, Calcagno & Eisser, 1971), the glomerular–tubular imbalance characterized by relative glomerular preponderance (Edelmann & Spitzer, 1971; Spitzer, 1971), and a possibly augmented sodium load to the macula densa (Kotchen et al., 1972), the loss of extracellular volume (Friis-Hansen, 1956), and an increased activity of the sympathetic nervous system. In addition, a diminished elimination of renin from the circulation by the immaturity of liver and kidney may contribute to the augmentation of PRC. The further increase of PRC in the first 48 h postpartum may be induced by dietary restriction.

PRC in mothers was significantly higher than in non-pregnant women as reported by several groups (Brown, Davies, Doak, Lever & Robertson, 1966; Geelhoed & Vander, 1968; Kokot & Cekański, 1970; Skinner et al., 1972). The time-interval until normalization of PRC after delivery (Brown et al., 1966; Geelhoed & Vander, 1968; Kokot & Cekański, 1970) might be dependent on a number of exogenous factors (diet, nursing); in our study PRC had decreased considerably 6 days after delivery, but was not yet normalized.

The decrease of PRC in children and adults was correlated to age by an exponential function (Fig. 1). We assume that this age-dependent decrease of PRC should be differentiated from the neonatal changes of PRC as the latter are most probably caused by processes of maturation.
Age-dependence of plasma renin

and adaptation. For the age-dependent decrease of PRC we have no explanation at the present time; however, previous studies have shown a decrease of glomerular filtration rate (Davies & Shock, 1950) and of functional size of the kidney (Friedman, Raizner, Rosen, Solomon & Sy, 1972) with age.

Fig. 1 shows that the degree of increase of PRC after upright posture was positively correlated to the basal PRC (Boyd, Jones & Peart, 1972), that means the absolute increase of PRC ($\Delta$PRC$_{upright}$ - PRC$_{recumbent}$) decreased with age. In contrast, the relative increase of PRC after upright posture (PRC$_{upright}$/PRC$_{recumbent}$) remained unchanged with age, the PRC in upright posture being about twice the basal PRC in all age groups.

In the case of renovascular hypertension presented here the determination of RRC and the microscopical evaluation of the kidney showed very small circumscribed areas causing and maintaining elevation of PRC and most likely hypertension; a similar case was recently reported by Leumann, Bauer, Slaton, Biglieri & Holliday (1970). The decrease of PRC with age is especially important in the critical examination of hypertension in childhood as the elevated PRC is used as a diagnostic tool in surgical correctable forms of hypertension. The comparison of PRC with control values of the same age group is necessary as the comparison with values obtained from adults would lead to the erroneous assumption of renovascular hypertension.

ACKNOWLEDGMENT

The work was supported by Deutsche Forschungsgemeinschaft.

REFERENCES


