

Plasma renin activity in infants with congenital heart disease

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SUMMARY Plasma renin activity was estimated in 11 infants with severe congestive heart failure. The infants had congenital heart disease with left to right shunts and were receiving diuretic treatment. Plasma renin activity was measured by radioimmunoassay of generated concentrations of angiotensin I. The mean (SD) plasma renin activity was 84 (21) ng angiotensin I/ml/hour, which is considerably above normal infant values. A hyperactive renin-angiotensin system may be detrimental in these patients. Angiotensin converting enzyme inhibitors may be of value in treating infants with severe congestive heart failure.

The advent of angiotensin converting enzyme inhibitors for the treatment of congestive heart failure has stimulated interest in how they affect the renin-angiotensin-aldosterone system. Adults, who have congestive heart failure due to myocardial disease, have been found to have raised plasma renin activity and plasma aldosterone concentrations after the acute phase of myocardial failure but these become less as the heart failure becomes chronic.¹

Infants with congestive heart failure on diuretic treatment often have a disturbed electrolyte balance, especially if they are failing to thrive and are receiving maximum medical management; and it seems likely that such disturbance would have an effect on the renin-angiotensin-aldosterone system. We report a study of the plasma renin activity in infants with congenital heart disease and congestive heart failure.

Patients and methods

We studied 11 infants with an age range of 14 to 84 days (mean 38 days). All were term babies except one born at 36 weeks' gestation. Their mean (SD) weight was 2820 (660) g at the time of the study. Patients were selected if they had congenital heart disease with predominantly left to right shunts, high pulmonary blood flow, and no obstruction in the systemic circulation (for example, coarctation). The infants studied comprised three with a ventricular septal defect, six with complete atrioventricular septal defect, one with double outlet right ventricle, and one with truncus arteriosus (type I). They all had sufficiently severe congestive heart failure that

they were failing to thrive on maximal medical management and for this reason had been admitted to hospital. All infants were taking frusemide and digoxin, and all but one were taking amiloride. Informed parental consent was obtained before taking the blood specimens; these were taken only when there was a clinical need for plasma electrolyte estimation.

Plasma renin activity was measured after the babies had spent a minimum of seven days in hospital receiving treatment for heart failure. The age of the infant, gestational age at birth, weight, diuretic and other drug treatment, cardiac diagnosis and feed content and volume were recorded. On the day of measurement for plasma renin activity the heart rate, respiratory rate, and blood pressure while resting (quiet or asleep) were measured. The systolic blood pressure was recorded with a standard sphygmomanometer, with a cuff that covered at least two thirds of the right upper arm, and a pulse Doppler device. The diastolic blood pressure was recorded from an automated blood pressure machine (Dynamap) using the diastolic value corresponding to the systolic value that most closely matched the systolic pressure obtained manually.

Plasma renin activity was measured, while the infant was supine, between two and three hours after the infant's last feed between 9 and 10 am. Blood was obtained from a peripheral vein, allowing blood to drip from a needle into a chilled tube containing edetic acid as an anticoagulant. The sample was transferred on ice to the laboratory for immediate cold centrifugation; the supernatant was separated and stored at -20°C until analysed. One

ml of whole blood was required for the angiotensin I assay: blood was taken for packed cell volume estimation and plasma sodium, potassium, urea, and creatinine concentrations at the same time. A urine specimen collected at roughly the same time as the blood sample was similarly analysed.

Plasma renin activity was assessed by the concentrations of angiotensin I generated at 37°C and pH 6.0; this was measured by radioimmunoassay in an antibody coated tube and calibrated against the Medical Research Council standard 71/328 (Kit SB-REN-2, CIS (UK) Ltd, High Wycombe, United Kingdom). All analyses were carried out in duplicate in the same batch; the mean intrabatch variation was 5.3%. Results are expressed as angiotensin I generated in ng/ml/hour. Included in the assay for comparison were five infants age 10–47 days who were expected to have normal values. These patients comprised two babies admitted because of cyanotic spells and subsequently found to be normal, one infant with a cleft palate, and two convalescent infants—one after repair of ileal atresia and the other after streptococcal peritonitis. All had normal plasma urea and creatinine concentrations.

Results

The mean plasma renin activity was 84 ng angiotensin I/ml/hour (SD 21; range 57–126). The mean (SD) concentration of plasma sodium at 132 (3.8) mmol/l was marginally low, and the range of urinary sodium concentration was from 6 to 110 mmol/l (median 33). The mean concentrations of plasma potassium, urea, and creatinine were within normal ranges. There was no correlation between plasma renin activity and plasma sodium, potassium, urea, or creatinine, or for urinary sodium, sodium:creatinine ratio; or sodium intake for the preceding 24 hours. Neither was there any correlation between plasma renin activity and age, weight, blood pressure (systolic or diastolic), packed cell volume, or dose and duration of diuretic; similarly, there was no correlation with degree of tachypnoea or tachycardia.

The infants who were expected to have normal values for plasma renin activity ranged from 5.2–31 ng angiotensin I/ml/hour (mean 19.6; SD 10.5). The plasma renin activities for the study group were significantly higher than those of the normal group ($p < 0.001$; Student's *t* test).

Discussion

The figure shows that the mean plasma renin activity in infants with heart failure is considerably above

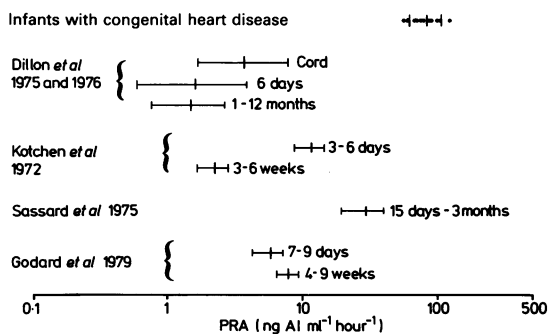


Figure Plasma renin activity plotted on a logarithmic scale for patients with congenital heart disease with reference normal values (mean SD) from previous publications.²⁻⁶

previously reported normal mean values for newborns and infants and falls outside normal ranges quoted for infants.²⁻⁶ In only one series, in which the normal population was a group of inpatients 15 days to 3 months old with benign adenoiditis, does the range overlap.⁵ Our 'normal' patients could conceivably have had conditions which might have influenced their renin activity; none the less, their plasma renin activity values were within previously reported normal ranges. Orally administered frusemide is known to produce an acute rise in plasma renin activity in normal infants,⁷ but the figures reported were considerably below the range of values in our infants.

We have not found any correlation between any of the variables assessed and the plasma renin activity. In normal infants the correlations have been confined to a variable decline in the plasma renin activity from the time of birth until 9 years of age and, in one report, a correlation was found with salt intake and urinary osmolality.⁶ The absence of correlations with factors known to influence renin activity may be related to the large numbers of relevant variables present in this small group of patients—for example, diuretics, blood volume, sodium balance, potassium, hypoxia, and age. No likely trends were observed, however, with individual variables; this gives no indication that expanded numbers in this study would have provided significant correlations.

Our results indicate that the renin-angiotensin-aldosterone system is hyperactive in this group of patients; this may be attributable to the congestive heart failure or to the treatment given. The question as to whether the response is appropriate cannot be answered at this stage. What may be an appropriate response in a subject with normal anatomy and physiology may be inappropriate in an infant with

major disturbances in communications between systemic and pulmonary circulations and a myocardium under stress.

It has been reported that plasma renin activity parallels angiotensin II concentrations in infancy.⁸ Angiotensin II is a potent vasoconstrictor contributing to the afterload on the left ventricle. Reduction of afterload has been shown to be beneficial in congestive heart failure.^{9 10} It may be that angiotensin converting enzyme inhibitors are an appropriate method of directly reducing the afterload by the removal of vasoconstrictive forces associated with a high plasma renin activity (and presumably angiotensin II) in infant heart failure.

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