

INFLUENCE OF URINARY SODIUM EXCRETION ON PLASMA RENIN ACTIVITY AFTER PROLONGED STANDING IN CHILDREN WITH ORTHOSTATIC DYSREGULATION

MAKOTO UCHIYAMA, M. D., TAKESHI OTSUKA, M. D.
AND
KAORU SAKAI, M. D.

Department of Pediatrics, Niigata University School of Medicine, Asahimachi-1, Niigata

(Received February 12, 1986)

ABSTRACT

In 39 children with orthostatic dysregulation (O. D.) and 28 control children aged 8 to 15 years, the relationship between plasma renin activity (PRA) after standing for 60 minutes and urinary sodium (Na) excretion was studied to elucidate the influence of Na balance on standing PRA in O. D..

Children with O. D. showed significant negative correlations between the standing PRA and 12-hour urinary Na/K ratio ($P < 0.01$), between the change in PRA on standing (standing PRA-supine PRA) and 12-hour urinary Na excretion ($P < 0.001$) and between the rate of increase in PRA on standing (standing PRA/supine PRA) and fractional excretion of filtered Na (FENa) ($P < 0.01$). Control children, however, showed no significant correlations between them.

Children with O. D. showed significant negative correlations between standing PRA and Na/creatinine ratio, Na/K ratio and FENa in urine collected during the 60-minute standing period ($P < 0.05$, $P < 0.001$, $P < 0.05$, respectively). Control children, however, showed positive correlations between them.

These findings suggest that the renin-angiotensin system may be activated to maintain circulatory homeostasis after prolonged standing according to the level of urinary Na excretion in O. D..

INTRODUCTION

Orthostatic dysregulation (O. D.) occurs most commonly during puberty and adolescence. Cardiovascular symptoms, e. g. postural hypotension, dizziness, and palpitations

are characteristic of O. D., but both gastrointestinal and other, more non-specific symptoms related to the unstable autonomic nervous system occur (1, 2).

In children with O. D., low levels of plasma renin activity (PRA) on standing (3) and a tendency of sodium (Na) retention (decreased urinary Na excretion) in the daytime (4) have been reported. There is usually a close relationship between Na balance and the renin-angiotensin-aldosterone (RAA) system (5), and in normal children supine PRA varies according to urinary Na excretion (6, 7). However, as we have previously demonstrated, 12-hour urinary Na excretion does not correlate with PRA in either a supine position or a short period of standing position (15 minutes) in children with O. D. (7). These findings suggest that there may be an abnormal interrelationship between Na balance and the RAA system in O. D.. This might cause various symptoms of O. D. if the RAA system is not activated sufficiently according to Na balance. We therefore examined PRA after standing for 60 minutes and urinary Na excretion in children with O. D..

MATERIALS AND METHODS

39 children with O. D. diagnosed according to the Japanese criteria (1) and 28 control children aged 8 to 15 years were studied at the Department of Pediatrics of Niigata University School of Medicine.

Blood for measurement of Na, potassium (K), creatinine and PRA was taken before breakfast after the children had been lying supine for 90 minutes. A second sample was taken for PRA after the children had been standing for 60 minutes. Urine was collected from all children for the 12 hours prior to blood sampling, and during the 60-minute standing period in 18 children with O. D. and 14 control children. It was analysed for Na, K and creatinine. Na and K concentrations were measured by flame photometry and creatinine by the Jaffe reaction on an autoanalyser. PRA was measured by radioimmunoassay using a CIS kit. Urinary excretion for 12 hours was corrected for body surface area obtained from the formula in use for Japanese children (8). Fractional excretion of filtered Na (FENa, %) was calculated from the formula: (urinary Na/plasma Na) \times (plasma creatinine/urinary creatinine) \times 100.

Simple correlation coefficients were calculated between urinary Na excretion and PRA after logarithmic transformation.

RESULTS

Examining first the relationship between PRA after standing for 60 minutes and 12-hour urinary Na excretion, significant negative correlations were demonstrated in the children with O. D. between the standing PRA and Na/K ratio (Fig. 1), between the change in PRA on standing (standing PRA-supine PRA) and Na excretion (mEq/m²/12 hours; Fig. 2) and between the rate of increase in PRA on standing (standing PRA-supine PRA) and FENa (Fig. 3). In control children, however, there was no significant relation-

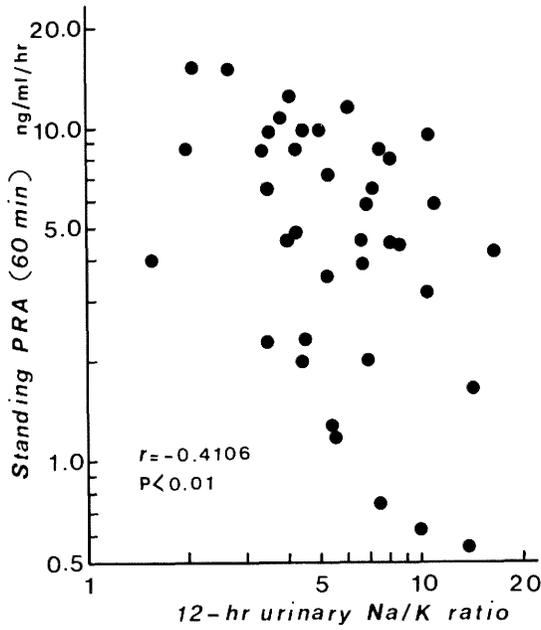


Fig. 1. Relationship between plasma renin activity after standing for 60 minutes and 12-hour urinary Na/K ratio in children with orthostatic dysregulation

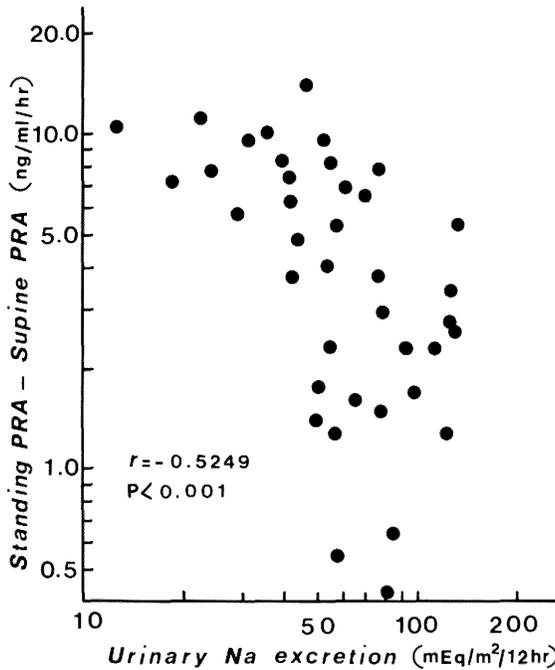


Fig. 2. Relationship between the change in plasma renin activity after standing for 60 minutes and 12-hour urinary Na excretion in children with orthostatic dysregulation

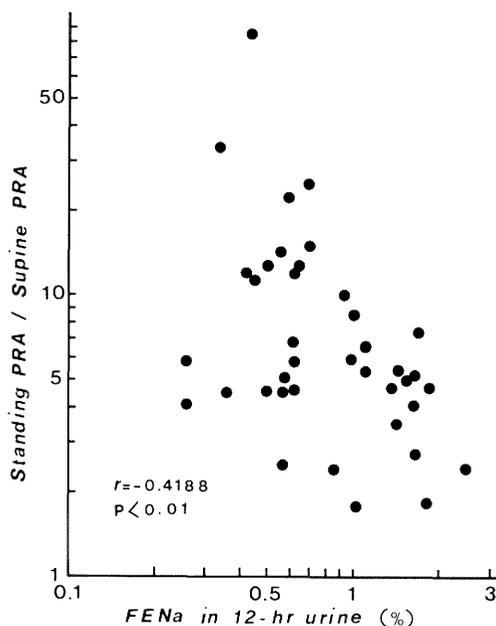


Fig. 3. Relationship between the rate of increase in plasma renin activity after standing for 60 minutes and fractional excretion of filtered sodium (FENa) in 12-hour urine in children with orthostatic dysregulation

ship between changes in PRA on standing and Na excretion in the preceding 12 hours (Table 1).

When standing PRA was compared with Na excretion in urine collected during the 60-minute standing period, significant negative correlations were again found in the children with O. D. this time between standing PRA and Na/creatinine ratio (Fig. 4), Na/K ratio (Fig. 5) and FENa (Fig. 6). Standing PRA was also negatively related to Na excretion per minute, but this was not found to be statistically significant ($r = -0.2604$, $P > 0.05$). In control children, however, significant positive correlations were seen between standing PRA and both Na/creatinine ratio (Fig. 4) and FENa (Fig. 6) in the 60-minute urine sample. Na/K ratio and Na excretion per minute were also positively related, but this did not reach statistical significance ($r = 0.5121$ shown in Fig. 5, $r = 0.5222$, $P > 0.05$, respectively).

Table 1. Correlation coefficients between plasma renin activity (PRA) after standing for 60 minutes and Na excretion in 12-hour urine in 28 normal children

	Na (mEq/m ²)	Na/K	FENa
Standing PRA	0.0106	0.0765	0.0742
Standing PRA-Supine PRA	-0.0665	0.0600	0.2014
Standing PRA/Supine PRA	-0.1977	-0.0935	0.1549

FENa: Fractional excretion of filtered sodium
 Statistical significance: $P > 0.05$, respectively

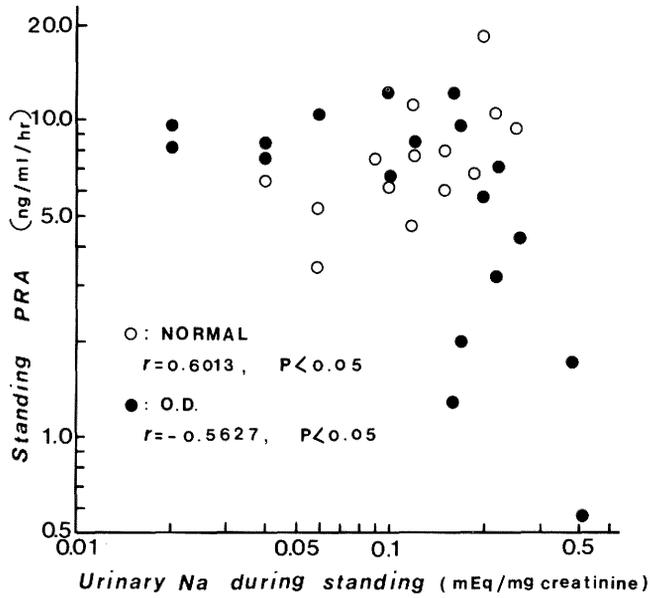


Fig. 4. Relationship between plasma renin activity after standing for 60 minutes and urinary Na/creatinine ratio during the 60-minute standing period in normal children and children with orthostatic dysregulation

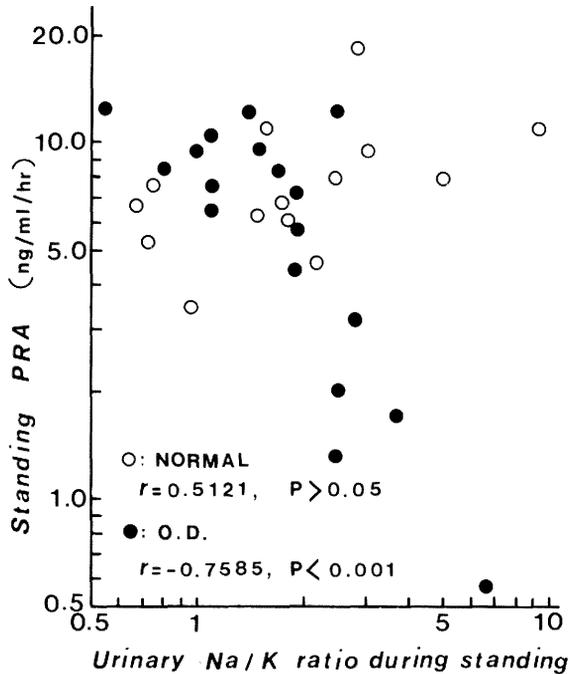


Fig. 5. Relationship between plasma renin activity after standing for 60 minutes and urinary Na/K ratio during the 60-minute standing period in normal children and children with orthostatic dysregulation

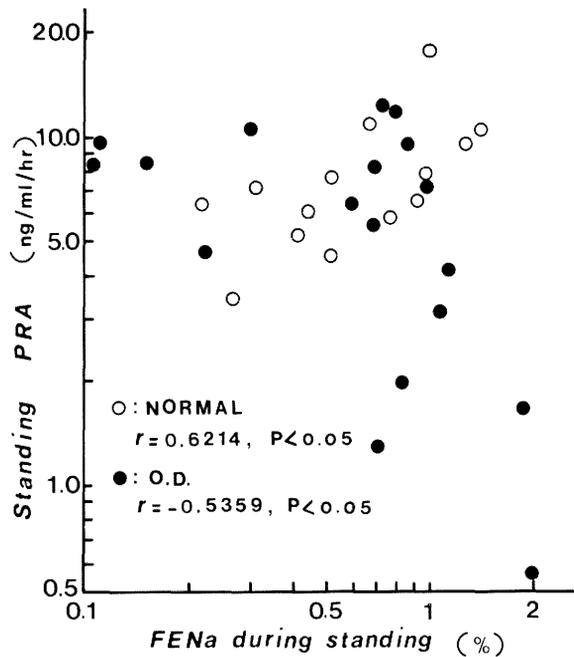


Fig. 6. Relationship between plasma renin activity after standing for 60 minutes and fractional excretion of filtered sodium (FENa) in urine collected during the 60-minute standing period in normal children and children with orthostatic dysregulation

DISCUSSION

There is no renin response to Na depletion in the denerved dog kidney (9), and in man, the renin response to diuretics can be blocked by a beta-adrenergic blockade (10). In addition, children with anorexia nervosa in whom sympathetic activity is decreased (11) demonstrate an insufficient renin response for their level of urinary Na excretion (6). These findings suggest that PRA may not be correlated with urinary Na excretion in conditions associated with a decrease in activity of the sympathetic nervous system such as O. D.. Children with O. D. have normal blood pressures after standing for 60 minutes, although they showed a profound postural drop when standing for only 15 minutes (12). Although activation of the sympathetic nervous system is slower in these children, it may be fully achieved following more prolonged standing. Normal children show an inverse relationship between supine PRA and 12-hour urinary Na excretion (6, 7), while in children with O. D. it is standing PRA which is negatively correlated with 12-hour urinary Na excretion. These findings suggest that in O.D. the RAA system may have a significant role in maintaining blood pressure on standing according to the level of urinary Na excretion.

Maruta (4) found that in the daytime (i. e. in a standing position), urinary Na

excretion is decreased in children with O. D. and increased in normal children, although in normal adults urinary Na excretion is known to decrease on standing. In the present study, PRA showed a negative correlation with urinary Na excretion on standing in children with O. D., suggesting that the activated RAA system may reduce urinary Na excretion on standing in O. D. However in our normal children, PRA showed a positive correlation with urinary Na excretion on standing. If activation of the RAA system is important in regulating urinary Na excretion on standing, this should be negative, but this has not been confirmed in either normal children or adults. Our results suggest that other systems may be involved in the regulation of Na excretion on standing in normal children and that the RAA system may only be attempting to compensate for these. Elucidation of the mechanism regulating Na balance on standing in the normal child was not the aim of this study, but we would hope to investigate this at a future data.

REFERENCES

- 1) Okuni, M.: Orthostatic dysregulation in childhood with special reference to the standing electrocardiogram. *Jpn Cir J* 1962; 27: 200-204.
- 2) Okuni, M.: Criteria for the diagnosis of O. D. and procedures of the tilting test. In: Ichihara, Y. et al., eds. Orthostatic dysregulation. Tokyo: Chugai-Igaku-sha, 1974: 7-18 (in Jpn).
- 3) Noda, M., Kato, K., Hisano, Y., Harayama, N., Omura, J., Shimizu, S., Iwagaki, H. and Oyama, K.: Plasma renin activity in orthostatic dysregulation (abstract). *Acta Paediatrica Japonica* 1975; 79: 942-943 (in Jpn).
- 4) Maruta, K.: A study on diurnal rhythm of urinary electrolyte excretion in patients with orthostatic dysregulation. *Journal of Tokyo Women's Medical College* 1969; 39: 480-493 (in Jpn).
- 5) Imai, M. and Sokabe, H.: Plasma renin and angiotensinogen levels in pathological states associated with oedema. *Arch Dis Childh* 1968; 43: 475-479.
- 6) Uchiyama, M., Otsuka, T., Shibuya, Y. and Sakai, K.: Electrolyte excretion in 12-hour urine and in spot urine. Relationship to plasma renin activity and aldosterone concentration in older children. *Acta Paediatr Scand* 1985; 74: 394-399.
- 7) Uchiyama, M.: Factors regulating plasma renin activity in children with orthostatic dysregulation. *The Autonomic Nervous System* 1983; : 258-266 (in Jpn).
- 8) Fujimoto, S., Watanabe, T., Sakamoto, A., Yukawa, K. and Morimoto, K.: Studies on the physical surface area of Japanese. Part 18, Calculation formulas in three stages over all age. *Jap J Hyg* 1968; 23: 443-450 (in Jpn).
- 9) Mogil, R. A., Itskovitz, H. D. and Russel, J. H.: Renal innervation and renin activity in salt metabolism and hypertension. *Am J Physiol* 1969; 216: 693-697.
- 10) Horký, K., Gregorová, I. and Dvoráková, J.: The effect of renin and aldosterone inhibition by beta-adrenergic blockade on the response to the new diuretic azosemide. *Eur J Pharmacol* 1981; 69: 439-446.
- 11) Fohlin, L.: Body composition, cardiovascular and renal function in adolescent patients with anorexia nervosa. *Acta Paediatr Scand (Suppl)* 1977; 268: 1-20.
- 12) Uchiyama, M.: The role of renin in children with orthostatic dysregulation. *Acta Medica et Biologica* 1983; 31: 115-128.