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Low urinary dopamine excretion associated to low sodium excretion in normotensive Piaroa Amazonian ethnia compared to urban subjects.

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Abstract. The objective of this work was to compare urinary dopamine, noradrenaline, adrenaline, sodium and potassium excretion in a group of normotensive Piaroa Amazonic ethnia who do not use salt in their regular food intake, against a group of urban normotensive citizens known to have a high salt intake in their regular meals. Twenty adult normotensive Piaroa subjetcs living in the Amazonas forest, 11 men and 9 women, 23-72 years old, and 33 normotensive urban citizens, 25-70 years old, 17 men and 17 women, were included in the study. After a 10 min. rest, an average of three supine systolic (SBP) and diastolic (DBP) blood pressure recordings was obtained. Piaroas subjects SBP and DBP were 111.3± 2.9 mmHg and 62.7± 1.9 mmHg respectively; urban subjects SBP and DBP were 111.8 ± 2.2 mmHg and 70.3 ± 1.6 mmHg respectively. Supine heart rate was lower in Piaroas (58.0 ± 1.8 beats/min) than in urban subjects (76.5± 1.9 beats/min), $p < 0.05$. Sodium urinary excretion was much lower in Piaroas (12.6 ± 5.2 mmol/24 h) when compared to urban subjects (210.7 ± 24.5 mmol/24 h), $p < 0.01$. No difference was found in daily urinary potassium excretion between Piaroas and urban subjects (50.4 ± 7.2 mmol/24 h *vs* 45.1± 7.4 mmol/24 h). Urinary dopamine excretion was lower in Piaroas (314.7 ± 40.1 µg/24 h) in comparison to urban subjects (800.4± 59,2 µg/24h), $p < 0.05$. Daily urinary noradrenaline and adrenaline excretion were 67.9 %and 85.4% respectively lower in Piaroas than in urban subjects. In conclusion, lower amounts of sodium daily intake are associated to lower kidney dopamine production in Piaroas as compared to urban subjects. Apparently indigenous tribes might require less kidney dopamine synthesis to excrete the very small amounts of salt they consume in their regular food intake.

The opposite was found in urban subjects; more kidney dopamine synthesis would be required for larger amounts of urinary sodium excretion. In this population, essential hypertension has been associated to a failure of the natriuretic mechanism triggered by dopamine on kidney tubules.

Reducción en la excreción de dopamina urinaria asociada a una baja excreción de sodio en etnia Piaroa Amazónica comparada con sujetos urbanos.
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Resumen. El objetivo de este trabajo fue comparar la excreción urinaria de dopamina, noradrenalina, adrenalina, sodio y potasio en un grupo de sujetos normotensos de la etnia Piaroa Amazónica, quienes no usan sal en su dieta normal; contra un grupo de sujetos normales los cuales consumen un alto contenido de sal en sus comidas. Se incluyeron en este estudio 22 sujetos adultos de etnia Piaroa que vivían aislados en el bosque amazónico, 11 hombres y 9 mujeres, de 23-72 años de edad y 33 sujetos urbanos normotensos de 25-70 años de edad, 17 hombres y 16 mujeres. Después de 10 min. en reposo, se tomó el promedio de las presiones arteriales sistólica (PAS) y diastólica (PAD) tomadas en 3 consultas semanales. Los sujetos Piaroa tuvieron una PAS y PAD de 111,3± 2,9 mmHg and 62,7 ± 1,9 mmHg respectivamente y en los sujetos urbanos la PAS y PAD fueron de 111,8± 2,2 y 70,3 ± 1,6 mmHg, respectivamente. La frecuencia cardíaca fue menor en los Piaroa (58,0 ± 1,8 lat/min) que en los sujetos urbanos (76,5± 1.9 lat/min), $p < 0.05$. La excreción urinaria de sodio fue extremadamente más baja en los Piaroa (12,6 ± 5,2 mmol/24 h) que en los sujetos urbanos (210,7 ± 24,5 mmol/24 h), $p < 0.01$. No se halló diferencia en la excreción urinaria de potasio entre sujetos Piaroa y urbanos (50,4 ± 7,2 mmol/24 h *vs* 45,1± 7,4 mmol/24 h). La excreción de dopamina urinaria fue más baja en los Piaroa (314,7 ± 40,1 µg/24 h) en comparación con los sujetos urbanos (800,4± 59,2 µg/24h), $p < 0.05$. La excreción diaria de noradrenalina y adrenalina fueron 67,9% y 85,4% respectivamente más bajas en los Piaroa que en los sujetos urbanos. La ingesta diaria muy baja en sodio parece estar asociada a una menor producción de dopamina renal; aparentemente, estas tribus indígenas requieren una menor síntesis de dopamina renal para excretar las cantidades mucho menores de sal que consumen en su dieta ordinaria. Lo opuesto fue hallado en los sujetos urbanos, en ellos la hipertensión arterial esencial ha sido asociada a un déficit en el mecanismo natriurético ejercido por la dopamina en los túbulos renales.

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INTRODUCTION

Sodium intake has been considered for a long time one of the ethiopathogenic factors involved in essential hypertension (9, 14) and high salt intake in salt-sensitive people usually rise blood pressure in a reversible fashion (7). Apparently this sensitivity seems to be genetically determined (12).

The impact of salt intake on blood pressure is a complex matter; while salt-resistant persons are regularly found upon a screening of high salt included in the diet, it has been observed that a small proportion (15.3%) of normotensive subjects increases their blood pressure upon drastic salt restriction (20). These subjects have been termed "counterregulators". A higher percentage (33-36%) of counterregulators has been found among hypertensive patients (15).

The salt-link in essential hypertension has been associated to kidney dopamine production. Apparently as salt intake increases, kidney dopamine synthesis from plasma dopa (27) is augmented (23). This tubular synthetized dopamine (3) inhibits proximal tubule sodium reabsorption through ATPase activity inhibition in proximal convoluted tubule cells (2), so favouring excretion of the salt overload (25).

An alteration of this kidney dopaminergic mechanism was described in hypertensive patients as a failure to increase their kidney dopamine production when challenged with a high salt intake (23).

On the other hand, noradrenaline has an opposite effect to dopamine on tubular sodium reabsorption, it reduces sodium excretion (4) through an increase of ATPase activity (5) in the ascending Henle's loop.

Studies made in indigenous populations have demonstrated that their blood pressure does not increase with age (19) as it occurs in urban living people; and this epidemiological phenomenon has been associated to several factors that include a lower salt consumption when compared to persons living in industrialized societies.

In those normotensive indigenous populations, the relationship between blood pressure, salt intake and urinary output of dopamine has not been studied.

The purpose of this work was to compare urinary dopamine, noradrenaline, adrenaline, sodium and potassium excretion in a group of normotensive Piaroa Amazonian indians who do not use salt in their regular diet, against a group of urban normotensive citizens known to have a high salt intake in their regular meals. Theoretically, if kidney dopamine synthesis is under the influence of the sodium load in the diet, Piaroa ethnia should have lower dopamine and sodium excretions when compared to matched urban subjects.

SUBJECTS AND METHODS

Piaroa subjects

Twenty adult (11 men and 9 women) Piaroa subjects from an ethnia living in the Amazonian forest (Venezuela's Amazonas State) were selected to participate in the study through the cooperation of the chieftain of the tribe and the general practitioner appointed to the town San Juan de Manapiare.

The medical doctor regularly visited four Piaroa ethnic settlements (Guara, Guayabalito, Paraíso, Cocurito) accounting for 530 inhabitants and sequentially selected the healthy normotensive subjects on the basis of clinical examination and after verbal consent to participate in the study.

The Piaroa subjects were asked to collect two successive 24 hours urine samples, and three weekly systolic (SBP) and diastolic (DBP) blood pressure measurements were performed in both arms with a mercury sphigmomanometer, after 10 min rest and upon standing.

Right arm blood pressure was taken in further visits. The procedures were done between january and march.

Age range of the group was 23-72 years old, as documented by the identity card provided by the Venezuelan Home Office authorities. Body mass index of Piaroas was 17.9 - 26.7 kg/m^2 (Table I). The tribe was partially isolated in the forest, no table salt was used for cooking because of cultural reasons, and industry processed foods were largely unavailable to them.

Urban subjects

On the same criteria as the one employed for the Piaroa subjects, thirty three healthy adult subjects of mixed race, 17 men and 16 women, age 25-70 years old were selected at the local infirmary of Villa de Cura, a city of approximately 100.000 inhabitants located at the northern part of Venezuela.

The subjects gave their consent for participating in the study.

Two succesive 24 hour urine samples were collected and the subjects were instructed to return weekly during three weeks for blood pressure recording with a mercury sphygmomanometer after 10 min rest and upon standing. The body mass index of the group was 19.2 -28.1 kg/m^2 (Table I).

Urine Dopamine, Noradrenaline and Adrenaline Assay

The first urine sample collection was over 0.5 g of sodium metabisulphite as antioxidant. Inmediately after collection, urine volume was measured and 10 mL duplicates were mixed with concentrated $HClO_4$ to reach 0.4 N concentration. The tubes were frozen and transported by air over dry ice to the laboratory. After thawing, samples were centrifuged at 5000 g x 10 min at 4 °C, the supernatant was kept at -60 °C in a deep freezer, for no longer than one month, until assay.

TABLE I

BIOMEDICAL PARAMETERS OF PIAROA INDIANS AND URBAN SUBJECTS

Parameter	Piaroa	Urban
	(Mean± SE)	
Age (years)	44.1± 4.8	42.3± 6.4
Men (n)	11	17
Women (n)	9	16
Body mass index (Kg/m^2)	22.9 ± 0.9	24.2 ± 0.4 .
Supine SBP (mmHg)	111.3 ± 2.9	111.8 ± 2.2
Supine DBP (mmHg)	62.7 ± 1.9	70.3 ± 1.6
Supine HR (beats/min)	58.0 ± 1.8	76.5 ± 1.9*
Standing SBP (mmHg)	107.4 ± 2.1	112.3 ± 2.24
Standing DBP (mmHg)	65. 6 ± 2.6	72.2 ± 1.8
Standing HR (beats/min)	66.1 ± 2.0	85.7 ± 2.1*

SE, standard error of the mean, n, number of subjects.
SBP, systolic blood pressure. DBP, diastolic blood pressure. HR, heart rate.
*$p < 0.05$ *vs* Piaroa ethnia.

Catecholamines were adsorbed onto purified alumina; noradrenaline and adrenaline were flourometrically determined according to the procedure of Anton-Sayre (1). From alumina eluates in O.O5 N acetic acid, dopamine was fluorometrically assayed by the method of Shellenherger (22). Aliquots from these samples were employed for the assay of dopamine, noradrenaline and adrenaline by high performance, reverse-phase liquid chromatography on a biophase ODS (25O x 4.6 mm - 5µm) from Bioanalytical Systems. Detection was performed with an electrochemical detector fitted with a glassy carbon electrode (Model MF 1OOO). The operating potential was +0.75 V against the $Ag/AgCl_2$ electrode (16).

No significant differences were found between HPLC and fluorometric catecholamine assays, so reported values correspond to fluorometric analysis.

Sodium and Potassium Quantitation

The second 24 hour urine collection, without any additive, was taken the day after the first urine collection. The volume was measured and 1O mL duplicates were frozen

and transported by air over dry ice to the laboratory.

After thawing, the tubes were centrifuged at 5000 g x 10 min and the supernatant employed for sodium and potassium assay by flame photometry (Cole-Parmer, Digital Flame, Model 2655-00). Urinary excretion of Na^+ and K^+ were expressed as mmol/24 hours and corrected by body weight.

Statistical Analysis

Comparison between means was done by Student's "t" test for unpaired samples; $p< 0.05$ was considered significant.

The record books of morbility (EPI-15) Kept at Piaroa and urban infirmaries were examined for reports of hypertension the year before (1992) and the year this work was done (1993).

Total number of consultations were registered and the number of hypertension reports were counted to have an estimate of hypertension morbility from both studied groups.

Differences between percentages of epidemiological data were evaluated with the Chi square test, at a level of significance $p < 0.01$.

RESULTS

There were no significant differences between Piaroa ethnia and urban normotensive subjects regarding age and body mass index (BMI). BMI was within normally accepted limits (8) and obese subjects were not included in both studied groups (Table I). However height was shorter in Piaroa ethnia than the one in urban subjects; $X \pm SE$, Piaroa men: 1.60± 0.03; women: 1.55± 0.04 m.

Supine and standing SBP and DBP were similar in both studied groups (Table I), but supine and standing heart rate was 18.5 and 19.6 beats/min respectively higher in urban citizens ($p <0.05$, Table I).

Daily urinary sodium excretion was 198.1 mmol/day lower in Piaroa subjects when compared to urban citizens. This difference did not account for the lower body weight of Piaroas because correcting the values for body weight, the difference (Table II) between both groups remains significant.

Daily urinary potassium excretion was almost the same in Piaroa ethnia and urban citizens, 5.3 mmol/day lower in urban citizens than in Piaroa subjects, which was not significant.

Urinary catecholamine excretion showed remarkable differences between both groups; daily dopamine excretion was 60.6% lower in Piaroas in comparison to the one in urban subjects (Table III).

The noradrenaline and adrenaline excretion in Piaroas were lower (67.9% and 85.4% respectively) than the one in urban subjects (Table III).

DISCUSSION

Normotensive Piaroa ethnia and age matched normotensive urban subjects were studied. Piaroa sub-

TABLE II

URINARY SODIUM AND POTASSIUM EXCRETION IN NORMOTENSIVE PIAROAS AND URBAN SUBJECTS

Group	Ion	mmol/24 hours	mmol/kg/24 hours
Piaroa	Na^+	12.6 ± 5.2*	0.26 ± 0.16*
	K^+	50.4 ± 7.2	1.26 ± 0.12
Urban	Na^+	210.7 ± 24.5	3.28 ± 0.46
	K^+	45.1 ± 6.4	0.88 ± 0.16

mmol/kg/24 hours represent values individually corrected by kg body weight.
* $p < 0.01$ *vs* urban subjects.

TABLE III

DOPAMINE, NORADRENALINE AND ADRENALINE DAILY URINARY EXCRETION IN NORMOTENSIVE PIAROAS AND URBAN SUBJECTS

Group	Dopamine	Noradrenaline	Adrenaline	n
		(µg/24 hours)		
Piaroa	314.7± 40.1*	23.3± 3.4*	3.8± 0.66*	20
Urban subjects	800.4± 59.2	72.7± 5.8	26.1± 4.0	33

Values represent the Mean ± standard error of the mean.
* $p < 0.01$ *vs* urban subjects.
n, number of subjects.

jects showed a supine and standing heart rate lower than urban subjects. This finding might be interpreted as the result of a reduced adrenergic drive to the heart in the amazonian group, a fact that coincides with a 67.9 and 85.4% lower urinary noradrenaline and adrenaline excretion when compared to urban subjects.

Low urinary sodium excretion in Piaroa closely follows their low Na^+ intake, in comparison with urban citizens. A similar finding was reported by Oliver y col. (19) in the Yanomami ethnia (Amazonas forest) and by Page y col. (21) among members of an indigenous population from the Solomon Islands (South Pacific). This finding was epidemiologically associated to a lower mean blood pressure, lower incidence of hypertension and absence of the age-related "physiological" increase of blood

pressure, which is observed in urban living people. These epidemiological facts are in agreement with the low percent morbility of hypertension observed in this Piaroa ethnia (O.182 and O.206% during the years 1992 and 1993, respectively).

The same data record obtained at the local infirmary where the urban subjects were enrolled for this study revealed a 10.5 and 11.7 times higher hypertension morbility (1.91 and 2,42% during the years 1992 and 1993, respectively) when compared to Piaroa ethnia.

This percent morbility data should be taken cautiously, it is rather biased since it includes blood pressure recordings from adult population only (blood pressure is not regularly taken to infants and adolescents in day to day practice). Nevertheless, this bias should be approximately the same in both studied groups.

In urban subjects, the sources of sodium in the diet are the refined salt (used for coking), canned preserved and industrially processed foods, which regularly contain sodium benzoate, sodium nitrate and sodium glutamate as preservatives and flavour enhancers. This kind of food ingredients are not likely consumed by the studied group of Piaroa ethnia. A detailed list of the dietary foods consumed by both studied groups was registered, but its description is beyond the scope of this work.

Sodium excretion found in our group of urban subjects was similar to the one reported for several western countries (200 mmol/day) in the INTERSALT study (14).

The association between a low incidence of hypertension and low salt intake is probably coincident with a high potassium intake, as it has been suggested from ethnical and experimental studies (24). It is worth mentioning that in hypertensive rats, a high potassium intake brings protection against stroke and kidney lesions probably because it induces natriuresis (26).

As vegetables are the most important source of potassium in the diet, and we found no significant difference in potassium excretion between Piaroa ethnia and urban subjects, this finding suggests that both studied groups have a rather similar intake of vegetables.

On the other hand, the urinary potassium excretion found in our study groups fall in the range reported in two groups of black and white people from the United States (13).

It appears to us that the most significant finding of our work is that the urinary dopamine output was very low in Piaroas when compared to the one of urban subjects. It is known that salt intake can increase kidney dopamine synthesis which in turn inhibits sodium reabsorption, favouring Na^+ ion excretion (23, 25). It seems reasonable to us to propose that very low levels of sodium intake in the regular food regime of Piaroa ethnia requires a low level of kidney dopamine production for promoting Na^+ excretion.

On the contrary urban subjects who consume and excrete an avera-

ge 12.3 g/day of salt require a high kidney dopamine synthesis.

This fact might have some implication in the pathophysiology of hypertension because salt-sensitive hypertensive patients show a low urinary dopamine excretion (11, 23).

A previous report has documented a low urine dopamine output associated with a low kidney sodium excretion in an Iranian group of normotensive urban subjects (6) in spite of their relative high salt intake (9.9 g/day)

A genetic defect of the catecholamines-synthesizing enzymes in the Piaroa ethnia is not ruled out. This possibility can only be excluded by specific biochemical tests for tyrosine-hydroxilase (the rate-limiting step of catecholamine synthesis) and dopamine -beta- hydroxilase enzyme activities. However, the presence of this genetic defect in the Piaroa subjects studied is quite improbable because none of them either complained or presented clinical signs of orthostatic hypotension, which is characteristic in patients bearing this kind of enzyme alterations (17, 18).

We would speculate that long-term high salt exposure through the regular diet can overcome the kidney dopaminergic homeostatic mechanism of natriuresis, leading to blood pressure increase, as one of the various factors involved in the pathogenesis of hypertensive disease.

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