

Characteristics of the association between salt intake and blood pressure in a sample of male working population in southern Italy

P. STRAZZULLO, M. TREVISAN, E. FARINARO, F. P. CAPPUCCIO, L. A. FERRARA, E. DE CAMPORA AND M. MANCINI

Institute of Internal Medicine and Metabolic Diseases, Center for Atherosclerosis and Metabolic Disorders, 2nd Medical School, University of Naples, Naples, Italy

KEY WORDS: Dietary salt intake, blood pressure.

A possible association between dietary salt intake and blood pressure was investigated in an unselected sample of 188 healthy Neapolitan men.

In univariate analysis diastolic pressure was positively correlated with age, body mass index and 24-h excretion of sodium, potassium and creatinine, but not with urine volume or sodium:potassium ratio. Systolic pressure was also related to age, body mass index and 24-h sodium, but to a lesser degree.

As a high level of intercorrelation was apparent, multivariate analysis was also carried out. Body mass index was shown to be the variable having the largest influence on diastolic pressure variability: nevertheless a significant independent role was still found for 24-h urinary sodium when the latter was included in a regression along with body mass index, age, urine volume and potassium excretion.

These results seem to support the possibility that dietary salt has a substantial influence on blood pressure levels.

Introduction

The role played by habitual high salt intake in the etiology of arterial hypertension is a crucial issue for a preventive approach to this mass disease.

Cross-cultural studies seem to demonstrate an association between the average salt intake and the prevalence of high blood pressure in different geographical areas^[1-11], although their findings have been the object of serious criticism^[12]. On the other hand within population comparisons have yielded most often negative results^[13-22]. As hypertension is a multifactorial disease caused by the interaction of genetic and environmental factors, it is possible indeed that the results of the investigation of a given ethnic group do not apply to others with different genetic backgrounds and life styles.

The present paper is a report of a study carried out in Southern Italy to explore the relationship of salt intake to blood pressure in an unselected sample of a healthy male population. It provides evidence of a statistically significant association between blood pressure and 24-h urinary sodium excretion, independent from a number of possibly confounding variables not often evaluated in previous studies. A working hypothesis is then proposed about the possible contributory role of chronic high salt intake in the genesis of arterial hypertension.

A preliminary report on this subject has been presented previously^[23].

Subjects and methods

Sixteen hundred and thirty-one men, 25-56 years of age, employed at the Olivetti factory in Naples, participated in 1976-1977 in a survey on the prevalence of cardiovascular risk factors in Southern Italy^[24]. They underwent, in random sequence, a medical examination, which included the collection of medical history, a physical evaluation, a

Received for publication 21 July 1982; and in revised form 30 November 1982.

Correspondence to: Dr P. Strazzullo, Semeiotica Medica, Nuovo Policlinico, Via S. Pansini 5, 80131-Napoli, Italy.

Presented in part at the second Joint Meeting of the Working Groups of the European Society of Cardiology, Pavia, 3-5, September 1981.

standardized blood pressure measurement and an ECG recording.

Blood pressure was measured with a random zero sphygmomanometer after a rest of 10 min in a seated position^[25]; two readings of systolic (SBP) and of 5th-phase diastolic (DBP) pressure were obtained 2 min apart from each other and their average was recorded. Body weight and height were taken with usual indoor clothing and without shoes; the body mass index (BMI) was calculated as the ratio weight/height², where the weight is in kg and the height in m.

For the purpose of the present study, a subgroup of 300 unselected participants consecutively examined over two months, was invited in addition to provide a complete 24-h urine collection: they received detailed methodological instructions and were requested to stay on their habitual diet.

Two hundred and forty-three subjects adhered to the invitation; fifty-five were later excluded from the study, being on treatment for high blood pressure or having admitted to missing some fraction of the 24-h urine collection. Eventually therefore the group included in the analysis was 188 men.

The urinary sodium and potassium concentrations were determined by flame photometry; creatinine by the picric acid method (Jaffé). As over 95% of the daily sodium losses take place through the renal route, under steady state conditions the 24-h urinary excretion of sodium can be taken as an estimate of its dietary intake.

Univariate and multivariate statistical analysis were carried out by standard methods^[26] and with the use of Olivetti P-652 and Hewlett Packard HP-85 computers.

Results

Table 1 gives mean values, standard deviation and range of distribution of the variables examined in our study population.

Out of 188 subjects, sixty had a DBP above 90; thirty-one had a DBP \geq 95, and seven between 104 and 113 mmHg. The exclusion of subjects with treated hypertension, the relatively young age of the participants and their extraction from a healthy population at work, were factors contributing to the low prevalence of severe hypertension in this group. It should be noted also that only a few of those with definite hypertension were aware of their condition.

The 24-h urinary sodium excretion ranged between 50 and 340 mmol, which indicated a salt intake in the range of 3 to 20 g/day, with an average

Table 1 Mean, standard deviation and range of distribution of specified variables in 188 men

Variable	M \pm SD	Range
Systolic BP	127.7 \pm 16.9 mmHg	94–190
Diastolic BP	83.4 \pm 12.2 mmHg	47–113
24-h sodium	176.8 \pm 59.3 mmol	50–342
24-h potassium	51.8 \pm 19.7 mmol	12–125
Na/K ratio	3.7 \pm 1.4 mmol	1.3–9.2
24-h creatinine	13.2 \pm 3.2 mmol	7.3–26.9
24-h urine volume	1000 \pm 281 ml	480–1870
Body weight	74.2 \pm 9.0 kg	50.3–97.2
Height	167.8 \pm 5.3 cm	156–182
Body mass index	26.3 \pm 2.9 cm	18.9–33.9
Age	40.6 \pm 7.4 yrs	28–56

of 10.5 g, a finding consistent with those from most Western countries^[9].

A correlation matrix is presented in Table 2. Significant correlation coefficients were found between DBP and respectively age, body weight, body mass index, sodium, potassium and creatinine excretion. SBP was related more weakly to the same variables, except for potassium excretion. The higher degree of association shown by diastolic as compared with systolic pressure is probably explained by its smaller intraindividual variability.

A high level of intercorrelation is evident: in particular, urinary volume, sodium, potassium and creatinine excretion were all interrelated and, in addition, they were significantly related to body weight and BMI.

These results are confirmed by cross-classification through quintile analysis; Table 3 gives mean values and standard deviation of each variable by quintile of diastolic blood pressure.

Statistically significant differences were found again for age, body weight, BMI, sodium, potassium and creatinine excretion, when comparing the mean values in the upper versus the two lower quintiles of DBP. By contrast no difference was observed with regard to height, Na/K ratio and 24-h urine volume.

It can be noted that 24-h sodium excretion rises markedly between the first and the third quintile of DBP distribution, with minor changes thereafter: this trend differs from that of most other variables (e.g. age or body weight) which show rather regular increments over the entire range of diastolic pressure.

Table 2 Correlation matrix, blood pressure and specified variables

	Systolic BP	24-h sodium	24-h potassium	Na/K ratio	24-h creatinine	24-h urine volume	Body weight	Height	Body mass index	Age
Diastolic BP	0.71***	0.27***	0.29***	0.01	0.23**	0.07	0.27***	-0.11	0.37***	0.20**
Systolic BP		0.14*	0.13	0.04	0.12	-0.00	0.20**	-0.08	0.24***	0.19*
24-h sodium			0.56***	0.25***	0.43***	0.46***	0.30***	0.07	0.29***	-0.07
24-h potassium				-0.53***	0.46***	0.27***	0.24***	-0.01	0.27***	-0.05
Na/K ratio					-0.06	0.11	0.11	0.05	0.09	-0.07
24-h creatinine						0.36***	0.23**	0.08	0.22**	0.06
24-h urine volume							0.28***	0.13	0.20**	-0.03
Body weight								0.44***	0.85***	0.00
Height									-0.04	-0.10
Body mass index										0.04

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

Table 3 Mean and standard deviation of specified variables by diastolic blood pressure quintile and level (mm Hg)

Variable	I (≤ 72)	II (73-79)	III (80-87)	IV (88-93)	V (≥ 94)
24-h sodium (mmol)	150 \pm 57	163 \pm 60	184 \pm 68	187 \pm 68	189** \pm 62
24-h potassium (mmol)	41 \pm 15	49 \pm 20	51 \pm 17	56 \pm 23	57** \pm 20
Na/K ratio	3.79 \pm 1.18	3.63 \pm 1.60	3.67 \pm 1.23	3.94 \pm 1.29	3.50 \pm 1.53
24-h creatinine (mmol)	12.1 \pm 3.5	13.2 \pm 3.0	13.4 \pm 3.7	14.3 \pm 4.1	13.9** \pm 2.2
24-h urine volume (ml)	1007 \pm 296	999 \pm 350	992 \pm 292	1041 \pm 296	1006 \pm 273
Body weight (kg)	71.3 \pm 10.0	72.0 \pm 6.4	73.4 \pm 10.6	75.1 \pm 9.9	77.7*** \pm 8.4
Height (cm)	168.9 \pm 6.8	168.8 \pm 7.3	167.5 \pm 7.0	166.6 \pm 7.3	168.2 \pm 7.6
Body mass index	24.8 \pm 2.7	25.5 \pm 2.3	25.8 \pm 3.0	26.8 \pm 3.1	28.1*** \pm 2.6
Age (yrs)	38.4 \pm 6.3	39.6 \pm 6.8	39.8 \pm 7.2	41.0 \pm 7.8	43.6*** \pm 6.7

** $P < 0.01$
 *** $P < 0.001$ } difference between V and (I+II) quintile.

Given the high level of intercorrelation observed between the variables examined, multiple linear regression was used to test further their relative influence on blood pressure variability in the 188 subjects included in this analysis (Table 4).

As sodium, potassium and creatinine excretion were all significantly associated with DBP and

further related to each other, they were added separately in three different equations, which also included a fixed set of other variables, i.e. 24-h urine volume, body weight, height and age (equations 1-3). The T-values obtained for sodium and potassium excretion were of comparable magnitude and both statistically significant; on the

Table 4 Regression equations of diastolic blood pressure on specified variables (coeff is coefficient and SE standard error)

Variable	Equation 1		Equation 2		Equation 3		Equation 4		Equation 5	
	Coeff	SE	Coeff	SE	Coeff	SE	Coeff	SE	Coeff	SE
24-h sodium (mmol)	0.046	0.002					0.046	0.002	0.034	0.002
	(T=3.01)**						(T=3.04)**		(T=1.99)*	
24-h potassium (mmol)			0.131	0.002					0.075	0.003
			(T=3.63)***						(T=1.54)	
24-h creatinine (mmol)					0.598	0.061				
					(T=2.05)*					
24-h urine volume (l)	-3.045	0.002	-1.217	0.002	-3.650	0.002	-4.002	0.002	-4.101	0.002
	(T=-1.07)		(T=-0.52)		(T=-1.03)		(T=-1.26)		(T=-1.33)	
Body weight (kg)	0.430	0.007	0.425	0.007	0.440	0.007				
	(T=4.21)***		(T=4.23)***		(T=4.43)***					
Height (cm)	-0.551	0.012	-0.524	0.012	-0.550	0.013				
	(T=-3.18)**		(T=-3.03)**		(T=-3.10)**					
Body mass index							1.253	0.020	1.260	0.021
							(T=4.38)***		(T=4.44)***	
Age (yrs)	0.326	0.008	0.313	0.007	0.332	0.007	0.342	0.008	0.339	0.007
	(T=2.88)**		(T=2.83)*		(T=2.96)*		(T=3.05)**		(T=3.04)**	
Regression		5559		6042		4432		5501		6223
Residual		19 762		19 226		20 870		19 975		19 688

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

other hand the contribution made by creatinine was more modest and was just of borderline significance.

In equation 4 BMI was substituted for body weight and height, but this change made no difference in the total variance explained by this set of variables.

Finally, when sodium and potassium were included in the same equation (equation 5) their single independent effect was reduced, as expected, but more so was that of potassium, which in this set was no longer statistically significant.

Discussion

A statistically significant association between urinary sodium output and blood pressure is shown by this cross-sectional examination of healthy Neapolitan men under no medical treatment; multivariate analysis indicates further that this association is independent of a number of potentially confounding variables rarely considered together in previous studies.

The 24-h urinary potassium excretion was also

found to be significantly associated with diastolic pressure in univariate analysis; however, when entered in a multiple regression equation along with sodium excretion, its effect on DBP variability appeared to be secondary to that of sodium. This finding is in accordance with the physiological connections in the renal handling of the two electrolytes, potassium being actively secreted in the urine in proportion to the amount of sodium and fluid delivered to the distal nephron and to the availability of sodium for cation exchange in the cortical collecting tubule^[27,28]; thus, the greater the salt content of the diet, the higher the rate of potassium excretion. Accordingly, from the present study no indication can be derived as to the proposed protective effect of high potassium diets against high blood pressure^[29,30].

The 24-h sodium excretion was significantly correlated with body weight and BMI, in agreement with previous reports^[18,31]. High salt intake in the obese is generally assumed to be a result of over-feeding; a recent report has described in addition a higher sodium/calorie ratio as a characteristic feature of the habitual diet of a sample of obese adolescents^[32].

In the present study, the results of multivariate analysis indicate BMI as the variable having the largest influence on DBP variability: nevertheless a significant independent role is still left to 24-h sodium excretion when the latter is added in a regression equation with either body weight or BMI. Such an association between sodium and blood pressure, independent from body weight, has been reported to our knowledge only by Joossens *et al.*^[20] from a Belgian male adult population, and by Cooper and coworkers^[31] in a study of Chicago school children: in other 'within population' studies either a significant correlation was not found^[15-18] or multivariate analysis was not done^[19-21].

At variance with the study by Cooper *et al.*^[31], our data do not suggest a strong independent association of 24-h creatinine with blood pressure: in fact, when entered in a regression equation with body weight, creatinine did not make an appreciable contribution to DBP variability. Its correlation with blood pressure in univariate analysis appears to be largely a result of cross association with body weight.

Similarly, there was no indication of any independent role played by 24-h urine volume, since this was totally unrelated to blood pressure.

The strength of the association between sodium and blood pressure was probably underestimated because of the large intraindividual variability of both variables. The information provided by single 24-h urine collections, although useful for group comparison, gives only a rough estimate of the habitual salt intake of individual subjects^[33]. Such methodological limitation has been often accepted in population studies as the majority of participants would refuse the burden of multiple collections. However, it significantly reduces the probability of demonstrating a possible biological correlation between dietary salt and any other variable; so also do possible inadequacies in urine collection which cannot be controlled with certainty in this type of study.

It seems noteworthy that the increase in 24-h sodium excretion, while remarkable between the first and the third quintile of DBP, was smaller for further increments in blood pressure. A similar observation has been made by Berglund and coworkers^[34,35], who found in a random sample of male population in Goteborg a positive association between urinary sodium and blood pressure only within the 'normotensive' range.

Sodium excretion thus appears to be increased in

subjects with high blood pressure compared with 'normotensives', but it is not significantly different within the hypertensive group. This finding might be explained by the exclusion from the present study of 'severe' hypertensives because of current medical treatment.

Alternatively, or in addition to the previous one, the relative loss of linearity in the association between these two variables beyond a certain blood pressure level may be due to the influence of other factors of environmental or genetic origin that potentiate the adverse effect of a 'high salt' diet.

Weinberger and coworkers^[36] have been able to induce a significant increment in the blood pressure of normotensive volunteers by raising their daily sodium intake to extremely high levels for a short period of time; however, similar experimental evidence has not been obtained through changes in dietary salt within the habitual range of Western communities.

On the other hand, a moderate decrease in the habitual salt intake has been proved to be effective in lowering blood pressure in patients with established arterial hypertension^[37]. The hypothesis can be made that a comparable dietary modification extended to the general population would be able to produce a marked shift in the entire blood pressure distribution, thereby significantly reducing the rate of hypertensive vascular diseases. A few pilot studies have tested the feasibility of intervention programs in this direction both in adults and children^[4,38].

References

- [1] Swales JD. Dietary salt and hypertension. *Lancet* (1980); 1: 1177-9.
- [2] Tobian L. Dietary salt (sodium) and hypertension. *Am J Clin Nutr* 1979; 32: 2659-62.
- [3] Dahl LK. Salt intake and hypertension. In: Genest J, Koiv E, Kuchel O, eds. *Hypertension*. New York: McGraw-Hill, 1977: 548-59.
- [4] Joossens JV. Dietary salt restriction. The case in favour. In: Robertson JIS, Pickering GW, and Caldwell ADS, eds. *The therapeutics of hypertension*. London: Academic Press and Royal Society of Medicine, 1980: 243-50.
- [5] Joossens JV, Geboers J. Nutrition and gastric cancer. *Nutr Cancer* 1981; 2: 250-61.
- [6] Oliver WS, Cohen EL, Neel JV. Blood pressure, sodium intake and sodium related hormones in the Yanomamo Indians, a 'no-salt' culture. *Circulation* 1975; 52: 146-51.
- [7] Page LB, Damon A, Moellering Jr RC. Antecedents of cardiovascular disease in six Solomon Islands societies. *Circulation* 1974; 43: 1132-46.

- [8] Page LB, Vandeventer D, Nader K, Lubin N, Page JR. Blood pressure, diet and body form in traditional nomads of the Qash'gai tribe, southern Iran. *Acta Cardiol* 1978; 33: 102-10.
- [9] Sinnett PF, Whyte HM. Epidemiological studies in a total highland population, Tukisenta, New Guinea. *J Chronic Dis* 1973; 26: 265-90.
- [10] Shaper AG. Cardiovascular disease in the tropics III. *Br Med J* 1972; 3: 805-7.
- [11] Sasaki N. The relationship of salt intake to hypertension in the Japanese. *Geriatrics* 1964; 19: 735-41.
- [12] Simpson FO. Salt and hypertension: a sceptical review of the evidence. *Clin Sci* 1979; 57 (suppl 5): 463s-480s.
- [13] Prior IAM, Brimley Evans JG, Harvey HPB, Davidson F, Lindsey M. Sodium intake and blood pressure in two Polynesian populations. *N Engl J Med* 1968; 279: 515-20.
- [14] Miall WE. Follow-up study of arterial pressure in the population of a Welsh mining valley. *Br Med J* 1959; 2: 1204-10.
- [15] Dawber TR, Kannel WB, Kagan A, Donabedian RK, McNamara PM, Paaronson G. Environmental factors in hypertension. In: Stamler J, Stamler R, Pullman TN, eds. *The epidemiology of hypertension*. New York: Grune and Stratton, 1967: 255-88.
- [16] Simpson FO, Waal-Manning HJ, Bolli P, Phelan EL, Spears GFS. Relationship of blood pressure to sodium excretion in a population survey. *Clin Sci Mol Med* 1978; 55: 373s-375s.
- [17] Grim CE, McDonough JR, Dahl LK, Hames CG. Racial differences in Evans Co, Georgia. *Circulation* 1970; 42 (suppl III): III, 85 (Abstract).
- [18] Schlierf G, Arab L, Schellenberg B, Oster P, Mordasini R, Schmidt-Gayk H, Vogel G. Salt and hypertension: data from the 'Heidelberg study'. *Am J Clin Nutr* 1980; 33: 872-5.
- [19] Dahl LK. Evidence for an increased intake of sodium in hypertension based on urinary excretion of sodium. *Proc Soc Exp Biol Med* 1957; 94: 23-9.
- [20] Joossens JV, Willems J, Claessens J, Lissens W. Sodium and hypertension. In: Fidanza F, Keys A, Ricci G, Somogyi GC, eds. *Nutrition and cardiovascular diseases*. Rome: Morgagni Edizioni Scientifiche, 1970; 91-110.
- [21] Doyle AE, Chua KG, Duffy S. Urinary sodium, potassium and creatinine excretion in hypertensive and normotensive Australians. *Med J Aust* 1976; 2: 898-900.
- [22] Pietinen PI, Wong O, Altschul AM. Electrolyte output, blood pressure and family history of hypertension. *Am J Clin Nutr* 1979; 32: 997-1005.
- [23] Strazzullo P, Trevisan M, Farinaro E, De Campora E, Furnari M, Ferrara LA, Mancini M. The association between urinary sodium excretion and blood pressure in a sample of Neapolitan population. *Eur Heart J* 1981; 2 (suppl A): 19 (Abstract).
- [24] Farinaro E, Panico S, Oriente P, Mancini M. Prevalence of risk factors in an urban working of Southern Italy. In: Carlson L, Paoletti R, Sirtori C, Weber G, eds. *Proceedings of the International Conference on Atherosclerosis*. New York: Raven Press, 1978: 375-8.
- [25] Wright BM, Dore CF. A random zero sphygmomanometer. *Lancet* 1970; i: 337-9.
- [26] Snedecor GW, Cochran WG, eds. *Statistical Methods*. Ames: The Iowa State University Press, 1967.
- [27] Duarte CG. Renal handling of potassium. In: Knox FG, ed. *Textbook of renal pathophysiology*. Hagerstown, MA: Harper and Row, 1978: 133-47.
- [28] Malnic G, Klose RM, Giebish G. Micropuncture study of distal tubular potassium and sodium transport in rat nephron. *Am J Physiol* 1966; 211: 529-47.
- [29] Walker G, Russell P, Whelton P, Hermann J. Relation between blood pressure, plasma renin activity, aldosterone, urinary sodium and potassium in 574 ambulatory subjects. *Circulation* 1978; 58 (suppl II): II-165 (Abstract).
- [30] Holly JM, Goodwin FJ, Evans SJ, Vanden Burg MJ, Ledingham JM. Re-analysis of data in two Lancet papers on the effect of dietary sodium and potassium on blood pressure. *Lancet* 1981; ii: 1384-7.
- [31] Cooper R, Soltero I, Liu K, Berkson D, Levinson S, Stamler J. The association between urinary sodium excretion and blood pressure in children. *Circulation* 1980; 62: 97-104.
- [32] Curtis Ellison R, Sosenko JM, Harper GP, Gibbons L, Pratter FE, Miettinen OS. Obesity, sodium intake and blood pressure in adolescents. *Hypertension* 1980; 2 (suppl I): 1-78-82.
- [33] Liu K, Cooper R, McKeever J, Byington R, Soltero I, Stamler R, Gosch F, Stevens E, Stamler J. Assessment of the association between habitual salt intake and high blood pressure: methodological problems. *Am J Epidemiol* 1979; 110: 219-26.
- [34] Berglund G, Wallentin I, Wikstrand J, Wilhelmsen L. Sodium excretion and sympathetic activity in relation to severity of hypertensive disease. *Lancet* 1976; i: 324-6.
- [35] Lyungman S, Aurell M, Bartford M, Wikstrand J, Wilhelmsen L, Berglund G. Sodium excretion and blood pressure. *Hypertension* 1981; 3: 318-26.
- [36] Weinberger MH, Luft FC, Bloch R, Henry DP, Wyman AE, Rankin LI. Blood pressure in sodium fed humans. In: Laragh JH, Buhler FR, Seldin DW, eds. *Frontiers in hypertension research*. New York: Springer 1981: 58-61.
- [37] Parijs J, Joossens JV, Van Der Linden L, Verstreken G, Amery AKPC. Moderate sodium restriction and diuretics in the treatment of hypertension. *Am Heart J* 1973; 85: 22-34.
- [38] Gillum RF, Elmer PJ, Prineas RJ. Changing sodium intake in children. The Minneapolis children blood pressure study. *Hypertension* 1981; 3: 698-703.