ORAL SODIUM LOADING IN NORMAL INDIVIDUALS

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At the commencement of the Peru Burn Project (1) in 1951, great apprehension was aroused in many by the use of large quantities of isotonic saline solutions[5] in the treatment of burned patients, for it was believed that such therapy in individuals retaining sodium due to the stress reaction would overload the circulation and lead to death in pulmonary edema. The reason for this fear was based upon the knowledge that man, in contrast to the dog, retained a great part of the sodium administered as isotonic sodium chloride over a considerable period of time (2, 3). Yet, during the course of the study of 110 burned children and 83 burned adults to whom had been given orally a quantity of an isotonic saline solution equivalent to 10 per cent of body weight during the first 24 hours after thermal injury and half that amount during the second 24-hour period, no untoward effects due to sodium, such as vomiting, generalized edema or massive pulmonary edema, were encountered (1), in spite of the fact that these patients demonstrated marked water and sodium retention (largely the result of accumulations in the burned area as edema fluid). The experimental conditions of sodium loading in previous studies of normal subjects did not duplicate those utilized in the treatment of burned patients Hence, a quantity of isotonic saline solution similar to that given to burned patients was administered to normal persons over the same time period in order to clarify the effects of such sodium loading upon the kidney and circulation.

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[5] The term 'saline solution' throughout this paper refers to a solution of a mixture of sodium chloride and sodium bicarbonate. For exact composition, see Materials and Methods.

MATERIALS AND METHODS

Renal function. Twelve healthy Peruvian males between the ages of 20 and 28 years were studied. None had a medical history of previous renal or cardiovascular disease. The subject was not permitted to take any liquid or food after 8 P.M. of the day previous to the performance of the study. After voiding on arrival at the hospital at 8 A.M., he was weighed nude and placed in bed in a recumbent position. The bladder was catheterized, venous pressure was measured carefully in the antecubital vein, and three twenty-minute clearance periods using inulin and sodium para-aminohippurate (PAH) by the technique of Goldring and Chasis (4) were accomplished. Five hundred cc. of water had been given approximately one and one-half hours previous to the measurement of the first clearance period, and suprapubic pressure and injection of air were used to empty the bladder. The catheter was then removed. At 11 A.M., after the subject had voided, a gastric tube was introduced into the stomach via the nose, and a constant drip of an isotonic saline solution containing 137 mEq. per L. of Na, 93 mEq. per L. of Cl and 44 mEq. per L. of HCO_3 was administered by the gastric tube at a uniform rate of 4 to 5.5 cc. per min. Each subject was given a total quantity of saline solution equivalent to 10 per cent of body weight over a period of 21 hours, during which time the subject remained recumbent and received no food or water. At 2-hour intervals the subject voided spontaneously, and the urine volume was measured and the urine saved. At 8 A.M. the next morning, when the total quantity of saline solution had been given, he was again weighed after voiding and then catheterized. Venous pressure was measured, and three clearance periods of 15 to 20 minutes each were repeated with inulin and PAH, this time without giving water previously. At the termination of the clearance studies the subject was weighed once more.

In the urine and plasma collected during the clearance periods PAH was analyzed by the method of Smith, Finkelstein, Aliminosa, Crawford, and Graber (5), inulin by the method of Schreiner (6), sodium and potassium by the flame photometer using lithium as internal standard (7), and chloride by the method of Van Slyke and Hiller (8). In the first blood sample drawn at the control period and the period after completion of the sodium loading test, hematocrit was determined by the Wintrobe method, total plasma protein by the copper sulfate method (9), alkaline reserve by the manometric

method of Van Slyke (10), and concentration of sodium and potassium in red blood cells separated from plasma after one-half hour centrifuging at 3,000 rpm by the flame photometer method. Sodium and potassium concentrations were determined also in the 2-hour urine samples collected. Afterwards, the separate 2-hour samples of urine were mixed and the total quantity of urine excreted over the period of sodium administration was analyzed for sodium and potassium. Glomerular filtration and renal plasma flow were calculated during the control period and at the termination of the oral sodium loading. Total quantity of sodium and potassium excreted (UV) during the same periods, as well as during the 2-hour collection periods, was calculated. In addition, percentage of filtered sodium excreted was calculated during all clearance periods.

Plasma volume study. Eleven healthy Peruvian males between the ages of 20 and 28 years (including seven of the former subjects who volunteered for this test one month after completion of the previous one) were studied. All of the same conditions were maintained as before, except for the fact that no renal clearances were performed. Instead, at 9 A.M. on the day of the beginning of the test, plasma volume was measured by the four sample techniques using T-1824 (11). Again the subjects received a quantity of the saline solution equivalent to 10 per cent of body weight via gastric tube uniformly by constant drip over a 21-hour period. After completion of administration of the saline solution (8 A.M.), plasma volume determination was repeated as on the day before.

RESULTS

Hemodynamics

In Table I are listed glomerular filtration rate, renal plasma flow and plasma volume during the control period and during the period just after the administration of a quantity of the isotonic saline solution equivalent to 10 per cent of body weight. In eleven of the twelve subjects the glomerular filtration rate increased significantly over the control value and in only one individual did it stay the same. The average value shows a significant increase (+ 32 per cent) over the control value after the sodium load. On the other hand, renal plasma flow increased over the control value in six of the twelve subjects, decreased in five and stayed the same in one. The average value of all the subjects does not show a significant increase over the control value. The plasma volume increased over the control value in four of twelve individuals, decreased in six and remained the same in one after the administration of the saline solution. The average value of all the subjects shows no significant change over the control value. Venous pressure was measured during the control period (average, 104 mm.) and after sodium load-

TABLE I

Hemodynamic studies in normal subjects with oral sodium loading

Subject	No. of clearances	Glomerular filtration *cc./min./1.73 m²*			Renal plasma flow *cc./min./1.73 m²*			Plasma volume *cc.*		
		Control*	After*	Diff.	Control*	After*	Diff.	Control	After	Diff.
J. C.	3	105	161	55	614	725	111	3,055	3,358	303
M. C.	2	160	253	93	599	925	326			
L. M.	2	129	195	66	752	730	−22	2,110	2,400	290
P. L.	2	162	198	36	1,099	1,375	276			
E. R.	3	130	126	−4	648	577	−71	2,610	2,483	−127
A. R.	3	108	139	31	759	587	−172	3,354	3,600	246
A. V.	3	138	167	29	668	668	0			
J. G.	3	103	146	43	635	605	−30			
V. F.	3	118	163	45	631	750	119			
L. Q.	3	145	186	41	825	863	38	3,027	2,731	−296
R. C.	3	102	133	31	685	649	−36	3,035	3,048	13
C. G.	3	114	137	23	728	768	40	2,800	2,650	−150
A. L.								3,510	3,097	−413
J. R.								2,256	2,320	64
J. E.								2,720	2,455	−265
J. M.								2,941	2,463	−478
Average values		126	167	41†	720	768	48	2,856	2,782	− 74
Standard error of average				6.9			40.7			84

* Each number represents the average value of the clearance periods.
† Significant at the 1 per cent level.

TABLE II

Water and electrolyte excretion in normal subjects with oral sodium loading

Subject	No. of clearance periods	Urine volume* cc./min.		$U_{Na}V$* mEq./min.			U_{Na}* mEq./L.		U_KV* mEq./min.		U_K* mEq./L.	
		Control	After	Control	After	Sum	Control	After	Control	After	Control	After
J. C.	3	2.65	4.22	0.345	0.660	1.005	135.3	158.8	0.0689	0.0390	26.4	9.3
L. M.	2	3.79	3.03	0.310	0.520	0.830	85.7	172.0	0.0425	0.0449	11.7	14.8
P. L.	2	4.88	4.40	0.560	0.934	1.494	118.8	212.5	0.0913	0.0892	19.8	20.3
M. C.	2	9.75	3.85	0.526	0.718	1.244	54.1	187.0	0.0911	0.0294	9.4	7.6
E. R.	3	3.80	6.53	0.485	0.701	1.186	130.6	113.2	0.1168	0.0684	31.2	10.8
A. R.	3	4.02	3.65	0.528	0.572	1.100	148.4	155.5	0.0473	0.0277	13.1	7.6
A. V.	3	3.96	4.15	0.403	0.794	1.197	103.0	192.9	0.1021	0.0543	26.2	13.2
J. G.	3	4.69	1.63	0.286	0.396	0.682	64.4	242.0	0.0642	0.0437	14.1	26.7
V. F.	3	4.14	4.43	0.457	0.758	1.215	125.6	176.3	0.0586	0.0701	16.4	16.5
L. Q.	3	1.66	4.01	0.422	0.751	1.173	265.0	91.6	0.0367	0.0260	23.0	4.9
R. C.	3	1.36	5.04	0.345	0.841	1.186	49.4	167.1	0.0390	0.0400	4.9	8.0
C. G.	3	5.29	9.33	0.613	0.961	1.574	124.7	103.2	—	—	—	—
Average value		4.16	4.52	0.440	0.717		117.1	164.3	0.0690	0.0484	17.8	12.7

Analysis of variance of $U_{Na}V$ †

Source	df	Sum of squares	Mean square	F
Mean	1	8.0342		
Total	23	0.8804		
Control vs After	1	0.4611	0.4611	68.82 ‡
Subjects	11	0.3455		
Interaction	11	0.0738	0.0067	
				$F_{.01}$ 9.65

* Each number represents the average value of the clearance periods.
† $U_{Na}V$ = Total Na excretion; U_{Na} = Na concentration in urine excreted.
U_KV = Total K excretion; U_K = K concentration in urine excreted.
df = Degrees of freedom.
‡ Significant at the 1 per cent level.

ing (average, 133 mm.) in nine individuals, but no significant change was noted.

Excretion of water and electrolytes

In Table II are shown the concentrations and total quantity of the ions, Na and K, excreted during the clearance periods performed before and after the administration of the saline solution. The concentrations of sodium increased significantly after sodium loading, while the concentration of potassium decreased. The total quantity of sodium excreted augmented significantly after sodium loading (+ 63 per cent), while potassium diminished (− 30 per cent). The sodium excreted during the control period represented 2.58 per cent of the filtered load, while the sodium excreted after the administration of the sodium load represented 3.33 per cent of the filtered load. Although the volume of urine increased in seven of twelve individuals, the average urine volume after sodium loading showed no significant increase over the

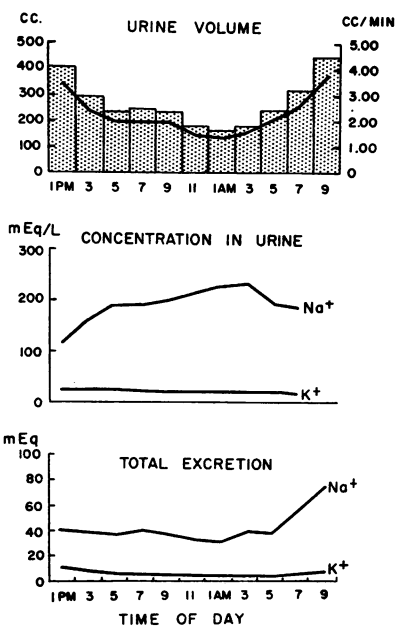

FIG. 1. DIURNAL VARIATIONS WITH ORAL SODIUM LOADING

TABLE III

Fluid and electrolyte balance in normal subjects with oral sodium loading *

Subject	Fluid intake cc.	Electrolyte intake mEq. Na	K	Cl	Urinary output cc.	Urinary excretion mEq. Na	K	Weight change Kg. After Na load	3 hrs. after Na load
M. C.	6,650	822	0	558	2,620	432	40	+2.1	+1.6
L. M.	5,300	685	0	465	3,340	455	43	+1.5	+0.7
	5,300	726	0	493	4,000	480	46	+0.5	
P. L.	6,000	822	0	558	4,860	690	53	+0.3	−1.1
E. R.	5,000	685	0	465	3,020	382	38	+1.7	+0.9
	5,400	740	0	502	2,540	315	62	+1.7	
A. R.	6,000	810	0	534	2,925	375	22	+2.4	+1.4
	6,000	810	0	534	960	232	38	+4.4	
A. V.	6,600	904	0	614	4,960	660	66	0.0	−1.1
J. G.	7,000	959	0	651	2,000	340	68	+3.3	+2.9
V. F.	6,000	822	0	558	3,600	490	59	+0.7	−0.5
L. Q.	6,000	822	0	558	3,500	517	39	+1.5	
	6,000	822	0	558	2,680	493	66	+2.2	
R. C.	7,000	959	0	651	3,300	609	64	+3.3	+2.5
	7,000	959	0	651	3,060	536	59	+3.3	+2.1
C. G.	6,300	863	0	586	3,900	554	78	+1.1	−0.4
	6,000	822	0	558	2,780	378	98	+2.0	
J. R.	5,000	685	0	465	1,540	408	55	+1.8	
J. E.	5,300	726	0	493	4,540	654	91	+0.3	
J. M.	6,300	863	0	586	1,540	442	31	+2.9	
Average	6,000	815	0	552	3,083	472	56	+1.85	+0.82

* Table does not include one subject in which the sodium load produced diarrhea and another who had large saliva loss.

control value due to the fact that the control value itself represented a slight water diuresis.

In Figure 1 are demonstrated the average urine volume, concentration of sodium and potassium and total excretion of sodium and potassium of the 2-hour urine collections during the administration of the saline solution. The first 2-hour sample showed an increase of water and sodium excretion as compared to the values prior to the administration of the saline solution. Water, sodium and potassium excretion all decreased during the night hours with sodium excretion rising notably during the early morning hours above the values encountered at the beginning of the test on the previous day. Sodium concentration in the urine rose during the administration of the sodium load with only a moderate effect noticeable due to changes in water excretion, while potassium concentrations remained relatively constant regardless of water excretion.

In Table III are listed the total intake and total output of water and electrolytes during the administration of the sodium load, together with the changes of weight affected by the sodium administration. It is noted that 51 per cent of the water and 58 per cent of the sodium administered were excreted via the kidney during the period of oral administration of sodium. From the weight data, it can be observed that at the completion of the sodium loading only 31 per cent of the water administered (1.85 Kg.) was retained, which rapidly diminished to 14 per cent (0.82 Kg.) three hours after the termination of the sodium administration. The different responses of a single subject receiving the same sodium load on two separate occasions are also given.

Blood analyses

Table IV demonstrates the changes in hematocrit, total plasma proteins, plasma concentration of sodium, potassium, chloride and bicarbonate and erythrocyte concentration of sodium and potassium before and immediately after the administration of the sodium load. Although some of

TABLE IV

Blood analyses in normal subjects with oral sodium loading

Analyses	Control Average ± S.D.	After Na loading Average ± S.D.
Hematocrit, %	46.2 ± 2.48	44.0 ± 7.2
Tot. Proteins, *gm.* %	7.66 ± 0.34	7.17 ± 0.47*
Plasma Na, *mEq./L.*	139.1 ± 3.51	137.2 ± 3.39
Plasma K, *mEq./L.*	4.13 ± 0.37	3.86 ± 0.30*
Plasma Cl, *mEq./L.*	101.3 ± 0.95	100.7 ± 0.55
Plasma HCO_3, *mEq./L.*	24.6 ± 0.41	23.0 ± 0.51*
RBC K, *mEq./L.*	90.8 ± 3.5	87.9 ± 4.2*
RBC Na, *mEq./L.*	14.5 ± 0.35	14.7 ± 1.84

* The difference between the control value and the value after the sodium load has statistical significance.

these values changed significantly due to the administration of the large quantities of saline solution, none of the changes appear to be of any real importance.

DISCUSSION

The excretion of 58 per cent of a large oral sodium load during the period of its administration challenges the widely held belief that man, unlike the dog, is sluggish in excreting sodium (2). Since previous studies in the literature concerned with sodium loading in man have all been performed giving smaller total amounts of physiologic sodium chloride solution (1 to 3 liters), but by more rapid intravenous infusion (13 to 65 cc. per min.), it is possible that the previously unreported experimental conditions used in this study are responsible for the observed difference.

Earlier investigators have held that man excreted sodium sluggishly compared to the dog due to the fact that glomerular filtration did not increase in man with the intravenous administration of sodium chloride. In the present study, however, there was usually a consistent and significant increase of glomerular filtration at the termination of oral sodium loading. Since the percentage of filtered sodium excreted increased significantly from 2.58 per cent to 3.33 per cent, it is evident that decreased tubular reabsorption over and above the increased amount filtered by the glomerulus accounted for a part of the augmented sodium excretion. Even though it is difficult to compare the results of this study with prior ones, it can be stated, nevertheless, that water and sodium excretion after oral sodium loading fell to values between those reported in non-prehydrated (2) and prehydrated (12) subjects maintained in the recumbent position.

The magnitude of the sodium and water diuresis after oral sodium loading is masked somewhat by the control values, since these latter values themselves demonstrated a slight water and sodium diuresis compared to data in the literature. The slight water diuresis during the control period was due to the administration of a small quantity of water before the commencement of the test. The slight sodium diuresis is more difficult to explain, but is most likely due to an augmented ingestion of sodium in the daily Peruvian diet prior to the test.

Although no attempt was made to study renal hemodynamics during the course of the administration of the sodium load, the gross data of sodium and water excretion on the 2-hour samples collected during that time demonstrated the well-known diurnal variations of water and sodium excretion without sodium loading, but at higher levels than reported under normal circumstances (13).

SUMMARY

1. Sixteen healthy young Peruvian males were given a quantity of an isotopic saline solution equivalent to 10 per cent of body weight in the recumbent position by constant drip via a gastric tube over a period of 21 hours. Renal hemodynamics and electrolyte excretion were studied in twelve of the subjects and plasma volumes in eleven of them before and after the administration of the sodium load.

2. Glomerular filtration rate increased an average of 32 per cent over the control value after administration of the sodium load, while effective renal plasma flow did not change significantly.

3. While body weight was increased significantly at the termination of the sodium load, plasma volume did not change significantly. The increase in body weight largely disappeared within 3 hours after termination of the load.

4. During the period of administration of the sodium load, 58 per cent of the administered sodium and 51 per cent of the administered water were excreted via the kidneys. The concentration and total quantity of sodium excreted in the urine increased significantly at the termination of the sodium load. An increased filtration of sodium by the glomeruli as well as a decreased reabsorp-

tion of sodium by the tubules are considered to be responsible for this phenomenon. Water excretion was augmented also, but its significance was masked by the slight water diuresis present in the control values. The diurnal variations of sodium and water excretion during the course of administration of the sodium load were evident, but at higher levels than under normal circumstances.

5. Total excretion of potassium as well as potassium concentration in the urine decreased after sodium loading.

6. There were no important changes in plasma concentrations of red blood cells, total proteins, or electrolytes.

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