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Research Article

STUDIES IN DIURNAL VARIATION OF WATER AND ELECTROLYTE EXCRETION: NOCTURNAL DIURESIS OF WATER AND SODIUM IN CONGESTIVE CARDIAC FAILURE AND CIRRHOSIS OF THE LIVER [1, 2]

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Clinicians have been aware that nocturia is an important symptom of disease, yet there has been little investigation of the underlying mechanisms. The nocturias of obstruction with overflow, of cystitis, and of pregnancy, have had obvious explanations. The nocturia of chronic glomerulonephritis has been explained by the inability of the kidney to perform its finer regulatory functions, thus producing a urine of essentially constant composition, varying in quantity chiefly in relation to changes in the filtration rate. Recently, the nocturia of cardiac failure has been studied by Brod and Fejfar (1) who report that inulin and PAH clearances show an increase in the renal plasma flow after the patient retires, followed by a fall in the filtration fraction and an increase in the filtration rate. These findings were further confirmed by Baldwin, Sirota and Villarreal (2), who also demonstrated by means of both creatinine and inulin clearances that the glomerular filtration rate increases at night when there is nocturia. The latter (3) caution, however, that fluctuations in the clearance of creatinine cannot be determined accurately by variations in the amount of creatinine in the urine, since there are unpredictable fluctuations in the serum creatinine. On the basis of these data they propose a simple explanation for the increase in the nocturnal flow of urine in patients with cardiac failure. In such patients an inadequate cardiac output is somewhat improved by shunting blood away from the kidneys to tissues with greater blood needs during the day. At night, when there is less peripheral demand for blood, more blood is diverted to the kidneys. During this period of increased filtration the water and electrolytes presented to the tubules exceed their respective tubular maxima, and the excess is excreted in the urine (4, 5). This concept is strengthened by the demonstration of a greater filtration fraction during the day than during the night. Yet, upon reviewing their data, Fejfar and Brod (6) and Baldwin, Sirota and Villarreal (2, 3) feel that the increased filtration alone does not account for the variations in urine composition, and that variations in distal tubular function also must be considered.

The object of the present study has been to gather some data on the nature of the diurnal urinary cycles in edema-forming conditions, and to test some of the theories of the mechanisms producing these cycles.

MATERIALS AND METHODS

Three groups of male patients were studied. Group I —eight patients served as controls and were in the hospital for diseases that did not affect kidney function. Four were convalescent from peptic ulcer, one was convalescent from lobar pneumonia, two had chronic myelogenous leukemia, and one had a carcinoma of the thyroid. Group II—eight patients with heart disease comprised this group; six had arteriosclerotic, and two rheumatic heart disease. All had been edematous in the past but were maintained free from edema at the time of the study on a regimen which included digitalization, a low sodium diet and frequent use of mercurial diuretics. Diuretics were omitted on the days on which urine was collected. Group III—13 patients with cirrhosis of the liver, who had ascites or who had had ascites in the recent past were investigated. Four of these were re-studied later on a dietary program which consisted of 300 ml. of milk given at intervals of four hours throughout the day and night.

[1] Reviewed by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions of the author are the result of his own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

[2] This investigation was supported (in part) by a research grant from the National Heart Institute, National Institutes of Health, Public Health Service.

Clinical data pertaining to the patients are summarized in Table I.

In order to facilitate accurate collection and measurement of specimens, the subjects were admitted to the Metabolic Ward for closer supervision. Four of the controls and all of the cardiac and cirrhotic patients were on a limited sodium intake. While the food was not weighed, analyses of sample menus and numerous determinations of sodium in 24-hour collections of urine showed that the amount of sodium ingested was always less than 1,500 mg. a day. In patients with poor appetites the intake of sodium was considerably lower. Meals were served according to the usual hospital schedule. Patients who had not been on the diet previously were allowed a period of two or three days for adjustment before collections of urine were begun. No restrictions were placed on fluid intake, but the subjects were encouraged to drink freely during the day and to limit fluids at night. Un-

TABLE I

Clinical data pertaining to patients

Patient	Diagnosis	Age	Ht.	Wt.	Date of study	B.P.	BUN	Remarks
Da	Duodenal ulcer	29	70	164	Dec. '49	130/70		
Ro	Duodenal ulcer	43	69	149	Jan. '50	128/80		
Sm	Duodenal ulcer	25	73	188	Feb. '50	100/70		
Gr	Duodenal ulcer	51	67	123	Mar. '50	105/60		
St	Carcinoma of thyroid	24	71	153	Dec. '49	100/70	15	Treated with radioiodine; doing well, July 1951
Br	Pneumonia, convalescent	25	64	105	Dec. '49	120/70		
To	Leukemia, chronic myelocytic	43	69	160	Nov. '49	130/80	10	Died Jan. 1951
On	Leukemia, chronic myelocytic	39	68	177	Aug. '49	120/75	14	Died Feb. 1951
Ka	Arteriosclerotic heart disease	57	67	145	May '49	110/80	25	Old myocardial infarction
Sm	Arteriosclerotic heart disease	49	72	169	Nov. '49	110/80	12	Old myocardial infarction; died Dec. 1949
Mo	Arteriosclerotic heart disease	46	68	146	Feb. '50	110/70	21	Old myocardial infarction; slightly ambulatory
Ho	Rheumatic heart disease	47	69	142	July '49	130/54	12	Mitral stenosis, aortic insufficiency, auricular fibrillation
Br	Arteriosclerotic heart disease	55	65	125	May '49	132/100	18	Old myocardial infarction; died Feb. 1950
Ba	Rheumatic heart disease	49	68	118	July '50	120/80	15	Mitral stenosis
Je	Hypertensive and arteriosclerotic heart disease	62	67	121	Sept. '50	190/85	26	Old myocardial infarction; aortic aneurysm
Pe	Arteriosclerotic heart disease	58	67	132	Sept. '50	110/70	16	Old myocardial infarction; died Jan. 1951 of new infarction
Si	Cirrhosis	53	70	131	Nov. '49	168/98	12	Slight ascites, more in past
Do	Cirrhosis	52	65	176	Sept. '49	162/112	8	Moderately severe ascites
Re	Cirrhosis	55	68	105	Oct. '50	130/80	36	Severe ascites
Le	Cirrhosis	52	71	154	Oct. '50	110/80	15	Severe, increasing ascites
Ro	Cirrhosis	55	70	113	July '50	105/80		Moderate, increasing ascites
Li	Cirrhosis	61	66	164	May '50	120/90	21	Moderately severe ascites
He	Cirrhosis with hepatoma	56	67	120	Oct. '49	120/80	16	Homologous serum jaundice. No alcoholism. Died March 1950, cirrhosis with multicentric hepatoma
Ma	Cirrhosis	58	71	189	Aug. '50	130/70	11	Moderate ascites. Died Sept. 1950 of hemorrhage
Lo	Cirrhosis	60	68	117	Sept. '49	140/60		Ascites in past; none during study
Bu	Cirrhosis	53	70	156	Sept. '49	130/88		Slight ascites
Va	Cirrhosis	72	68	144	Jan. '50	150/95	14	Moderate ascites, homologous serum hepatitis. Died March 1950
Buw	Cirrhosis	54	68	139	Oct. '49	130/80	13	Moderate ascites. Died April 1950. Necropsy suggested infectious hepatitis despite alcoholic history
Du	Cirrhosis	39	66	160	Sept. '49	90/60	9	Moderate, decreasing ascites

less otherwise indicated, patients were up and about the ward during the day and remained in bed from 9 p.m. to 7 a.m.

Urine collections were started at midnight and spontaneously voided specimens were obtained under supervision of the nursing staff at intervals of four hours until the end of the experimental period. In order to reduce casual irregularities and to compensate for differences in regimen from day to day, collections were made for three successive days. The volume of each specimen was recorded and the sodium and potassium were determined using the Beckman Flame Photometer (7). In about half of the patients the specimens were analyzed for creatinine by the method of Bonsnes and Taussky (8). The final data were collected for each of the comparable daily periods and the average amount of each four-hour excretion was reported as a percentage of the 24-hour output.

TABLE II

Control subjects

Patient	Total excreted	Per cent of total excretion per collection period Hours of collection 0–4	4–8	8–12	12–16	16–20	20–24
	Water *ml.*						
Da	3,092	3.7	8.7	23.9	24.6	23.8	15.5
Ro	2,822	5.4	6.7	23.7	25.2	21.7	17.2
Sm	3,490	5.5	7.3	21.6	27.1	19.1	19.6
Gr	4,497	7.7	8.7	18.0	24.9	18.4	22.5
St	3,430	2.0	2.5	37.9	23.9	20.7	13.0
Br	2,780	10.2	8.3	18.2	19.4	18.5	25.6
To	1,410	10.9	13.5	17.5	20.3	21.2	16.5
On	1,172	12.7	11.7	18.2	20.6	17.2	19.6
Average		7.3	8.4	22.4	23.3	20.1	18.7
	Sodium *gm.*						
Da	1.182	3.3	5.8	26.1	19.4	32.5	13.1
Ro	1.037	14.4	13.2	13.2	19.3	19.8	20.1
Sm	2.708	14.9	11.3	17.7	14.3	21.3	20.5
Gr	0.714	13.6	12.5	16.2	22.7	18.5	16.6
St	4.284	2.6	4.0	19.7	34.3	21.8	17.5
Br	1.777	5.2	7.6	22.1	26.4	24.2	14.6
To	6.502	10.9	13.5	17.5	20.3	21.2	16.5
On	3.988	13.4	8.7	18.8	24.3	16.6	18.3
Average		9.8	9.6	18.9	22.6	22.0	17.2
	Potassium *gm.*						
Da	2.059	10.8	7.9	23.8	26.0	17.9	13.5
Ro	2.549	10.1	16.0	18.6	22.1	19.4	13.8
Sm	2.344	6.4	9.0	25.6	26.6	21.1	11.3
Gr	3.388	9.7	13.6	18.4	23.4	20.3	14.7
St	3.187	6.7	5.7	26.5	30.9	15.4	14.8
Br	3.155	11.2	14.9	20.9	18.9	17.2	16.9
To	2.340	8.8	16.2	19.8	17.6	20.8	16.9
On	2.819	10.8	16.8	22.1	21.5	17.7	11.0
Average		9.3	12.5	22.0	23.4	18.7	14.1
	Creatinine *gm.*						
Ro	1.643	15.3	16.2	16.8	17.8	17.7	16.1
Sm	2.056	16.9	15.9	16.9	15.0	18.2	15.6
Gr	1.522	15.2	16.4	15.5	19.0	18.2	15.8
Br	1.605	14.1	16.4	17.2	20.9	20.2	11.3
Average		15.4	16.2	16.6	18.2	18.6	14.7

RESULTS

The data pertaining to the control group are presented in Table II. Although variations are obvious within the group, it is to be noted that in most individuals there was a minimal output of water, sodium and potassium from midnight until 8 a.m., a gradual rise to a maximum between noon and 4 p.m., followed by a slight subsequent decline to midnight. In general, the potassium appears to fall more rapidly from its maximum than does the water or the sodium. The values for creatinine reveal only a slight and inconstant fluctuation with a tendency to a daytime maximum and a nocturnal minimum. Both here, and elsewhere in this study, there appears to have been no consistent correlation between increases in output of creatinine and increases in output of water, sodium or potassium.

The data referable to the patients with compensated congestive heart disease are summarized in Table III. It will be noted that two of them presented patterns which closely resemble the normal. However, the remaining six patients had a marked alteration of pattern, with the maximum output of water and sodium between midnight and 8 a.m. and the minimum between 8 a.m. and 4 p. m. The output of potassium in this group was extremely erratic, and no consistent trend could be demonstrated. Excretion of creatinine was also erratic, but two points are apparent—the range of variation for each four-hour period was small, and there was no constant relationship between the values for output of creatinine and any of the other values determined.

Table IV summarizes the data from the patients with cirrhosis of the liver. It will be noted that reversal of the normal day/night ratio for excretion of water and sodium was even more consistent than in patients with heart disease. The peak excretion of water and sodium was between midnight and 8 a.m. in most cases, and was more marked in regard to excretion of sodium than to excretion of water. Despite alterations in excretion of water and sodium, the excretion of potassium, except for a moderately delayed peak, was remarkably similar to the normal. Values for output of creatinine showed only a very slight tendency to increase during the night-time hours, and continued to be erratic in relationship

TABLE III

Congestive heart failure

Patient	Total excreted	Per cent of total excretion per collection period, Hours of collection 0–4	4–8	8–12	12–16	16–20	20–24
	Water *ml.*						
Ka	2,683	27.2	25.4	7.2	10.8	16.0	13.4
Sm	1,025	32.1	26.5	10.0	7.7	8.9	14.9
Mo	2,655	14.1	10.2	16.7	15.5	28.3	15.2
Ho	1,792	9.8	6.6	26.1	29.3	16.2	12.0
Br	2,333	26.0	21.7	11.0	10.6	9.7	21.0
Ba	1,293	15.3	9.3	7.9	16.2	23.7	27.5
Je	1,579	25.9	12.0	12.4	10.5	13.0	26.3
Pe	955	17.6	11.5	14.2	19.5	15.2	21.7
Average		21.0	15.4	13.2	15.0	16.4	19.0
	Sodium *gm.*						
Ka	0.200	46.8	30.6	2.7	3.5	6.7	9.7
Sm	0.044	23.3	27.3	12.2	12.8	11.7	12.8
Mo	0.082	8.0	4.5	23.0	21.1	34.3	9.2
Ho	0.193	11.3	5.0	18.1	28.7	26.6	10.3
Br	0.076	27.6	31.8	10.2	6.1	6.7	17.4
Ba	1.022	20.5	15.6	7.9	11.3	25.9	18.9
Je	0.650	34.7	18.5	6.9	5.2	8.5	26.6
Pe	0.370	22.3	19.8	15.9	14.9	12.7	14.4
Average		24.2	19.1	12.1	12.9	16.6	15.3
	Potassium *gm.*						
Ka	2.713	18.6	15.2	11.1	19.0	20.7	15.4
Sm	0.786	22.3	19.9	14.6	13.7	12.6	17.0
Mo	2.640	11.2	10.7	16.5	22.3	27.9	11.3
Ho	2.172	8.3	9.0	25.7	21.4	20.5	14.7
Br	1.420	22.9	19.5	11.2	12.7	13.4	20.3
Ba	2.267	9.6	9.5	16.8	24.8	23.6	15.7
Je	2.293	19.8	14.6	14.6	11.3	16.0	23.4
Pe	2.170	14.7	13.4	17.6	18.4	18.9	17.1
Average		15.9	14.0	16.0	18.0	19.2	16.9
	Creatinine *gm.*						
Mo	1.184	15.4	14.0	17.4	18.7	19.2	15.5
Ba	1.237	16.5	15.0	16.3	17.7	19.5	15.1
Je	0.980	18.4	14.3	17.4	12.8	15.6	21.6
Pe	1.166	16.1	14.6	17.9	17.0	17.2	17.5
Average		16.6	14.5	17.3	16.6	17.9	17.4

to other substances excreted during a given period.

Because there is a delayed response to a water load in cirrhosis of the liver, it was thought advisable to include a group of patients with cirrhosis to whom equal amounts of food and fluid were given at equal intervals throughout the day and night. The data on the four patients so studied showed that with one exception the cycle continued to be abnormal. Some allowance must be made for the fact that this alteration in the feeding pattern was quite disturbing to the patients. These data are summarized in Table V.

Examination of the effect of the various conditions upon the excretion of water revealed that in at least three-fourths of the patients with congestive heart failure and cirrhosis of the liver

TABLE IV

Hepatic cirrhosis

Patient	Total excreted	Per cent of total excretion per collection period, Hours of collection 0–4	4–8	8–12	12–16	16–20	20–24
	Water *ml.*						
Si	3,298	8.6	4.2	17.4	31.1	18.8	19.9
Do	1,092	16.9	12.1	8.1	9.2	21.4	32.4
Re	1,476	31.2	17.0	7.9	13.0	18.0	13.1
Le	1,020	17.0	9.0	5.2	8.4	22.5	37.8
Ro	1,388	19.8	6.8	4.9	13.5	25.7	29.3
Li	1,593	17.2	11.4	12.3	21.6	15.3	22.4
He	1,908	23.4	11.5	15.0	16.6	15.5	18.0
Ma	1,406	41.3	13.4	5.1	8.1	10.1	22.1
Lo	2,025	19.6	14.4	7.4	11.9	15.3	31.4
Bu	916	14.3	13.2	15.2	21.3	20.8	21.8
Va	2,718	14.0	6.3	10.1	20.0	24.5	25.1
Buw	883	18.1	16.0	21.1	15.3	14.2	15.3
Du	2,018	14.5	7.8	19.0	18.7	17.0	23.0
Average		19.7	11.0	11.4	16.1	18.4	23.9
	Sodium *gm.*						
Si	1.414	16.9	10.6	7.3	14.5	24.2	26.7
Do	0.886	31.7	22.2	1.5	11.1	11.5	22.2
Re	0.259	30.3	44.4	6.0	4.4	7.1	7.0
Le	0.696	17.3	17.7	5.7	3.4	26.3	29.9
Ro	0.442	33.4	18.0	5.5	4.5	12.7	26.0
Li	0.589	46.2	38.6	1.0	1.0	1.0	12.6
He	0.522	24.6	21.0	7.4	12.0	11.8	23.3
Ma	0.027	40.0	11.2	10.0	11.2	15.0	12.5
Lo	2.839	14.2	23.4	9.2	11.0	24.7	17.5
Bu	0.210	23.6	35.7	6.2	6.2	5.9	28.4
Va	0.057	19.2	12.6	20.5	15.2	17.6	15.0
Buw	0.033	9.0	10.0	46.0	11.0	16.0	8.0
Du	0.560	19.7	25.5	17.8	11.9	11.9	15.2
Average		25.1	23.0	11.1	9.0	14.3	18.8
	Potassium *gm.*						
Si	2.602	11.9	10.9	15.0	21.9	23.2	17.1
Do	1.753	16.7	19.5	13.0	16.4	18.3	15.9
Re	1.927	19.6	18.9	11.0	16.0	22.0	15.1
Le	1.507	16.1	14.5	12.9	16.2	23.8	16.4
Ro	1.876	14.0	12.5	13.2	13.3	28.4	18.5
Li	2.780	17.8	15.8	9.4	15.6	23.2	18.1
He	1.776	15.6	13.7	13.4	15.3	19.3	23.2
Ma	1.201	19.9	16.0	9.4	15.9	19.3	19.7
Lo	2.805	6.7	16.4	14.8	19.8	23.9	18.3
Bu	1.273	14.4	16.5	14.5	19.1	18.9	16.5
Va	0.932	14.3	10.1	16.5	20.0	22.5	16.7
Buw	1.670	15.1	15.1	19.8	16.8	18.1	15.2
Du	2.264	7.4	13.2	15.9	27.2	22.6	13.7
Average		14.6	14.8	13.7	17.9	20.3	17.3
	Creatinine *gm.*						
Re	1.207	17.1	17.6	13.9	15.4	19.5	16.4
Le	1.011	17.9	13.3	13.7	17.7	21.9	15.6
Ro	0.965	20.4	15.5	16.0	14.4	20.0	13.7
Ma	1.372	17.7	14.2	11.2	21.1	18.6	17.6
Va	1.089	17.3	15.3	16.8	17.3	17.2	16.2
Li	1.529	17.6	17.1	15.8	14.8	18.5	16.1
Average		18.0	15.5	14.6	16.8	19.3	15.9

there was an increase in the nocturnal excretion of water, with a reversal of the diurnal cycle. In general, the excretion of sodium demonstrated the same nocturnal increase, but was more marked than that of water. Excretion of potassium was relatively unaffected by reversals of the diurnal cycle of water and sodium excretion in the conditions studied. However, in three cardiac and three cirrhotic patients with extreme degrees of inversion of excretion of water and sodium, the potassium cycle was also inverted.

In 14 cases excretory cycles of creatinine were studied with those of water, sodium and potassium. It was found that the diurnal variations were proportionately much smaller than were the variations of the other substances studied. It was also noted that the cycle was often inconstant from day to day, and therefore averages for a three-day study often produced results which were not consistent with actual daily patterns. The relationship between the four-hour creatininuria and the excretion of the other substances studied was not always consistent, since excretion of creatinine often varied in one direction, while the excretion of water, sodium, or potassium varied in the opposite direction with respect to a preceding or a following period. However, when the excretory cycle of water and sodium was markedly reversed, there was a tendency for the excretion of creatinine to show a lesser degree of similar reversal. It was observed that when there was a general flattening of the excretory cycle there was not infrequently an exceptionally

TABLE V

Hepatic cirrhosis

(Feedings every four hours)

Patient	Total excreted	Per cent of total excretion per collection period, Hours of collection 0–4	4–8	8–12	12–16	16–20	20–24
	Water *ml.*						
Li	692	22.6	33.1	13.6	12.6	8.9	9.3
Re	1,914	28.6	23.5	13.4	11.5	12.5	10.5
Le	525	16.6	11.8	15.0	20.7	14.3	21.5
Ro	970	19.7	8.2	12.6	9.8	14.1	35.6
Average		19.4	19.2	13.6	13.6	12.5	19.2
	Sodium *gm.*						
Li	0.212	31.8	52.3	6.4	3.1	3.0	3.5
Re	1.504	25.8	21.5	8.4	5.1	6.7	33.1
Le	0.630	7.9	5.5	19.1	28.1	17.7	21.1
Ro	0.475	25.8	7.3	12.6	11.2	18.2	24.8
Average		22.8	21.7	11.6	11.9	11.4	20.6
	Potassium *gm.*						
Li	1.978	19.3	28.0	12.4	15.3	11.5	13.5
Re	2.800	11.3	12.4	17.1	18.7	12.6	26.1
Le	1.484	13.0	16.3	21.5	21.5	10.8	16.8
Ro	3.203	15.5	12.3	20.5	14.6	19.2	17.4
Average		14.8	17.0	17.9	17.5	13.5	18.5
	Creatinine *gm.*						
Li	1.418	22.0	24.2	12.9	17.0	11.6	12.3
Re	0.916	17.9	14.0	16.4	16.9	13.7	21.1
Le	0.790	18.3	12.6	16.2	18.5	12.2	22.4
Ro	0.946	17.7	10.3	18.8	14.6	20.1	18.8
Average		19.0	15.3	16.1	17.0	14.4	18.7

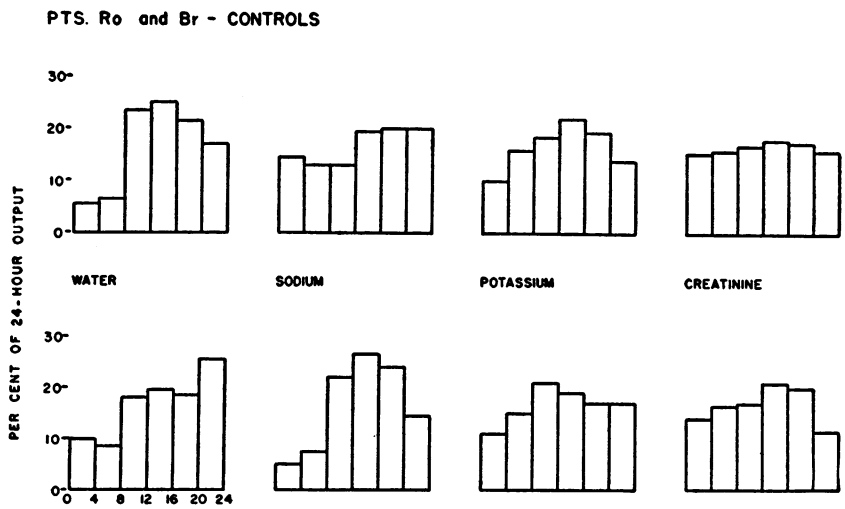

FIG. 1. TYPICAL DISTRIBUTION OF EXCRETION OF WATER, SODIUM, POTASSIUM AND CREATININE IN TWO NORMAL INDIVIDUALS

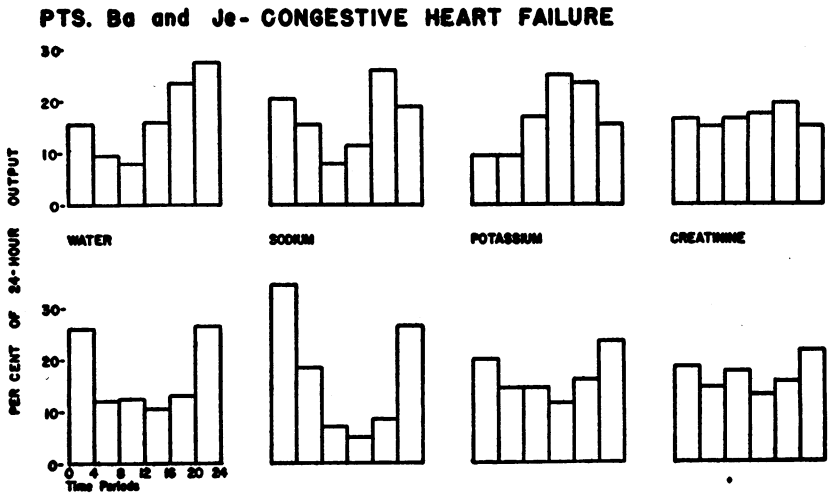

FIG. 2. TYPICAL DISTRIBUTION OF EXCRETION OF WATER, SODIUM, POTASSIUM AND CREATININE IN TWO PATIENTS WITH COMPENSATED CONGESTIVE CARDIAC FAILURE

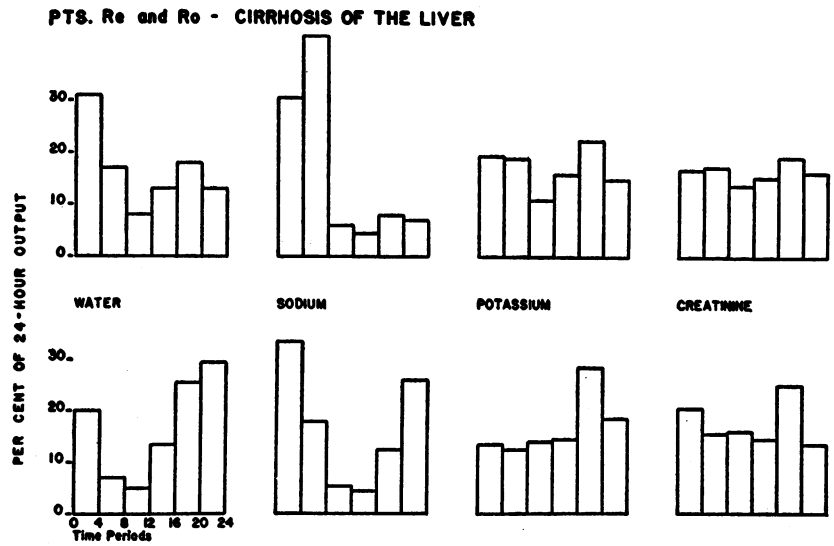

FIG. 3. TYPICAL DISTRIBUTION OF EXCRETION OF WATER, SODIUM, POTASSIUM AND CREATININE IN TWO PATIENTS WITH CIRRHOSIS OF THE LIVER WITH ASCITES

erratic period demonstrating a marked and unexplained diuresis. The figures illustrate patterns observed in two essentially normal individuals (Figure 1), in two patients with congestive cardiac failure (Figure 2), and in two patients with cirrhosis of the liver and ascites (Figure 3).

DISCUSSION

The diurnal variation of urinary excretion in the control group was in accord with reported observations (9–16). The work of earlier investigators who employed a routine of equal feedings equally spaced throughout the day demonstrated that normally the diurnal cycle of excretion was independent of the rhythm of ingestion. The work by these investigators also suggested that wakefulness, rather than daytime activity, was the usual controlling factor. Since nocturia is a physiological abnormality when it occurs in association with the customary daily routine, the normal daily cycle of wakefulness, activity, and ingestion of food and fluids was taken as the starting point for these studies.

Since a similar abnormal nocturnal diuresis of water and sodium exists in both cirrhosis and congestive cardiac failure, the same mechanism may be effective in both diseases. Brod (17) has reported that there is a nocturnal increase in urinary creatinine in congestive cardiac failure, and more recent studies (1, 2) have shown by direct methods that there is a concomitant increase in the filtration rate. The resulting nocturnal increase in tubular loading would explain the nocturia and the increased diuresis of sodium that is associated with it, and would be in accord with the concept that sodium diuresis results from increased glomerular filtration. In a preliminary report, Baldwin, Sirota and Villarreal (2) found that while there is a nocturia during cardiac failure, this nocturia disappears upon cardiac compensation and the elimination of edema. Six of our eight patients who had had congestive cardiac failure continued to have nocturia despite carefully controlled compensation. As has been pointed out, the excretion of creatinine found in this study, while usually paralleling the excretion of water and electrolytes, did not do so consistently. Therefore, although it must be conceded that there is probably an increased nocturnal filtration rate, our data did not produce a consistent relationship between creatinine and sodium excretion.

Arborelius (18) has reported that there was a marked decrease in the difference in water and chloride output between the period of maximum excretion and the period of minimum excretion in several patients with acute liver disease when compared to normal controls. Patients with liver disease also exhibit a delayed diuresis following a water load, and Adlersberg and Fox (19) have used this as a test of liver impairment. There is a similarly delayed diuresis in Addison's disease, and this fact forms the basis of the Robinson-Power-Kepler water test (20). Levy, Power and Kepler (21) have shown that liver disease will produce a falsely positive water test. It is apparent that the liver and adrenal (22) must have an effect upon diuresis and the diurnal cycle by mechanisms which have not yet been clarified. Because of the delayed diuresis following a water load, it was important to determine whether the nocturia was a late response to the normal daytime intake of water. For this reason several patients with cirrhosis were subjected to a test in which the dietary intake was the same at all feedings and the feedings were evenly spaced. This procedure failed to alter the abnormal rhythmicity. Recently, Farnsworth and Krakusin (23) have pointed out that cirrhosis causes a greater conservation of sodium than does cardiac failure. This observation has been confirmed by our own data as well as those of other workers (24, 25).

The abnormal rhythmicity in the case of congestive cardiac failure can be explained by hemodynamic factors which vary the renal plasma flow and the glomerular filtration rate. But such a cardio-renal hemodynamic explanation cannot be applied to the abnormal rhythmicity in hepatic disease since there is no reason for the cardiac output to be decreased, or evidence that the filtration rate is decreased (26). However, data on these factors are incomplete, and the glomerular filtration rate may be decreased by mechanisms which are not apparent. Similarly, adjustment of the tubular work capacity by a humoral agent has not been ruled out. The liver may elaborate or inactivate such a substance, and thus the effect may be independent of renal hemodynamics. An abnormal liver may be unable to meet its physiologic demands during activity, but the increase in hepatic blood flow with the assumption of the horizontal position (27) may enable the liver to carry out its functions in a more normal manner.

SUMMARY AND CONCLUSIONS

1. The diurnal variation in the excretion of water, sodium and potassium was studied in 29 individuals, and the variation in the excretion of creatinine was studied in 14 of these.

2. Eight individuals without evidence of sodium or water-retaining diseases were found to have maximum excretion of these substances during the day and minimum excretion during the night.

3. Eight patients were studied who had had congestive heart failure, but were edema-free and compensated. Six demonstrated a reversal of the normal cycle of water and sodium excretion with maximum excretion during the night. Three of this latter group continued to have a normal daytime maximum excretion of potassium.

4. Thirteen patients with cirrhosis of the liver and ascites were studied; eight had reversed water and eleven had reversed sodium excretory cycles.

Only three had definitely reversed cycles of potassium excretion, the others were flattened or normal.

5. Four patients with cirrhosis of the liver were given equal feedings equally spaced throughout the day and night; in three the excretory cycle continued to be abnormal. This suggests that the abnormal excretory cycle is independent of the intake cycle.

6. Creatinine excretion showed only small variations from period to period. Casual fluctuations were frequent and followed no apparent basic rhythm. Ordinarily there was a slight daytime maximum, but in some of the patients with increased nocturnal diuresis of water or sodium there was a nocturnal peak excretion of creatinine. Fluctuations in water and sodium diuresis from period to period were not always associated with a similarly directed fluctuation in excretion of creatinine.

7. Ultimately, all variations in urinary excretion must be associated with fluctuations in glomerular filtration, in tubular activity, or a combination of both. The cardio-renal hemodynamic explanation for the nocturnal diuresis of sodium and water in congestive heart failure does not appear satisfactory as an explanation for the similar nocturnal diuresis in cirrhosis of the liver. It is possible that there may be a nocturnal increase in renal plasma flow and glomerular filtration rate in cirrhosis of the liver, but such a mechanism has not yet been demonstrated. It is also possible that the nocturnal diuresis may be the result of an alteration in tubular function which is mediated by a humoral agent that can be affected by the liver.

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