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Research Article

THE EFFECTS OF ADRENALINE UPON RENAL FUNCTION AND ELECTROLYTE EXCRETION [1]

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The subcutaneous and intravenous infusion of adrenaline in man at a rate of 8 to 10 gamma per minute has previously been shown to produce a decrease in both renal plasma flow and glomerular filtration rate (1–4). The changes are not, however, proportional; and thus with a greater reduction in the plasma flow, a rise in filtration fraction results. The effects of the adrenaline-induced renal ischemia and hypofiltration on electrolyte excretion have not been adequately described. It is the purpose of this report to present data concerning the effect of intravenous adrenaline on both renal function and electrolyte excretion.

METHODS

Studies of renal function and determinations of electrolyte excretion were conducted on 12 young men without evidence of cardiovascular or renal disease. The experimental subjects received a normal hospital diet which contained between 7 and 15 grams of sodium chloride daily. The experiments were performed with the patients in the basal state after adequate hydration by the oral ingestion of one liter of water 60 to 90 minutes before the study. After three control periods of 15 minutes each, 0.45 to 0.80 mg. of adrenaline was administered by a constant injection syringe during a 45 minute period. The renal clearance studies were repeated during the administration of adrenaline. Renal plasma flow was determined by the clearance of para-aminohippurate as previously described (5). The glomerular filtration rate was measured by the clearance of inulin utilizing the method of Roe, Epstein, and Goldstein (6). The average priming solution of sodium para-aminohippurate and inulin consisted of 3 cc. and 50 cc., respectively. The average sustaining solution contained 14 cc. of sodium para-aminohippurate and 100 cc. of inulin, diluted to 200 cc. with triple distilled water. Approximately 150 cc. of sustaining solution was used for each experiment.

Sodium and potassium were determined by an internal standard Perkin-Elmer flame photometer. Chloride was determined by the titrimetric iodate method of Sendroy as modified by Van Slyke and Hiller (7).

RESULTS

The control values for renal hemodynamic and electrolyte studies are the averages of three consecutive periods. The values during the constant infusion of adrenaline are the averages of two periods beginning 15 minutes after the start of the infusion.

There was a marked and significant decrease in the mean renal plasma flow ($t = 7.82$, $P < 0.01$). In nine subjects the rate of glomerular filtration decreased, and in the other three it increased slightly. The mean change in the filtration rate was statistically significant ($t = 2.62$, $P < 0.02$). The filtration fraction increased in all patients, and the mean change was highly significant ($t = 9.32$, $P < 0.01$). The clearance data are recorded in Table I.

The serum sodium and chloride concentrations were unchanged by the administration of adrenaline. However, the serum potassium fell in each instance. The mean decrease in serum potassium was highly significant ($t = 3.90$, $P < 0.01$). Serum electrolyte concentrations are recorded in Table II.

A decrease in urinary sodium, chloride, and potassium excretion occurred in each subject. The mean change for each of the electrolytes studied was very significant ($P < 0.01$). The rate of urine flow decreased in eight subjects and increased in the other four. The mean change for the group was + 9.4 per cent. The urinary electrolyte excretion was independent of the rate of urine flow. Data for urinary electrolyte excretion are recorded in Table III.

The data presented in this report afford a means of studying the interrelationships of hypofiltration and electrolyte excretion. There was a moderate direct correlation between per cent change in uri-

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TABLE I

Renal hemodynamic studies before and during adrenaline infusion

Patient	Renal plasma flow (*cc. per min.*)			Glomerular filtration (*cc. per min.*)			Filtration fraction (*per cent*)		
	Control	During adrenaline	Per cent change	Control	During adrenaline	Per cent change	Control	During adrenaline	Per cent change
W. A.	669.2	363.5	−45.7	121.4	94.1	−22.5	18.1	25.9	+43.1
K. C.	532.7	361.8	−32.1	104.0	106.3	+2.2	19.5	29.4	+50.8
L. R.	682.1	370.5	−45.7	108.7	97.1	−10.7	15.9	26.2	+64.8
R. H.	673.1	331.0	−50.8	109.8	78.0	−29.0	16.3	23.6	+44.8
D. J.	583.5	208.5	−64.3	117.3	62.5	−46.7	20.1	30.0	+49.3
A. T.	544.8	386.0	−29.2	108.0	118.8	+10.0	19.8	30.8	+55.6
G. T.	604.1	326.3	−46.0	123.8	88.7	−28.4	20.5	27.2	+32.7
O. K.	766.3	475.1	−38.0	143.7	121.7	−15.3	18.8	25.6	+36.2
R. Ho.	697.2	392.8	−43.7	122.6	100.1	−18.4	17.6	25.5	+44.9
E. R.	625.7	549.1	−12.2	122.4	128.5	+5.0	19.6	23.2	+18.4
D. B.	663.5	367.6	−44.6	110.6	101.4	−8.3	16.7	27.6	+65.3
S. L.	498.2	313.9	−37.0	92.3	72.6	−21.3	18.5	23.1	+24.9
Mean	628.4	370.5	−40.8	115.4	97.5	−15.3	18.5	26.5	±44.2
S. D.	±78.2	±83.5	±12.8	±12.9	±20.0	±16.2	±1.6	±2.6	±14.5

nary sodium and per cent change in renal plasma flow ($r = 0.65$), and a high direct correlation between per cent change in urinary sodium and per cent change in glomerular filtration (Figure 1) ($r = 0.84$). Eliminating the effect of glomerular filtration, by the method of partial correlation (8), reduced the correlation between per cent change in urinary sodium and per cent change in renal plasma flow to insignificance (partial $r = 0.46$, $P > 0.1$).

Analysis of the data on chloride excretion and renal function was similar to that for sodium but yielded somewhat lower correlations. The correlation between per cent change in urinary sodium and per cent change in urinary chloride was 0.66.

An insignificant correlation was found between per cent change in the urinary potassium and per cent change in renal plasma flow ($r = 0.55$, $P > 0.05$). Similarly, an insignificant correlation was found between per cent change in urinary potassium and per cent change in glomerular filtration rate ($r = 0.55$, $P > 0.05$). There was no correlation between the per cent change in urinary potassium and the per cent change in serum potassium

TABLE II

Serum electrolyte concentrations before and during adrenaline infusion

Patient	Serum sodium (*milli-equivalents per liter*)			Serum potassium (*milli-equivalents per liter*)			Serum chloride (*milli-equivalents per liter*)		
	Control	During adrenaline	Per cent change	Control	During adrenaline	Per cent change	Control	During adrenaline	Per cent change
W. A.	144.0	133.7	−7.2	4.02	3.91	−2.7	104.6	104.9	+0.3
K. C.	147.3	141.1	−4.2	4.72	3.62	−23.3	105.8	105.9	+0.1
L. R.	149.0	143.5	−3.7	3.83	2.64	−31.1	105.6	104.0	−1.5
R. H.	148.3	148.3	0.0	4.43	3.52	−20.5	104.4	105.9	+1.4
D. J.	146.4	146.6	+0.1	4.25	3.04	−28.5	103.9	98.1	−5.6
A. T.	142.7	143.1	+0.3	4.81	3.83	−20.4	100.5	100.0	−0.5
G. T.	143.3	143.1	−0.1	4.27	3.77	−11.7	106.6	107.8	+1.1
O. K.	149.2	149.4	−0.1	5.39	4.09	−24.1	109.5	110.5	+0.9
R. Ho.	138.3	138.2	−0.1	4.52	4.19	−7.3	104.0	104.9	+0.9
E. R.	147.5	147.7	+0.1	4.56	4.31	−5.5	101.0	102.0	+1.0
D. B.	151.8	152.0	+0.1	4.54	3.75	−17.4	104.5	104.5	0.0
S. L.	147.7	146.6	−0.8	4.53	3.83	−15.5	102.0	102.9	+0.9
Mean	146.3	144.4	−1.3	4.49	3.71	−17.3	104.4	104.3	−0.1
S. D.	±3.6	±5.1	±2.4	±0.50	±0.47	±9.1	±2.5	±3.3	±6.4

TABLE III

Urine electrolyte excretions before and during adrenaline infusion

Patient	Urine sodium excretion (*micro-equivalents per minute*)			Urine chloride excretion (*micro-equivalents per minute*)			Urine potassium excretion (*micro-equivalents per minute*)		
	Control	During adrenaline	Per cent change	Control	During adrenaline	Per cent change	Control	During adrenaline	Per cent change
W. A.	168	54	−67.9	153	55	−64.1	107	34	−68.2
K. C.	162	110	−32.1	185	114	−38.4	102	43	−57.8
L. R.	114	65	−43.0	87	63	−27.6	93	54	−41.9
R. H.	143	46	−67.8	140	28	−80.0	118	24	−79.7
D. J.	179	35	−80.5	145	30	−79.3	72	24	−66.7
A. T.	149	136	−8.7	153	105	−31.4	117	54	−53.9
G. T.	206	69	−66.5	112	45	−59.8	68	18	−73.5
O. K.	156	82	−47.4	225	94	−58.2	167	78	−53.3
R. Ho.	165	89	−46.1	178	94	−47.2	105	28	−73.3
E. R.	122	96	−21.3	108	73	−32.4	51	37	−27.5
D. B.	63	54	−14.3	49	19	−61.2	62	17	−72.6
S. L.	111	47	−57.7	139	34	−75.5	126	20	−84.1
Mean	145	74	−46.1	140	63	−54.6	99	36	−62.7
S. D.	±37	±30	±23.2	±47	±33	±18.9	±32	±18	±16.5

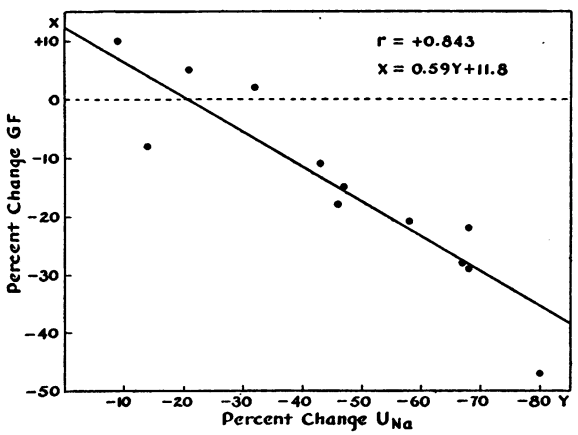

FIG. 1. CORRELATION BETWEEN PER CENT CHANGE IN GLOMERULAR FILTRATION RATE (GF) AND PER CENT CHANGE IN URINARY SODIUM EXCRETION (U_{Na})

($r = -0.01$). This pattern for potassium was not altered by applying the method of partial correlations.

DISCUSSION

There are three major factors which regulate the renal excretion of sodium and chloride; namely serum concentration, glomerular filtration rate, and tubular reabsorption. No evidence exists that these ions are cleared by tubular excretion. Under ordinary circumstances the serum concentration of these ions remains relatively constant. It is therefore apparent that this factor, *per se*, has no influence on the urinary excretion of these electrolytes. The constant infusion of adrenaline did not alter the serum concentration of either sodium or chloride, and thus this factor did not contribute to the changes in the excretion of these electrolytes.

It is impossible to assess adequately the relationship of glomerular filtration and tubular reabsorption to the ultimate excretion of sodium and chloride. Formulae which are used to express tubular reabsorption or rejection fractions are fallacious since under normal circumstances they merely express the constancy of the serum ion concentration. Furthermore, it is not possible to assess tubular reabsorption activity as an independent entity when the filtration rate is changing (9). The perplexity of the problem is manifested by the conflicting opinions expressed in the current literature (9–13).

Under the conditions of this experiment there was a high degree of correlation between hypofiltration and diminution in urinary sodium and chloride. Such a relationship could result from any or all of the following factors: (*1*) decreased load, (*2*) increased rate of tubular reabsorption, and (*3*) decreased velocity of flow in the tubular lumen. Since the serum electrolyte concentration was constant, decreased load and hypofiltration are synonymous. If hypofiltration were the sole factor and the percentage of tubular reabsorption of the filtered load were constant, then the percentage changes in glomerular filtration and urinary elec-

trolyte excretion would be comparable. However, the changes in urinary sodium and chloride were more than three fold those of filtration rate. Since hypofiltration is associated with proportionately greater changes in urinary sodium and chloride, other factors must be involved. In view of these disproportionate changes, tubular reabsorption cannot be evaluated as an independent entity (9). While increased tubular reabsorption must be at least a contributing factor, this does not necessarily infer increased specific activity of tubular cells for reabsorption of sodium and chloride. Hypofiltration may influence reabsorption by increasing the time of contact of electrolytes with tubular cells.

The problem of evaluating potassium excretion is much more complex than that for sodium and chloride since both tubular reabsorption and tubular excretion are involved. With the infusion of adrenaline the problem is further complicated by a decrease in the serum concentration of potassium. The alteration in serum potassium is not, however, correlated with the changes in renal function nor with urinary excretion, and must reflect an intracellular shift. A similar decrease in serum potassium has been noted by Keys following the injection of epinephrine (14). This author also noted a return above pre-injection levels within 50 minutes. It is to be noted that our studies were carried out during the constant infusion of epinephrine, and the serum potassium was not determined subsequently. The decreased urinary excretion of potassium during adrenaline infusion cannot be adequately explained by either the changes in serum concentration or by hypofiltration.

CONCLUSIONS

1. The constant intravenous infusion of adrenaline in doses of 10 to 18 gamma per minute caused a decreased renal plasma flow, a decreased glomerular filtration rate, and an increased filtration fraction.

2. There was a decrease in the urinary excretion of sodium, chloride and potassium. The serum sodium and chloride were not altered but the serum potassium decreased.

3. A high degree of correlation was demonstrated between the percentage changes in urinary sodium and chloride and the percentage change in glomerular filtration rate. This was not true for potassium.

4. Tubular reabsorption could not be evaluated in the presence of reduced filtration rate. The reasons for this have been discussed.

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