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Control by Plasma Potassium Concentration of Sodium Excretion by Isolated Perfused Dog Kidney*

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Summary. The experiments demonstrate that sodium and water rejection by isolated kidney submitted to saline loading is related to hypokalaemia caused by haemodilution. Since there is no change in glomerular filtration, it is demonstrated that sodium rejection is due to decreased tubular reabsorption caused by hypokalaemia. The experimental results suggest that escape from sodium retaining steroids could be related to the combined effect of sodium retention and potassium depletion on sodium tubular reabsorption. They explain also the uncontrollable sodium losses observed in the clinical states of potassium deprivation.

In a previous note (Nizet [6]), we have described a series of experiments demonstrating that isolated dog kidneys, artificially perfused at a constant pressure by heparinized blood, are able to reject a sodium and water load. Interference of extrarenal hormonal factors is excluded. Rejection of load is related more to a decrease in reabsorption than to an increase of glomerular filtration. Although lowering of haematocrit and of plasma protein levels and increase of plasma flow are likely to play a role in the control of sodium and water excretion, it is unlikely that they are the only factors involved.

One consequence of plasma dilution by saline is a decrease in potassium concentration and an increase in sodium/potassium ratio. In the present series of experiments, we have investigated the possible role of plasma potassium concentration on saline rejection.

Methods

The technique has been described in a previous note [6]. Two kidneys of the same pair are perfused by two identical machines, using identical heparinized blood in equal amounts, and at the same pressure (110 mm Hg). Kidneys and blood are taken from anesthetized dogs after injection of heparin; sodium, potassium, chloride, plasma proteins and urea are drawn in the middle of each collection period. Creatinine clearances are measured. Continuous injection of potassium, urea, glucose and creatinine is insured. For technical details, we refer to previous papers (Nizet [5]; Cuypers, Nizet and Baerten [1]; Nizet [6]; Nizet, Cuypers, Deetjen and Kramer [7]).

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A load of 150 ml solution of NaCl 9 *p* 1000 is added to both perfusion equipments. On one side, potassium concentration is restored and maintained to normal levels by initial addition of 0,75 mEq and continuous injection of a supplement of 0.2 mEq/hour of KCl. Water loss by urine secretion has not been compensated by addition of fluid to the machines.

Experimental results

The average results of five double experiments are summarized in the table. The results being based on the comparison of kidneys of the same pair, individual differences of donor dogs are minimized and

Table. *Control by plasma potassium concentration of sodium rejection by isolated dog kidney. (Average values of 5 double experiments)*

	Control kidney 450 ml blood + 150 ml normal saline			450 ml blood + 150 ml normal saline + potassium supplementation		
Time (minutes)	30—60	60—90	90—120	30—60	60—90	90—120
Renal blood flow (ml/gm/min)	4.56	5.4	5.76	4.32	5.64	6.4
Haematocrit (p. 100)	43.8	46	51	43.4	44.6	47.6
Plasma Na (mEq/l)	154	165	183	158	162	182
Plasma K (mEq/l)	2.84	2.62	2.62	5.18	4.56	4.42
Plasma Cl (mEq/l)	126	137	144	128	137	148
Plasma urea (gm/l)	0.21	0.19	0.18	0.19	0.19	0.19
Plasma proteins (gm/l)	45.5	55.5	66.8	47.9	48.5	55.5
Plasma osmolality (mOsm)	309	327	361	311	323	357
Urine flow (ml/100 g/min)	2.78	6.28	6.12	1.82	4.36	3.9
Urine Na (mEq/l)	116	72	73	97	43	36
Urine K (mEq/l)	18.3	8.6	7.4	31.2	13.9	12.2
Urine Cl (mEq/l)	107	61	66	111	51	42
Urine urea (gm/l)	1.45	0.75	0.61	1.63	0.89	0.79
Urea osmolality (mOsm)	313	202	207	281	171	167
Glomerular filtration rate (ml/100 gm/min)	46	58	41	44	57	44
Na load (μEq/ 100 gm/min)	7,023	9,383	7,554	6,881	9,346	8,007
Na rejection (p. 100 of load)	4.58	4.85	5.92	2.59	2.1	1.78
Total urine volume (ml)		202			132	
Kidney weight (gm)		40.5			39.5	

statistical significance of differences has been evaluated by the method of pair comparison, which has been applied to the results corresponding, to the second and third periods of urine collection.

The comparison of corresponding results in the two series of perfusions (with and without potassium supplementation) and at corresponding intervals of time leads to the following observations: at least during the first 90 min, there is no significant difference in total blood flow ($2\,p = 0.65$), haematocrit, plasma flow, plasma protein ($2\,p = 0.55$), sodium, chloride and osmolality, glomerular filtration rate ($2\,p = 0.65$) and sodium load ($2\,p = 0.85$). On the contrary, there is a significant decrease of urine flow ($2\,p < 0.005$) and a still greater decrease of sodium rejection ($2\,p < 0.005$) after correction of hypokalaemia.

Discussion

The results demonstrate that hypokalaemia is at least partly responsible for sodium and water rejection after dilution of blood by a saline and water load. Restoration of plasma potassium level to a normal value reduces sodium and water excretion. Since there is no significant change in glomerular filtration, it must be admitted that potassium acts through a change in tubular reabsorption of sodium and water.

Our previous results obtained with isolated kidneys (NIZET [6]) demonstrated that decreased reabsorption plays a major role in the elimination of a water and sodium load. The present experiments show that sodium reabsorption is decreased by hypokalaemia. There is no clear relationship between the absolute amounts of sodium and potassium excreted; moreover, there is no significant difference between the total amounts of potassium excreted by the control kidney and by the kidney submitted to potassium supplementation.

It appears therefore that one at least of the factors controlling excretion of a water and saline load is related to potassium dilution, rather than to plasma volume expansion. Whether the control is related to the change in potassium concentration in the blood and in the tubular fluid, or in the tubular cells has still to be elucidated.

It is interesting to point out that prolonged and severe hypokalaemia may induce reversible histological lesions with vacuolization at the level of proximal tubules (FOURMAN, MCCANCE and PARKER [2]; RELMAN and SCHWARTZ [8]; LAROCHE, LAGRUE, CAQUET and LAUDAT [3]).

On the basis of the present experiments, a renal mechanism could be suggested to explain escape phenomenon; the action of mineralocorticoids tends to increase plasma Na and decrease plasma K; Na reabsorption decreases as an immediate consequence of hypokalaemia or potassium cell depletion, and the result is a compensation by the kidney itself for excess sodium retention.

It is also possible to offer an interpretation of other clinical facts. MAHLER and STANBURY [4] and SQUIRES and HUTH [9], have observed that potassium depletion is followed by an uncontrollable natriuresis that persists even under salt-poor diet. These observations are easily explained on the basis of a decreased sodium reabsorption caused by hypokalaemia.

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