Effect of Potassium Salts Administration on the Renal Excretion of Bicarbonate during Acute Respiratory Acidosis and Hypochloremic Alkalosis in the Dog

Previous work from this laboratory[1] has shown that hypochloremia increases the tubular reabsorption of bicarbonate in the dog. Others have demonstrated that the administration of KCl decreases tubular bicarbonate reabsorption in normal dogs[2] and in animals submitted to acute respiratory acidosis[3]. The infusion of NaCl during respiratory acidosis was also found to decrease bicarbonate reabsorption in the dog[4]. In order to separate the respective effects of the K and Cl ions, it was therefore found necessary to study the action of two potassium salts, KCl and $KHCO_3$, on bicarbonate excretion in two situations characterised by an increase in tubular bicarbonate reabsorption: respiratory acidosis and hypochloremia. The data to be reported show that in some experimental conditions the effect of KCl administration is mainly due to the action of the Cl ion on bicarbonate excretion.

Methods. Two groups of experiments were performed. In the first group (8 experiments), acute respiratory acidosis was induced in Penthotal-anesthetised dogs by inhalation of 20% CO_2 in O_2 through a tracheal tube. At the same time, plasma bicarbonate concentration was raised by the infusion of a 6% $NaHCO_3$ solution, and tubular bicarbonate reabsorption calculated from data obtained by conventional clearance technique, using creatinine clearance as a measure of glomerular filtration rate. A $KHCO_3$ or a KCl solution (270–300 *mM*/l) was then infused, and tubular bicarbonate reabsorption calculated again while plasma potassium concentration was rising (Table I).

In the second group (7 experiments), hypochloremic alkalosis was induced in unanesthetised dogs by intermittent peritoneal lavage, using a sterile isotonic $NaHCO_3$ solution (145 *mM*/l) containig 3·5 *mM* KCl/l and 1 g glucose/l. After a 30–90 min interval, the solution was removed and replaced by fresh isotonic $NaHCO_3$ solution. The procedure was repeated according to the size of the animal. By this method we removed 5 to 9 mEq of Cl/kg body weight. As for the respiratory acidosis experiments, tubular bicarbonate reabsorption was studied before and after the administration of $KHCO_3$ or KCl 270–300 *mM*/l solution (Table II).

Results

1.—*Respiratory Acidosis* (Table I and Fig. 1): As expected, tubular bicarbonate reabsorption is much increased in the respiratory acidosis experiments where arterial pCO_2 reaches values from 125 to 145 mm Hg. The values of the bicarbonate excretion rate, expressed in *mM*/l of glomerular filtrate, are directly proportional to plasma bicarbonate concentration values (black circles, Fig. 1, left) because arterial pCO_2 remains fairly constant from one experiment to the other.

Due to the threshold phenomenon of bicarbonate excretion, the dotted line constructed from the data of the control periods cuts the abcissae at a plasma bicarbonate concentration value of 26 *mM*/l. It follows that the ratio (excreted bicarbonate, *mM*/l glomerular filtrate)/(plasma bicarbonate concentration – 26) is the constant which determines the slope of the curve. This ratio has a mean value of 0·561[6] for the control periods of the 8 experiments (24 clearance periods) before potassium administration. During potassium infusion, the mean value of this ratio increases to 0·790 for KCl (24 clearance periods) and to 0·797 for $KHCO_3$ (24 clearance periods). The differences between the means are highly significant when the potassium administration periods are compared to the control periods ($P < 0{\cdot}001$) but the effect of KCl is not significantly different from that of $KHCO_3$.

It should be noted that the mean plasma chloride concentration rises from 104 to 109 mEq/l in the KCl and from 104 to 105 mEq/l in the $KHCO_3$ experiments. The small amplitude of the plasma chloride concentration increment observed during KCl infusion is readily explained by the expansion of the extracellular fluid compartment produced by the simultaneous infusion of the 6% $NaHCO_3$ solution (Table I). It is obvious that KCl and $KHCO_3$ show an identical effect on the tubular reabsorption of bicarbonate under these experimental conditions.

2.—*Hypochloremic alkalosis* (Table II and Fig. 2): As was previously observed in hypochloremic alkalosis produced by an artificial kidney in the dog[1], this state does not induce any significant decrease in the glomerular filtration rate. In the 7 experiments here described, the GFR mean values were respectively 74 and 70 ml/min before and after the induction of hypochloremia.

As for the respiratory acidosis experiments, the bicarbonate excretion is much decreased in hypochloremic alkalosis. The correlation between the bicarbonate excretion rate values and the plasma bicarbonate concentration values is also linear in this condition (black circles, Fig. 2, left), and the dotted line cuts the abcissae at a plasma bicarbonate concentration value of 28 *mM*/l. If the same mode of calculation used for the respiratory acidosis experiments is applied here, the ratio (excreted bicarbonate, *mM*/l glomerular filtrate)/(plasma bicarbonate concentration – 28) has a mean value of 0·929 for the control periods of the 7 experiments (21 clearance periods). After potassium administration the mean value of this ratio increases to 1·467 for KCl (18 clearance periods) and to 1·247 for $KHCO_3$ (24 clearance periods). The differences between the means are not significant when the effect of KCl is compared to that of $KHCO_3$ or when the $KHCO_3$ periods are compared to the control periods. Contrastingly, the difference between the KCl and the control periods is very significant ($P < 0{\cdot}01$).

It is important to note that the mean chloride concentration of the plasma rises from 84 to 97 mEq/l during KCl and does not change during $KHCO_3$ infusions.

Conclusions

In respiratory acidosis, *K* administration produces an important decrease in the tubular reabsorption of bicarbonate as has been shown by ROBERTS *et al.*[3]. Since bicarbonate reabsorption can also be markedly depressed by the administration of NaCl in normal[5] and respiratory acidotic dogs[4], it should be expected that KCl would show a greater effect than $KHCO_3$ in our experiments. That such is not the case is related to the lack of increase in plasma chloride concentration in the KCl experiments. These data confirm that the flooding of the cells of the

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Table I

Experiment illustrating the effect of KCl and $KHCO_3$ infusions on bicarbonate excretion in the same dog during respiratory acidosis
Dog A, 28 kg.

1. KCl infusion 3. 4. 58

Time	Plasma						GFR	Bicarbonate		
min	$BHCO_3$ mEq/l	Cl mEq/l	Na mEq/l	K mEq/l	pH	PCO_2 mm Hg	ml/min	Excreted mEq/min	Filtered mEq/min	Reabsorbed mEq/l glomer. filtrate
–47	Start infusion $NaHCO_3$ 6%, 7 ml/min									
–37	Start inhalation CO_2 20% in oxygen									
0–28	46·0	106	164	3·08	7·16	140	106	1·02	5·12	38·6
29–45	49·5	105	169	3·08	7·17	140	91	1·07	4·73	40·2
50	Start infusion KCl 270 *mM*/l in $NaHCO_3$ 6%, 6 ml/min									
66–93	49·4	107	170	6·02	7·18	136	108	2·05	5·54	32·3
94–118	49·0	111	170	7·37	7·18	136	104	2·13	5·36	31·1

2. $KHCO_3$ infusion 9. 5. 58

Time	Plasma						GFR	Bicarbonate		
min	$BHCO_3$ mEq/l	Cl mEq/l	Na mEq/l	K mEq/l	pH	PCO_2 mm Hg	ml/min	Excreted mEq/min	Filtered mEq/min	Reabsorbed mEq/l glomer. filtrate
–45	Start infusion $NaHCO_3$ 6%, 7 ml/min									
–35	Start inhalation CO_2 20% in oxygen									
0–30	40·0	108	164	3·20	7·14	126	91	0·74	4·01	35·9
31–60	42·7	106	167	3·32	7·15	129	106	1·03	4·77	35·5
65	Start infusion $KHCO_3$ 300 *mM*/l in $NaHCO_3$ 4·2%, 5 ml/min									
80–112	47·0	107	168	5·77	7·18	129	112	1·98	5·52	31·6
113–143	49·3	110	168	7·37	7·19	133	109	2·05	5·63	32·8

Table II

Experiment illustrating the effect of KCl and $KHCO_3$ infusions on bicarbonate excretion in the same dog during hypochloremic alkalosis
Dog B, 29 kg.

1. KCl infusion 16. 5. 57

Time	Plasma						GFR	Bicarbonate		
min	$BHCO_3$ mEq/l	Cl mEq/l	Na mEq/l	K mEq/l	pH	PCO_2 mm Hg	ml/min	Excreted mEq/min	Filtered mEq/min	Reabsorbed mEq/l glomer. filtrate
–29	Start infusion $NaHCO_3$ 3%, 7 ml/min									
0–28	41·0	77	146	2·20	7·68	37	74	0·73	3·17	33·0
29	Start infusion KCl, 270 *mM*/l in $NaHCO_3$ 3%, 6 ml/min									
49–77	39·1	86	153	4·24	7·68	35	89	1·20	3·65	27·5
78–107	38·7	92	155	5·02	7·67	35	99	1·52	4·00	25·0

2. $KHCO_3$ infusion 19. 6. 57

Time	Plasma						GFR	Bicarbonate		
min	$BHCO_3$ mEq/l	Cl mEq/l	Na mEq/l	K mEq/l	pH	PCO_2 mm Hg	ml/min	Excreted mEq/min	Filtered mEq/min	Reabsorbed mEq/l glomer. filtrate
–39	Start infusion $NaHCO_3$ 2·4%, 7 ml/min									
0–34	37·8	76	145	2·21	7·68	32	75	0·50	2·82	31·1
36	Start infusion $KHCO_3$, 300 *mM*/l in water, 6 ml/min									
50–83	43·6	76	142	3·40	7·67	33	71	0·66	3·08	34·1
84–112	43·0	76	142	4·17	7·65	38	68	0·89	2·94	30·1

distal tubule by large amounts of potassium deviates the ionic exchange $Na^+ \rightleftarrows H^+$ to $Na^+ \rightleftarrows K^+$ in respiratory acidosis. This deviation depresses H^+ secretion and consequently decreases bicarbonate reabsorption.

In hypochloremic alkalosis, the increase of tubular bicarbonate reabsorption is certainly not due to a stimulation of H^+ secretion as in respiratory acidosis. It is secondary to the distortion of the anionic pattern of the plasma. The reabsorption of sodium/l of glomerular filtrate remains constant and equals the sum of the thresholds of chloride and bicarbonate. It follows that a decrease of plasma chloride concentration enhances the reabsorption of bicarbonate. The comparison between the effects of KCl and $KHCO_3$ administration in hypochloremic alkalosis shows that the important decrement of bicarbonate reabsorption observed in the KCl experiments

is mainly, perhaps solely, due to the chloride ion of the *K* salt. The depression of bicarbonate reabsorption is not as impressive during the infusion of $KHCO_3$.

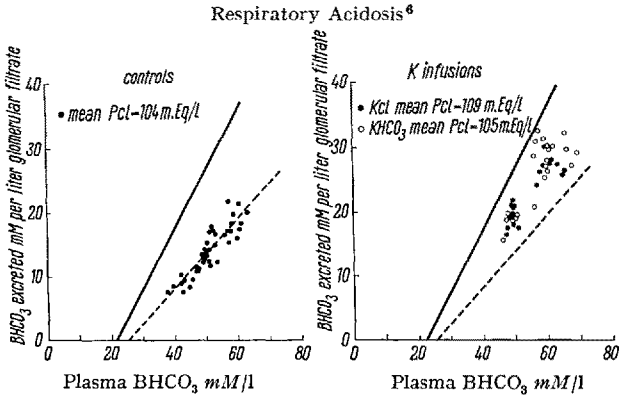

Fig. 1.—*Left:* Comparison between the control periods of the present respiratory acidosis experiments (---) and the curve obtained by PITTS and LOTSPEICH[5] in normal dogs infused with hypertonic $NaHCO_3$ solutions (—).

Fig. 1.—*Right:* Comparison between the control periods of the respiratory acidosis experiments (---) and the KCl (black circles) and $KHCO_3$ (open circles) infusions experiments and the curve obtained by PITTS and LOTSPEICH[5] (—).

The marked susceptibility of bicarbonate reabsorption to the K^+ ion in respiratory acidosis compared to hypochloremic alkalosis is explained by the fact that potassium can deviate the distal ionic exchange $Na^+ \rightleftarrows H^+$ to $Na^+ \rightleftarrows K^+$ in acidosis but not in alkalosis where the process of K secretion is already working maximally[1].

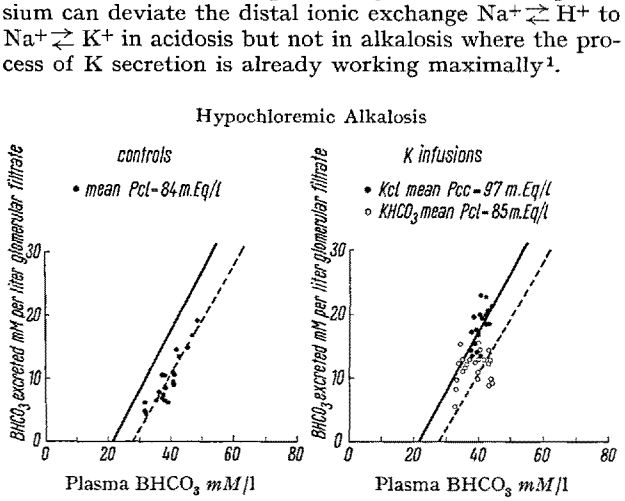

Fig. 2.—*Left:* Comparison between the control periods of the hypochloremic alkalosis experiments (---) and the curve obtained by PITTS and LOTSPEICH[5] in normal dogs infused with hypertonic $NaHCO_3$ solutions (—).

Fig. 2.—*Right:* Comparison between the control periods of the hypochloremic alkalosis experiments (---) and the KCl (black circles) and $KHCO_3$ (open circles) infusions experiments.

The lack of stimulation produced by $KHCO_3^-$ compared to KCl on bicarbonate excretion in hypochloremic alkalosis further demonstrates the existence of at least two distinct mechanisms for bicarbonate reabsorption: (1) ionic exchange $Na^+ \rightleftarrows H^+$ under the dependence of carbonic anhydrase, and (2) active reabsorption of sodium, with the obligatory reabsorption of HCO_3^- and Cl^- in the respective proportion they are found in the tubular urine. The first mechanism is sensitive to the potassium ion and the latter to the chloride ion.

These experiments show that the influence of KCl administration on bicarbonate excretion in various clinical and experimental conditions should be carefully analysed before definite conclusions can be drawn as to the effect of the potassium ion itself for some of the results observed might be due to the chloride ion.

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Résumé

L'effet d'infusions de KCl et de $KHCO_3$ a été étudié chez des chiens soumis à deux situations aiguës caractérisées par un accroissement de la réabsorption du bicarbonate: l'acidose respiratoire et l'alcalose hypochlorémique. Les deux sels diminuent fortement la réabsorption du bicarbonate au cours de l'acidose respiratoire mais le KCl est beaucoup plus efficace dans l'alcalose hypochlorémique où le $KHCO_3$ paraît dépourvu d'effet.

Über die Bedeutung der Innervation für die Adrenalinsynthese im Nebennierenmark

Selbst langdauernde elektrische Reizung des *Nervus splanchnicus* führt zu keiner nennenswerten Verminderung des Katecholamingehaltes im Nebennierenmark. Die Resynthese hält offensichtlich auch mit der Abgabe grosser Hormonmengen Schritt (ELLIOTT[1], HÖKFELT und MCLEAN[2], HOLLAND und SCHÜMANN[3]).

Um einen direkten Anhaltspunkt dafür zu gewinnen, dass die Innervation der Nebenniere für die Geschwindigkeit der Adrenalinsynthese von Bedeutung ist, haben wir an Kaninchen durch mehrtägige Behandlung mit Reserpin das Nebennierenmark weitgehend an Adrenalin verarmt, sodann die linke Nebenniere durch Splanchnicotomie denerviert und 3, 4 und 6 Tage später den Adrenalingehalt beider Nebennieren kolorimetrisch und fluorimetrisch bestimmt (KRONEBERG[4] und SCHÜMANN[5]).

Die Ergebnisse sind in der Tabelle zusammengestellt: Frühere Untersuchungen[4] an 7 Kaninchen hatten ergeben, dass der Adrenalingehalt beider Nebennieren im Mittel 86 µg/kg Körpergewicht beträgt (43 µg/kg pro Nebenniere). Nach dreimaliger intravenöser Injektion von je 0,3 mg Reserpin/kg im Abstand von 24 h ist am 4. Tag der Adrenalingehalt der rechten Nebenniere im Mittel von 3 Versuchen auf 6,4 µg/kg, derjenige der linken Nebenniere auf 6,6 µg/kg abgesunken (Kontrolltiere, Gruppe I). Wie die Verarmung beider Nebennieren nahezu gleich gross ist, so ist auch die Resynthesegeschwindigkeit der Katecholamine in beiden Nebennieren praktisch identisch (Scheinoperierte Tiere, Gruppe II). Bei den Versuchstieren (Gruppe III) wurde nach dreimaliger Injektion von

[6] The slope of the curve obtained during respiratory acidosis should be theoretically (as in Fig. 2) the same as the one observed by PITTS and LOTSPEICH[5] in normal dogs infused with $NaHCO_3$ hypertonic solutions. Actually, the slope of the curve in respiratory acidosis is reduced because, due to dilution, plasma chloride concentration falls while plasma bicarbonate concentration rises during the bicarbonate infusion.

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