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Relationship of Plasma Potassium and Hydrogen Ion Concentrations in Acidosis-Induced Hyperkalemiaand Hyperkalemia-Induced Acidosis†

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=Abstract=**The relationship between the plasma potassium concentration and blood pH was evaluated in acidosis-induced hyperkalemia and hyperkalemia-induced acidosis in rabbits. In the first group of animals, metabolic acidosis was induced by an intravenous infusion of 0.1 N hydrochloric acid, and in the second group, hyperkalemia was induced by an intravenous infusion of 20 mM potassium chloride solution. The third group of animals was infused with both hydrochloric acid and potassium chloride. All three groups showed metabolic acidosis, hyperkalemia, and compensatory respiratory alkalosis. The degree of alkalosis was most extensive in HCl infused, and least in KCl infused animals. The simultaneous infusion of HCl and KCl induced the most extensive change in the acid-base status, and the hydrogen and potassium ion concentrations. However the quantitative relationship between potassium and hydrogen ion concentrations was similar in all three groups. It is, therefore, presumed that acidosis-induced hyperkalemia and hyperkalemia-induced acidosis involve a common mechanism.**

Key Words: *Metabolic acidosis, Hyperkalemia, Blood pH, Compensatory respiratory alkalosis, Rabbit*

INTRODUCTION

The relation between blood pH and plasma potassium is complex and is influenced by several factors.

The patient with metabolic or respiratory acidosis tends to be hyperkalemic(Fenn and Cobb 1935; Elkinton *et al* 1955; Fenn and Asano 1956; Nichols 1958; Lade and Brown 1963; Saki and Paton 1965; Rimmer *et al* 1987; Magner *et al.* 1988), while the patient with metabolic or respiratory alkalosis tends to be hypokalemic(Keating *et al.* 1953; Giebisch *et al* 1955. Liebman and Edelman 1959; Kurtzman *et al* 1990). In general, plasma potassium changes less with alkalosis than with acidosis(Adroguë and Madias 1981), less with respiratory acidosis than with metabolic acidosis(Polak *et al* 1961; Brown and Goott 1963; Schwartz *et al* 1965; Carter *et al* 1967; Adroguë and Madias 1981), and less with organ-

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ic acid-induced acidosis than with HCl-induced acidosis(Burnell *et al* 1956; Tobin. 1958; Simmons and Avedon 1959; Adroguë and Madias 1981; Adroguë *et al.* 1985).

On the contrary, hyperkalemia can induce metabolic acidosis. The potassium homeostasis is easily impaired by disease states as well as by pharmacologic agents. Hyperkalemia is frequently associated with renal insufficiency, diabetes mellitus, and diseases with metabolic acidosis(Rimmer *et al.* 1987). Potassium chloride, nonsteroidal anti-inflammatory drugs, captopril, digoxin, heparin sodium, β-blockers and potassium-sparing diuretics can also elevate serum potassium concentration, and consequently induce mild metabolic acidosis(Ponce *et al.* 1985; Rimmer *et al.* 1987).

A number of studies have described a quantitative relationship between the plasma potassium concentration and the blood pH change in acidosis-induced hyperkalemia (Burnell *et al.* 1956; Schwartz *et al.* 1965; Adrogué and Madias 1981). However, no quantitative comparison of the plasma potassium concentration and the blood pH between acidosis-induced hyperkalemia and hyperkalemia-induced acidosis has been made.

In the present study, we attempted to compare the changes in plasma potassium concentration and blood pH between animals with HCl infusion(acidosis-induced hyperkalemia), KCl infusion(hyperkalemia-induced acidosis) and the simultaneous infusion of HCl and KCl.

MATERIALS AND METHODS

Rabbits of either sex (2.1 - 2.6 kg) were used. Each animal was anesthetized with pentobarbital sodium(30 mg/kg, i.v.). An arterial catheter was inserted into the right common carotid artery toward the heart, which was used for monitoring the blood pressure with a pressure transducer and for sampling of the arterial blood. A venous catheter was inserted into the jugular vein and was used for infusion of the test solution.

Animals were divided into three groups. The first group was infused with the normal saline containing 0.1 N HCl, the second group was infused with the normal saline containing 20 mM KCl, and the third group was infused with the normal saline containing both the HCl and KCl. The rate of infusion was adjusted according to the changes in blood pressure and pH.

The arterial blood was sampled at thirty minute intervals using a heparinized syringe. The pH and pCO_2 were measured at 37° C with an IL pH/pCO_2 meter and the concentration of HCO_3^- was calculated by the Henderson-Hasselbalch equation(the solubility coefficient of CO_2 was assumed to be 0.0301). The concentration of K^+ was measured by a flame photometer.

RESULTS

The changes in acid-base status are drawn in the pH-[HCO_3^-] diagram as depicted in Figures 1(group I, infused with 0.1 N HCl), 2 (group II, infused with 20 mM KCl), and 3(group III, infused with 0.1 N HCl and 20 mM KCl). Data points from the same rabbit are interconnected.

When animals were infused with HCl(group I, Fig. 1), their acid-base status moved to the left and in a downward direction in the pH-[HCO_3^-] diagram, revealing a metabolic acidosis and a compensatory respiratory alkalosis.

Likewise, when animals were infused with KCl(group II, Fig. 2), their acid-base status moved to the left and in a downward direction, but in this case, the degree of the compensatory respiratory alkalosis was less than with the HCl infusion (group I).

When animals were infused with both HCl and KCl(group III, Fig. 3), the acid-base status changed similarly, but much more extensively than those with HCl or KCl alone. The degree of compensatory respiratory alkalosis was less than that with HCl, but was greater than that with KCl.

Figures 4(group I), 5(group II), 6(group III) illustrate time courses of plasma H^+ and K^+ concentration changes. The absolute values are listed in Table 1, 2, and 3, respectively.

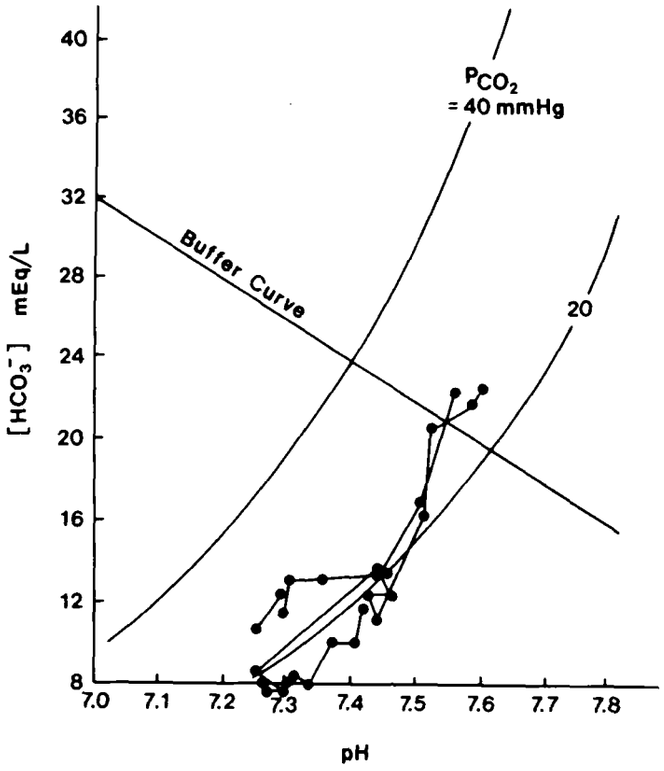

Fig. 1. Changes in blood acid-base status during intravenous infusion of 0.1N hydrochloric acid in rabbits. Data from the same rabbit are interconnected.

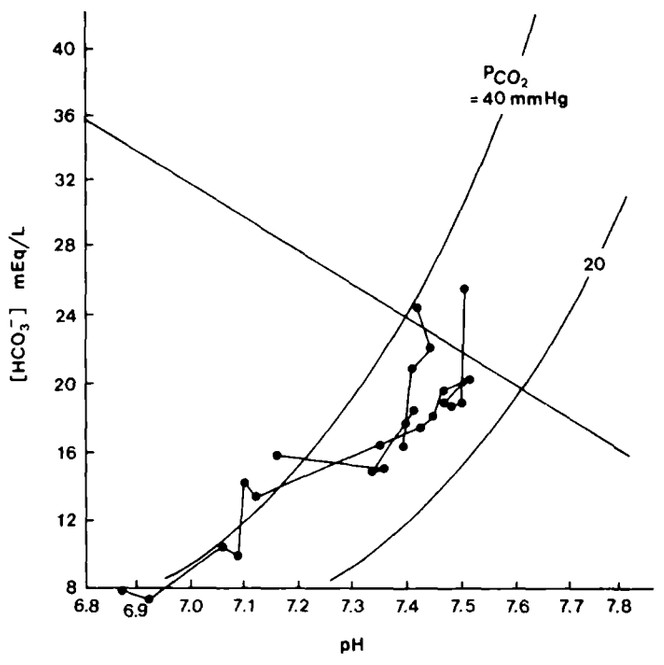

Fig. 2. Changes in blood acid-base status during intravenous infusion of 20mM potassium chloride in rabbits. Data from the same rabbit are interconnected.

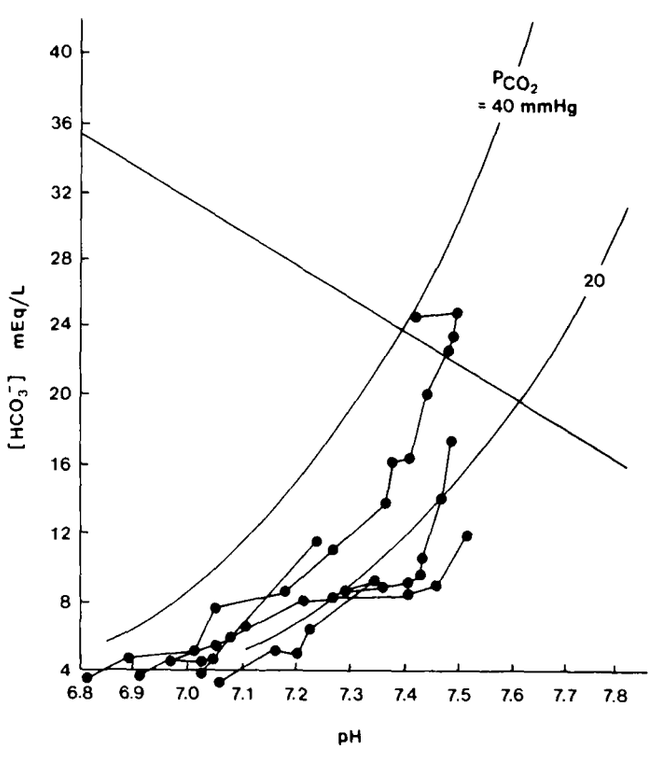

Fig. 3. Changes in blood acid-base status during intravenous infusion of 0.1N hydrochloric acid and 20mM potassium chloride in rabbits. Data from the same rabbit are interconnected.

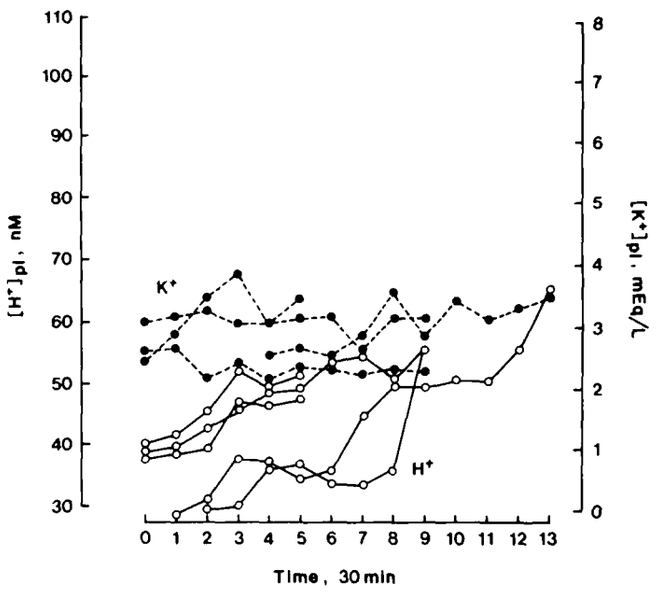

Fig. 4. Time courses of plasma hydrogen ion and potassium ion concentrations during intravenous infusion of 0.1N hydrochloric acid. Interval between each sample is 30min.

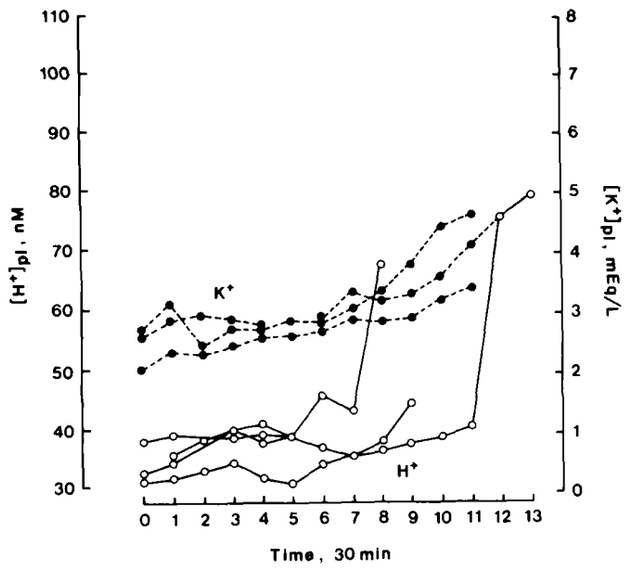

Fig. 5. Time courses of plasma potassium ion and hydrogen ion concentrations during intravenous infusion of 20mM potassium chloride. Interval between each sample is 30min.

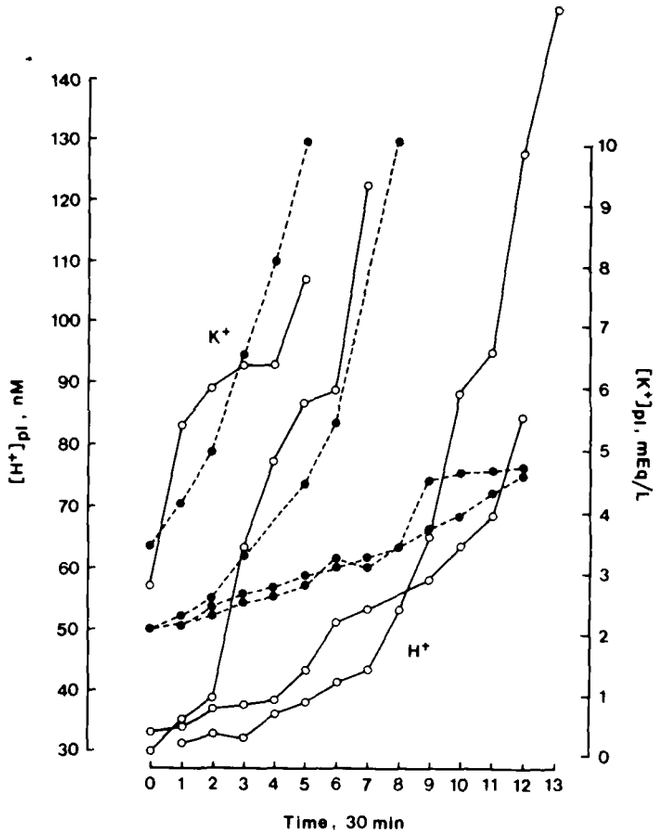

Fig. 6. Time courses of plasma potassium ion and hydrogen ion concentrations during 0.1N hydrochloric acid and 20 mM potassium chloride simultaneously. Interval between each sample is 30min.

In group I (Fig. 4 and Table 1), the H^+ concentration increased from 35 to 66 nM. The concurrent increase in K^+ concentration was observed from 2.8 to 3.5 mM. Thus, the relative change was much greater in the H^+ concentration than in the K^+ concentration.

In group II (Fig. 5 and Table 2), the concentration of K^+ increased from 2.6 to 4.0 mM. The consequent increase in H^+ concentration was from 34 to 60 nM. Thus, the relative increase was similar between the two cases.

In group III (Fig. 6 and Table 3), the H^+ concentration increased from 32 to 151 nM, and the K^+ concentration increased from 2.4 to 6.2 mM/L. Among three cases, the magnitude of change in this case was much greater than those in other groups.

But there were no differences in the quantitative relationship of K^+ and H^+ in all three groups.

DISCUSSION

The distribution of K^+ between intracellular and extracellular fluids is affected by the extracellular pH. Change in blood pH is minimized by cellular uptake and loss of H^+(Scribner *et al.* 1955; Scribner and Burnell 1956; Schloerb *et al.* 1967). This movement of H^+ is accompanied by a reciprocal movement of K^+. Consequently, acidosis causes plasma K^+ to rise while alkalosis causes it to fall.

There have been many arguments regarding the mechanism of this phenomenon(Simmons and Avedon 1959; Brown and Goott 1963; Magner *et al* 1988). It is, however, generally accepted that the hyperkalemic effect of acidosis is resulted from two mechanisms: (1) a shift of K^+ from intracellular to extracellular space as H^+ ions move into cells as a result of the H^+-K^+ exchange in the cell membrane throughout the body, and (2) an inhibition of K^+ secretion by the distal tubule in the kidney(Burnell *et al.* 1956; Simmons

Table 1. Changes in plasma hydrogen ion and potassium ion concentrations during intravenous infusion of 0.1N hydrochloric acid in rabbits

$[H^+]_{pl}$

		Sample number												
		0	1	2	3	4	5	6	7	8	9	10	11	12	13
	1														
	2	39.8	41.7	45.7	52.5	50.1	51.9								
	3	38.0	38.9	39.4	46.8	46.8	47.8								
Rabbit	4	30.9	31.8												
	5		28.2	30.9	37.2	37.2	34.7	35.9	44.7	50.1	50.1	51.3	51.3	56.3	66.1
	6	25.1	26.3	29.5	30.2	36.3	36.7	33.9	33.9	36.3	56.2				
	7	38.5	38.9	42.7	46.2	49.0	49.5	53.7	55.0	51.3	56.2				
	M	34.5	34.8	37.6	42.7	43.9	44.1		44.5	45.9			51.3	56.2	66.1

$[K^+]_{pl}$

	1	3.0	3.7												
	2			2.2	3.5	2.2	2.9								
	3	3	3.1	3.2	3	3.0	3.4								
Rabbit	4														
	5					2.5	2.6	2.5	2.8	3.5	2.8	3.4	3.1	3.3	3.5
	6	2.5	2..6	2.1	2.3	2.0	2.3	2.3	2.2	2.3	2.3				
	7	2.4	2. 7			3.0	3.1	3.1	2.5	3.1	3.1				
	M	2.45	2..7	2.75		2.75	2.66	2.63	2.8	2.73	2.73		3.1	3.3	3.5

Blood samples were drawn in thirty-minute intervals.

and Avedon 1959; Kurtzman *et al.* 1990).

The hypokalemic effect of alkalosis can be also explained by the H^+-K^+ exchange in the cell membrane and the increased K^+ secretion in the kidney.

But hyperkalemia is not a necessary concomitant of all types of metabolic acidosis. HCl causes marked hyperkalemia, whereas infusion of organic acids(such as lactic acid and β-hydroxybutyric acid) causes a much smaller rise in plasma K^+(Burnell *et al* 1956; Tobin 1958; Simmons and Avedon 1959; Magner et al. 1988). The difference between HCl and lactic/ β–hydroxybutyric acid effects is explained by the fact that organic anions readily enter cells, whereas Cl^- is actively extruded. During organic acidosis, the H^+ movements into cells are accompanied by lactate/ketone anions, preserving the intracellular electroneutrality, and thus K^+ exit from the cell is not required(Kurtzman *et al.* 1990).

Besides the nature of the acid load, other factors also influence the degree of hyperkalemia. These include the chronicity of acidosis, the change in ECF volume, the associated hormonal changes, and the presence of tissue necrosis(Magner *et al.* 1988).

In the present study, there was no difference in the quantitative relationship between the plasma K^+ and H^+ concentrations in all three groups. We, therefore, assume that the genesis of acidosis-induced hyperkalemia and that of hyperkalemia-induced acidosis involve a common mechanism. This assumption, however, is applied only to the acute metabolic acidosis induced by HCl, since in other types of metabolic acidosis the quantitative relationship between the plasma K^+ and H^+ may be different.

The simultaneous infusions of HCl and KCl resulted in a greater change in the plasma K^+

Table 2. Changes in plasma potassium ion and hydrogen ion concentrations during intravenous infusion of 20mM potassium chloride in rabbits

$[H^+]_{pl}$

		Sample number											
		0	1	2	3	4	5	6	7	8	9	10	11
	1	32.4	34.7		39.8	38.0	38.9						
	2	29.5	45.7										
Rabbit	3	37.6	35.1	38.0	39.8	40.7	38.9	45.7	43.2	67.6			
	4	38.0	38.9	38.9	38.9		38.9	37.2	35.9	36.7	38.0	39.8	40.7
	5	30.9	31.6	32.7	34.3	31.6	30.9	34.3	35.9	38.0	44.7	75.9	79.4
	M	34.7	35.1	36.5		36.8	37.9	39.1	39.6	42.2	43.1	48.5	50.4

$[K^+]_{pl}$

	1	3.5	10		4.6	3.8	3.9						
	2	2.4	2.6										
Rabbit	3	2.6	2.8	2.9	2.8	2.7	2.8	2.8	3.3	3.2			
	4	2.0	2.3	2.3	2.4	2.6	2.6	2.7	2.9	2.8	2.9	3.2	3.4
	5	2.6	3.1	2.4	2.7	2.7	2.8	2.8	3.0	3.3	3.8	4.4	4.6
	M	2.4	2.6	2.5	2.6	2.7	2.7	2.8	3.1	3.1	3.4	3.8	4.0

Blood samples were drawn in thirty-minute intervals.

Table 3. Changes in plasma hydrogen ion and potassium ion concentrations during intravenous infusion of 0.1N hydrochloric acid and 20mM potassium chloride in rabbits

$[H^+]_{pl}$

		Sample number													
		0	1	2	3	4	5	6	7	8	9	10	11	12	13
	1	30.2	34.7	38.9	60.3	77.7	87.1	89.1	123.0						
	2	33.1	34.3	37.2	37.6	38.9	43.7	51.3	53.7	44.7	58.9	61.7	69.2	85.1	
Rabbit	3	57.5	83.2	89.1	93.3	93.3	107.2								
	4	38.0	31.6	33.1	32.4	36.3	38.5	41.7	43.7	53.7	66.1	89.1	95.5	128.8	151.4
	M	31.7	34.5	38.1	43.4	50.9	56.4	60.7	62.5		73.5	75.4	82.4	107.3	152.4

$[K^+]_{pl}$

	1	2.0	2.2	2.5	3.3	3.9	4.4	5.4	10.0						
	2	2.0	3.0	2.3	2.5	2.6	2.8	3.2	3.1	3.4	3.7	4.3	3.9	4.6	
Rabbit	3	3.4	4.1	4.9	6.5	8.0	10.0								
	4	2.0	2.1	2.4	2.6	2.7	2.9	3.1	3.2	3.4	4.5	4.6	4.2	5.5	6.2
	M	2.0	2.2	2.4	2.6	2.7	2.9	3.2	3.2	3.4	4.1	4.5		5.1	6.2

Blood samples were drawn in thirty-minute intervals.

and H^+ concentrations as compared with their separate infusions. It may be that H^+ can move into cells as a result of the H^+-K^+ exchange in low concentrations of extracellular K^+, but the movement of H^+ into cells is interfered with in high concentrations of extracellular K^+. If this

were the case, then the infused HCl cannot be efficiently buffered, and consequently the extracellular H^+ level may increase extensively. As a result, the concentrations of H^+ and K^+ change in the broad range when HCl and KCl are infused simultaneously.

REFERENCES

Adrogué HJ, Chap Z, Ishida T. Role of the endocrine-pancreas in the kalemic response to acute metabolic acidosis in conscious dogs. J Clin Invest 1985; 75:798-808

Adrogué HJ, Madias NE. Changes in plasma potassium concentration during acute acid-base disturbances. Am J Med 1981; 71:456-67

Brown EB Jr, Goott B. Intracellular hydrogen ion changes and potassium movement. Am J Physiol1963; 204(5):765-70

Burnell JM, Villamil MF, Uyeno BT. Effect in humans of extracellular pH change in relationship between serum potassium concentration and intracellular potassium. J Clin Invest 1956; 35:935-9

Carter N, Rector F Jr, Campion DS, Seldin D. Measurement of intracellular pH of skeletal muscle with pH-sensitive glass microelectrodes. J Clin Invest 1967; 46:920-33

Elkinton JR, Singer RB, Barker ES, Clark JK. Effects in man of acute experimental respiratory alkalosis and acidosis on ionic transfers in the total body fluids. J Clin Invest 1955; 34:1671-90

Fenn WO, Asano T. Effects of carbon dioxide inhalation on potassium liberation from the liver. Am J Physiol 1956; 186:567-81

Fenn WO, Cobb DM. Evidence for a potassium shift from plasma to muscles in response to an increased carbon dioxide tension. Am J Physiol 1935; 112:41-55

Giebisch G, Berger L, Pitts RF. The extrarenal response to acute acid-base disturbances of respiratory origin. J Clin Invest 1955; 34:231-45

Keating RE, Weichselbaum TE, Alanis M, Margraf HW, Elman R. The movement of potassium during experimental acidosis and alkalosis in the nephrectomized dog. Surg Obstet Gynecol 1953; 96:323-30

Kurtzman NA, Gonzalez J, DeFronzo R, Giebisch G. A patient with hyperkalemia and metabolic acidosis. Am J Kidney Dis 1990; 15(4):333-56

Lade RI, Brown EB Jr. Movement of potassium between muscle and blood in response to respiratory acidosis. Am J Physiol 1963; 204:761-4

Liebman J, Edelman IS. Interrelations of plasma potassium concentration, plasma sodium concentration, arterial pH and total exchangeable potassium. J Clin Invest 1959; 38:2176-88

Magner PO, Robinson L, Halperin RM, Zettle R, Halperin ML. The plasma potassium concentration in metabolic acidosis: a re-evaluation. Am J Kidney Dis 1988; 11(3):220-4

Nichols G Jr. Serial changes in tissue carbon dioxide content during acute respiratory acidosis. J Clin Invest 1958; 37:1111-22

Polak AG, Hynie D, Hays RM, Schwartz WB. Effects of chronic hypercapnia on electrolyte and acid-base equilibrium. I. Adaptation. J Clin Invest 1961; 40: 1233-37

Ponce SP, Jennings AG, Madias NE. Drug-induced hyperkalemia. Medicine 1985; 64:357-70

Rimmer JM, Horm JF, Gennari FJ. Hyperkalemia as a complication of drug therapy. Arch Intern Med 1987; 147:867-9

Saki Y, Paton BC. Physiologic effects of rapid hemodilution. Arch Surg 1965; 91:887-91

Schloerb PR, Brackett GL, Grantham JJ. Carbon dioxide dissociation in potassium depletion. Am J Physiol 1967; 212:953-6

Schwartz WB, Brackett NC, Cohen JJ. The response of extracellular hydrogen ion concentration to graded degrees of chronic hypercapnia. The physiologic limits of the defense of pH. J Clin Invest 1965; 44: 291-301

Scribner BH, Fremont-Smith K, Burnell JM. The effect of acute respiratory acidosis on the internal equilibrium of potassium. J Clin Invest 1955; 34:1276-85

Scribner BH, Burnell JM. Interpretation of the serum potassium concentration. Metabolism 1956;5: 468

Simmons DH, Avedon M. Acid-base alterations and plasma potassium concentration. Am J Physiol 1959; 197:319-26

Tobin RB. Varying role of extracellular electrolytes in metabolic acidosis and alkalosis. Am J Physiol 1958; 195:687-92