Role of Acid-Base Disturbance on Potassium Transport Along the Nephron

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SUMMARY. We evaluated the role of acidosis on the regulation of transepithelial potassium transport in rabbit early proximal convoluted tubules (PCT) and cortical collecting ducts (CCD) by using in vitro microperfusion and conventional microelectrode methods. In PCT, when the bath medium pH declined from 7.4 to 6.8, transepithelial voltage (Vt) and net potassium flux (JK) increased; however, in CCD, Vt and JK decreased significantly without changing net Na flux. In CCD, basolateral acidosis decreased basolateral membrane voltage and increased transepithelial resistance, with an increment of calculated fractional resistance of apical membrane in principal cells. Inhibition of JK by basolateral acidosis remained significant in the presence of 2mM luminal BaCl₂. Elimination of ambient bicarbonate (Hepes buffer solution) did not affect the inhibitory effect of basolateral acidosis on JK. Basolateral 1 mM amiloride diminished the inhibitory effect of basolateral acidosis on JK. The ⁸⁶Rb and ²²Na efflux coefficients were not significantly affected by basolateral acidosis.

In conclusion, the present study demonstrates that basolateral acidosis affects JK in both PCT and CCD, but it does so in opposite directions. In CCD, basolateral pH is indeed an important modulator of epithelial K transport. Mechanistically, basolateral acidosis appears to inhibit apical K conductance independently of Na conductance or ambient bicarbonate in rabbit CCD.

Introduction

The maintenance of potassium balance is vital in several respects; in particular, a high intracellular potassium concentration is essential for operating cell functions and for keeping the normal electrical gradients across the cell membranes, which is essential for various forms of electrolyte transport. Since the maintenance of potas-
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Potassium balance is critical for the maintenance of cellular metabolism, potassium homeostasis should be efficiently regulated in a narrow range by several mechanisms. The acid-base balance is also critical for cell viability, therefore, several buffering systems should be necessary. It has long been known that changes in acid-base balance have significant effects on both renal and extrarenal potassium homeostasis [1]. It has been generally accepted that acidosis increases, while alkalosis decreases, plasma potassium concentration [2]. A common rule of thumb states that for every 0.1 unit change in blood pH the potassium concentration will change in the opposite direction by approximately 0.1–1.2 mEq/l [3,4]. Whether the acidosis is respiratory or metabolic in origin has an important effect on the magnitude of the hyperkalemic response. Respiratory acidosis causes little increase in the plasma potassium concentration; for every 0.1 unit change in blood pH the plasma potassium concentration increases by only 0.1–0.3 mEq/l [5]. Recent studies have indicated that the relationship between changes of blood pH and plasma potassium concentration is quite complex, and is influenced by several factors, including the origin of the acid-base disturbance, the nature of the anion accompanying the increase in hydrogen ion, change in plasma bicarbonate concentration, per se, duration of acidosis, and extent of intracellular buffering. Extrarenal potassium homeostasis is very important in keeping plasma potassium levels within a narrow range, especially in a rapid potassium loaded condition such as occurs just after meals. Several factors, such as insulin, catecholamines, aldosterone, and maybe other peptides, by controlling renal and/or extrarenal potassium regulatory systems, may contribute to keeping plasma potassium levels constant [1].

We have examined the relationship between acid-base disturbance and potassium transport in hemodialyzed patients [6]. In hemodialyzed patients, erythrocyte potassium concentration increased in patients with severe metabolic acidosis, and the amount of potassium removed into the dialysate was significantly smaller than that in patients without metabolic acidosis. These findings clearly showed the shift of potassium into the cells when metabolic acidosis was corrected by hemodialysis. To confirm this finding, in vitro 86Rb uptake was examined in erythrocytes of control subjects and uremic patients. 86Rb uptake was performed by incubation of cell suspensions of erythrocytes for 60 min with HEPES buffer. Acidification of the incubation medium, from 7.4 to 6.8, diminished Rb uptake significantly, by 15% [7]. In the presence of 10^{-3}M ouabain, Rb uptake was markedly inhibited, and the pH-dependent suppression of Rb uptake was also abolished. In the presence of 10^{-5}M amiloride and furosemide, acidification of the incubation medium failed to suppress Rb uptake in control subjects; however, in uremic patients, furosemide did not affect the pH-dependent suppression of Rb uptake. These data suggested that 1) in extrarenal potassium regulatory mechanisms, erythrocytes also play an important role in regulating plasma potassium level, 2) metabolic acidosis depletes erythrocyte potassium contents, and rapid correction of metabolic acidosis during hemodialysis shifts potassium into erythrocytes, and 3) metabolic acidosis, directly or indirectly suppresses ouabain-sensitive Na-K ATPase activity. In renal potassium homeostasis, a number of clearance studies have demonstrated that both metabolic and respiratory acidosis decrease urinary potassium excretion; in contrast, both metabolic and respiratory alkalosis increase urinary potassium excretion [8–11]. In renal potassium regulatory mechanisms, increased plasma potassium concentration, itself, stimulates urinary potassium secretion [12,13]; however, both metabolic and respiratory