A recent editorial from Goodfriend1 and the article by Chapman et al.,2 published in Hypertension, addressed the noteworthy pharmacological effects of low doses of spironolactone in patients who failed to respond to 3 antihypertensive drugs. Although the mechanisms responsible for the blood pressure–lowering effects of spironolactone are still unclear, the simple fact that a 1-mmol/L increase in serum K was associated with greater systolic blood pressure reduction implies that a reassessment of the role of aldosterone and K ions in essential hypertension is warranted. In this context, 3 major points deserve consideration.

First, the equivocal assumption that serum K accurately reflects body K or cell K function, despite the clinical and experimental evidence, is questionable. In the article by Chapman,2 serum K was measured at 6-month intervals, and despite treatment with drugs affecting cell K uptake and renal K handling, there was no assessment of intracellular K in these subjects. Second, considering that the renin-angiotensin-aldosterone axis plays a critical role in cell K homeostasis, why was aldosterone blockade not considered in these patients at the time of spironolactone treatment? This is a critical point considering the current view on hyperkalemia-related morbidity during aldosterone treatment.3

Third, if such low doses of spironolactone improve the management of hypertension, the use of spironolactone should be carefully reevaluated on the bases of Na intake, body K homeostasis, and used doses. For instance, an increased aldosterone level in a “no-salt” culture, such as Yanomamo, represents a physiological adjustment,4 very different from the mild-to-high levels of aldosterone in hypertensive subjects with a much higher Na intake. This hormonal adjustment may explain why a low dose of aldosterone blockade might be physiologically helpful in hypertensive subjects, whereas large doses may impair both Na/K homeostasis and BP response.

Our findings of nonsodium-dependant low red-cell K transport in essential hypertensive subjects and in half of the normotensive offspring strongly suggest a defective mechanism (genetic?) in cell K transport,5 in which an increased plasma aldosterone could be a nonclassical feedback for such cell K depletion, as recorded in normotensive offspring with lower red blood cell K content. Furthermore, studies documenting that aldosterone plays a physiological role in body K homeostasis and cell K distribution6 might be linked to the protective effects of K in hypertension and organ-target disease as described by Tobian et al.7

These foregoing considerations, thus, may apply to broader aspects in the evaluation and management of essential hypertension, in which a different approach is necessary for the understanding of body K physiology and disorders that occur in hypertensive subjects or that may follow the administration of antihypertensive drugs.8 In brief, aldosterone and cell K physiology in essential hypertension remain fascinating topics as they were decades ago, and this editorial and research article certainly confirmed it.

Disclosures

None.

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Hypertension. 2007;50:e165-e164; originally published online September 10, 2007; doi: 10.1161/HYPERTENSIONAHA.107.099408
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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