

hypokalemia included severe cramps, headaches and vertigo in addition to hypotension. Since death, cardiac arrhythmias and even decreases in blood pressure are the gross end-points of the adverse effects of hypokalemia, these findings are interesting. There are, in fact, a multitude of biochemical effects of potassium deficiency and the accompanying alkalosis that are extremely debilitating but not often clinically recognized. In aggregate, these manifestations of potassium depletion are probably more disabling than the commonly reported cardiac arrhythmias and the more "objective" findings associated with hypokalemia.

It has been proposed that potassium depletion or alkalosis, or both, results in alterations of the potassium-ammonia axis.⁵ Potassium depletion and alkalosis are associated with an increase in the ratio of serum ammonia to blood urea nitrogen⁵ (serum urea). Vascular headaches,⁵ seizures,⁶ memory defects and syncope may occur as consequences of alterations of the ratio. Many of the symptoms, particularly headaches and memory defects, are resolved or greatly reduced by potassium chloride administration.

There is a host of adverse neuromuscular, cardiac and even cognitive effects of hypokalemia. What we need is less debate and more penetrating scientific inquiry to answer the many important questions that remain.

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The recent paper by Drs. Larochelle and Logan comparing the effects of hydrochlorothiazide-amiloride with those of hydrochlorothiazide alone on blood pressure and serum potassium level suffers from a number of deficiencies and omissions that may have the same cause.

The authors state that their concern about diuretic-induced hypokalemia is prompted by studies that have linked hypokalemia to complex ventricular ectopic activity. As Kassirer and Harrington¹ recently pointed out, treatment or prevention of diuretic-induced hypokalemia has been promoted for decades, but the rationale for this effort has undergone many twists and turns. Initially hypokalemia was simply considered unhealthy; later it was felt to induce carbohydrate intolerance and hypercholesterolemia. Both of these theories have since fallen by the wayside. Currently the use of potassium-sparing diuretics or potassium supplements is advocated on the grounds that potassium has a hypotensive effect or because hypokalemia may be linked to sudden cardiac death.

Just as the older arguments for the treatment of hypokalemia were justified by citation of the literature, Larochelle and Logan give three references as substantiating evidence for their thesis. However, they do not inform their readers that the issue of hypokalemia and sudden cardiac death is not one-sided. Three other studies appear to minimize or eliminate the spectre of serious cardiac arrhythmias consequent to mild hypokalemia.²⁻⁴

Moreover, if the authors felt obliged to recommend the use of a potassium-sparing agent along with a diuretic, why did they choose a fixed-dose combination product instead of two separate drugs? The problems associated with adjusting the dose of a combination product to achieve optimum therapeutic results are well known, and, except in a limited number of circumstances, single drugs are considered superior.⁵

The single cause of all of these

problems is, I believe, the source of money that helped to finance the study. Merck Frosst Canada Inc. is acknowledged at the end of the paper as providing financial assistance; it makes the only combination hydrochlorothiazide-amiloride product available in Canada (Moduret), and Moduret is widely promoted for its benefits in preventing hypokalemia-induced arrhythmias.

As one professor of pharmacology has stated, the major pharmaceutical manufacturers do not support comparative studies that might show their product to be inferior.⁶

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Cancer risks among residents of Manitoba Indian reserves, 1970-79 [correction]

In Table I of the article by Drs. T. Kue Young and N.W. Choi (*Can Med Assoc J* 1985; 132: 1269-1272), the site or type of cancer for code 189 should have read (with the correction in italics) "Kidney/other urinary".—Ed.