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Magnesium (Mg) and potassium (K) deficiencies frequently coexist in clinical practice, most commonly as a result of poor gastrointestinal absorption or renal conservation, secondary to intrinsic disease or its treatment. Suboptimal Mg intake makes its renal conservation critical, especially in seriously ill catabolic hospitalized patients, many of whom have protein-calorie-malnutrition, which further compromises cation homeostasis. Precription of diuretics and other agents that cause Mg- and K-wasting can readily provoke loss of intracellular (i.c.) cations, that is not diagnosed by tests of serum levels. Direct i.c. measurements may disclose major deficiencies, that can exist in the presence of normal serum values. In the case of Mg, loading tests may provide indirect evidence of i.c. deficiency, that can complicate the care of high risk patients. Mg deficiency disrupts cellular function and integrity, with impairment of cellular bioenergetics, increased membrane permeability, and dysfunction of the Na/K adenosine triphosphatase pump and other enzyme systems, resulting in K-depletion and Ca-overload. K-therapy, alone, may fail to correct low serum and/or i.c. K- levels. Indeed, the frequent use of high doses of K, without correction of the Mg deficiency, can further exacerbate the combined deficiencies, through stimulation of aldosterone secretion.

Deficiency of either Mg or K is arrhythmogenic; the aged ischemic myocardium in the setting of myocardial infarction is particularly vulnerable to the cation deficiencies. Refractory ventricular and atrial arrhythmias have responded to repletion of either or both cations, after failure of conventional antiarrhythmic agents that were given without correction of the deficiencies. Digoxin toxicity frequently occurs despite non-toxic serum levels, with the toxicity attributable to Mg and K deficiency from concomitant diuretic therapy. Occult Mg deficiency may be at least as common as hypokalemia in this setting, and the gratifying response to Mg therapy, regardless of a normal serum value, may be in keeping with an i.c. deficit, as well as with the well documented pharmacologic efficacy of Mg and K in digoxin toxic arrhythmias. Increased cardiac mortality in mild hypertension trials such as the Mr FIT and the comparable HDFP programs have led to speculation as to the arrhythmogenicity of the diuretic-associated hypokalemia as a risk factor for sudden death. Extracellular (e.c.) changes in K are more important in determining resting membrane potential and electrical stability of the heart than are i.c. cardiac levels - which may be preserved in the face of total body deficiency - provided there is not concomitant Mg depletion. Thus, complacency regarding total body K, in the face of small changes reported in hypertensives treated with diuretics is unfounded, in view of the critical roles of i.c. K and Mg - both of which can be depleted by long-term use of diuretics. Catecholamine surges can also have profound adverse effects on e.c. K, through enhanced skeletal muscle K uptake. This can be especially critical in patients with myocardial infarction. Diuretic-induced intensification of Mg deficiency increases the vulnerability to arrhythmia of hypertensive patients, both through direct effect on K, and by increasing the secretion of catecholamines - which in turn adversely influences myocardial Mg uptake, and induces lipolysis, which further reduces the available Mg pool. K is antiarrhythmic in patients with myocardial infarction in combination with glucose and insulin. It has been suggested that addition of Mg to GIK (termed MAGIK by E.B. Flink) might improve the therapeutic effect.