Does Hypomagnesemia Have an Adaptive Role in Hypertension?

To the Editor:

Northcott and Watts investigate association of hypomagnesemia with hypertension; these authors conclude that activation of phosphatidylinositol 3-kinase by low extracellular magnesium concentration enhances arterial tone.1 As indicated by these authors, despite many experimental and clinical studies, the cause–effect relation between magnesium and hypertension nevertheless remains uncertain.

Magnesium supplementation has not produced consistent results in hypertensive patients.1 The specific cardiac and generally adaptive role of magnesium depletion in a wide variety of clinical conditions unassociated with hypertension has not been appreciated.2,3 Whereas the clinical futility of magnesium supplementation in acute myocardial infarction (AMI) has finally been accepted after many randomized clinical trials (RCTs),4 because the end-point of trials in hypertension is rather nebulous when compared with the end-point of trials in AMI (death), the issue of the cause–effect relation between hypertension and hypomagnesemia is unlikely to be resolved by trials. Randomization is a purely mathematical strategy that uses the uncertainty principle.5 RCTs attempt to eliminate through mathematical logic natural patient-to-patient idiosyncracy, including the placebo effect, these being biologically irreducible realities. Results of RCTs, therefore, express the outcomes of uncertainty at several levels, and the biological impact of the placebo effect probably can neither be identified reliably nor eliminated completely. In no 2 patients with hypertension (as well in the same patient on different occasions) can we expect the impact of the many known factors that influence blood pressure, including the emotional state, to be identical during the pretrial, placebo run-in, or trial periods regardless of parallel or crossover designs. In the absence of sufficient conceptual groundwork, RCTs tend to misguide clinicians particularly in conditions that are subject to spontaneous variations.

Further studies in humans of magnesium supplementation to revert upregulated signaling pathways to normal do not appear warranted. By enhancing arteriolar tone, magnesium depletion in hypertension possibly limits tissue hyperperfusion as a homeostatic function. This teleologic function may be important in vital tissues such as lungs and brain; failure of such adaptation may set the stage for the development of hyperperfusion states such as pulmonary (left ventricular failure) or cerebral (hypertensive encephalopathy) edema. Paradoxically, such an adaptive function of hypomagnesemia would be attenuated by exogenous administration of magnesium in hypertensive patients.

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