Circulating magnesium and cardiovascular events

Dear Sir:

In their systematic review and meta-analysis of prospective studies, Del Gobbo et al (1) showed an inverse association of magnesium concentrations with the incidence of cardiovascular disease, including fatal and nonfatal ischemic heart disease (IHD). Yet, another recent meta-analysis (2) has reported a beneficial effect of dietary magnesium on cardiovascular disease mortality among women but not among men. However, the meta-analysis by Del Gobbo et al (1) went one step further by analyzing circulating magnesium, which may suggest the key mechanism of the whole issue.

All of the studies included in the meta-analysis by Del Gobbo et al (1) that investigated magnesium in women, either by dietary intake or by circulating concentrations, showed a significant protective effect against IHD incidents (3–5). Among studies that reported strictly on circulating magnesium in women, Chiuve et al (4) showed an inverse association with sudden cardiac death, whereas Liao et al (3) reported a trend toward the decreased risk of IHD. Circulating magnesium is directly regulated by renal function (6). On the contrary, dietary magnesium is mostly associated with individual nutrition and dietary habits. Importantly, there is a low correlation between dietary intake and circulating magnesium concentrations.

There are reasons why we should distinguish between circulating magnesium concentrations and dietary magnesium and also separate men from women. Prolonged corrected QT (QTc) interval is associated with an increased risk of potentially fatal ventricular tachyarrhythmias (7–13). Intravenous magnesium has been used for treatment and prevention of ventricular tachycardia (8, 11), ventricular fibrillation (10, 13), and polymorphic ventricular tachycardia (7, 12). Because QTc prolongation is more often present in women, we suggested that the beneficial effect of magnesium could be more pronounced in female patients (14). Pathophysiologic mechanisms may include antagonism at the L- and T-type calcium channels (15), membrane stabilization (16), reduced frequency of ventricular ectopic beats (17, 18), and conversion to sinus rhythm (7, 8, 10, 19, 20). Accordingly, there is a compelling evidence of benefit from intravenous magnesium application, and so the effect of the circulating magnesium concentration could be substantial for its cardiovascular effects. The facts that intravenous magnesium is effective against ventricular tachyarrhythmias through mechanisms which include prolongation of the QT interval, and that QTc interval is more often prolonged in women could underlie a better antiarrhythmic protection in women than in men.

Perhaps Del Gobbo et al could separate the effect of circulating magnesium in men and women and provide the pooled results. The problem of a low correlation between dietary and circulating magnesium must be accounted for in future research.

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REFERENCES
Vitamin D concentration and disease risk: the concerns

Dear Sir:

In their interesting retrospective cohort study, Quraishi et al (1) highlight the increased risk of hospital-acquired bloodstream infection (HABSI) in 2135 adult patients from 2 Boston teaching hospitals with lower serum 25-hydroxyvitamin [25(OH)D] concentrations. The study analysis in adult patients shows that 25(OH)D concentrations <10 ng/mL before hospitalization were associated with significantly increased odds of developing HABSI. Current research on vitamin D has highlighted its important role as a key regulator of innate and adaptive immune systems that may influence host susceptibility to infections. The study by Quraishi et al has also necessitated the initiation of randomized trials to test the role of vitamin D supplementation to reduce the burden of HABSI. In this regard, several interesting facets of 25(OH)D concentrations warrant attention. First, the requirement of optimal 25(OH)D concentrations for the induction of antimicrobial host-defense mechanisms via Toll-like receptor (TLR2, TLR1) stimulation provides a crucial basis for clinical observations in infections (2). This is discussed by Quraishi et al in addition to discussion of depressed macrophage phagocytosis, chemokinesis, and proinflammatory cytokine production as a result of low 25(OH)D concentrations (1). Reports also show that activation of TLRs results in secretion of antimicrobial peptides by tracheobronchial epithelial epithelial cells that facilitate the development of adaptive immune responses at the site of infection (3). Therefore, the presence of vitamin D metabolites is important for the proper induction of host-defense mechanisms and suggests that vitamin D supplementation should be carefully examined. Second, substantial seasonal variation in concentrations of 25(OH)D at the population level is an important aspect that needs attention (4). Quraishi et al (1) analyzed the 25(OH)D concentrations in patients before hospitalization between 1993 and 2010. Their observational findings depend on multivariable analyses and suggest that vitamin D supplementation may provide a novel approach to lowering HABSI risk. However, the seasonal variation in vitamin D concentrations adds to the complexities in vitamin D epidemiology and requires much consideration before widespread supplementation is implemented (5). Third, it was importantly noted that vitamin D metabolism and concentrations vary widely according to race-ethnicity (6). Interestingly, baseline 25(OH)D concentrations are lower in blacks, and their response to supplementation with respect to clinical outcomes may differ from that in whites (7), suggesting caution for supplementation with an emphasis on racial information. Fourth, 25(OH)D concentrations are known to induce the genomic regulation of fetal development and hence add to risk factors for childhood diseases (8). The Vitamin D Antenatal Asthma Reduction Trial (VDAART; registered at clinicaltrials.gov as NCT00856947) aims to supplement 25(OH)D in pregnant mothers to reduce the risk of asthma in their children. Therefore, the 25(OH)D concentrations in mothers may add some crucial findings in studies with children population. Fifth, interestingly, Welsh et al (9) explained 25(OH)D deficiencies as “reverse causality” in which there is a chance that poor health conditions will dictate low 25(OH)D concentrations, rather than the reverse. Conversely, studies suggest that 25(OH)D concentrations decrease significantly during the acute-phase response (10). In conclusion, all of these factors are crucial in the context of 25(OH)D-related population studies, potentiating the need for a multifaceted approach during further interventions.

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