Low Serum Magnesium and Obesity – Causal Role or Diet Biomarker?

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The association between low magnesium (Mg) status, and insulin resistance and the metabolic syndrome has been shown repeatedly in adults [1], and higher Mg intakes have been shown to have a protective role [2]. This leads to the tantalizing conclusion of a mechanistic involvement of Mg in weight gain and insulin resistance through its critical role as a cofactor in several enzymes in carbohydrate metabolism [1]. However, the Km of Mg for these enzymes is close to its intracellular concentration, which does not decline easily on Mg deficient diets [3]. The effect is also subtle: the adjusted risk for diabetes with quite low (<1.7 mg/dL) serum Mg levels have been shown to increase modestly by about 1.5 fold [4]. Furthermore, reverse causality is also possible: diabetes is known to increase renal Mg excretion, and insulin resistance decreases Mg uptake. Therefore, the theoretical framework that links low Mg status to obesity and insulin resistance is not simple. The relation between obesity and Mg is also not clear. Several studies have assessed the association between body mass index and Mg intake or status in adults, but the results are still controversial [2,5]. This may be because the associations of low serum Mg with obesity related outcomes are subtle and subject to type 2 errors. In this issue of *Indian Pediatrics*, Jose, *et al.* [6] have found that serum Mg was lower in obese Indian children, but this counter-intuitively occurred with apparently higher Mg intakes. The authors are careful not to imply any mechanistic linkage either way, but speculate that the

aggravation of the insulin resistant state with low serum Mg could start early in childhood. Measuring Mg status accurately is challenging, since serum Mg is only about 1% of the total body Mg, and most probably reflects its renal handling rather than its dietary intake. A very low Mg diet (<10%) in a human subject in 'excellent health' led to a drop by about 0.4 mg/dL in serum levels, along with negative balances, but no drop in intracellular levels [3]. On the other hand, intracellular Mg depletion has been found with normal serum Mg concentrations [1]. The point is that Mg intake cannot easily be related to serum level or status. Pre-analytical factors, including the effect of prior exercise on serum Mg, are also important. Nevertheless, given the observation that the obese children had a higher energy adjusted Mg intake [6], the low serum Mg levels are likely to be an 'effect' rather than a cause. The authors' opinion is that the observed differences could have been due to decreased Mg absorption or increased excretion. Both these mechanisms are plausible. The questions relate to how and why. For example, one could enquire whether the obese children had a higher calcium (Ca) intake, since this is known to interfere with Mg absorption. Indeed, dairy products are high in Ca and low in Mg content. The intake of carbonated soft drinks, with higher intakes of phosphorus could also interfere with absorption while caffeine can increase renal Mg excretion [7]. A vegetarian and unprocessed food-based diet, such as with whole grains, nuts, and green leafy vegetables, is high in Mg, which is lost during processing. Therefore, in studies that investigate associations between serum Mg and other outcomes, it is critical to have a close inspection of the dietary environment. Observational studies such as those by Jose, *et al.* [6] are important in a transitioning society with changing processed food intake; however, longitudinal studies with detailed food intake assessment are required to assign causality or to assess the potential interaction with insulin resistance. Until then, the role of Mg will remain enigmatic, the need for supplements unclear, and serum Mg may simply have to continue to be considered as a biomarker for a particular type of diet. *Competing interests:* Dr Kurpad is a member of the Kraft Health and Wellness Global Advisory Board; *Funding:* None.

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