Dietary Micronutrients Reduce Insulin Resistance via Adipose Tissue Modulation in Mice Fed a High Fat Diet

Zeyu Yang, Ruslan Kubant, Jacqueline Beaudry, and G. Harvey Anderson

University of Toronto

Objectives: Obesity is associated with increased insulin resistance (IR) and white adipose tissue (WAT) dysregulation (e.g., decrease in PPAR-γ mRNA expression and impaired leptin sensitivity). Dietary vitamins A, B1, B6, and B12, selenium (Se) and zinc (Zn) have been shown to reduce IR in obesity in animals and humans, but mechanisms have not been defined. The objective of this study is to investigate the effects of selected micronutrients on adipose tissue metabolism and IR in a mouse model of diet-induced obesity (DIO). We hypothesize that these additions modulate genes regulating IR in WAT and improve leptin sensitivity.

Methods: 28 DIO male mice were randomly assigned to two high fat (HF, 60 kcal % fat) diets with or without the inclusion of a mineral-vitamin mixture (MVM: 5 × vitamin A, B1, B6, B12, zinc, and 2 × selenium), respectively. Similarly, 28 lean mice were randomized into a low-fat diet (LF, 10 kcal % fat) with or without the MVM. Mice were fed diets ad libitum for 8 weeks. Bodyweight (BW), IR, serum glucose, fasting insulin, C-peptide, leptin, as well as mRNA expression of genes involved in insulin signaling and adipokine secretion were measured in epididymal white adipose tissue (eWAT).

Results: Compared to HF mice, HF-MVM mice exhibited reduced body weight gain over time (by 6%, $P < 0.05$), improved insulin sensitivity ($P < 0.05$), reduced fasting glucose (by 18%), insulin (by 45%), C-peptide concentrations (by 26%) and Homeostatic Model Assessment for Insulin Resistance (by 47%, HOMA-IR, $P < 0.05$ for all). Similarly, LF-MVM had reduced fasting glucose level ($P < 0.05$) compared to LF mice. As expected, serum leptin concentration (adjusted for a visceral fat mass) was 6-fold higher in HF mice compared to LF mice; HF-MVM mice had lower leptin level compared to the HF mice suggesting improved leptin sensitivity. Ppar-γ gene expression in eWAT was 77% lower in HF vs LF group, suggesting eWAT dysfunction and systemic IR in DIO mice; the addition of MVM to LF diet attenuated this effect.

Conclusions: This MVM mixture may reduce IR through the up-regulation of the PPAR-γ system in WAT and improve leptin sensitivity in DIO. Understanding the mechanism of action of micronutrients in reducing IR in a highly relevant animal model will provide new avenues for identifying food component solutions to modify IR in humans.

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