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Review Article and Clinical Experience: The Roles of Micronutrients in The Treatment of Diabetes Mellitus (Focus on Chromium and Specific Nutrients)

Abstract

It is estimated that the glucose disposal of whole body insulin sensitivity reflected by the muscles, liver, and adipose tissues are approximately 60%, 30%, and 10%, respectively. However, the adipose tissue may play a pivotal role in the induction of Insulin Resistance (IR) in the muscles and the liver. Marked impairments in insulin’s intracellular signaling cascades are present in fat cells of Type-2 Diabetes Mellitus (T2DM), including: 1. reduced IRS-gene and protein expression, 2. reduced IRTK activity, 3. impaired insulin-stimulated PI3-kinase activity, 4. impaired PKB / Akt activity, and 5. reduced GLUT 4 expression. These impairments are also found in some (~30%) normoglycemic individuals with genetic predisposition for T2DM. The Syndrome-X was firstly coined by Reaven in 1995 and then to be provided in 1999 by the name: the Metabolic Syndrome-X. This Syndrome represents a "Cluster" of metabolic disorders and cardiovascular risk factors which includes: 1. Insulin Resistance / Hyperinsulinemia, 2. Central Obesity, 3. Glucose Intolerance, 4. Atherogenic Dyslipidemia (&uarr; TG, &darr; HDL-Chol., &uarr; Apo-B, &uarr; Small Dense LDL), 5. Hypertension, 6 Proteombotic State (&uarr; PAI-1, &uarr; F-VII, &uarr; Fibrinogen), 7. Endothelial Dysfunction, and 8. Hyperuricemia. Such a &ldquo;Cluster&rdquo; may lead to the development of T2DM and Coronary Heart Disease (CHD). An excessive Free Radicals (FR) production (caused by the antioxidant's levels to fall below the normal in T2DM) is thought to play significant roles in the development of Diabetic Vascular Complications (DVDs). Several antioxidants such as Raxofelast (600 mg bid), Thiotic Acid (Alpha Lipoic Acid), Vit.C, Vit.E, Zn have been reported to be successful in overcoming Oxidative Stress. Hence, it is rational to deduce that antioxidant micronutrients would be useful in patients with T2DM). Clinical evidences indicate the benefit effects of selected minerals, trace elements, and vitamins such as: Cr, Mg, Zn, Cu, (and others: Mn, I, Se, Fe), and vitamins (B1, B6, B12, Folic Acid, Niacin, Biotin, C, E). Such beneficial effects include: the improvement of insulin secretion and peripheral sensitivity, carbohydrate metabolism, and lipid profiles, even the protective effect against tissue damage caused by lipid peroxidation. It can be summarized from several studies that supplemental Chromium (Cr), 200ug until 1000 ug per day to patients with T2DM for 1-10 months showed beneficial effect; increased insulin binding to cells, insulin receptor number, and activated Insulin Receptor Tyrosine Kinase = IRTK (8-fold) leading to increased insulin sensitivity. Chromium also inhibits Phospho Tyrosine Phosphates (PTP-IB) that inactivates the insulin receptor. Theactivation of IRTK by Cr and the inhibition of insulin receptor tyrosine phosphatase lead to the increased phosphorylation of the insulin receptor and to the increased insulin sensitivity. In a double blind, placebo controlled study (with T2DM patients), Cr was shown to improve glucose, insulin, cholesterol blood levels and AIC in a dose-dependent manner (200-1000 ug/day) after 4 months. A Cluster of determinant factors for the risk of Cardiovascular Diseases called Syndrome-37 will be listed. Conclusion: Insulin resistance and compensatory hyperinsulinemia lead to the development of the Metabolic Syndrome-X. Oxidative Stress in Diabetes Mellitus caused the increased risk of atherosclerosis. Clinical evidences show beneficial effects of micronutrients especially in insulin secretion and peripheral sensitivity, glucose homeostasis, and lipid profiles, even in neutralizing free radicals. Hence, micronutrients (esp. Chromium) have potential therapeutical benefits for patients with Diabetes Mellitus.

Keyword : micronutrients, Diabetes, Mellitus, chromium, ,

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