

Relationship Between Insulin Resistance and Endothelial Dysfunction/ Cardiovascular Diseases: The Importance of Method Consideration in Interpretation of Serum Insulin Level

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In recent years, it has been demonstrated that insulin resistance and endothelial dysfunction play a crucial role in the pathogenesis of atherosclerosis. Insulin resistance is the primary pathophysiological problem responsible for certain metabolic and cardiovascular disorders known as metabolic syndrome. Endothelial-derived nitric oxide (NO) deficiency is thought to be the main defect linking the insulin resistance to endothelial dysfunction. NO deficiency results from decreased synthesis with over consumption in tissues by high levels of reactive oxygen and nitrogen species, that are produced by cellular disturbances in glucose and lipid metabolism. Inflammatory reaction caused by lipid accumulation and oxidative stress in the vessel wall causes the release of chemoattractants and cytokines. This worsens insulin resistance and endothelial dysfunction. Clinically, experimental evidence revealed the success of treatments that improve insulin resistance and endothelial dysfunction. These therapies reduce cardiovascular morbidity and mortality such as remedies or nutrients rich for NO and treatments that reduce insulin resistance [1]. NO is produced via the classical L-arginine-NO-synthase pathway and enterosalivary nitrate-nitrite-NO pathway. This alternate pathway has revealed the importance of dietary nitrate from the aspect of the cardioprotective effect of a diet rich in vegetables and fruit. In clinical trials with dietary nitrate, improvements in blood pressure, endothelial function, ischemia-reperfusion injury, arterial stiffness, platelet function, and exercise performance have reported with a simultaneous increments of markers of NO status [2].

Some issues should be considered in the evaluation of insulin resistance. Insulin analysis is frequently used for both research and clinical purposes. Currently there is no reference method for insulin assays [3]. Insulin measurement improves the classification and management of diabetes mellitus and helps in treating subjects with insulin resistance. In addition, calculating homeostasis model assessment (HOMA), frequently used in research studies, is currently problematic mostly due to its dependency on the absolute value of insulin. In a study comparing serum insulin measurements with different assays including two chemiluminescence, four ELISA, and two IRMA methods, maximum of 1.8-fold difference was reported [4]. This difference should be taken into account when interpreting circulating insulin levels. Care should be taken when comparing the results of insulin levels and insulin sensitivity/resistance indices from different research studies.

We conclude that insulin resistance measurements and nitric oxide precursor rich nutritional supplements may be beneficial in order to prevent cardiovascular diseases, to take precautions in the early period, and to support the treatment protocols of patients. Also, it should be considered to follow patient insulin levels by using laboratory results performing the same insulin measurement method.

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