Insulin Resistance: Quest for Surrogate Markers

Insulin resistance (IR) is defined as a decreased response of the peripheral tissues to insulin action. IR results from the inability of insulin to act normally in regulating nutrient metabolism in peripheral tissues. Individuals with IR are prone to develop type 2 diabetes mellitus. IR has been recognized as the integral feature of the so-called metabolic syndrome, which includes glucose intolerance, IR, obesity, hypertriglyceridemia, low HDL cholesterol, hypertension, and accelerated atherosclerosis.[1]

The presentation of IR depends on the type and stage of the resistance. Many patients do not develop overt diabetes despite extreme IR. Other patients present with cases of severe hyperglycemia that require large quantities of insulin and may present with the classic symptoms of diabetes mellitus, such as polyuria, polydipsia, polyphagia, and weight loss. Others may present as metabolic syndrome, obesity, history of hypertension, coronary artery disease, etc.[2]

IR is an established independent predictor of a range of disorders. As resistance to insulin sets in long before any disease signs start appearing, so it is important to categorize and treat individuals with IR as early as possible.[3] Moreover, IR affects a wide array of disease, so medical science is always on the lookout for sensitive and specific surrogate markers for IR so as to have early detection and treatment. Besides markers serve as sensitive detectors of early target organ damage.[4]

Various methods employed to measure IR include – hyperinsulinemic-euglycemic glucose clamp, oral glucose tolerance test, measurement of fasting insulin levels, glucose/insulin ratio, insulinogenic index, homeostasis model assessment, quantitative insulin sensitivity check index, etc.[5] However, most of these methods are difficult to apply in clinical practice for various reasons – require repeated blood sampling, require measurement of insulin levels, and analytical methods for measuring insulin levels are not standardized across all laboratories;[6] there is need to have secondary derived surrogate markers for IR.

Various derived markers in use for IR are – Matsuda index, Gutt index, Stumvoll index, and Avignon index; all applying mathematical equations.[5] Some newly marked markers for IR, mostly products/substrate of inflammation are – insulin growth factor binding protein-1, C-reactive protein, ferritin, adiponectin, and tumor necrosis factor-alpha, etc.

However, the buck does not stop here. Recently, the relationship of leptin and adrenomedullin has been studied as markers of IR particularly in polycystic ovary disease patients, and a positive association has been found.[7,8] These two may prove to be markers of the future for IR

and may augment the already enriched kitty of markers for IR.

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