Insulin-Resistance in Non-Diabetic Volunteers Provides a Trade-off for Better or Worse

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Editorial

Recently, my group published a series of papers examining the presence of Insulin Resistance (IR) estimated by Fasting Blood Glucose levels (FBG) on many aspects of health during the “continuum of risk” phase of glucose-insulin balance in non-diabetics [1]. To clarify, the continuum of risk phase represents a diagnostic range which has not yet reached a level that establishes presence of a definitive medical perturbation in the case of diabetes mellitus for our purposes a consistent level of fasting blood glucose below 125 mg/dl [2]. The major reason behind these publications was to more firmly establish a need for early preventive measures to deter serious future chronic metabolic health maladies via sustaining the most optimal state of insulin sensitivity and avoiding resistance. Employing data attained from relatively healthy non-diabetic volunteers, correlations between the relatively mild IR and a variety of chronic metabolic perturbations associated with aging and even the aging process itself that had both good and bad outcomes (trade-offs) were scrutinized [1-4]. To further clarify using the concept of continuum of risk here, we originally based our supposition concerning glucose-insulin metabolism on common clinical knowledge concerning blood pressure. It is generally accepted that systolic blood pressure in the non-hypertensive range is best kept at the lowest level short of hypotension for optimal health [5]. Accordingly, would maintaining a low FBG (indicating a low level of IR) short of hypoglycemia provide enough benefit for a longer happier life span possibly by ameliorating long-term effects of IR on elements making up the Metabolic Syndrome (MS) including type 2 Diabetes Mellitus (T2DM) and Non-Alcoholic Fatty Liver Disease (NAFLD) [3,6]. However, before proceeding, it becomes necessary to establish use of Fasting Blood Glucose (FBG) as a surrogate for IR [1,7]. Characteristically, circulating glucose and insulin rise gradually over time. Nevertheless, despite the persistent elevations, both will remain in the continuum of risk range in most individuals the scenario of most interest in the present report. Suffice it to say, this occurs because insulin often loses sensitivity over time in its actions to enhance glucose uptake of principal organs such as liver, fat and muscle. Much of sensitivity loss of Insulin (IR) is due to lifestyle shortcomings in diet and exercise, as well as the aging process itself [8,9]. In response to this evolving IR, more insulin is released attempting to bring the circulating glucose back toward normal; but this goal, more often than not, is not often achieved. Eventually circulating insulin continues to increase in the circulation. This back and forth interplay of rising glucose-insulin levels in non-diabetics frequently persists. Although in the majority of cases, this interaction may not lead to diagnosed diabetes, it theoretically can do damage anyway [10,11]. Based on the above, we submit that the rise in FBG in response to IR can be that practical surrogate for IR [7]. What strengthens this belief? Throughout the literature, serum insulin levels have been proposed to be an ideal reflection of IR [12,13]. Nevertheless, FBG values offer a more ideal representative than insulin, because they are checked routinely and readily available in offices and clinics for analyses [14]. More reassuring of value, FBG has been shown to correlate positively with insulin measurements [1]. Using FBG as a surrogate for IR, statistically significant positive correlations were found in non-diabetes between FBG and body weight, fat mass, systolic blood pressure, levels of triglycerides, markers for inflammation [hsCRP, WBC and neutrophil count], as well as ALT to indicate higher levels of fat accumulation in the liver [1,14]. In keeping with the diagnosis of MS, HDL-cholesterol was shown to have a significantly negative correlation with FBG [1,14]. So, FBG at non-diabetic levels corresponds closely with many risk factors recognized in T2DM, MS, and NAFLD [1,15,16]. This leads us to our recognition of a trade-off. Insulin rise gradually over time. Nevertheless, despite the persistent elevations, both will remain in the continuum of risk range in most individuals the scenario of most interest in the present report.
when attempting to lower circulating glucose to healthier levels [21]. More appropriate to our interpretation of trade-off centering on non-diabetics, the trade-off focuses on the natural compensatory attempt to lower glucose levels through enhanced insulin release. In this situation, the immediate pro is the lowering of the circulating glucose levels; the con is the long-term, heightened insulin activity and other compensatory responses adversely affecting the rest of the body. These unfortunate changes during a continuum of risk period are not routinely perceived and if casually so are not readily treated by means that could produce a real beneficial response by ameliorating the low-grade IR. Important to reemphasize, it has been postulated previously that IR, even in relatively mild forms, could lead to serious health situations with the passage of time [3,6]. In support of this statement, lowered FBG levels along with many of associated manifestations including general inflammation have been shown to decrease in elderly surviving volunteers in our studies after age 65 years despite gradual steady elevations prior this later age period [3,6]. This has been de-scribed as the “Aging Paradox.” If due to “Survivor Bias’ because of maintenance of a more ideal glucose-insulin status over their lifespan Implications. J Am Coll Nutr. 2019;10:1-9.

References


