Insulin resistance in Human Diseases

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ABSTRACT

Insulin resistance may play an aetiopathogenetic role in NIDDM, hypertension and coronary artery disease. Insulin resistance has been demonstrated in a variety of conditions. The exact mechanism of insulin resistance has yet to be elucidated. It may occur at the pre-receptor, receptor or post-receptor level.

INTRODUCTION

Insulin resistance is a fairly common phenomenon and has gained importance relatively recently because of its possible aetiopathogenic role in the clinical course of three inter-related disease entities: non-insulin-dependent diabetes mellitus (NIDDM), hypertension (HT) and coronary artery disease (CAD). Insulin resistance per se is an accompaniment of a variety of conditions, some congenital, others acquired (1). With better means of detection it is being discovered in many more conditions. Further, the mechanisms of this resistance are becoming clearer giving better insight into the subject.

REVIEW OF LITERATURE:

Resistance to insulin was first demonstrated 50 years ago when a classification of diabetes based on insulin resistance was suggested. The 'insulin resistant' diabetes that was proposed at that time found a near synonym in NIDDM, as evidenced by the elevated plasma free fatty acid concentrations in NIDDM (2). Further studies indicated a partial resistance to insulin in NIDDM. This resistance did not affect insulin-stimulated glucose uptake but prevented insulin from lowering plasma free fatty acid (FFA) concentrations (3).

One of the first relationships of insulin resistance with hypertension came to be known with discovery of post-prandial hyperinsulinemia in patients with mild essential hypertension (4). Further studies (5-7) stressed this, particularly in the presence of obesity, and pointed to a possible cause-effect relationship. This may have serious implications because free fatty acid concentrations as a result of insulin resistance may play a major role in the pathogenesis and mortality of CAD (8).

Insulin resistance has been demonstrated in a variety of conditions such as hypo-and hyper-thyroidism (9), aplastic anemia (10), post cardiac surgery (11), polycystic ovarian syndrome (12), tropical diabetes (13), diabetic ketoacidosis (14), old age (15), uraemia (16), S jogren's syndrome (17) and acromegaly (18).

Although mechanisms of insulin resistance are being elucidated, we are as yet far away from a complete understanding of the same. Possible mechanisms suggested include post-receptor binding defects in pyruvate dehydrogenase (19), defects pertaining to pancreatic amylin and calcitonin gene related peptide (20), insulin-like growth factor I receptors (21), dietary carbohydrate (22), insulin receptor kinase (23), insulin receptor autophosphorylation (24), cytosolic free calcium concentration (25) and insulin receptor antibodies (16). Various therapeutic modalities appear to decrease this resistance to insulin. These include exercise (26), d-fenfluramine (27), metformin (28), interferon (29), dexamethasone (30), weight reduction (31) and oral vandate therapy (32).

CONCLUSIONS:

1. Insulin resistance is a common phenomenon intimately related to the trial of obesity, hypertension and NIDDM and found in a number of other distinct disease entities.

2. This insulin resistance, by causing persistently elevated plasma FFA concentrations, is an important factor in the development of CAD.

3. Mechanisms of insulin resistance are manifold and may be at pre-receptor, receptor and post-receptor level.

4. If the problem of insulin resistance is overcome it could decrease the mortality due to CAD.

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