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Effect of Weight loss on Insulin Resistance

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Abstract

Insulin resistance refers to the diminished physiological response to insulin, particularly in target tissues such as the liver, skeletal muscle, and adipose tissue. This condition can arise from both genetic and acquired factors, with lifestyle aspects like physical inactivity and increased central fat being significant contributors. The most prevalent complications associated with insulin resistance include Type 2 Diabetes Mellitus and non-alcoholic fatty liver disease. Additionally, due to the reduced clearance of glucose related to insulin resistance, there is an increase in insulin production by beta cells, which results in hyperinsulinemia. Interleukins IL-1 and IL-6 also play minor roles in insulin resistance by affecting insulin signaling pathways and the functioning of both beta and alpha cells. Effective management strategies for insulin resistance primarily involve controlling weight through dietary changes and engaging in regular physical activity.

Keywords

Diet; Physical activity; Insulin resistance Insulin sensitivity; Metabolic syndrome; Type 2 diabetes; Weight loss.

Introduction

The B cells in the pancreas produce insulin, an anabolic hormone that plays a critical role in regulating blood glucose levels. Insulin resistance refers to a diminished biological response to insulin stimulation. While insulin receptors are present in various tissues, the skeletal muscle, liver, and adipose tissue are the most responsive. Both genetic and acquired factors may contribute to insulin resistance. Type A and Type B insulin resistance represent two genetic forms [1]; Type A is rare and results from mutations in the insulin receptor gene, leading to complications such as impaired glucose homeostasis, skin tags, and acanthosis nigricans. In contrast, Type B is driven by an autoimmune reaction against insulin receptors, initially noted in diabetic patients exhibiting severe insulin resistance. It is now understood that antibodies

against insulin receptors can cause glucose regulation issues, producing effects from intense insulin resistance to life-threatening hypoglycemia [2].

Acquired causes include decreased physical activity and increased body fat, along with medications such as glucocorticoids, selective estrogen receptor modulators, protease inhibitors, and atypical antipsychotics. Hormonal disorders such as acromegaly, Cushing's syndrome [3], and hypothyroidism also contribute to insulin resistance. In response to insulin resistance, the pancreas increases beta-cell insulin production, which leads to hyperinsulinemia. Metabolic consequences of this condition include hyperglycemia, hypertension, dyslipidemia, endothelial dysfunction, and a prothrombotic state, with type 2 diabetes (T2D) being the most prevalent outcome. It is believed that insulin resistance can develop 10 to 15 years prior to the onset of T2D.

Interleukin-6 (IL-6) and the balance between IL-1 and IL-1 receptor antagonists are significant in this pathological framework. IL-1α and IL-1β can disrupt insulin signaling by modifying insulin receptor substrate phosphorylation and reducing the expression of various components essential for insulin-regulated glucose transport [4]. These interleukins are likely implicated in the pathophysiology of insulin resistance and type 2 diabetes by affecting insulin signaling pathways and the function of beta and alpha cells. Thus, the primary focus of treating insulin resistance should be lifestyle modifications. Nutritional strategies are essential, emphasizing calorie reduction and the avoidance of carbohydrates that elevate insulin demand. Additionally, physical activity can enhance energy expenditure and improve insulin sensitivity in skeletal muscle [5].

Method

In order to conduct this systematic review, we searched the medical literature for studies that discussed the insulin resistance and weight loss from December 2024 to March 2025, an English only literature search was conducted utilizing he electronic databases of MEDLINE (via PUBMED), EMBASE, SCOPUS, OVID, and Cochrane Library Only publications that had undergone peer review were used in the final Analysis and key words were employed Insulin resistance, Weight loss, Metabolic syndrome Additionally, we looked through the references of the most pertinent review articles for any new research that our original literature search had miss.

According to literature review

longitudinal observational a cohort study in Palermo, the largest city in Sicily (Italy), At the 4-year follow-up visit, 707 adults without diabetes were part of the cohort. A validated Food Frequency Questionnaire for the local population was used to evaluate the habitual intake of energy and macronutrients over the previous 12 months. Insulin resistance was measured using the Homeostatic Model Assessment of β-cell Function and Insulin Resistance (HOMA-IR). Furthermore, PNPLA3 underwent genotyping. When energy intake (EI) consistently surpasses energy expenditure, obesity results. The possible metabolic factors, such as insulin resistance, are still unknown, though. This study examined variables linked to variations in body weight over an extended period of time [6].

Furthermore, another study done on adults who are overweight or obese, an elevated lipoprotein insulin

resistance (LP-IR) score is indicative of insulin resistance; however, there is insufficient information on how exercise interventions affect LP-IR. This study aimed to analysis the impact of a weight loss and miniating ideal weight on the LP-IR score in adults who are overweight or obese.

In adults who were overweight or obese, the LP-IR score increased during weight loss and remained stable during the PA-REC group's weight maintenance phase. Aerobic exercise, at least according to chronic weight loss guidelines, can maintain improvements in LP-IR scores and may suggest a lower risk of type 2 diabetes in adults who are overweight or obese [7].

Moreover, another study done on 172 post pubertal adults, they undergo long term weight loss therapy and after time body composition, total fat, blood glucose, lipid level and leptin level were measured in this population the study showed that regardless of visceral fat reduction, all groups under analysis showed positive effects on body composition. In the population under investigation, visceral fat was discovered to be an independent predictor of insulin resistance. Improved metabolic and inflammatory parameters were twice as evident in obese adolescents who lost a larger percentage of visceral adipose tissue (>1.8 cm) as in those who showed smaller losses. Visceral fat reduction was shown to be positively correlated with hepatic enzymes, lipid profiles, glucose metabolism, and the homeostasis model evaluation of the insulin resistance index [8].

In addition, another study done on Insulin resistance (IR) and its metabolic abnormalities in both young and old have been associated with metabolic syndrome (MS), diabetes mellitus (DM), and cardiovascular disease (CVD). More young people are MS diagnoses these days.

From January 1, 2022, to January 7, 2022, a case-control study was carried out at the Clinical Pathology and Internal Medicine Departments and Clinic at Qena University Hospital in Egypt. 110 participants were split into two groups for the study: 20 age- and sex-matched healthy controls and 90 MS obese cases with a body mass index (BMI) of greater than 30 kg/m2. Serum fasting glucose, fasting insulin, and lipid profile (total cholesterol, LDL, HDL, and triglycerides) were all clinically assessed and examined. The HOMA IR was calculated. Findings: MS has been linked to both diabetes and hypertension (P = 002). Weight, waist circumference (WC), midarm circumference (MAC), BMI ($p<0.0001$), triglycerides, VLDL ($P<0.005$), uric acid (P=0.009), fasting glucose (P=0.0002), insulin (P=0.007), HOMA-IR (P=0.0201), and a significant drop in HDL levels ($p<0.0001$) were all significantly higher in MS patients, who were also significantly older. Triglycerides (r=0.216 P=0.031), VLDL (r=0.216;), and BMI (r=0.266; 0.007) all showed positive correlations with HOMA-IR [9].

Meta-analysis (Liu and colleagues). focused on elements like IR in order to assess the effects of mind-body exercise interventions on patients with MetS. Analysis was done on 14 randomized controlled trials (RCTs) with 1148 patients. According to the findings, mind-body exercise considerably reduced blood pressure, fasting blood glucose, triglycerides (TG), high-density lipoprotein (HDL) cholesterol, IR, WC, BMI, and blood pressure. According to subgroup analysis, fitness qigong interventions that lasted 24–48 weeks and were done six–7 times a week were especially successful in lowering risk factors in patients with MetS. The study found that patients with MetS benefit from mind-body exercise and suggested low-to-

moderate-intensity fitness qigong interventions. a cross-sectional study that is retrospective [10].

Furthermore, lifestyle modification like physical activity and stress management plays fundamental role in the treatment of insulin resistance Diet control along with aerobic excise significantly improve insulin resistance and stress reduction like yoga along with adequate sleep have positive impact on metabolic diseases [11]. Reducing excessive carbohydrate intake while increasing protein and fat consumption may improve longevity and cardiovascular health, according to research based on the Korean Genome and Epidemiologic Study (KoGES) dataset, which found that the carbohydrate-to-protein or fat intake ratio was linked to mortality [12].

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