Integrative Obesity and Diabetes

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Obesity and Type 2 diabetes mellitus

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Abstract

Worldwide obesity is showing no signs of lessening and is fueling an angry outburst in numbers of Type 2 Diabetes Mellitus (T2DM). In spite of apparent links between obesity and T2DM, actual mechanisms are intricate given that some people with obesity materialize to be protected in some way from developing T2DM. Obesity and T2DM form part of the metabolic syndrome, which combined with hypertension and Dyslipidaemia result in impulsive mortality from cardiovascular disease in millions of people each year. Long-term microvascular complications from T2DM and multiple co-morbidities associated with obesity (psychological, musculoskeletal, respiratory and reproductive) also have a major adverse collision on quality of life and masquerade a mammoth financial burden on global health authorities. The relationship between obesity and diabetes is of such interdependence that term 'diabesity' has been coined. Major factors causative towards 'diabesity' include chronic overconsumption of energy-dense food, lifestyle, genetic makeup and environment play important roles in adipose tissue function or dysfunction. T2DM is characterized by impaired fat metabolism in adding up to glucotoxicity. Overconsumption of energy-dense foods results in excessive fat deposition and enhanced insulin resistance. Free fatty acids (FFAs) delivered to liver via the portal vein result in fatty liver. FFAs spill into systemic circulation result in lipotoxicity of organs such as pancreas, heart and muscles initiate a viscous cycle of fat damage, inflammation, worsening insulin resistance and beta cell insulin secretion, and eventually demonstration of T2DM. Visceral fat content is an independent predictor of insulin resistance, whilst adipokines such as adiponectin protect against obesity-induced T2DM. Further study of the precise mechanisms of lipotoxicity in development of T2DM will enable development of novel strategies to manage and prevent onset of T2DM in context of obesity. In this review, we elaborate associations between obesity and T2DM.

Introduction

Obesity has become a real concern worldwide due to its increasing prevalence and associated cluster of diseases that reduce life quality and expectancy. Abnormal deposition of fat in the adipose tissue due to chronic over nutrition or reduced physical activity or hereditary reasons is called as obesity [1]. Obesity increases the risk of type 2 diabetes, cardiovascular disease, cancer, and premature death. The global epidemic of obesity and T2DM is deterioration According to updated World Health Organization (WHO) reports; worldwide obesity has almost doubled since 1990 [2]. More than 1.1 billion people are estimated to be overweight of which around 320 million are calculated to be obese. More than 2.5 million deaths each year are attributed to higher BMI (body mass Index), a figure that is expected to double by 2030. Incidence rate of obesity is about 300 million adults worldwide [3].

T2DM is a heterogeneous disorder most commonly characterized by insulin resistance, a state of reduced insulin-mediated glucose uptake, in the presence of incapacity of the pancreatic beta cells to produce and provide sufficient insulin to meet the required needs [4]. A history of 2-3 years of T2DM does not produce irreversible damages to the beta cells, but as long as the energy overload persists through years, irreversible impairment of the beta cells occurs, and insulin is required in order to control plasma glucose [5]. Updated WHO reports mention that 347 million people worldwide have Diabetes Mellitus (DM) [6,7], of which T2DM comprises the vast majority (90%). T2DM is closely associated with excessive body fat and physical inactivity. It is predicted that there will be a growing burden of DM, and that the world prevalence of DM amongst adults aged 20-79 years will increase to 439 million by 2030 [8]. It has been reported that 86% of adults with T2DM are overweight or obese; 52% have obesity and 8.1% have morbid obesity [9].

Obesity and diabetes are closely related to each other as about 80% diabetics are obese. Obesity is a common finding in T2DM. There is impaired insulin sensitivity of peripheral tissues such as muscle and fat cells to the action of insulin in obese individuals (insulin resistance). Weight reduction in such obese patients produces improvement in the diabetic state [10]. Obesity increases the risk of T2DM, cardiovascular disease, cancer, and premature death [11]. Pharmacological factor involved in obesity and diabetes includes lipoprotein lipase, having a central role in the metabolism of both triglyceride rich particles and High-Density Lipoproteins (HDL). Lipoprotein lipase is determinant of serum triglyceride and HDL concentrations [12].

It is a well-known fact that if you are overweight or obese, you are at greater risk of developing type 2 diabetes, particularly if you have excess weight around your tummy (abdomen). Abdominal fat causes fat cells to releases 'pro-inflammatory' chemicals, which can make the body less sensitive to the insulin it produces by disrupting the function of insulin responsive cells and their ability to respond to insulin. This is known as insulin resistance - a major trigger for type 2 diabetes. Having excess abdominal fat (i.e. a large waistline) is known as central or abdominal obesity, a particularly high-risk form of obesity [13].

Obesity is also thought to trigger changes to the body's metabolism. These changes cause fat tissue (adipose tissue) to release fat molecules

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into the blood, which can affect insulin responsive cells and lead to reduced insulin sensitivity. Another theory put forward by scientists into how obesity could lead T2DM is that obesity causes prediabetes, a metabolic condition that almost always develops into type 2 diabetes [13]. The links between obesity and type 2 diabetes are firmly established without the intervention of a healthy diet and appropriate exercise; obesity can lead to type 2 diabetes over a relatively short period of time. The good news is that by reducing your body weight, by even a small amount, can help improve your body's insulin sensitivity and lower your risk of developing cardiovascular and metabolic conditions such as type 2 diabetes, heart disease and types of cancer. According to the NHS, a 5% reduction in body weight followed up by regular moderate intensity exercise could reduce your type 2 diabetes risk by more than 50% [14].

The influence of obesity on type 2 diabetes risk is determined not only by the degree of obesity but also by where fat accumulates. Increased upper body fat including visceral adiposity, as reflected in increased abdominal girth or waist-to hip ratio, is associated with the metabolic syndrome, type 2 diabetes, and cardiovascular disease [14], although underlying mechanisms remain uncertain.

Whether subcutaneous fat lacks the pathological effects of visceral fat or is simply a more neutral storage location, for example, requires further study. Beyond differences in body fat distribution, emerging evidence suggests that different subtypes of adipose tissue may be functionally distinct and affect glucose homeostasis differentially. Adult humans have limited and variable numbers of brown fat cells [15], which play a role in thermo genesis and potentially influence energy expenditure and obesity susceptibility [16]. Improved understanding of the function of different fat cell types and depots and their roles in metabolic homeostasis is a priority for investigation into the pathogenesis and complications of obesity. Likewise, adipose tissue is composed of heterogeneous cell types. Immune cells within adipose tissue also likely contribute to systemic metabolic processes. As the study of adipose biology progresses, it will be important to consider whether additional subtypes of adipocytes or other cell types can be identified to refine our understanding of obesity complications and generate novel approaches to prevention.

At least three distinct mechanisms have been proposed to link obesity to insulin resistance and predispose to T2DM: 1. Increased production of adipokines /cytokines, including tumor necrosis factor-a, resistin, and retinol binding protein, that contribute to insulin resistance as well as reduced levels of adiponectin [17]; 2. ectopic fat deposition, particularly in liver and perhaps also in skeletal muscle, and dysmetabolic sequelae [18]; and 3. mitochondrial dysfunction, evident by decreased mitochondrial mass and/or function [19]. Mitochondrial dysfunction could be one of many important underlying defects linking obesity to diabetes, both by decreasing insulin sensitivity and by compromising b-cell function.

Conclusion

Obesity and T2DM, whether individually or whether co-existing as "diabesity" are of major significance with regards to premature mortality, quality of life, associated chronic microvascular complications (in the case of T2DM), obesity-associated co-morbidities, and the global healthcare economy. A better understanding of the causative and therapeutic interrelationships between these two conditions is essential. Tackling the worsening global epidemic of diabesity effectively will require a multifaceted approach focused on both adults and children that includes governments, changes to environments, changes to cultures (particularly around food) and development of novel, safe and effective therapies that promote weight-loss and improve the dysmetabolic state. These efforts should be a major priority.

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