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THE RELATIONSHIP THE LEPTIN HORMONE, OBESITY AND DIABETES

ABSTRACT

Leptin, which is adipocytes, secreted of the hormone, over food intake regulation, energy expenditure has also an important role in acting as neuroendocrine hormone, and metabolic function.it is interested in glucose metabolism and interacts with insulin metabolism. In addition to distrusting metabolism, leptin also impairs endocrine, immune functions, reproductive function, adipose tissue metabolism and energy order. Leptin also exerts peripheral effects directly on glucose metabolism and gluconeogenesis. it is obvious that leptin deficiency or leptin resistance is responsible for obesity which is also correlated with body fat stores, here we have to refer that is the obesity is one of the most causes of diabetes also it leads to insulin resistance. In these studies, we will focus on the relationship between leptin and diabetes mellitus type 2 and insulin resistance with obesity. In this study, we will focus on the relationship between the leptin hormone and obesity with diabetes.

Keywords: Leptin, Obesity, Diabetes, Human, Metabolism

1. INTRODUCTION

Leptin is a protein hormone consist of 146 amino acids with 16 kD, it is synthesized by adipose tissues [1]. In 1994, Friedman etc. al. found that in ob/ob, the obese (ob) gene, responsible for the phenotype of the typical obesity, diabetes and insulin resistance was copied [2]. They also found very closely homologue gen for humans which are identical to the mice about 84%. Adipocyte body weight regulation is the fact that a decrease in starvation adiposity causes hyperphagia, reduces the amount of energy, and eventually returns body weight back to the previous level [3 and 4]. This hormone also has effects on fatty acid (FA), and was found to cause an increase in the oxidation capacity to FA and a decrease in triacylglycerol stores [5]. The energy balance created by this hormone is seen in glucose and lipid metabolism, reproduction, cardiovascular function, and immunity. The directly affects other organs of mammals and is clearly regulated by the nutritional status to meet the needs of brain, and skeletal muscle [6]. Hereby many previous studies it clear that the leptin hormone is responsible for obesity in mammals by regulation of food intake and energy expenditure [7, 8 and 9]. Also, there is another idea to indicate that the Hyperleptinemialeads to leptin resistance which is cause obesity [10 and 12]. Studies to date indicate a strong relationship between obesity and diabetes [13 and 14]. The relationship between obesity and type 2 Diabetes Mellitus, excessive tissue triglycerides causing were observed to cause insulin resistance. This result was demonstrated by epidemiological studies and experiments [15 and 16].

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2. RESEARCH SIGNIFICANCE

This study was to highlight that the relationship between diabetes mellitus, leptin and obesity should be clarified by more studies to be carried out, it is believed that this study will support and shed light on further studies on this topic.

3. DIABETES

Diabetes is a metabolic disease. Insulin secretion is a metabolic disease with hyperglycemia caused by insulin disorder, or both. The chronic creates long-term damage and dysfunction of different organs, especially the eyes, kidneys, heart, and blood vessels, nerves. The autoimmune damage of the pancreatic cells results in insulin deficiency to irregularities that result in resistance to insulin action. Insulin disorder leads to irregularities in carbohydrate, fat and protein metabolism in diabetes target tissues [17]. Polyuria, weight loss, and blurred vision are among the most common symptoms of hyperglycemia. In addition, susceptibility to certain infections can cause chronic hyperglycemia. If diabetes is not controlled, its serious has been dangerous. Consequences diabetes is hyperglycemia with ketoacidosis or the non-ketotic hyperosmolar syndrome. Diabetes leads to retinopathy due to potential vision loss and visual function ends. Diabetes is a common chronic disease in the world, and there are several studies that predict it will increase from 171 million in 2000 to 366 million in 2030 [18]. The most commonly diagnosed patient about 90% is type 2 diabetes mellitus [19]. The WHO prepares a Report in 2002 counts the most risk factors that impact on current humanity and the overall load of disease. This report focused on the importance of obesity and indolence in daily activity in increasing the possibility of exposure to type two diabetes. According to this report, it is expected that 58% of the global load of T2DM, are attributable to BMI (body mass index) [20]. Diabetes affected by low physical activity directly by insulin sensitivity and also indirectly by obesity .one of the recognized factors of diabetes mellitus type 2 is obesity [21]. The obesity may lead to insulin resistance, as a result, because the diabetes mellitus type 2 the no esterified fatty acids (NEFAs) that adipose tissue in obese human secret it may cause of the hypothesis that insulin resistance and β-cell dysfunction [22, 23 and 24].

4. OBESITY

Obesity is one of the most common chronic diseases in the world. It is considered a dangerous epidemic at any age. Obesity is one of the major causes of increasing the risk of type 2 diabetes. This disease includes morbidity, hypertension, dyslipidemia, coronary heart disease, stroke, calcification from hypertension, sleep apnea and breathing problems are the cause of prostate, and colon cancers [25]. Obesity people must understand that to avoid the risk of this dangerous epidemic requires a life-long effort. There is a common measure important for assessing overweight and total body fat content is BMI (body mass index) which is the symbols of obesity, BMI is calculated as the weight of the body (kg)/squared height (m^2), BMI<18.5 Underweight, BMI 18.5-24.9 Normal, BMI 25-29.9 overweight, BMI>30 obesity.

5. ROLE OF LEPTIN IN THE REGULATION OF GLUCOSE METABOLISM

In addition to the regulation of energy and food intake, there is evidence suggesting that leptin hormone also plays a key role in glucose metabolism [26]. In fact, rodents models that have low blood leptin levels are characterized by insulin resistance and diabetes [27

and 28]. Some studies demonstrate that in the case of leptin therapy may lead to decreasing in blood glucose and insulin levels [29]. Other leptin models not associated with obesity, characterized by loss of adipose tissue as a result of mutations that damage adipogenes, counteract severe insulin resistance and diabetes phenotype characteristic [30, 31 and 32]. As a result of the study, it was concluded that leptin regulates glycaemia balance and energy balance in both rodent models and clinical settings [33]. The effect of the central nervous system (CNS) on the energy balance of leptin are considered to have critical role in allocating the current mainstream in the brain, and leptin on energy homeostasis that the glucose lowering effects of leptin are realized through the brain. Therefore administration of leptin directly to the brain, at normal doses, normalizes blood glucose levels in rodent models [34, 35, 36 and 37].

6. LEPTIN AND DIABETES

There was a relationship between diabetes mellitus and blood leptin levels [38]. In previous studies shown that leptin can harm insulin production, and some data have shown that leptin is involved in the development of peripheral insulin resistance [39]. Leptin interferes with insulin resistance. In obese subjects, type 2 diabetes may have high leptin levels as observed in obesity. Consequently, glucose dependent insulin secretion by the pancreas can lead to hyperglycemia [40]. Probably Insulin resistance, also made by hyperleptinaemia, contributes to glucose intolerance and eliminates suppression of leptin induced insulin secretion and can promote hyperinsulinemia (insulin in the blood rises to normal upper levels).High serum leptin levels in obesity cause desensitization of the receptor and defective leptin receptor signal in their cells. As a result, this leads to chronic hyperinsulinemia and may contribute to the pathogenesis of diabetes [41]. Leptin which prevents triglyceride accumulation in various tissues makes a protective antidiabetic effect by increasing peripheral insulin sensitivity [42 and 43]. Mutations in the leptin or leptin receptor gene were not sufficient in screenings of the human ob gene in Type 2 diabetic subjects. Although evidence of the growth of type 2 diabetes or reduced glucose tolerance was not sufficient [44 and 45]. Leptin levels are comparable in type 2 diabetic patients and nondiabetics that BMI or fat mass is taken into account [46, 47 and 48]. Briefly, leptin can inhibit insulin secretion at the level of the pancreas, while concurrently glucose utilization by enhancing insulin action. In humans, insulin associated with leptin levels. However, the hypothesis that explaining whether insulin can actively regulate leptin levels in humans remains controversial.

7. DIABETES AND OBESITY

Obesity and weight gain are associated with the risk of diabetes [49 and 50] and weight loss less sensitive to the risk of diabetes risk than obese people [51]. There is some survey evince that by global commonness of type 2 diabetes is attached to elevate rates of obesity in part a sequel of social tendencies to higher energy intake and reduced energy expenditure [52]. Neel reported that glucose should be used efficiently as a biological fuel. He also suggested that the evolutionary pressure to separated glucose to be used as body fuel during starvation by the brain led to a genetic tendency against insulin resistance in peripheral tissues [53]. Fat is considered as store energy in most efficiently biological systems. It has been suggested that obesity and diabetes cause outbreaks when eating high calorie foods unlimitedly [54 and 55]. Adipocyte which secretes hormones (leptin and ghrelin) regulates appetite and metabolism, a

passive fuel tank. In fact, it is considered an endocrine organ that communicates with the brain and peripheral tissues [56]. According to the above functions, the location of the adipose tissue (visceral versus subcutaneous) [57] is average adipocyte in the tissue and by adipocyte metabolism of glucose and corticosteroids. There are some special cases in which obesity increasing in the level of leptin, the resistance at which the leptin effect increases at the cellular level increases concentration of leptin in blood, hence, this special case may be associated with insulin resistance [58]. Other factors derived from adipose tissue have been shown to participate in systematic insulin resistance. One of these factors is elevation of free fatty acid level which is derived from adipose tissue that has been shown to participate to insulin resistance in muscle and liver in obesity [59 and 60].There are many protein secreted from the adipocytes exception the leptin and ghrelin that modulate glucose metabolism and the action of insulin [61].

8. DISCUSSIONS

Diabetes mellitus is a hyperglycemic disease that results from insulin secretion, the effect of insulin, or both [62]. Insulin resistance is defined as a disturbance in the biological response to insulin in the pathogenesis of type 2 diabetes [63]. Obesity is one of many factors that affect insulin sensitivity. It has been observed in many studies that an increase in fat tissue, particularly in the abdominal region, increases the risk of insulin resistance [64 and 65]. In addition, the possible relationship between leptin and diabetes, which has an important role in the regulation of body weight and metabolism, is very important and has been the subject of numerous studies. Although the relationship between type 2 diabetes and leptin has been studied in many ways, it is still not fully clarified. In this context, it has been shown that leptin levels are elevated in obese and non-diabetic individuals, and leptin levels are significantly lower in patients with type 2 diabetes [66 and 67], but other studies have shown that plasma leptin levels in patients with type 2 diabetes are no different from those without diabetes and have the same BMI, and leptin level is associated with BMI [68 and 69]. While in obese individuals, serum leptin concentration is positively correlated with body mass index (BMI) and body fat ratio, which are indicators of obesity [70], numerous studies have shown that there is a positive relationship between serum fasting leptin and insulin levels and insulin resistance in obese individuals [71 and 72]. Although there is a positive relationship between leptin level and body mass index (BMI) in obese women and men, this relationship is not observed in normal weight [73 and 74]. The hormone leptin, which reduces appetite and increases energy expenditure, should be less theoretically in obese people, but studies do not confirm this. Serum leptin levels are significantly higher in obese individuals than in normal individuals [75]. The obesity observed in humans is not only caused by the absence of leptin. A higher leptin level is necessary to overcome leptin resistance, therefore, more leptin is released from the fatty tissue, and more leptin release leads to an increase in the fatty tissue that produces it [76]. Diabetes mellitus is a disease that disrupts a person's quality of life and lasts for a lifetime, which must be monitored and treated in the process; damage, dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart and blood vessels can develop. The objective of this study was to highlight that the relationship between diabetes mellitus, leptin and obesity should be clarified by more studies to be

carried out, it is believed that this study will support and shed light on further studies on this topic.

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