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The role of Apelin hormone at insulin resistance disorder

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Abstract

Insulin resistance is a metabolic disorder that precedes type 2 diabetes, where cells begin to show a state of non-responsiveness to the hormone insulin. Such physiological conditions naturally cause high blood glucose levels, which may be caused by obesity. Adipose tissue has the ability to secrete the hormone Apelin, which is a peptide hormone. Apelin act to target fat and glucose metabolism pathways, and therefore can be used as a treatment in cases of insulin resistance induced by obesity.

Keywords: Insulin resistance; Apelin; Adipose tissue; Type 2 diabetes

1. Introduction

Insulin resistance is a disorder that occurs in the response of insulin receptors to the hormone insulin found in the liver, muscles and most tissues of the body. The most important causes of insulin resistance are weight gain, genetic predisposition, lifestyle, and others. The most important complications of insulin resistance are causing type A diabetes. Apelin is known as a hormonal peptide because it works according to the theory of hormone action, it's pre-pro-protein consisting of 77 amino acids and is classified as an adipokine. Apelin was first discovered in 1998 via Masahiko Fujino.

2. Insulin resistance disorder

2.1. Definition

Insulin resistance is defined as a impair the response to insulin by insulin-stimulated tissues. All tissues that have insulin receptors are susceptible to insulin resistance, such as hepatocytes, adipocytes, and skeletal muscle cells. The presence of insulin resistance contributes effectively to increased insulin production and secretion due to high blood glucose levels [1]. There are many studies that assume that hyperinsulinemia precedes insulin resistance, and therefore hyperinsulinemia itself is a condition that causes insulin resistance. Such hypotheses work on the duality of hyperinsulinemia with the abundance of calories consumed, which in turn leads to insulin resistance, which is considered a main disorder in the body's metabolism. The most important health consequences resulting from insulin resistance are hyperglycemia, hyperurecemia and hypertension, and it can also cause a disorder in prothrombotic state. Insulin resistance can develop into other medical complications, such as type 2 diabetes, fatty liver and etc.. insulin resistance is classified as a genetic disease with specific genes causing it. It can be classified as an acquired disorder due to the accumulation of fat in the body, but so far there are no definitive tests for the disease. Rather, the complications of insulin resistance are relied upon to identify the disease [2]. The insulin resistance signs and symptoms concluded in figure 1.

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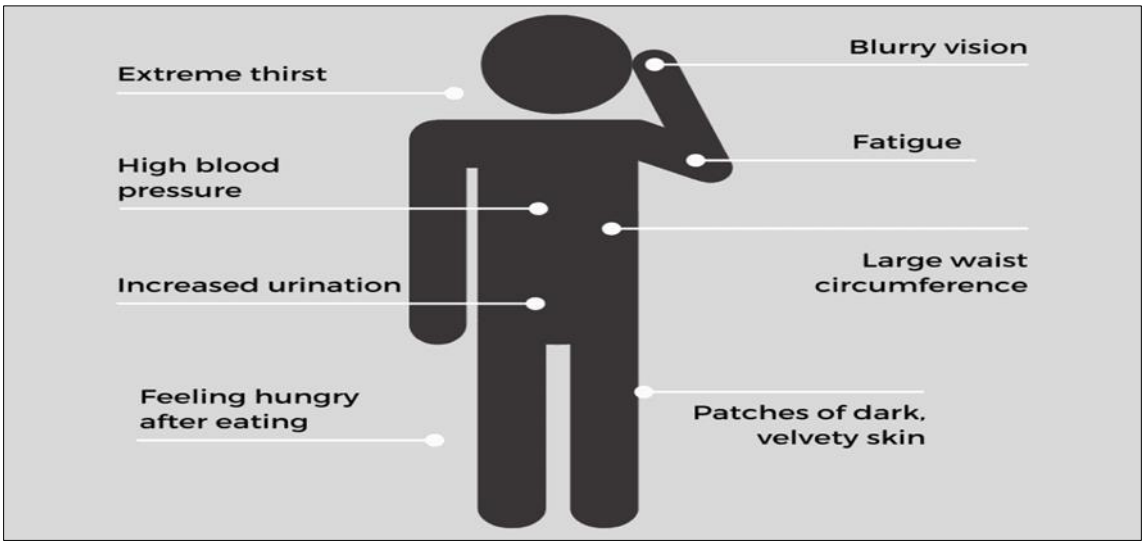

Figure 1 Insulin resistance signs and symptoms

2.2. Etiology

Insulin resistance disorder has several causes, and these causes are classified as genetic and acquired. Genetic causes of insulin resistance disorder include for example Werner syndrome, Alstom syndrome, polycystic ovary syndrome and others [3]. On the other hand, there are acquired causes of insulin resistance disorder, for example lack of physical activity, increased visceral obesity, increased sodium due to foods rich in sodium, medications (such as glucocorticoids drugs) and other causes [4]. In addition, insulin resistance disorder can be classified into two main types:-

- -Type A- insulin resistance: The main cause is in the insulin receptor itself, as there is a genetic problem that led to the encoding of an insulin receptor in a shape and structure that differs from the normal receptor.
- -Type B- insulin resistance: The main cause is the presence of autoantibodies in the insulin receptor that lead to the failure of the receptor's response to the insulin hormone [5].

2.3. Pathophysiology

Insulin resistance occurs in three main organs and areas of the human body, the first of which is skeletal muscles, the liver and adipose tissue. The increase in calories inside the muscles without their expenditure leads to insulin resistance, The abundance of calories and their conversion to glucose, the muscles are the most important primary site for glucose consumption. The presence of high accumulated calories leads to an increase in the accumulation of fatty acids inside the muscles. Where diacylglycerol is considered the most important fatty acid in muscle cells, which represents the surplus energy in the cell. Diacylglycerol activates PKC-theta kinase, which causes insulin signals to decrease and thus a decrease in the glucose transporter (GLUT4), which causes inhibition of glucose absorption inside the cell and thus the transfer of glucose to the liver. The presence of high sugar concentrations causes it to be converted in the liver into fat through the de novo lipogenesis. Excess glucose enters hepatocytes via insulin-independent pathways that stimulate de novo lipogenesis by pushing out substrate, resulting in the creation of more fatty acids from excess glucose. These fats in turn tend to accumulate in visceral tissues and cause obesity [6].

3. Apelin

Apelin is known as a hormonal peptide because it works according to the theory of hormone action, it's pre-proprotein consisting of 77 amino acids and is classified as an adipokine. Apelin was first discovered in 1998 via Masahiko Fujino [7], see figure 2.

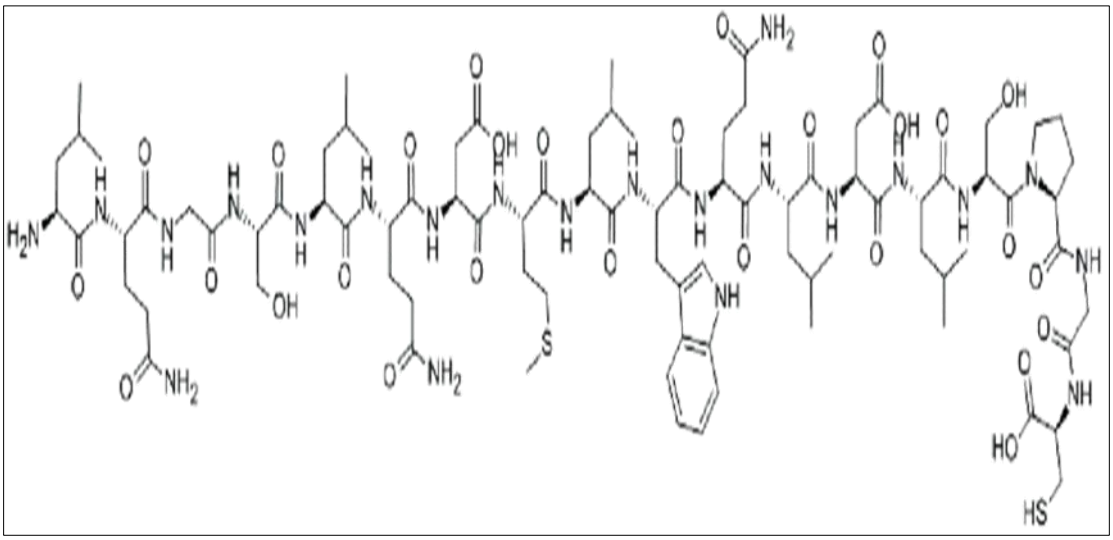

Figure 2 Apelin structure

Apelin is secreted mainly from two sources in the body, the first is adipose tissue and the second is the gastric membrane, but adipose tissue is considered the basis for the secretion of Apelin. Apelin is called in some sources the satiety hormone because it plays an important role in the feeling of satiety. The mechanism of Apelin's action is not fully understood yet, but Apelin works as a chemical messenger to transmit a signal to a target tissue, such as the brain, and therefore it works according to the theory of hormone action. Apelin works in the energy balance in the body through its effects on the hypothalamus region of the brain, which works to regulate metabolism and energy balance in the human body through its effects on the central nervous system. On the other hand, Apelin has the ability to interact with the hormone insulin to regulate glucose metabolism in the body [8]. Apelin has a positive correlation with nutrition and the density of adipose tissue in the body, while It has an negative correlation with fasting, as its level decreases during fasting, see figure 3.

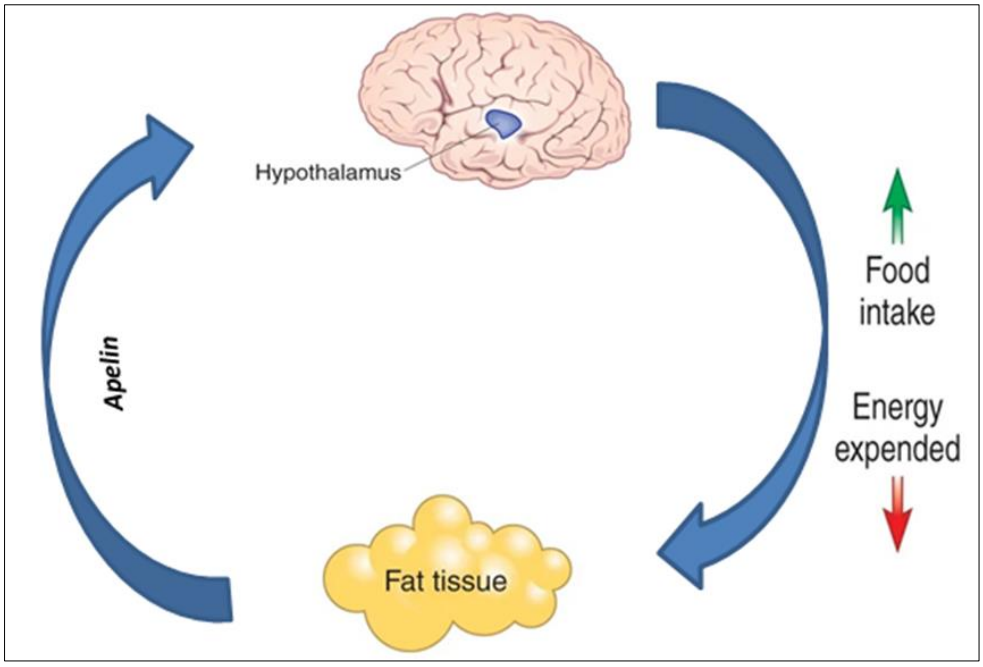

Figure 3 Effect of Apelin from adipose tissues on hypothalamus region

In addition, the Apelin hormone plays an effective role in the body's immunity, as it works as an inflammatory factor.

Apelin is affected by energy and food levels in the body, as increasing energy reserves enhances Apelin secretion, which is called constitutive secretion, because gastric Apelin is affected by food and meals [9]. When Apelin is secreted and enters the bloodstream, it reaches the hypothalamus directly, and binds to its own receptor to give a signal of satiety. In addition to what is mentioned, Apelin has other peripheral effects, For example, interacting with cholecystokinin in the stomach, Apelin increases vagal afferent activity controlling the gastric emptying which in turn contributes to satiety. Apelin also works in the intestine to enhance carbohydrate absorption by enhancing the supply of glucose transporters such as the sodium-glucose transporter-1. At fast the food and lipids become unavailable, therefore the Apelin levels reduce, thus promote food intake to ensure a steady supply of metabolic fuel. It is reasonable to imagine that decreased Apelin levels to increase food intake produce a stronger signal than increased levels of this hormone to reduce food intake as a survival function resulting from the long-term evolutionary challenges of food scarcity [10].

4. Apelin hormone with insulin resistance

Many studies around the world have shown that there is a positive correlation between the level of Apelin and the state of insulin resistance, including Boucher et al. (2005), where he proved during his study that the level of Apelin begins to increase with the onset of high insulin levels, which occurs as the first stage in the case of insulin resistance [11]. Li et al. (2006) also showed that insulin resistance has a positive correlation with the increase in accumulated adipose tissues that cause obesity, as the higher the percentage of accumulated fats, the higher the level of Apelin in the body [12]. In other experiments, Li C, Cheng H (2022) proved that the Apelin hormone acts to increase the process of fatty acids oxidation and also improves the process of glucose absorption in the body because Apelin targets the Apelin-APJ system, and therefore can be used as a treatment for insulin resistance [13].

5. Conclusion

The current study aims to show the importance of the role of Apelin in insulin resistance disorder, as it showed an important role for Apelin in the case of high accumulated fat in the body that induced to insulin resistance. Its role is evident in Apelin hormone acts to increase the process of fatty acids oxidation and also improves the process of glucose absorption in the body because Apelin targets the Apelin-APJ system, and therefore can be used as a treatment for insulin resistance.

Compliance with ethical standards

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