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Lipid metabolism and insulin sensitivity

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Abstract. Diabetes mellitus is known to be a serious chronic disease that requires great attention because it is the "cancer that never dies" and affects many people worldwide; its later complications are often numerous and frightening, and some of them may even affect their children as hereditary diseases. The relationship between lipid metabolism and insulin sensitivity in relation to diabetes is therefore even more important in this context. Insulin plays an important role as a key metabolic hormone in regulating glucose intake and maintaining lipid metabolic homeostasis. Insulin resistance interferes with the homeostasis of lipid metabolism while triggering related metabolic diseases such as type 2 diabetes. This review focuses on the relationship as well as interactions between lipid metabolism as well as insulin sensitivity and the specific factors affecting lipid metabolism and insulin sensitivity in terms of excess lipid accumulation, lipid deficiency, altered lipid composition, and specific lipid species. Finally, interventions based on the factors affecting lipid metabolism and insulin are proposed to improve metabolic health and reduce the risk of metabolic diseases such as diabetes.

Keywords: lipid metabolism; insulin sensitivity; insulin resistance; diabetes mellitus.

1. Introduction

Diabetes remains a significant metabolic disease, with the World Health Organization's global diabetes statistics for the year 2021 suggesting that 537 million adults are living with diabetes, increasing to an even higher 643 million by 2030 [1]. As a disease characterized by hyperglycemia due to elevated blood glucose, the cause is due to insufficient insulin secretion to produce sufficient insulin resistance. At the same time, an excessive increase of lipids in the liver, which is the main organ regulating lipid and glucose metabolism, impairs insulin sensitivity and leads to abnormal lipid metabolism [2]. For example, in type 2 diabetes mellitus, the regulation of lipid metabolism is affected by insulin resistance and insufficient insulin secretion. Such abnormalities in lipid metabolism can also lead to the development of other health problems.

In this review, I describe the relationship between lipid metabolism and insulin sensitivity to elucidate the effects of lipid metabolism on insulin sensitivity and provide appropriate interventions. By understanding the effects and interventions, it will be possible to better understand lipid metabolism in diabetic patients and to choose optimal treatments to improve insulin sensitivity.

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2. Overview of lipid metabolism

Lipid metabolism often involves several interdependent or cross-regulated pathways [3]. These pathways include lipid digestion, absorption, transport, storage, lipid catabolism, and biosynthesis [4]. In the digestive system, pancreatic lipase breaks down triglycerides into fatty acids, monoglycerides, and some free small molecules of glycerol [5]. These fat digests are then absorbed into the enterocytes, where they resynthesize triglycerides in the endoplasmic reticulum and are moved and transported around the body in transporters incorporated into celiac particles, relying on those lipoprotein particles that are formed through the transport of cholesterol and triglycerides in combination with proteins [4].

The normalization or lack thereof of lipid metabolism plays an important role in diabetes and insulin sensitivity. Firstly, lipid metabolism helps to maintain energy homeostasis [6], storing a lot of energy and ensuring nutritional homeostasis. However, the accumulation of specific lipid metabolites contributes more to lipid-induced insulin resistance, and insulin sensitivity tends to decrease when intracellular concentrations of lipid metabolites are elevated [7]. As a result, the effect of insulin per unit of glucose is reduced, and the body's ability to break down sugars is correspondingly reduced, with a decrease in the cellular capacity for glucose uptake, leading to an increase in glucose concentrations in the blood and the development of type 2 diabetes mellitus. This abnormality in lipid metabolism is strongly associated with insulin sensitivity and can lead to diabetes and its associated complications.

Therefore, by understanding these concepts of lipid metabolism and insulin sensitivity, it is possible to gain a deeper understanding of the mechanisms of diabetes as well as to find out if there is an increase in insulin sensitivity when there is sufficient insulin secretion, which is a good area of research for improving insulin sensitivity and treating diabetes.

3. Link between lipid metabolism and insulin sensitivity

Insulin resistance is a pathological condition that occurs when insulin signaling is impaired [8] and is also a key factor in the pathogenesis of type 2 diabetes [9]. Lipid accumulation, lipodystrophy due to lipid overaccumulation, lipid deficiency, alterations in lipid composition, and the effects of specific lipid species often leads to dysregulation of lipid metabolism.

3.1. Lipid overaccumulation

Adipose tissue directs lipid metabolism as well as its products [6], Obesity and diabetes are metabolic disorders resulting from excessive lipid accumulation. When lipids in cells and tissues are not absorbed and free fatty acids (FFA) are spilled due to increased metabolic disorders, these FFA interfere with insulin signaling thereby increasing insulin resistance. At the same time, excessive lipid burden can lead to hampered cellular functions [10]. To add insult to injury, excessive accumulation of lipids induces inflammation and produces inflammatory cytokines which impair insulin sensitivity, leading to impaired insulin signaling and systemic insulin resistance [11].

3.2. Excessive lipid deficiency

Conversely, adipose malnutrition can also lead to severe insulin resistance [12]. Because adipose tissue is unable to store excess energy [13], the body's fat metabolism is abnormally low, leading to a decrease in lipid storage, and therefore a greater than usual release of FFA from the plasma, which is abnormally high and interferes to some extent with insulin signaling [9], increasing insulin resistance. However, when the body is over-nourished, leptin, the hormone responsible for regulating appetite, triggers appetite, increases tissue uptake of glucose by activating the sympathetic nerves, protects pancreatic β-cells from lipotoxicity, and increases insulin sensitivity [13].

3.3. Altered lipid composition

Alterations in the iron content, lipocalin content, and resistin content of lipids at various levels may affect insulin sensitivity.

When iron content is increased in adipocytes, iron acts as a strong oxidant that catalyzes cellular reactions and increases the level of oxidative stress [14], damaging pancreatic β-cells and creating

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insulin resistance [6], as lipocalin is affected and inhibited during secretion, which increases abnormalities in lipid metabolism and increases fat accumulation, which reduces insulin sensitivity. sensitivity.

Resistin, a small protein secreted by adipose tissue [6], plays a role in the mechanisms of lipid metabolism and insulin resistance. Elevated resistin is known to trigger insulin resistance in vitro and in vivo [6] and vice versa. However, to date, there is no definitive information to suggest a correlation between resistin and insulin resistance [15].

3.4. Effects of specific lipid species

3.4.1. Diacylglycerol (DAG). Diacylglycerol, a lipid metabolite that serves as a link between lipid metabolism and insulin resistance, is hypothesized to phosphorylate the insulin receptor Thr1160 and inhibit tyrosine kinase activity in the insulin receptor along with activation of protein kinase C (PKCε) in the cell [16], which impedes insulin signaling [17]. In the study of the lipid tract model of hepatic insulin resistance, it can be understood that intrahepatic DAG and hepatic insulin resistance have a clear link, and the increase and accumulation of DAG are accompanied by a corresponding increase in the degree of hepatic insulin resistance so that the two are positively correlated with each other. At the same time, increased DAG reduces insulin sensitivity in humans, and both are strongly associated with type 2 diabetes [16]. These conditions interfere with insulin signaling, thus diminishing insulin action on cells, increasing glucose uptake, and affecting lipid metabolism. However, correct dietary DAG intake can effectively improve insulin sensitivity in type 2 diabetic patients [16]. Similarly, reducing the expression of PKCε can then avoid damaging insulin signaling and also reduce hepatic insulin resistance.

3.4.2. Ceramides. Ceramide, a bioactive lipid molecule that regulates cell signaling [18], may disrupt insulin sensitivity and lead to its decline [19]. It is known that there may be a link between insulin resistance and ceramides [17] and that ceramides may increase in tissues due to an increase in fatty acids [18]. Of course, reduced insulin sensitivity does not necessarily correlate with the accumulation of fatty acids in its entirety. Ceramides affect insulin signaling in several ways, including inhibition of phosphatidylinositol 3-kinase (PI3K) signaling, and blocking activation of the anabolic enzyme Akt/PKB [18,20]. In these ways, glucose uptake becomes abnormal and nutrient storage is compromised [19].

3.4.3. Free fatty acids (FFA). Free fatty acids are known to enhance glucose-induced insulin secretion [21]. When a person is overly obese, levels of circulating FFA derived from lipolysis in adipocytes are elevated [22], and excess FFA leads to the accumulation of lipid intermediates in muscle [10], resulting in disturbed insulin signaling as well as dysregulation of lipid metabolism, which increases the occurrence of insulin resistance. In the presence of this resistance, glucose cannot be taken up efficiently, ultimately leading to elevated blood glucose. At the same time, the body produces more insulin to allow FFA to enter the plasma from the fat cells. The abnormal elevation of FFA in plasma is mainly due to the continuous accumulation of lipid derivatives such as diacylglycerol and ceramides in the cells [10].

By studying the link between lipid metabolism as well as insulin sensitivity, researchers can use these to understand the specific causes as well as mechanisms of insulin resistance. This provides a theoretical foundation for the later provision of relevant and specific measures to improve diabetes mellitus.

4. Factors affecting lipid metabolism and insulin sensitivity and interventions

4.1. Factors Affecting Lipid Metabolism and Insulin Sensitivity.

4.1.1. Dietary structure. Dietary structure has an important influence on insulin sensitivity and people with type 2 diabetes. Red meat consumption is positively associated with the risk of type 2 diabetes [14]. Red meat tends to be heme iron-containing, and according to the above article about increased iron

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content in lipids leading to insulin resistance [6], it is understood that red meat intake is highly correlated with heme iron intake [14]. And there is also a positive correlation between red meat intake and the risk of weight gain, thus high amounts of refined carbohydrates [23], as well as high fat and sugar as the main components leading to lipid accumulation, can lead to disorders of lipid metabolism, while obesity mediates the intake of red meat and the risk of diabetes mellitus [14]. Sodium and nitrite contained within processed meats are also toxic to pancreatic β-cells when converted to nitrosamines and also increase the risk of diabetes [14].

Excessive intake of animal proteins and low intake of plant-based proteins in the human body exacerbates insulin resistance [24], as well as worsens metabolic control in diabetic patients, increasing the incidence of type 2 diabetes mellitus. When animal protein is ingested, this ingredient, together with amino acids, activates glucagon secretion, and when plasma glucagon is persistently elevated, the intake of animal protein may induce insulin resistance and type 2 diabetes; in patients with type 1 diabetes, metabolic control is worsened, and vascular damage may occur [24]. High animal protein intake also impairs the inhibitory effect of insulin on glucose in the liver, thus affecting insulin sensitivity in the long term.

4.1.2. Genetic factors. Genetic factors play a significant role in lipid metabolism and insulin sensitivity in humans. The development of insulin resistance in an individual may also be determined by genetic factors [25]. Abnormalities in insulin structure as well as mutations in insulin receptor substrates can be used to explain genetic variation. These mutations lead to abnormalities in lipid metabolism, which in turn affects insulin signaling pathways and conduction, and ultimately insulin sensitivity. It is clear that while exploring genetic factors, the impact of lifestyle, as well as environmental factors, needs to be taken into account [25].

4.1.3. Living environment. Lifestyle also plays an important role in determining insulin resistance and metabolism [25]. Lithium in the environment accumulates in the liver [26], bone, and muscle through the food chain, and high levels of lithium can impair insulin signaling and interfere with intracellular signaling pathways, thus affecting lipid metabolism and insulin sensitivity. Some pollutants in the environment tend to damage the human body, and even at low levels of exposure, chronic diseases can be suffered from prolonged exposure to highly polluted environments. Some persistent organic pollutants, such as organochlorine pesticides, arsenic, and non-dioxin polychlorinated biphenyls (PCBs), affect human endocrine function. In particular, arsenic impairs pancreatic β-cell function and even alters the expression of genes associated with insulin resistance thereby increasing the risk of type 2 diabetes [27]. Constant exposure to highly polluted environments can also lead to increased oxidative stress and inflammatory responses, affecting the balance of lipid metabolism.

Extreme external temperatures can also affect insulin sensitivity. In cold environments, plasma concentrations of insulin are subsequently reduced, while still allowing for glucose uptake and metabolism. Slightly higher temperatures increase the affinity of the insulin receptor for glucose, which affects the uptake of glucose by cells. In addition, high temperatures lead to the loss of insulin receptors, resulting in reduced insulin binding capacity [27].

In addition to this, for example, seasonal changes, sunlight exposure, and sea level height can affect insulin sensitivity.

4.1.4. Physical activity. When many people become fat due to a lack of exercise, the excessive accumulation of lipids in the body cannot be metabolized in time, which will lead to lipid metabolism disorders and related metabolic diseases. At the same time, lack of exercise will not be able to promote cellular uptake of glucose, resulting in the accumulation of glucose in the plasma and increased insulin resistance. Lack of exercise does not increase the synthesis and stabilization of nitric oxide in the vasculature, which has a vasodilatory effect, improving vascular function and inhibiting insulin delivery and glucose uptake [28].

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4.2. Improving Metabolic Health through Interventions.

4.2.1. Dietary composition. Insulin sensitivity is primarily regulated through the influential factor of dietary structure. Weight loss does not enhance insulin sensitivity, and reducing animal protein intake [24], adjusting dietary heme iron intake, and substituting plant foods can enhance insulin sensitivity. Avoiding diets high in animal protein [24] and limiting saturated fat intake [23], such as consuming nuts, low-fat dairy products, or diets high in grains and fiber instead of animal protein can help to slow the release of glucose and reduce the need for insulin, which can significantly reduce the risk of developing diabetes [14,24]. Vegetable-related dietary fiber can increase insulin sensitivity and improve insulin resistance. Reducing the consumption of red meat, especially processed meat, and eating healthier foods can also reduce diabetes risk and cardiovascular risk.

4.2.2. Increase exercise. Proper aerobic exercise has been shown to be effective in preventing cardiovascular risks [28], and of course, resistance exercise has been shown to be most beneficial for glucose metabolism [29], stimulating the release of factors such as bradykinin and increasing glucose uptake [27]. It improves insulin resistance as well as enhances insulin sensitivity through enhanced signaling after receptor enhancement, promotes regulation of lipid metabolism, reduces the excessive accumulation of lipids in tissues, prevents and manages overweight conditions, and maintains a healthy body. At the same time, exercise has been shown to have a weight loss effect [28] and can have a meaningful impact on blood pressure, metabolism, and quality of life. According to one report, 2 years of aerobic exercise resulted in an increase in plasma HDL cholesterol levels of nearly 3-9% [30], which can reduce the incidence of type 2 diabetes. Exercise reduces hyperactivity of sympathetic nervous activity, favoring insulin resistance and improving autonomic nervous system homeostasis [28].

4.2.3. Managing the living environment. To minimize the impact of environmental factors on insulin resistance, the body needs to reduce exposure to high levels of pollution and chemicals and take care of personal environmental cleanliness; however, it also needs to ensure a certain amount of outdoor exercise in order to ensure adequate sunlight exposure. The body needs to be able to sense temperature extremes and make appropriate choices to maintain normothermia, such as adding or subtracting clothing to minimize the effects of temperature extremes on insulin sensitivity. Medical testing and interventions where appropriate.

5. Conclusion

The discussion in this review shows that there is indeed a strong link between lipid metabolism and insulin sensitivity in many ways. Disturbances in lipid metabolism due to excessive accumulation of lipids, triggering an overabundance of FFA and production of inflammatory cytokines; accumulation of DAG as well as ceramides; all of these interfere with normal insulin signaling and ultimately lead to a decrease in the cellular insulin response.

There is no cure for diabetes, so it is important to prevent it. Finding interventions for lipid metabolism and insulin sensitivity is also an important strategy. Dietary changes, lifestyle modifications, physical activity, and the living environment are some of the ways to improve lipid metabolism and insulin sensitivity and reduce insulin resistance and the risk of metabolic diseases. These in-depth studies help to better explain the molecular mechanisms underlying these relationships and provide a theoretical basis for future research and the development of novel therapeutic strategies.

There are many areas where lipid and insulin metabolism need to be investigated for new therapeutic strategies in the future. First, concerning genetic factors, researchers can provide more personalized, unique lipid interventions based on an individual's genetic profile and metabolic status, taking into account genomics, metabolomics, and proteomics. At the same time, researchers can also actively explore new pharmacological treatments to improve normal insulin transmission by regulating the balance of lipid metabolism.

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Going forward, this review is equally important in all respects. For these metabolic diseases, an understanding of lipid metabolism and insulin sensitivity can help in the diagnosis of these diseases as well as provide the rationale for new therapeutic strategies and the development of preventive measures to minimize the long-term effects of the disease on the patient. For patients with metabolic disorders, this information will enable them to understand the mechanisms of disease and health education, as well as to learn to better manage their health by promoting lifestyle changes. For society, these studies can help advance discovery and exploration in clinical practice, deepen understanding of the medical field, and promote cutting-edge research on related diseases.

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