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The Harm of High Fructose Intake to Human Health

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Abstract: Fructose consumption has increased significantly in many countries in recent years. As a sweetener, fructose has been widely used in processed foods and beverages due to its low cost and high sweetness. However, a high-fructose diet can damage human health in many ways. This paper mainly studies the influence of high fructose intake on human metabolism, aiming to explore the harm of high fructose intake on human health. This paper adopts the method of review, it found that high fructose intake can inhibit insulin production, cause insulin resistance, and lead to cardiovascular disease and type 2 diabetes. High fructose intake can lead to lipid production in the liver, lipid dysregulation, and postprandial increase of triglycerides; In addition, high fructose intake can induce hypertriglyceridemia, hyperuricemia, and increase the incidence of asthma. In summary, it can be seen that excessive fructose intake is very harmful to the human body, and we should reasonably control the daily fructose intake in our lives.

Keywords: High fructose, Insulin, Triglyceride

1. Introduction

According to expert recommendations, adults do not consume more than 50 grams of fructose per day, and it is best to control below 25 grams per day. Most studies have separately investigated the effects of high fructose intake on metabolism, cardiovascular, lipid, and disease, but no comprehensive study has been conducted. This paper summarized the comprehensive effects of high fructose intake on human body: By using the method of review, this paper sorted out the comprehensive effects of high fructose intake on human body, and discussed the effects of high fructose intake on human insulin, body weight, cardiovascular, lipid and respiration. Through this paper, readers can clearly obtain the comprehensive impact of high fructose intake on the human body.

2. Effects of high fructose intake on human metabolism

2.1. Resistance in insulin production

In the deuterated glucose disposal test by Kimber L. Stanhope and Peter J. Havel, it was found that during the 10-week intervention period, compared to subjects who consumed glucose-sweetened beverages, Fasting insulin concentrations increased significantly in subjects who consumed fructose-sweetened beverages. Specifically, after 10 weeks of drinking fructose-sweetened beverages, fasting

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insulin concentrations increased in the subjects, while no significant changes were observed in the subjects who drank the glucose-sweetened beverages [1].

Waleska C Dornas, Wanderson G de Lima, Maria L Pedrosa, and Marcelo E Silva designed animal and human experiments and found that after four weeks of feeding rats on a 35% fructose diet, Insulin sensitivity was reduced in rats. At the same time, Waleska C Dornas et al. found that a high-fructose diet was significantly associated with the development of Insulin resistance(IR) and the disturbance of glucose homeostasis in rodents. For example, rats fed fructose instead of starch showed multiple changes in glucose and lipid metabolism over several weeks. Lipid metabolism disorders are closely associated with IR, as ectopic lipid deposition may produce toxic lipid-derived metabolites (such as diacylglycerol, fatty acyl-CoA, and ceramides), Moreover, intracellular accumulation of liver triglyceride (TG) leads to increased serine/threonine phosphorylation of insulin receptor substrate 1 (IRS-1), which reduced insulin signaling. An increase in TG content is observed as early as 1 week, and fasting hyperinsulinemia occurs within 2 to 5 weeks, indicating systemic insulin resistance. In another study, rats fed 66 percent fructose had significantly less insulin receptor mRNA and insulin receptor number in skeletal muscle after 3 weeks compared to rats fed a standard diet. In the same 4-week study in human men, dietary fructose was found to reduce insulin sensitivity and increase liver steatosis and circulating TG levels [2].

In her study, Salwa W Rizkalla found that consuming an additional 1000 kcal of fructose per day for a week led to insulin binding and reduced insulin sensitivity compared to consuming the same amount of glucose. For the same amount of glucose sweetened drinks, daily consumption of high-fructose sweetened drinks (25% of total energy) for 10 weeks resulted in increased fasting plasma glucose and insulin levels, which in turn led to reduced insulin sensitivity. However, if moderate amounts of fructose are controlled to only 30 grams or 60 grams per day, there is no adverse effect on insulin sensitivity in healthy subjects compared to consuming the same amount of sucrose. Salwa W Rizkalla also found that a high-fructose diet resulted in a decrease in pancreatic beta cell mass, an increase in apoptotic cells, and an increase in glucose-induced insulin release. These changes lead to increased insulin secretion and, despite reduced beta cell mass, lead to hyperinsulinemia, impaired glucose tolerance, and insulin resistance [3].

2.2. The causation of cardiovascular disease and type 2 diabetes

In experiments on rats, İlter İlhan et al. found that a high-fructose diet in rats caused manifestations of metabolic syndrome, including obesity, insulin resistance, dyslipidemia and hypertension, and also changed the composition of the gut microbiota, increasing the number of harmful bacteria and decreasing the number of beneficial bacteria, which led to type 2 diabetes. In a study by Titer lhan et al., long-term fructose intake was found to increase the levels of cardiomyocytes, vascular endothelial cells, and inflammatory cytokines (such as IL-1β and TNF-α), thereby increasing the risk of cardiovascular disease. Excessive intake of fructose can increase the level of cellular oxidative stress. It also reduces the mitochondrial mass in heart muscle cells, resulting in mitochondrial dysfunction, which affects the normal function of the heart. At the same time, free radicals produced during fructose metabolism can cause cell damage and trigger an inflammatory response. They also looked at high-fructose corn syrup (HFCS), and they found that HFCS intake leads to increased uric acid synthesis in the liver, triggering oxidative stress and impairing endothelial nitric oxide production, leading to endothelial dysfunction. These are all important factors that lead to cardiovascular disease [4].

In Salwa W Rizkalla's study, plasma triglyceride (TG) and very low density lipoprotein triglyceride (VLDL-TG) levels were found to increase after high fructose intake, as was Kimber L. Stanhope and Peter J. Havel: Excessive fructose intake leads to a significant increase in the area under the triglyceride (TG) curve (AUC) 24 hours after meals, while glucose consumption tends to decrease,

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thereby increasing the risk of cardiovascular disease. They also found that excess fructose intake increased the concentrations of low-density lipoprotein cholesterol (LDL-C), apolipoprotein B (apoB), small and dense low-density lipoprotein (sdLDL), and oxidized LDL, promoted lipoprotein remodeling, and increased postprandial-like residual granular lipoprotein (RLP) -TG and RLP -cholesterol. These changes can also lead to an increased risk of vascular disease [1,3]

3. Effects of high fructose intake on body weight

3.1. An increase in visceral fat

Kimber L. Stanhope and Peter J. Havel found that excessive fructose intake led to a significant increase in visceral fat (VAT), while glucose intake mainly led to an increase in subcutaneous fat (SAT). The metabolism of fructose in the liver is not regulated by the energy status, resulting in a larger intake of fructose by the liver and less fructose entering the circulatory system, resulting in visceral fat accumulation [1].

Waleska C Dornas, Wanderson G de Lima, Maria L Pedrosa, and Marcelo E Silva found that increased excess fructose intake leads to lipid synthesis in the liver, resulting in increased reesterification of non-esterified fatty acids (NEFA) and downregulation of lipid oxidation in the liver. It causes an imbalance between the "input" and "output" of lipids in the liver, resulting in a net accumulation of fat in the liver [2].

GAN Qianyun, SUN Xueqian, SONG Ge, et al., after feeding SD rats a diet containing 35% fructose for 4, 8 and 12 weeks, the expression levels of IKKβ, IκB and NF-κB/p65 proteins in the NF-κB pathway were up-regulated and significantly activated in a time-dependent manner. The increase of serum lipids and the accumulation of lipids in the liver were induced. At present, several studies have found that by regulating AMPK signaling pathway, fat accumulation caused by high fructose is reversed. According to other studies, high fructose intake increases liver fat accumulation by inhibiting the expression levels of leptin and adiponectin, preventing calcium ions from activating CaMKK, and inhibiting AMPK phosphorylation [5].

In the experimental study of CHE Yingjuan et al., a large number of large fat vacuoles, enlarged liver cells, abnormal morphology and blurred boundaries were observed in the liver of rats in the high-fat and high-fructose diet group, all of which were manifestations of liver fat accumulation. In contrast, fat accumulation was also observed in the high-fat diet group, but to a lesser extent, mainly manifested by more small fat vacuoles within and between hepatocytes. It can be seen that Fructose is metabolized by ketohexokinase to produce fructose-1-phosphate, a substrate for fatty acid synthesis that further promotes fat accumulation in the liver.

The fructose component of a high-fat, high-fructose diet increases the raw material for fatty acid synthesis during metabolism, thus exacerbating the phenomenon of liver fat accumulation [6].

DU Mongyu, HE Shuxuan et al. found through their studies on fructokinase that fructokinase is a key enzyme in fructose metabolism and can promote the rapid conversion of fructose to fructose-1-phosphate. Fructose-1-phosphate is decomposed into dihydroxyacetone phosphate and glyceraldehyde by aldolase B. Both of these products are critical in the process of lipid synthesis and storage [7].

3.2. Lipid imbalance

In their study on fructose metabolism, DU Mengyu, HE Shuxuan et al. found that the increase in ATP consumption and oxidative stress caused by fructose metabolism could indirectly affect the expression and activity of genes related to lipid metabolism. However, a high-fat and high-fructose diet can interfere with the normal metabolic process of lipids by affecting the intake, synthesis, oxidation and storage of fatty acids. Metabolites produced during fructose metabolism can activate

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signaling pathways such as AMPK and SREBP-1c. The disturbance of fructose metabolism will affect the normal function of these signaling pathways, resulting in dysregulation of lipid metabolism [7].

Excessive fructose consumption has been shown to promote fat production and store fat in the liver, which can trigger obesity and non-alcoholic fatty liver disease (NAFLD). Gan Qianyun, Sun Xueqian, Song Ge et al. studied the signaling pathway and found that the activation of PI3K/AKT signaling pathway is related to adipogenesis and insulin resistance, and the activation of MAPK signaling pathway is related to adipocyte differentiation, lipid accumulation and inflammatory response, which indirectly promote lipid dysregulation. Inhibition of AMPK signaling pathway leads to increased fatty acid synthesis, promotes liver fat accumulation, and increases the risk of NAFLD. In addition, fructose rapidly consumes adenosine triphosphate (ATP) in the metabolic process, which is irreversible, and eventually causes adenosine monophosphate (AMP) to accumulate in the body, and high fructose also leads to lipid accumulation through multiple signaling pathways [4].

3.3. The increase in postprandial triglycerides

Salwa W Rizkalla designed animal experiments and found that a high-fructose diet (75% fructose) significantly increased liver triglyceride synthesis and serum triglyceride levels in rats. He also designed acute and chronic studies in humans. In acute studies, dietary fatty acids were significantly increased in VLDL within 4 hours after eating a high dose of fructose (0.75g/kg body weight) compared to glucose in healthy subjects, suggesting that fatty acids produced by fructose metabolism can be packaged into very low density lipoprotein (VLDL), resulting in increased plasma triglyceride (TG) levels. Fructose also inhibits liver lipid oxidation and promotes fatty acid reesterification and VLDL-TG synthesis. Moreover, even small doses of fructose mixed with glucose in drinks can immediately increase postprandial triglyceride levels. In the chronic study, Salwa W Rizkalla found that fructose-sweetened beverages increased postprandial triglyceride and fasting apolipoprotein B concentrations in overweight and obese women over a 10-week study compared to glucose-sweetened beverages. One meta-analysis found that fructose intake. At 50g/ day, there was no significant effect on postprandial triglyceride; When fructose intake is less than 100g/ day, it has no significant effect on fasting triglyceride, but increases postprandial triglyceride level [3].

Waleska C Dornas et al. found that excess fructose intake leads to lipid conversion and triglyceride secretion and clearance in the liver, suggesting that de novo lipid (DNL) may be a key biochemical process induced by fructose. Fructose increases fatty acid and triglyceride synthesis by stimulating the DNL pathway in the liver, resulting in higher triglyceride levels after meals [2].

Kimber L. Stanhope and Peter J. Havel found sex differences in the effects of fructose on postprandial triglycerides. Compared with men, healthy young female subjects showed a significantly reduced metabolic response to fructose, manifested by a smaller increase in postprandial triglyceride levels (Couchepin et al., 2008). Kimber L. Stanhope and Peter J. Havel also compared the effects of fructose, glucose, high-fructose corn syrup (HFCS), and sucrose on postmeal triglycerides. The results showed that the postprandial triglyceride reaction of sucrose and HFCS was comparable to that of pure fructose and significantly higher than that of glucose [1].

4. The increase in high fructose intake in the incidence of disease

4.1. The induction of hypertriglyceridemia

CHE Yingjuan et al. conducted a study on rats, and the results showed that the serum uric acid content of rats in the high-fat and high-fructose diet group was significantly higher than that of the model group (rats given only adenine and potassium oxazinate), indicating that the high-fat and high-fructose diet would further increase the uric acid content of hyperuricemia (HUA) rats. Both high-fat

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diet and high-fat high-fructose diet have negative effects on hyperuricemia rats to varying degrees, especially high-fat high-fructose diet can further increase uric acid level, aggravate kidney injury and liver fat accumulation [6].

4.2. The induction of asthma incidence

Luanne R. DeChristopher and Katherine L. Tucker analyzed the frequency of consumption of 100% fruit juice, soda/sports drink/fruit juice drink, and found that the incidence of asthma in children who consumed 100% fruit juice daily was about twice that of children who consumed no or occasional fruit juice. The incidence of asthma in children who consumed these beverages regularly or daily was about two and a half to three times higher than in children who did not consume them or who consumed them occasionally. The fructose-glucose ratio in high-fructose corn syrup and apple juice exceeds 1:1, and when this excess free fructose is not absorbed in the gut, it may react with partially digested dietary protein to form immunogens, triggering asthma. These immunogens bind to asthma-mediated receptors, such as RAGE, and may trigger airway mucus secretion and airway hyperresponsiveness. At the same time, they found that higher rates of asthma in African Americans and Puerto Ricans may be related to higher rates of fructose malabsorption in these populations [8].

5. Conclusion

This paper mainly discusses the overall damage of high fructose intake to the human body. Found that excessive fructose intake can lead to insulin resistance; Cause cardiovascular disease and type 2 diabetes; Lead to increased or dysregulated lipids, elevated postprandial triglycerides and hypertriglyceridemia; and increased incidence of asthma. Although the effects of high fructose intake on the human body were discussed in this paper, the damage to the liver and intestinal mucosal barriers was not involved. Future research will focus on liver and intestinal damage from fructose intake.

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