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Metabolism and Clinical Significance of Triglycerides

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ABSTRACT: Triglycerides, the principal form of fat storage in animals and humans, are essential in view of their roles in energy metabolism and regulation. Indeed, they have been ascribed very vital functional significance in a plethora of physiological processes, which extends to energy storage, metabolic signaling, and disease pathology. Biochemistry and metabolism of triglycerides is a multivaried area of science that includes different mechanisms that control synthesis, storage, and utilization in organisms. For many years, the issue of triglycerides and their relationship to cardiovascular disease (CVD) has been one of the central themes of research. Elevated triglyceride levels frequently associate with an elevated cardiovascular risk, but the situation is complex and multifaceted at all. It has now been reported that triglycerides could act not only as a biomarker regarding cardiovascular risk but also play an actual part in the fostering of cardiovascular disorders. The present literature review juxtaposes key findings on triglyceride metabolism, thereby underlining implications for health and disease, with the end to identify works currently associating triglyceride implications in cardiovascular health, and further to explore determinants of triglyceride levels gap that warrant further investigation.

INTRODUCTION

Triglyceride levels are determined by multiple factors, including genetic, lifestyle, and behavioral factors. Healy et al. (2011) note that low energy expenditure is strongly associated with unfavorable changes in biomarkers of disease, including elevated triglyceride levels, and, thus, it may be seriously recommended to modify lifestyle in the management of cardiovascular health. This is in support of findings by Ekelund et al. (2012) that high levels of moderate to vigorous physical activity are associated with lower triglycerides and improved cardiometabolic health. Genetic factors are paramount in the regulation of triglyceride metabolism. Nordestgaard (2016) emphasized the potential role of genetic-targeted interventions for the therapeutic lowering of triglycerides and therefore cardiovascular risk in this review with reference to, in particular, genetic variants in the ANGPTL3 gene. It is practice-changing that this relation of genetic variants with lower triglyceride levels makes it seem plausible that knowledge of individual genetic susceptibilities might similarly inform personalized treatment approaches.

The tissue of the fat body serves as the major reservoir for triglycerides and facilitates energy storage and release, which are essential for growth and reproduction. Lipid metabolism provided the bulk of energy homeostasis which is crucial in periods of fasting via the mobilization of triglycerides from cytoplasmic lipid droplets. The work reminds of the major role played by triglycerides as an energy reserve system, reflecting on how insects deal with metabolic challenges and giving implications to general triglyceride functions in different organisms.

It has to be remembered that the first choice in managing these levels are dietary options and changes in lifestyle. According to Dongiovanni et al. (2015), levels of triglycerides can drastically be reduced by imitating fasting-mimicking diets, especially in people at metabolic risk. This strongly implies that the dietary approach could be effective in changing metabolic parameters to lower cardiovascular risk. Moreover, Lin et al. (2015) reported that lifestyle changes, such as exercise and diet, were vital in triglyceride reduction and having a healthy heart. This was supported even by the meta-regression conducted by Nordestgaard et al. (2016) which detailed the value of exercise as a major intervention in handling triglycerides and hence its role in the prevention of cardiovascular disease.

METABOLISM

It was undertaken to study the metabolism of SCFAs and MCFAs, that is, the short- and medium-chain fatty acids derived in the liver from the hydrolysis of dietary triglycerides. It was found that these fatty acids served as regulators of different processes in lipid metabolism and energy homeostasis (e.g. glycolysis and lipogenesis). The authors proposed that varying responsiveness of an

individual to dietary sources might be at least one way how the relationship between triglycerides and fatty acid metabolism can be so complex. This has to encourage further research into how differently profiled fatty acids influence the overall lipid profile.

As emphasized by Chiang (2013), the regulation of hepatic lipid homeostasis is a key contribution of bile acids. They act in the emulsification and absorption of dietary lipids, such as triglycerides. The conversion of cholesterol to bile acids is necessary to avoid triglyceride accumulation in the liver; thus, bile acid metabolism is connected with triglyceride regulation. Such studies reveal a rather intricate interaction of bile acids with lipid metabolism, which in its turn might open up new possibilities for the treatment of dyslipidemia and associated metabolic disorders.

Activation of peroxisome proliferator-activated receptors, especially PPAR-α and PPAR-γ, has been remarked for significant effects on metabolism of triglycerides. Tyagi et al. (2011) have reported that activation of PPAR-α lowers triglyceride levels and increases oxidation of fatty acids, whereas PPAR-γ enhances insulin sensitivity. Knowledge of these pathways is a prerequisite in developing special therapies, which are aimed to elevate lipid profiles and to fight metabolic disorders through connection of triglyceride biochemistry with more general metabolic functions.

Triglyceride metabolism, as centrally coordinated by the liver, is delineated in the work of Alves-Bezerra and Cohen (2017) focus on the pathogenesis of NAFLD. They stress that overnutrition and obesity slam up triglyceride storage in the hepatocyte, reviewing at the molecular level how fatty liver is formed. The findings further justify more research on how regulatory pathways that control lipid metabolism in the liver are coordinated and their role in the pathogenesis of metabolic diseases.

In their study, Musunuru et al. (2010) discuss the genetic underpinning of hypolipidemia associated with ANGPTL3 mutations, which are related to low levels of triglycerides. Knowledge of the genetic control concerning triglyceride metabolism will contribute to the influence of hereditary components on lipid profiles and their implications for cardiovascular health. Such research goes a long way to place in perspective genetic investigations on triglyceride metabolism vis-à-vis their clinical relevance to the broader population.

Recently, the involvement of microRNAs in the regulation of triglyceride and cholesterol metabolism has gained much attention. MiR-33a and its homologue MiR-33b are among such miRs that play a role in the regulation of lipid homeostasis, hence likely druggable for the treatment for dyslipidemia to reduce cardiovascular risk, in a review increasing consciences are put on the molecular mechanisms that regulate lipid levels as well as their relationship with triglyceride metabolism.

In their study, Chau et al. (2010) proposed fibroblast growth factor 21 (FGF21) as a metabolic regulator that lowers triglycerides. FGF21-dependent activation of AMPK and SIRT1 improves mitochondrial oxidative function, a key player in lipid metabolism. The work really strongly brings out the provision of FGF21 as a potential therapeutic target in the treatment of obesity and diabetes, with triglyceride metabolism related to much broader metabolic regulatory networks.

Parhofer (2012015) discusses the mTOR complexes in triglyceride metabolism via control of lipogenesis and adipogenesis by them. Knowledge about the mTOR signaling pathways and the influence of nutrient availability on triglyceride accumulation will certainly help solve the issue of metabolic health in the presence of obesity and insulin resistance.

TRIGLYCERIDES AND CARDIOVASCULAR DISEASE

It is widely accepted within the literature that elevated triglyceride levels are an independent risk factor for CVD. In their study, Miller et al. (2011) stress that assessment of cardiovascular risk really includes triglycerides, especially in the gradually enlarging epidemic of obesity and metabolic diseases such as insulin resistance and type 2 diabetes mellitus. Atherogenicity of triglyceride-rich lipoproteins has been reliably proven; it reflects their participation in atherogenesis and subsequently developing cardiovascular events. And this accords with the findings of Chapman et al. (2011) who also state that raised TRLs do add to the cardiovascular risk in individuals, especially those who have underlying cardiometabolic abnormalities.

Moreover, the meta-analysis by Nordestgaard et al. (2016) supports that high triglycerides and their remnants are important causal factors for myocardial infarction. This finding strongly reiterates the case for highly effective strategies targeting triglyceride reduction that must be pursued in the clinical setting. Together, these results show the need to assess triglycerides as part of the risk stratification for cardiovascular disease.

In humans, high levels of triglycerides are strongly associated with the risk of cardiovascular disease (CVD). In their paper from 2011, Miller et al. discuss triglycerides as important biomarkers in the assessment of CVD risk, with an emphasis on the contribution of triglyceride-rich lipoproteins (TRLs) to atherogenesis. The process of metabolism of triglycerides is well known, and this knowledge is key to the development of strategies for therapy aimed at avoiding the most common and hazardous risks of hypertriglyceridemia. This research paper relates biochemistry of triglycerides to clinical outcomes, which gives reason to pay much attention to efficient lipid level control in CVD prevention.

INSULIN RESISTANCE AND TRIGLYCERIDE METABOLISM

In 2010, Guerrero-Romero et al. developed the triglycerides and glucose (TyG) index as an alternative marker in the evaluation of insulin resistance, indicating also that triglyceride metabolism should be considered the cornerstore of metabolic assessment. What

they found is that triglyceride and glucose measured in fasting were closely related, indicating a connection between lipids and carbohydrate metabolism. This relationship alone provides a better understanding of both metabolic syndrome and type 2 diabetes, justifying further research into the influence of triglyceride levels on insulin sensitivity.

CONCLUSION

Triglyceride biochemistry and metabolism, coordinated by a web of important regulatory mechanisms, are anything but simple in the maintenance of homeostasis and the prevention of disease. This review attempts to draw a broad picture of the critical findings on triglyceride metabolism from insect physiology to human health. Continued study in this area is considered important to develop therapeutics that will address the rise in prevalence of metabolic disorders that have been associated with disregulated triglyceride levels. It has been proven long ago that a relationship exists between triglycerides and cardiovascular problems, with the elevation of triglyceride levels being tantamount to both a risk factor and a risk in itself for cardiovascular issues. The determinants of triacylglycerol levels are many and varied, including genetic, lifestyle-related, and dietary factors. While much progress has been made in understanding this relationship, important knowledge gaps remain with the mechanisms underlying the impact of triglycerides on cardiovascular health. Future research should address these gaps and look into personalized approaches to triglyceride management, assessing the long-term effects of various interventions on cardiovascular outcomes.

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