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REVIEW ARTICLE

The postprandial situation as a pro-inflammatory condition

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Abstract Postprandial lipemia has been associated with cardiovascular disease. The current pathophysiological concept is that postprandial remnant lipoproteins migrate into the subendothelial space and that remnants activate circulating leukocytes and endothelial cells. Activated monocytes adhere to endothelial adhesion molecules, facilitating subendothelial migration of monocytes. These cells differentiate into macrophages, with the risk of foam cell formation, due to uptake of remnants and modified lipoproteins. Evidence is emerging that specific interventions may reduce the atherogenic postprandial inflammation. Fruits rich in polyphenols, virgin olive oil, carotenoids and exercise have recently been found to reduce postprandial inflammation. Pharmaceutical interventions with fibrates or statins not only improve the overall lipid profile, but reduce postprandial inflammation as well. This review will deal with the current concept of postprandial inflammation in relation to the development of atherosclerosis and potential interventions to reduce postprandial inflammation.

PALABRAS CLAVE
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La situación posprandial como condición proinflamatoria

Resumen La lipidemia posprandial está relacionada con la enfermedad cardiovascular. El concepto patofisiológico actual es que las partículas remanentes traspasan el endotelio, activan los leucocitos y las células endoteliales. Los monocitos activados se adhieren a la pared endotelial por mediación de moléculas de adhesión, facilitando así la migración de los monocitos

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al espacio subendotelial. Estas células se transforman en macrófagos, convirtiéndose definitivamente en células espumosas después de haber internalizado las partículas remanentes y otras lipoproteínas modificadas. Recientes estudios sugieren que existen intervenciones efectivas para modular la inflamación posprandial, y de esta forma rebajar el riesgo cardiovascular. Frutas ricas en polifenoles, aceite de oliva virgen, el caroteno y el ejercicio son ejemplos que han demostrado una reducción de la inflamación posprandial. El tratamiento con estatinas y fibratos no solo mejora el perfil lipídico, sino que también rebaja la lipidemia posprandial. Esta revisión describe los recientes conceptos de la inflamación posprandial relacionada con la generación de ateroesclerosis y también trata las intervenciones que pueden influir positivamente en la inflamación posprandial.

Introduction

When thinking of lipids in association with cardiovascular disease (CVD), the relationship between low-density lipoprotein cholesterol (LDL-C) and atherosclerosis is usually the first one that comes to mind. This is due to the great number of papers published during the last two decades addressing the effect of LDL-C reduction on incident CVD.[1]

However, atherosclerosis is a multifactorial disease and elevated LDL-C is just one of the many lipid risk factors involved.[2] All apolipoprotein (apo) B containing lipoproteins, which include chylomicrons, chylomicron remnants, very-low density lipoproteins (VLDL), intermediate-density lipoproteins (IDL) and LDL, are atherogenic. Increased fasting and non-fasting triglycerides, high plasma apo B concentrations and increased remnant cholesterol, together with elevated lipoprotein(a) and low high-density lipoprotein cholesterol (HDL-C) concentrations, are now recognized as independent risk factors beyond LDL-C.[3–5] Elevated triglycerides and remnant cholesterol levels are associated with postprandial lipemia, and most investigators in the field acknowledge the relevance of postprandial hyperlipidemia as a contributing, or even independent, risk factor for atherosclerosis.[6] The usual concept in this respect is that the generation of postprandial remnant particles, which can migrate into the subendothelial space and induce a local inflammatory process ultimately leading to foam cell formation, is responsible for vascular deterioration and plaque formation.[7] Recent work from different laboratories has expanded this hypothesis to the widely accepted inflammatory pathogenesis of the atherosclerotic plaque.[7–9] Novel data suggest that remnants may interact with circulating inflammatory cells, such as neutrophils and monocytes, and with endothelial cells. This interaction induces the generation of chemokines and oxidative stress, causing an intravascular inflammatory response preceding the subendothelial reaction described earlier.[8,10–12]

In order to improve our understanding of this intravascular inflammation, it is important to comprehend the processes involved in intravascular remodeling of the triglyceride-rich lipoproteins (TRLs).[10,13] This review will address the current knowledge about postprandial lipemia and inflammation, and it will give an overview of lifestyle changes and pharmacological interventions.

Classical concept of postprandial lipemia: chylomicron synthesis and secretion

Dietary lipids and fat-soluble vitamins are transported from the intestine to the blood by chylomicrons. Chylomicrons are the largest TRLs, and they contain triglycerides, cholesterol, phospholipids and proteins, with apo B48 as the structural protein.[14] Ingested triglycerides are digested into free fatty acids (FFAs) and 2-monoacylglycerol (MAG) by pancreatic lipase. FFAs and MAG are absorbed from the intestinal lumen and are carried to the endoplasmatic reticulum (ER), where they are resynthesized to triglycerides.[15–17] Within the ER, a prechylomicron is formed from two different primordial chylomicrons. One primordial chylomicron consists of phospholipids, cholesterol and one apo B48 molecule, and is chaperoned by the microsomal transfer protein (MTP) complex.[18] The other primordial chylomicron contains cholesterol esters, triglycerides and a single apo A-IV molecule.[19] The prechylomicron is then transported to the Golgi, where apo A-I is attached and a mature chylomicron is formed.[19–21] This mature chylomicron is secreted into the lymphatic system.[21] This process is illustrated in Fig. 1.

Common pathways for chylomicrons and very-low density lipoproteins in lipolysis and clearance

In the circulation, chylomicrons are hydrolyzed by lipoprotein lipase (LPL), which converts triglycerides into glycerol and fatty acids,[22] resulting in the formation of cholesterol-dense lipoprotein remnants, which are taken up by the liver.[23,24] Recently, the important role in the hydrolysis of triglycerides of glycosylphosphatidylinositol-anchored high-density lipoprotein binding protein 1 (GPIHBP1) has been identified. This protein serves as a binding site for LPL to the endothelium, and thus provides a docking platform for chylomicrons and VLDL, facilitating the triglyceride lipolysis from these lipoproteins.[25,26] The dietary FFAs that are