Abstract

Biochim Biophys Acta. 2011 Oct 7. [Epub ahead of print]

Lipolysis of triglyceride-rich lipoproteins, vascular inflammation, and atherosclerosis.

Schwartz EA, Reaven PD.

Division of Research, Phoenix VA Health Care System, 650 E. Indian School Rd., Phoenix, AZ 85012, USA.

BACKGROUND: Epidemiological and interventional studies have implicated elevated triglyceride-rich lipoprotein (TGRL) levels as a risk factor for cardiovascular disease and vascular inflammation, though the results have not been entirely consistent. This appears particularly relevant in model systems where the lipolysis occurs in the setting of established inflammation (e.g., in pre-existing atherosclerotic plaques), rather than in the tissue capillary beds where lipolysis normally occurs.

FINDINGS: Two main mechanisms seem to link TGRL lipolysis to vascular inflammation. First, lipolysis of TGRL leaves behind partially lipolyzed remnant particles which are better able to enter the vessel wall than nascent TGRL, have a rate of egress substantially lower than their rate of entry, and contain 5-20 times more cholesterol per particle than LDL. Furthermore, remnants do not require oxidation or other modifications to be phagocytized by macrophages, enhancing foam cell formation. Second, saturated fatty acids and oxidized phospholipids released by lipolysis induce inflammation by activating Toll-like receptors of the innate immune system, via oxidative stress, or by greatly amplifying existing pro-inflammatory signals (caused by subclinical endotoxemia) via mitogen-activated protein kinases. However, n-3 and unbound n-9 unsaturated fatty acids released by lipolysis have anti-inflammatory effects.

CONCLUSION: Thus, the contribution of TGRL lipolysis to inflammation likely depends less on the TGRL concentration than on the balance between pro- and anti-inflammatory factors, and on the setting in which the lipolysis occurs. In the setting of the typical "Western" diet, enriched in saturated and oxidized fatty acids and excessive in size, this balance is likely to be tilted towards increased vascular inflammation and atherosclerosis.

PMID: 22001233