GLOBALIZATION OF FOOD CONSUMPTION, SERUM AMYLOID A AND ATHEROGENESIS

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ABSTRACT

Coronary artery disease (CAD) is increasing worldwide and has become the number one (1) cause of death in the Philippines. Globalization which includes radical shifts in food consumption to a western diet that has supplanted traditional eating believed to be responsible for about 30% of CAD worldwide. The current study aimed to investigate the contribution of inflammation attending the globalization of food consumption to atherogenesis and its fatal consequence, CAD. The study utilized quantitative scientific procedures, and instruments which include chromatographic columns, ultracentrifuge, electron microscope, spectrophotometer and other similar instruments. Subjects are animal models such as rabbits and mice. Data analyses include quantitative results of biochemical assays such as cholesterol and apoprotein level determinations, and visualization of electron photomicrographs. Included is the simple review of published related studies. The qualitative descriptive analysis was done for the data. The data showed that although high levels of HDL and, its major apoprotein, apoA-I are known to be atheroprotective, during inflammation characterized by >1000-fold increases of the inflammatory marker protein, serum amyloid A (SAA), HDL decreases precipitously, SAA displaces apoA-I compromising HDL's protective function. Dietary cholesterol from animal-based diet evoked increases in SAA suggesting that inflammatory processes resulting from globalization of food consumption contribute to the increase of CAD worldwide. Preventive measures "should emphasize consumption of the "most healthful and nourishing diet" of whole grain, nuts, legumes, fruits, and vegetables reflecting a turn-of-the-century advocacy progressively being verified by scientific data.

Keywords: *coronary heart disease, atherosclerosis, inflammation, HDL, SAA, global dietary shifts*

INTRODUCTION

Coronary heart disease is the number one (1) cause of death in the United States and other industrialized nations (American Heart Association, 2017). Although the death due to coronary heart disease is decreasing in developed countries, it is increasing in developing and transitional countries, according to the World Health Organization, accounting for more than 60% of the global burden of coronary heart disease (World Health Organization, 2009). As one of those developing countries, heart disease has now become the number 1 cause of death in the Philippines (Department of Health, 2016). The relationship between inflammation, food consumption and the development of atherosclerosis will have to be established.

The root cause of coronary heart disease is atherosclerosis. Lipoproteins play a major role in the development of atherosclerosis. Lipoproteins are vesicles in blood plasma that transport the non-polar lipids, triglycerides, and cholesteryl esters from their place of production (liver) or dietary absorption (intestines) to their place of utilization (cells) or excretion (liver).

Composed of a core made up of the lipids that they transport surrounded by a surface layer of non-covalently linked membrane-like phospholipid embedded with apoproteins (apo), these vesicles classified according to their ultracentrifugal flotation densities include: very low-density lipoprotein (VLDL), low-density lipoprotein (LDL), and high-density lipoprotein (HDL).

High levels of LDL, the so-called “bad cholesterol” is a risk factor for atherosclerosis while high levels of HDL, also known as “good cholesterol,” is protective against the disease (Soran et al., 2012). Their apoprotein contents function as structural proteins, ligands for receptors, and co-factor of enzymes involved in lipid metabolism. These include apoB, the structural protein of LDL, apoA-I, and apoA-II the structural proteins of HDL, apoE which shuttles between VLDL and HDL and the apo Cs (CI, CII, and CIII) found mostly in VLDL. High levels of apoB are pro-atherogenic while a high level of apoA-I is associated with longevity (Kwiterovich & Sniderman, 1983). High

levels of apoE-containing particles suggest a defective lipid clearance and are associated with early development of atherosclerosis (Mahley & Angelin, 1984). Because of their role in the patho/physiologic mechanisms of atherogenesis, lipoprotein analyses are vital in the diagnoses of lipid-related cardiovascular abnormalities.

Statement of the Problem

This study aimed to show the connection between inflammation, food consumption and the development of atherosclerosis.

Specifically, the study sought to answer the following questions:

1. How do normal lipoprotein vesicles look like?
2. What is the effect of the inflammation and tissue destruction to the lipoproteins particularly HDL and LDL?
3. What is the effect of inflammation on the serum amyloid A (SAA)?

METHODOLOGY

Research Design

The study utilized quantitative scientific procedures, especially the use of laboratory procedures. It also utilized qualitative analysis of the literature to support the quantitative results of the study.

Subjects of the Study

Subjects are animal models such as rabbits and mice. Likewise, literatures that were included in the analysis are part of the subjects of the study.

Instrumentation

Instruments used in the study include chromatographic columns, ultracentrifuge, electron microscope, spectrophotometer and other similar instruments.

Data Analysis

Data analysis includes quantitative results of biochemical assays such as cholesterol and apoprotein level determinations, visualization of electron photomicrographs. The qualitative descriptive analysis was done for the data with the simple review of published related studies.

RESULTS AND DISCUSSION

Lipoprotein Vesicles in Normal Plasma

Figure 1

Electron photomicrograph of lipoproteins particles, unpublished data

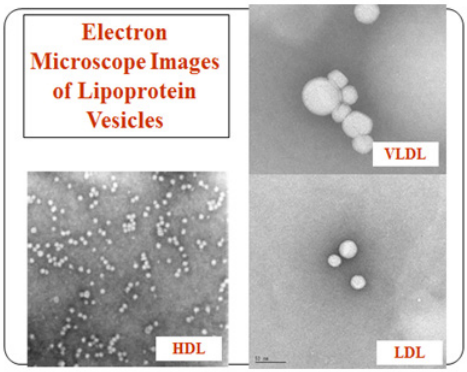


Figure 1 shows electron photomicrographs of lipoprotein vesicles in normal plasma. Plasma lipoproteins can be divided into seven classes based on size, lipid composition, and apolipoproteins (chylomicrons, chylomicron remnants, VLDL, IDL, LDL, HDL, and Lp (a)). Chylomicron remnants, VLDL, IDL, LDL, and Lp (a) are pro-atherogenic while HDL is anti-atherogenic (Feingold & Grunfeld, 2015).

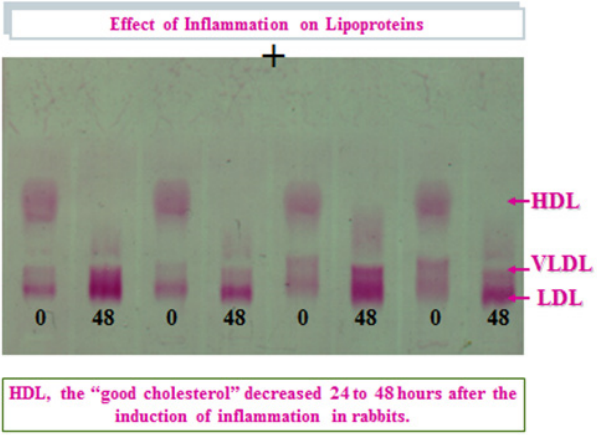
Inflammation and atherosclerosis

Inflammation is a component of the innate immune response. According to Getz (2005), "It is now widely recognized that atherosclerosis is a specific example of a chronic inflammatory response mainly to dyslipidemia and other risk factors."

Cabana et al. (1983) have shown the massive decrease of HDL and increases of LDL within 24-48 hrs following the induction of inflammation and tissue destruction laboratory animals as shown in Figure 2.

Figure 2

Agarose electrophoresis of rabbit plasma taken before (0 hr) and 48 hrs after the injection of 1% croton oil (v/v mineral oil) to induce inflammation. LDL increased while HDL was undetectable in the 48 hrs plasma (Cabana et al., 1983)



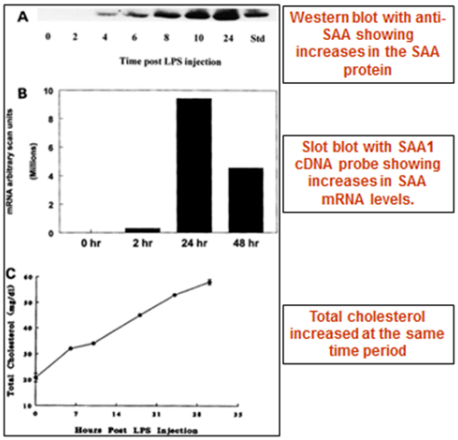
Similar changes occur in human subjects undergoing inflammatory conditions (Blackman et al., 1993; Cabana et al., 1997). Lipid analyses of the sera from the individuals undergoing inflammation showed increases in triglyceride and cholesterol in the VLDL and LDL fractions and massive decreases in HDL cholesterol and apoA-I. The remaining particles became enlarged, dense and enriched with serum amyloid A (SAA), SAA replacing apoA-I from the particles thereby affecting the atheroprotective functions of HDL.

SAA is a protein usually undetectable in normal plasma. Together with another protein, the C-reactive protein (CRP), SAA increases in concentration from 0 to >1000 ug/ml 24 to 48 hr following the induction of inflammation (Figure 3).

CRP and SAA are the only two proteins known for their rapid and massive increase. The biological significance of their increase remains unknown. Recent data suggest that CRP and SAA independently predict risks of future cardiovascular disease or death from cardiovascular causes. Whether they are active participants in the disease process or are simply markers of inflammation is not clear. The studies focused on SAA. The increase in concentration resulted from de novo production as shown by increases in both the mRNA and the protein (Figure 3). Plasma cholesterol levels increase at the same period.

Figure 3

Increases in SAA and cholesterol 24 hr after the induction of inflammation. Top, increases in SAA protein. Middle, increases in SAA mRNA. Bottom, increases in plasma cholesterol level adapted from Cabana et al. (1996) and Cabana et al. (1999)

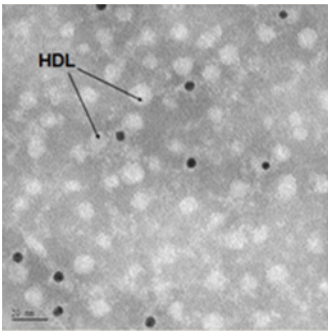


The biological significance of their increase remains unknown. SAA circulates in plasma bound to HDL (Figure 4).

SAA can be formed in the absence of the immune response and can bind lipid forming nascent like particles (Figure. 4). Various roles have been speculated for SAA. Getz (2005) suggested that SAA promotes early atherogenesis.

Figure 4

Electron photomicrograph obtained with anti-SAA labeled gold particles (unpublished data) showing SAA (black dots) bound to HDL (white particles)



Indirect evidence suggests that SAA may play a role in the initiation/progression of atherosclerosis, possibly involving the disruption of the atheroprotective function of HDL (Tolle et al., 2012). SAA may alter the level and function of HDL and displace apoA-I from the particles (Cabana et al., 1989). During the inflammatory conditions, HDL becomes proatherogenic (Van Lenten et al., 1995). SAA may bind cholesterol and affect the transfer of cholesterol from the tissues to HDL thereby altering a process called "reverse cholesterol transport" for the elimination of excess cholesterol (Banka et al., 1995). Dietary cholesterol evoked increases in SAA and atherosclerosis in mice (16) and human (Lewis et al., 2004). SAA was found in the fatty deposits of blood vessels (Tannock et al., 2005), was produced by endothelial cells, the cells that line and protect the lumen of blood vessels (Liang & Sipe, 1995) and induced the migration, adhesion, and infiltration of monocytes, the cells involved in the deposition of fatty streaks in the blood vessels (Meek et al., 1994; Badolato et al., 1995). Recently, Dong et al. (2011) and Badolato et al. (2000) showed that Serum amyloid A directly accelerates the progression of atherosclerosis in apolipoprotein E-deficient mice while King et al. (2011) and Dong et al. (2011) is of the opinion that SAA plays a causal role in atherosclerosis.

Lifestyle, inflammation, and atherosclerosis

Lifestyle is a major factor in the development of atherosclerosis and its fatal consequence, coronary heart disease. The American Heart Association imperative on lifestyle changes include: "stop smoking, choose good nutrition, reduce blood cholesterol, lower blood pressure, be physically active every day, aim for a healthy weight, manage diabetes, reduce stress, limit alcohol" (American Heart Association, 2017). Next to stopping smoking, choosing good nutrition is the second most effective preventive measure. Getz (2005) stated that "In both human and experimental atherosclerosis, hypercholesterolemia is the major exciting factor for the development of vascular lesions."

SAA as a marker of inflammation is associated with dietary cholesterol. For example, the study of Subramanian et al. (2008) showed that "atherosclerosis is increased in the presence of diet-induced obesity, insulin resistance, and elevated SAA levels and worsened by dietary cholesterol." Lewis et al. (2004) showed that "Increase in serum amyloid A evoked by dietary cholesterol is associated with increased atherosclerosis in mice." Recent data by Imayama et al. (2012) showed that caloric restriction with or without exercise reduced biomarkers of inflammation. Moreover, increased SAA is associated with obesity in animal models (Imayama et al., 2012) and that inflammation may be the link between obesity and cardiovascular disease (King et al., 2010).

Globalization of Food Consumption

It has been said that the world has become a village. Globalization includes shifts in food consumption. In an editorial, Hu (2008) stated that "Radical dietary shifts in many developed and developing nations are supplanting traditional patterns of eating with a Western diet high in animal products and refined carbohydrates and low in whole grains, fruits, and vegetables. In China, for example, consumption of animal products increased by nearly 40% between 1989 and 1997, and fast-food sales more than doubled between 1999 and 2005. Furthermore, consumption of soft drinks has soared in the United States and worldwide." Hu (2008) stated further that, "Fueled by urbanization and the advent of the global economy, these changes in eating patterns are

the most rapid and dramatic in the course of human history. The term "Coca-colonization," a reference to the ubiquitous presence of Coca-Cola, Pepsi, and McDonald's, describes a world that is moving toward a common diet, one accompanied by the more sedentary lifestyles associated with increased risk of chronic disease." Iqbal et al. (2008) estimated that about "30% of myocardial infarction could be attributed to unhealthy diet worldwide."

CONCLUSION

These results suggest that inflammatory processes coupled with changing lifestyle and globalization of food consumption may be contributing to the increases in death from heart disease worldwide especially in developing and transitional countries. Preventive measures should include lifestyle changes as advocated by the American Heart Association (2017) especially involving a choice of good nutrition which, according to Hu (2008) and Iqbal et al. (2008) "should emphasize replacing saturated and trans fats with unsaturated fats from natural vegetable oils, fish, and nuts and replacing refined grain products and sugar with whole grain products, legumes, fruits, and vegetables. Regular consumption of fast foods and soft drinks should be strongly discouraged." These recommendations reflect the counsel of Ellen G. White (1905) that nuts, fruits, grains, and vegetables are the most healthful and nourishing diet.

RECOMMENDATIONS

Considering the findings of the study, the following are recommended:

Health care providers at the community level should focus on the education on the inclusion in the diet of unsaturated fats from natural vegetable oils, fish, and nuts and be replacing refined grain products and sugar with whole grain products, legumes, fruits, and vegetables.

Families should also consider the above recommendations and discouraging members of the family with regards to regular consumption of fast foods and soft drinks.

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