Free high density lipoproteins and cardiovascular disease essay example

Health & Medicine

Lipids are a group of structurally diverse hydrophobic compounds that are not very soluble in water. Cholesterol is a common lipid that can be obtained from the diet and is synthesized in most cells of the human body. It is a component of cell membranes, maintains membrane fluidity, and acts as the precursor of other important biological compounds such as steroid hormones and bile salts (Smith, Marks, and Lieberman 54, 163).

High concentrations of cholesterol in the blood can cause accumulation of fatty deposits on arterial walls that can lead to the formation of atherosclerotic plaques, which are associated with heart attacks, strokes, and other cardiovascular diseases (CVDs). High amounts of saturated fat in the diet can lead to increased levels of unhealthy cholesterol in the blood and contribute to the development of atherosclerosis (Smith et al. 19, 579, 620).

A certain kind of lipoprotein produced in the liver and the intestine is called high density lipoprotein (HDL). HDL is considered to be the “ good cholesterol” because it accepts cholesterol from various tissues, such as the walls of blood vessels, and returns it to the liver in a process called reverse cholesterol transport (named so because cholesterol goes back to the liver). Other functions of HDL include exchange of proteins and lipids with other lipoproteins. The liver reuses the returned cholesterol to synthesize other lipoproteins, converts it into bile salts, or excretes it directly into the bile. Through reverse cholesterol transport, HDL therefore has the ability to lower blood cholesterol levels, which in turn correlate with lower risk of atherosclerosis (Smith et al. 580, 620, 642).

It is postulated that higher levels of HDL in the blood help reduce the

occurrence of atherosclerotic cardiovascular diseases. However, HDL cholesterol levels do not necessarily reflect the anti-atherosclerotic functions of HDL. Thus, HDL cholesterol levels may not be causally linked to CVDs. Instead, Rohatgi et al., in the paper entitled " HDL Cholesterol Efflux Capacity and Incident Cardiovascular Events," focus on what is called HDL cholesterol efflux capacity, particularly pertaining to the transfer of cholesterol from macrophages to HDL particles. This efflux capacity reduces the formation of foam cells (lipid-laden macrophages that engulf oxidized LDL cholesterol) within the blood vessel wall. Foam cells are indicative of the early stages of the development of atherosclerotic plaque (Smith et al. 634). Macrophage-specific cholesterol efflux capacity has been shown to be directly and causally associated with the prevention of atherosclerosis in various animal models; Rohatgi et al. attempted to explore this causality in human subjects.

Various clinical studies have successfully employed strategies for the measurement of cholesterol efflux capacity. These studies have revealed inverse correlations between cholesterol efflux capacity and prevalent cardiovascular disease, and have shown these correlations to be independent of HDL cholesterol levels. However, previous studies have not explored the correlation between cholesterol efflux capacity and incident (i. e. those that occur for a period of time after the initial sample collection) cardiovascular events in population samples. It is also not previously known or studied whether cholesterol efflux capacity is affected by factors such as sex, age, race, adiposity, insulin sensitivity or resistance, and inflammation. The aforementioned factors were addressed by Rohatgi et al. by employing a

cohort strategy in their study.

The participants of the research by Rohatgi et al. were also subjects of another study called the Dallas Heart study, whose members come from various ethnicities and reside in the Dallas County. A total of 2924 adults, 30 to 65 years of age at the start of the sampling and not diagnosed with any cardiovascular disease participated in the study by Rohatgi et al. Moreover, 57% of the participants were women, and 49% were black. Although 2924 participants were included in the analysis of baseline characteristics, only 2416 participants were included in the analysis of cardiovascular outcomes; data from the other 508 participants were excluded by the researchers based on their criteria.

Blood samples from the participants were analyzed for HDL cholesterol level, HDL particle size and concentration, and cholesterol efflux capacity. HDL cholesterol, as well as other plasma lipids, was measured using methods described in previous publications of the Dallas Heart Study. HDL particle size and concentration were analyzed using nuclear magnetic resonance (NMR) spectroscopy. Finally, cholesterol efflux capacity was measured using the efflux of labeled cholesterol from macrophages to plasma without apolipoprotein B.

The study had two clinical end points. The primary end point was a composite of the outcome of atherosclerotic CVD, which the authors defined as including the following: nonfatal heart attack (the first one only if the subject has had multiple attacks throughout the duration of the study) or stroke, certain types of coronary artery bypass (or revascularization), and cardiovascular complications resulting in death. The secondary end point

was to determine the total outcome of CVD, defined by the authors to include the aforementioned events of the primary end point, surgical treatment for peripheral vascular (or leg artery) disease, heart surgery and hospitalization, and the A-fib cardiac dysrhythmia.

The results of the study revealed that cholesterol efflux capacity was inversely associated with the composite CVD outcome. Multivariate adjustments for traditional risk factors, HDL cholesterol level, and HDL particle concentration did not significantly influence the inverse association. Similar findings were obtained for the other end point of total cardiovascular disease; inverse correlations between efflux capacity and total CVD outcome were observed as well. The results also showed no significant association between efflux capacity and traditional risk factors, adiposity, insulin sensitivity, or inflammation. Finally, other factors such as age, sex, or race did not significantly affect the association between cholesterol efflux capacity and atherosclerotic CVDs.

The cohort study established that in humans, cholesterol efflux capacity is the primary function by which HDL lowers risks of cardiovascular disease. The protective function of HDL was also determined to be distinct from other factors such as HDL cholesterol level, HDL particle concentration, and traditional risk factors. Moreover, the results of the study were consistent with multiple researches on the effects of HDL reflux on CVDs, such as those employing genetically modified mice. Previous studies have also shown that efflux capacity is a more accurate predictor of atherosclerosis severity than circulatory (blood) levels of HDL cholesterol. Other studies have also demonstrated that impaired cholesterol efflux capacity correlates with

increased platelet reactivity in vitro, which impairs the capacity of HDL to promote endothelial repair and induce blood vessel formation or angiogenesis. Thus, the results of the study by Rohatgi et al. corroborate the idea that HDL cholesterol efflux has multiple atheroprotective functions.

There were several limitations to the study. First, the population sample used was relatively young, implying low overall cardiovascular risk, which could have resulted in the small number of first events of atherosclerotic CVD. Second, the population sample does not reflect the general distribution of population, especially because of the oversampling of African ethnicity. Third, the levels of HDL cholesterol in the study sample were mostly within the normal range, so the data (and ultimately the generalizations) cannot be extended to persons with abnormal levels of HDL cholesterol. Finally, the researchers were not able to establish the association between efflux capacity and type A apolipoprotein.

The following are personal recommendations of this essay's author to the authors of the cohort study reviewed and summarized in this paper. The researchers should start by addressing the limitations of the study. Increasing the population sample, and without oversampling of a particular race, to reflect a more general population distribution could be in order. However, testing for more sample groups would take a lot of time and others resources. In this regard, the researchers could do meta-analyses of similar researches or to use data that would fit their inclusion criteria. Also, the researchers could do preliminary analysis of sample groups with either high or low HDL cholesterol level. They could keep the sample group small while maintaining consistent parameters so that multivariate adjustments would

not skew or affect the data. Moreover, since the researchers observed that age, sex, or ethnicity does not affect the atheroprotective abilities of HDL through efflux, the researchers can venture into a more molecular approach, such as by finding genetic controls or epigenetic factors affecting HDL efflux in humans. In particular, if the genes for HDL efflux have already been well-characterized, the researchers can look specifically at polymorphisms and their effect in cardiovascular disease risk. Finally, the researchers could also explore atherosclerosis in liver-impaired individuals who can’t produce or process HDL.

Works Cited

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