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Mini Review

Atherosclerosis and wine

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Abstract

One of the most important risk factors for the origin and development of atherosclerosis is certainly excessive intake of fat in everyday nutrition. This risk factor, and the way it affects the origin and development of atherosclerosis, is described in the article "Atherosclerosis and lymph/risk factors". In this article, based on verified and proven facts, it is suggested that the primary causes and initiators of atherosclerotic changes in the arterial system of the circulatory system are chylomicrons, especially large ones, which occur under the influence of several risk factors.

In light of today's scientific knowledge about the causes and process of atherosclerosis, how to explain and interpret the fact, seemingly very illogical, that the French do not have a high mortality from coronary diseases caused by atherosclerosis, despite the high fat content of everyday nutrition? Such epidemiological ilogenicity called the French Paradox, has been attributed to daily, moderate consumption of red wines, which proved correct [1]. It has been proven that the beneficial effects of red wine in the process of preventing atherosclerosis can be attributed to the effects of the polyphenols present, likewise, these effects do not only apply to red wine but also to other drinks, alcoholic and non-alcoholic, containing polyphenols [2]. Studies conducted on beer consumption have produced similar results [3]. It should be noted that the effect of alcohol is described by the J curve, suggesting that moderate alcohol consumption reduces the risk of atherosclerosis, unlike abstinence and excessive alcohol lovers, where this risk is noticeably higher. This effect of red wine is attributed, among other agents, to a significantly increased concentration of high-density lipoprotein (HDL) [4]. The paper discusses the effect of HDL particles on nascent chylomicrons in the lymphoma system, which, by entering the circulatory system, affects possible association with atherosclerosis.

"Atherosclerosis is the result of the arterial wall/circulating blood element interactions triggered by environmental factors that influenza individual genetic components. Vascular alteration in the coronary bed comprises some key elements such as early endothelial dysfunction, inflammatory cellular infiltration, lipid deposition, vascular Wall cell proliferation, and Thrombotic complications at lesion sites" [5].

Atherosclerosis, a disease of the blood system that is one of the main causes of death in modern civilization, has been published in the past fifty years, several scientific papers explaining and confirming all aspects and characteristics of this disease, from risk factors to consequences, as well as prevention from its occurrence. Unfortunately, despite all this, the fact remains that the mechanism of atherosclerosis is still unknown, with a not-so-optimistic prediction of its immediate solution. The articles published so far [6-8] discussed the reasons for such a situation. The conclusion that emerged was that the primary cause and driver of atherosclerotic changes

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in the artery wall is chylomicron, namely chylomicron of large and extra large dimensions, insufficiently structured, formed under the influence of several risk factors to which we are exposed. It should be noted that the basic and primary role of chylomicrons is the transport and delivery of consumed lipids, of all kinds, to organs and tissues in the body that are needed for their functionality. On their way, through the lymph, to the circulatory system, chylomicrons are exposed to the influence and influence of many factors, which determine their final size, structure, and functionality at the moment of entry into the circulatory system.

One also forgets or underlines, the very important fact that the primary role of chylomicron is their attachment to the endothelial arteries and capillaries to deliver its lipids (triglyceride) content to the tissue in need. It is precisely in this fact that there is danger and possibility of disturbances in the process of attachment to cells of endothelial arteries and capillaries of such atypical, extremely large, with diameter > 10 times, and with mass n^3 time's larger, chylomicron. This particularly applies to the area of large blood flow turbulence [9], when binding forces are not sufficient to maintain such a large particle on the endothelial surface, resulting in injuries to the arterial endothelium or uncontrolled decay of the chylomicron itself, resulting in an inflammatory process at this site [7,8].

Atherosclerosis is a chronic inflammatory disease manifested as coronary artery disease - myocardial infarction, cerebral arteries - stroke, or peripheral vascular insufficiency, and tends a progressive process that begins probably in early youth [10]. The process itself is multifactorial and mostly depends on risk factors, obesity, sedentarism, smoking, and the presence of some metabolic disorders. Progress in this process can be reduced or even stopped, by avoiding risk factors by changing the lifestyle (weight loss, smoking cessation, exercise, adequate nutrition), and moderate consumption of alcohol, especially red wine, should be added to this.

Moderate consumption of alcohol, especially red wine, leads to an increased concentration of HDL and triglycerides in the blood [11,12]. Since it is known that increased HDL blood concentrations have a protective effect against coronary artery diseases [13], this may also be a mechanism by which the consumption of red wine contributes to the protection against atherosclerotic complications. How?

"Levels of high-density lipoprotein (HDL) cholesterol are generally inversely associated with the risk for the development of atherosclerosis. The mechanism by which HDL imparts protection from the initiation and progression of occlusive vascular disease is complex and multifactorial. The major anti-atherosclerotic effect of HDL is felt to be reverse cholesterol transport. HDL has been demonstrated to scavenge cholesterol from the peripheral vasculature with transport to the liver, where is it excreted in the biliary system. However, HDL exhibits multiple other physiologic effects that may play a role in the reduced risk for atherosclerosis. HDL *has been demonstrated to exhibit beneficial effects on platelet function, endothelial function, coagulation parameters, inflammation, and interactions with triglyceride-rich lipoproteins. Increasing amounts of clinical and experimental data have shown that HDL cholesterol has significant antioxidant effect that may significantly contribute to protection from atherosclerosis"* [14].

The first convincing evidence of this connection between HDL and cholesterol and the occurrence of atherosclerotic changes in the circulatory system, and the emergence of cardiovascular diseases, was obtained in a well-known Framingham heart study, after which a generally accepted concept on the role of HDL in preventing cardiovascular diseases was proposed. It was also concluded in this regard that there is „good" HDL cholesterol and"bad" LDL cholesterol. Following such conclusions, many investigations were initiated during the '80s and '90s, to influence the risk of cardiovascular diseases by the therapeutic intervention of an increase in blood cholesterol. Although there have been significant new findings in the understanding of molecular and genetic regulation of HDL metabolism in plasma, the method itself did not yield results and proved to be unsuccessful.

"Despite this, most attempts to raise plasma HDL-C concentrations in a cardioprotective way have failed. Recently, hypotheses about the atheroprotective effects of HDL have shifted away from quantity to quality, mostly HDL function in reverse cholesterol transport. Plasma HDL from CVD patients is a poorer acceptor of cellular cholesterol than plasma from healthy controls, independent of plasma HDL-C concentrations. The function of HDL is likely determined by two other factors, stability and composition. The kinetic instability of HDL, which varies according to subclass, is a likely determinant of its reactivity in response to many HDL-modifying activities. HDL composition is also heterogeneous and variable; all HDL particles contain apo AI but only about two-thirds contain apo AII. This occurs despite the fact that apo AI and apo AII are hepatically secreted on separate HDL that later fuse in plasma. HDL also contains traces of other proteins, some of which have not yet been associated with HDL function. One minor HDL species are those that are secreted with intact signal peptides, which enhance their binding to HDL; these HDL have special properties that are independent of cholesterol transport" [15]

All the aforementioned beneficial effects of HDL in the process of atherosclerosis can be accepted in the context of possible but not finally scientifically proven effects, while the fact that HDL particles interact with triglycerides, chylomicrons, and VLDL lipoproteins has been scientifically proven and confirmed for a long time now [16], which in the context of these considerations has an extremely large, perhaps crucial significance.

The generally accepted concept of reversible transport of cholesterol indicates that it is a process by which HDL removes the surplus of cholesterol accumulated in the intercellular space of tissues, including skin and arterial walls, and it is returned to the circulatory system by the lymphoma system and excreted via the liver via feces from the body.

"Cholesterol is essential for all cells in the body and it is used extensively as a major structural component of cell membranes and as a substrate for the synthesis of other steroids such as bile

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acids, vitamin D, and sex hormones such as estradiol, progesterone, androsterone and testosterone, as well as adrenocortical hormones such as aldosterone and cortisone. The liver and small intestine are two crucial organs for cholesterol homeostasis. Indeed, high cholesterol biosynthesis in the liver leads to more VeryLow-Density Lipoprotein (VLDL) secreted into plasma, thereby increasing plasma total and LDL cholesterol concentrations. Increased quantities of dietary cholesterol also cause plasma cholesterol concentrations to rise in most individuals. Accumulated evidence has clearly demonstrated that elevated total and LDL cholesterol levels in plasma are an important risk factor for the development of cardiovascular diseases in humans and laboratory animals"[17].

"Accumulated evidence from human and animal studies has clearly demonstrated that one of the most important biological functions for HDL is to regulate reverse cholesterol transport that promotes cholesterol transport from the peripheral tissues, including the aortae, to the liver for biliary excretion. This indicates that HDL plays a critical role in protecting against the development of atherosclerosis through reverse cholesterol transport. It is well known that plasma contains numerous HDL particles that are involved in reverse cholesterol transport.105 In addition, it has long been suspected that the lymphatics may also play an important role in transporting newly effluxed cholesterol from the site of efflux to the circulation because interstitial and lymphatic fluid contains a lot of HDL and apoA-I.109 It is estimated that there is a lymph transport of more than 300 mg per day in humans.110 Most importantly, recent observations have found that the lymphatic vessel route is critical for efficient reverse cholesterol transport from multiple tissues, including the arterial wall.111 Removal of cholesterol by lymphatic vessels is dependent on the uptake and transcytosis of HDL by scavenger receptor class B type I (SR-BI) expressed on lymphatic endothelium,112 which challenges the current view that lymphatic endothelium is a passive exchange barrier for cholesterol transport. Accordingly, these findings may connect lymphatic function to atherosclerosis because lymphatic transport function may facilitate cholesterol clearance in therapies aimed at reversing atherosclerosis.113-115" [17].

However, it would be uncritical to conclude that this is the only role of HDL in the body. The above-mentioned fact that HDL particles directly participate in the transfer of apolipoproteins C-II, C-III, and E to ascending chylomicrons, so that these become "ripe chylomicrons", which means structurally stable and ready to enter the vascular system [16] Since the nascent chylomicron contains about 25 copies of apoE and about 180 copies of apoC, [18] it can be assumed how many HDL particles are needed to mature each nascent chylomicron. However, this is not only a problem, but also because chylomicrons are very different in terms of particle size, depending on the length and intensity of lipid absorption, and ranging from 75 to over 1000 nm. The question arises how much does the HDL of particles need at the moment of arrival of particularly large chylomicron particles into the lymph system (cisterna chyli)? We know that each chylomicron particle contains only two chains of ApoB, [18] which poses a great danger to the stability of such large lipid particles in the aqueous medium, therefore it is necessary to present and interact with HDL particles, which contribute to their stability by handing over their apoproteins and probably cholesterols and phospholipids.

And now we finally come up with questions from the beginning of the debate, how does red wine affect the appearance and development of atherosclerosis?

Conclusion

In the context of all the above facts and the results of the research presented in this discussion, a very convincing conclusion is reached that red wine (polyphenols present in it) significantly increases the presence of HDL particles in blood and lymph, affects the increased reversible transport of cholesterol via lymph, where HDL particles contribute and participate in the final formation of imagined chylomicron particles before they enter into the blood circulation.

The lack of decrease in the number of HDL particles in the lymph, especially at the moment of arrival of large structural unfinished and unstable scents of chylomicron particles, leads to the danger that such chylomicrons enter the blood circulation, where they may cause changes in the vascular endothelium, especially the aorta and arteries that come out of it, coronary and cerebral, in a highly turbulent blood flow through the area.

The result of this effect of red wine has significantly reduced the possibility of atherosclerosis, which has been confirmed in practice. Therefore, the benefits of a moderate drink of red wine, as well as other polyphenols-containing drinks, are real and multiple, from comfort to health preservation. Proven risk factors crucial to the occurrence of atherosclerosis, obesity, insufficient physical activity, smoking, and insufficient consumption of polyphenol can also be considered as specified risk factors. This is why red wine, due to its universal application and acquired civilization habits, has become a very important help for the preservation of health.

Syntagm "In vino veritas" from this discussion has proved to be very appropriate because the consumption of wine, its properties, and effects, confirms and indicates that it is chylomicrons that we have to pay full attention to, to get closer to the truth about the causes and mechanism of atherosclerosis, a chronic civilization disease, for which we do not yet have a concrete answer or explanation.

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