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"STATIN DRUGS ARE NOT THE ANSWER TO PREVENTING HEART DISEASE"- A CRITICAL REVIEW

Statins drugs are a highly prescribed class of medications that are used primarily for hypercholesterolemia. Due to their LDL-lowering effects, Statins prescriptions have been increasing rapidly because the number of people requiring reduction in high cholesterol has been increasing rapidly, likely due to the increasing rates of fast-food consumption, especially in the United States. It is estimated that the regular fast-food consumption increases by at least 2.2% every year [1]. Hypercholesterolemia has a significant number of negative effects that it can cause in patients with cardiovascular disease. It is a common trend for people that have hypertension, chronic kidney disease, heart failure, coronary artery disease, etc. to also have hyperlipidemia. Due to this trend, almost every patient who is being treated for cardiovascular disease, is also receiving Statin therapy. Therefore, Statins are not only being used widely for their lipid-lowering effects, but also for their ASCVD prevention effects. In theory it makes perfect sense for someone who has a high risk for an ASCVD event, to be put on Statin therapy to decrease the risk. However, there has been some controversy regarding its widespread use, as many people believe that using a synthetic drug like Atorvastatin to decrease cholesterol is actually doing more harm than good.

A podcast in the program Terry Talks Nutrition titled "Statin Drugs Are Not the Answer to Preventing Heart Disease" makes the following argument against Statin drugs. Terry Lemerond states that "Statin drugs are not only useless in preventing heart disease but they also significantly increase the risk of cancer, diabetes mellitus, and even heart attack and stroke." Terry's main reason for the previous statement is that there is no research evidence that has confirmed high cholesterol as the main contributor to heart disease, heart attacks or stroke. Many healthcare professionals, including Terry, believe that lowering cholesterol is not the answer for ASCVD prevention due to cholesterol being a natural product synthesized by the human body. They refer to cholesterol as our friend, not our enemy. It is well known that cholesterol is vital for many metabolic processes in the body. A few examples include synthesis of sex hormones, conversion of sunshine to Vitamin D, metabolism of fat-soluble vitamins, and brain function [2]. Many people also believe that the body makes as much cholesterol as it needs for that individual. Therefore, when Statins are prescribed to a patient with "high cholesterol", it is possible the reduction in cholesterol that will take place is doing more harm than good by causing the body to decrease production of a vital compound.

There is no doubt that Statin drugs are highly effective in reducing cholesterol levels. In a 6-week, double blind clinical trial with Atorvastatin 2.5-80 mg once daily, plasma LDL levels showed dose-dependent reductions by 25-61% [3]. However, many people believe that only a small percentage of the population may actually benefit from this reduction. The small percentage is referring to 48–65-year-old men, who already have had a heart related disease. Due to the proven LDL cholesterol-lowering effects that have been demonstrated by Statins,

millions of patients with a risk of ASCVD event greater than 5% are on Statin therapy. Statin therapy is indicated in almost every set of guidelines for any cardiovascular disease. A few examples where statins are prescribed, not specifically for their LDL effects but for their potential to lower risk of an ASCVD events - include patients with diabetes, chronic kidney disease, stable ischemic heart disease, acute coronary syndrome, coronary heart disease and heart failure. As a result, many people believe that Statin drugs have been largely over-prescribed and have resulted in a major revenue generating medication for the entire healthcare system. Lipitor, otherwise known as atorvastatin, has generated more revenue than any other drug on the market over the years. It is estimated that in 2013, statin usage increased by 149% to a total of roughly 92 million users by 2018 [4]. This was largely due to the adoption of statin therapy in the 2013 ACC/AHA guidelines. A Fact Versus Fiction article published by the American College of Cardiology stated that the most common complaint associated with Statin therapy, myopathy, was reported in up to 33% of patients [5]. In The Crestor 20 mg Versus Placebo in Prevention of Cardiovascular Events (JUPITER) trial, new-onset diabetes was found in 25% more cases in Statin versus placebo groups [5]. Another trial, known as "Lipitor In The Prevention Of Stroke, For Patient Who Have Had A Previous Stroke (SPARCL)", showed a slight increase in hemorrhagic strokes in the statin versus placebo group [5].

Another main piece of evidence to claim that statin therapy is ineffective in reducing the risk of cardiovascular disease, particularly heart attacks, is that a national study showed that nearly 75% of all heart attack victims have normal cholesterol levels [6]. A book called "The Great Cholesterol Myth" by Jonny Bowden and Stephen Sinatra supported claims that cholesterol is a minor player in heart disease, half of the people with heart disease have normal cholesterol levels, and half of the people with elevated cholesterol have healthy hearts, concluding that lowering cholesterol has extremely limited benefits. Another important claim to mention about Statins drugs includes the adverse effects that they can cause. It has been estimated that for every 100 patients who receive Statin therapy for 5 years, a heart attack will be prevented in only one or two patients [7]. However, it is thought that one or more patients out of the same 100 patients will develop diabetes and more than 20% of patients will experience significant adverse effects including muscle weakness, fatigue, and memory loss.

If high cholesterol (specifically LDL) is not the cause of heart disease, then what is? There is reasoning that low HDL (good cholesterol that carries bad cholesterol out of the body), inflammation of the blood vessels, and oxidation of LDL leading to plaque formation is the real cause of heart disease [8]. There are many natural products that can help reduce inflammation, prevent LDL oxidation, and increase LDL to achieve a "safer" and "more effective" option for patients who qualify for ASCVD prevention. The first natural product that should be mentioned is grape seed. Grape seed is a powerful antioxidant that has shown clinically significant reductions in high blood pressure levels, arterial plaque formation and inflammatory triglycerides [9]. Pomegranate is also a good source of antioxidants. Pomegranate is thought to prevent LDL from getting oxidized, hence preventing the synthesis of arterial plaques that can lead to vascular damage and cause many more complications. A clinical trial showed pomegranate supplementation produced significant protective actions on atherosclerosis [10]. Amla, also known as Indian Gooseberry, has also been shown to have clinically significant

positive effects on the heart. In a clinical trial, Amla was shown to significantly decrease total cholesterol levels, while increasing HDL levels [11,12]. Amla has also shown to significantly decrease inflammatory c-reactive protein levels and prevent LDL from oxidizing [11].

There are also several vitamins that are key for good heart health. These include vitamin A, D3 and K2. Vitamin A is vital for many organs and processes in the body, including heart development and maintenance. It has demonstrated antioxidant effects that decrease the production of free radicals, limiting the ability of them to cause heart disease [13]. Vitamin D3 is also a very important vitamin that plays a vital role in bone health by helping absorb calcium but also reducing inflammation, which has significant positive effects on heart health [14]. Vitamin K2 has shown evidence to reduce arterial calcification, thus reducing the risk of heart disease.

The last natural product to mention is Mesoglycan, which is a mixture of glycosaminoglycans (GAGs). GAGs are known to be the "building blocks" of joints, intestines, and the inside of blood vessels. Mesoglycan has demonstrated a significant improvement in circulation and a significant reduction in arterial stiffness [15]. In summary, there are several natural products that have shown evidence to be cardioprotective. Grape seed and pomegranate are effective in building the "foundation", amla is effective at decreasing cholesterol oxidation, Vitamins A, D3, and K2 are effective at preventing hardening of the arteries, and Mesoglycan is effective at rebuilding damaged blood vessels.

Overall, my time listening to this podcast was well spent. Before listening to this podcast episode, I was very fond of Statin therapy. I have been learning a great deal about how statin therapy is highly recommended by various sets of guidelines for many different indications. It is well known that statins are effective in reducing LDL levels and for that reason have been the first line therapy for patients with hyperlipidemia for many years now. It hasn't been until the last 10-20 years that Statins have been increasingly prescribed for other indications besides high cholesterol. In the ACC/AHA guidelines, Statin therapy is indicated for almost any patient who has greater than a 5% ASCVD 10-year risk score to attempt to lower the chances of future cardiovascular disease.

There are a lot of claims that suggested the evidence that Statins have produced in reducing the risk of cardiovascular disease, is not existent. However, that is just not the case. I firmly believe that the American College of Cardiology would not be pushing as hard as they do for patients to be on Statin therapy if the evidence was not significant. However, I do strongly agree that lowering LDL may not be the only effective way in preventing cardiovascular disease. The claim that everyone's body makes the amount of cholesterol their body needs to function, makes a lot of sense to me. Although some people's cholesterol levels are significantly higher than others (hyperlipidemia patients), that does not exactly mean the person's body is producing too much cholesterol. It could simply mean that the patient's body and cellular processes require a higher level of cholesterol to function efficiently. Therefore, when providers focus on trying to prevent someone's risk of cardiovascular disease by lowering their LDL levels, it could be very possible that they are creating more problems rather than preventing them. However, it makes perfect sense to use a medication that has shown to be effective in reducing the amount of arterial plaque

formation by preventing LDL oxidation to decrease the risk of someone developing cardiovascular disease because it is well known that plaque formation in the arteries only leads to negative outcomes. Before listening to Terry Lemerond talk about the natural products that can be used for ASCVD prevention, I was not aware of the evidence that has supported the use of the herbs mentioned previously. That is largely due to the fact that a lot of natural products lack clinical evidence from trials to back them up, causing a lot of Pharmacologists to shy away from them. However, Terry provided solid evidence for each one of the natural products he has talked about in this episode. That being said, I am still not comfortable recommending someone who has a ASCVD 10-year risk score of over 20% to take a pomegranate supplement to hopefully reduce their risk of ASCVD. In that case, I would prefer the patient to receive Statin therapy along with lifestyle modifications to lower their ASCVD risk because the benefits would likely outweigh the risks. However, for a patient who has slightly elevated blood pressure with an ASCVD 10-year risk score of 6%, I would feel it would be more beneficial recommending a natural product along with lifestyle modifications to hopefully decrease their risk of an ASCVD event rather than initiating a moderate-intensity statin that could potentially cause more harm than good, for example new-onset diabetes.

In conclusion, there is still a lot of research to be done to find the best approach to preventing ASCVD events. However, people like Terry, who bring a unique approach to the conversation, offer a significant contribution to getting closer to finding the answer. However, I believe that both sides of the conversation, Statins versus natural products, should work together, not apart, in building the evidence for both sides to hopefully lead to better understandings of what can be done to decrease ASCVD risk patient to patient.

References:

1. *Fast Food Statistics: July 2023*. The Barbecue Lab. (2023, July 5). https://thebarbecuelab.com/fast-food/

2. Cleveland Clinic medical. (n.d.). *What is cholesterol?*. Cleveland Clinic. https://my.clevelandclinic.org/health/articles/23922-what-is-cholesterol

3. Reduction of LDL cholesterol by 25% to 60% in patients with primary hypercholesterolemia by atorvastatin, a new HMG-COA reductase inhibitor | arteriosclerosis, thrombosis, and Vascular Biology. (n.d.). https://www.ahajournals.org/doi/full/10.1161/01.atv.15.5.678

4. Elsevier. (2023, April 11). *Statins utilization trends and expenditures in the U.S. before and after the implementation of the 2013 ACC/AHA guidelines*. Saudi Pharmaceutical Journal. https://www.sciencedirect.com/science/article/pii/S1319016423000841?via%3Dihub

5. *American College of Cardiology*. ACC Maintenance. (n.d.-a). https://www.acc.org/Latest-in-Cardiology/Articles/2018/04/09/13/25/Assessing-Severity-of-Statin-Side-Effects

6. ScienceDaily. (2009, January 13). *Most heart attack patients' cholesterol levels did not indicate cardiac risk*. ScienceDaily. https://www.sciencedaily.com/releases/2009/01/090112130653.htm#:~:text=Summary%3A,t

o%20current%20national%20cholesterol%20guidelines.

7. Lindsey C. Yourman, M. (2021, February 1). *Time to benefit of statins for the primary prevention of cardiovascular events*. JAMA Internal Medicine. https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2773065

8. Hong, C. G., Florida, E., Li, H., Parel, P. M., Mehta, N. N., & Sorokin, A. V. (2023). Oxidized low-density lipoprotein associates with cardiovascular disease by a vicious cycle of atherosclerosis and inflammation: A systematic review and meta-analysis. *Frontiers in cardiovascular medicine*, *9*, 1023651. https://doi.org/10.3389/fcvm.2022.1023651

9. Cao, A. H., Wang, J., Gao, H. Q., Zhang, P., & Qiu, J. (2015). Beneficial clinical effects of grape seed proanthocyanidin extract on the progression of carotid atherosclerotic plaques. *Journal of geriatric cardiology : JGC*, *12*(4), 417–423. https://doi.org/10.11909/j.issn.1671-5411.2015.04.014

10. Alalawi, S., Albalawi, F., & Ramji, D. P. (2023). The Role of Punicalagin and Its Metabolites in Atherosclerosis and Risk Factors Associated with the Disease. *International journal of molecular sciences*, *24*(10), 8476. https://doi.org/10.3390/ijms24108476

11. Upadya, H., Prabhu, S., Prasad, A., Subramanian, D., Gupta, S., & Goel, A. (2019). A randomized, double blind, placebo controlled, multicenter clinical trial to assess the efficacy and safety of Emblica officinalis extract in patients with dyslipidemia. *BMC complementary and alternative medicine*, *19*(1), 27. https://doi.org/10.1186/s12906-019-2430-y

12. Gopa, Biswas et al. "A comparative clinical study of hypolipidemic efficacy of Amla (Emblica officinalis) with 3-hydroxy-3-methylglutaryl-coenzyme-A reductase inhibitor simvastatin." Indian journal of pharmacology vol. 44,2 (2012): 238-42. doi:10.4103/0253-7613.93857

13. Mayo Foundation for Medical Education and Research. (2023, September 14). *Vitamin A*. Mayo Clinic. https://www.mayoclinic.org/drugs-supplements-vitamin-a/art-20365945#:~:text=Vitamin%20A%20also%20has%20antioxidant,disease%2C%20cancer%20and%20other%20diseases

14. *Vitamin D*. The Nutrition Source. (2023, March 7). https://www.hsph.harvard.edu/nutritionsource/vitamin-d/#:~:text=It%20is%20a%20fat%2Dsoluble,control%20infections%20and%20reduce%20inflammation

15. Tufano, A., Arturo, C., Cimino, E., Di Minno, M. N., Di Capua, M., Cerbone, A. M., & Di Minno, G. (2010). Mesoglycan: clinical evidences for use in vascular diseases. *International journal of vascular medicine*, *2010*, 390643. https://doi.org/10.1155/2010/390643