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The Effect of Vitamin D on Cardiovascular Disease

ABSTRACT

This research aims to identify the critical factors in the relationship between Vitamin D and coronary heart disease. The hypothesis is that vitamin D can decrease the risk of coronary heart disease. Previous data show how Vitamin D reduces atherosclerosis and homocysteine levels and how Vitamin D incorporates and decreases fat and calcium in the rest of the body, whether through renal excretion or intestinal absorption. It is shown that Vitamin D reduces plaque in the carotid artery as well, which is a more dangerous place for atherosclerosis to occur, as it affects blood flow into the brain. By studying the effect of Vitamin D on the risk of coronary heart disease, this research paper explores possible treatment options that increase Vitamin D levels and reduce the risk of heart attacks, such as getting more sunlight and taking dietary supplements for molecules such as calcitriol.

Introduction

Over 1 billion people in the world are Vitamin D deficient. Vitamin D is a fat-soluble vitamin found in the body as 25-hydroxy-vitamin D2 (ergocalciferol) and 25-hydroxy-vitamin D3 (cholecalciferol). The enzyme 1-alpha breaks down the vitamin into 1,25 dihydroxyvitamin D, the active form that helps to absorb calcium through the intestines while also decreasing renal excretion. Vitamin D can be obtained from the UV rays of sunlight or milk, or even fatty fish livers. A safe level of Vitamin D is between 30 ng/mL and 88 ng/mL. A person is deficient when levels are below 20 ng/mL (Givler et al. 2022).

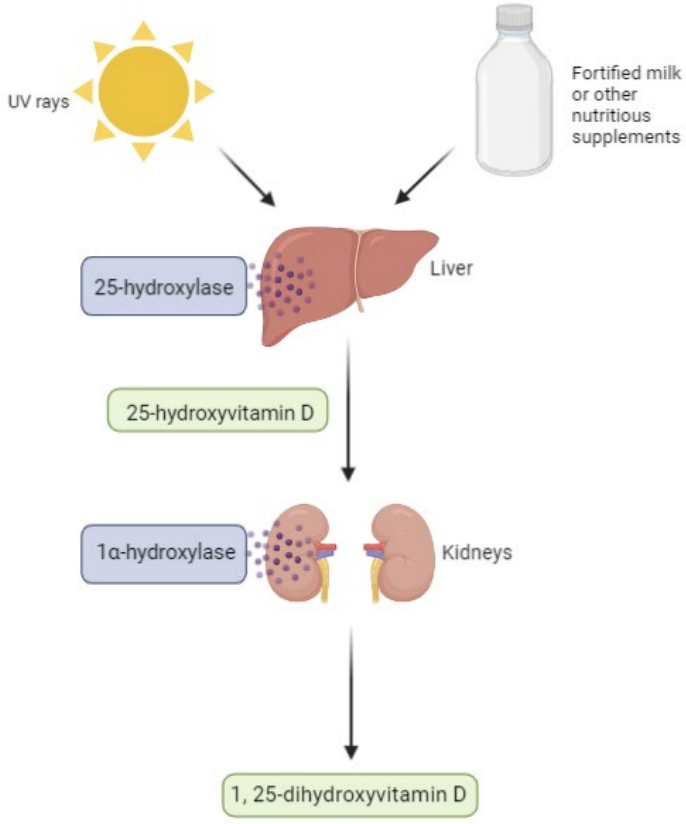

Figure 1. Diagram of how Vitamin D is absorbed and converted into the body (Figure made by Pramodani Arulkumar)

Coronary artery disease is a significant cause of death worldwide. It can cause atherosclerosis, a plaque build-up in the coronary arteries throughout the cardiovascular system. The disease is especially harmful when atheromatous plaques form in the carotid arteries, two large blood vessels on the sides of the neck. Recent research has shown a correlation between Vitamin D deficiency and an increased risk of heart attacks, inhibiting cholesterol uptake by certain macrophages called foam cells, which deposit fat into the endothelium, increasing the risk of atherosclerosis and plaque (Aggarwal et al. 2016).

Another factor that is the topic of recent research is homocysteine. Homocysteine, similar to cysteine, is found in extremely low levels in the bloodstream and is usually broken down by Vitamin B and changed to other substances to provide nutrition to the body. However, high levels of homocysteine can cause an increase in coronary heart disease or cardiovascular diseases in general. The chemical does this by making blood clotting easier and damaging the lining of the arteries (Ganguly et al. 2015). Establishing a relationship between Vitamin D deficiency and high homocysteine levels could reveal homocysteine to be a potential biomarker for cardiovascular disease.

This research aims to investigate the effects of Vitamin D deficiency on the various causes of coronary heart disease by identifying the functions of Vitamin D in the body and how it relates to homocysteine levels. By discovering these connections, we can consider treatment options and prevention techniques to decrease the risk of cardiovascular diseases. The research will also provide a clearer understanding of the relationship as it addresses conflicting studies done in the past. By finding out how Vitamin D deficiency increases the risk of coronary heart disease, we can discover potential treatment options that are more efficient and beneficial. The hypothesis is if Vitamin D levels in the body are decreased, there will be a significant increase in atherosclerosis and levels of homocysteine, causing an increased risk of coronary heart disease.

How Vitamin D Decreases Atherosclerosis

Vitamin D's primary role in the body is to retain and absorb calcium and phosphorus and use the calcium for bone development. Vitamin D, specifically the active form 1,25 dihydroxyvitamin D, regulates the contracting of vascular smooth muscle cells by using intracellular calcium (Aggarwal et al. 2016). In addition, Vitamin D inhibits macrophages carrying low-density lipoproteins (LDLs) and cholesterol uptake, decreasing plaque formation in the arteries. By inhibiting cholesterol uptake, vitamin D also regulates the transport of high-density lipoproteins (HDLs) through the bloodstream and prevents them from settling into the lining of the arteries (Aggarwal et al. 2016). Calcium and phosphorus are also found in plaque formations in the artery as calcification, which is extremely harmful to the body. Vitamin D also regulates the production of inflammatory cytokines that are part of the immune system. Increasing inflammation in the blood vessels could restrict blood flow and lead to a greater risk of heart attacks. The immune process of atherosclerosis can also be suppressed by the proliferation of T-cells in the body (Muscogiuri et al. 2017). Considering vitamin D's various roles in the body, we should also consider that vitamin D can decrease the risk of coronary heart disease and heart attacks.

The carotid arteries are two blood vessels on the sides of the neck that help blood flow to the brain (Carotid Artery Disease 2016). Atherosclerosis in the carotid arteries can cause them to narrow and form plaque. Plaque is comprised of fat, cholesterol, and calcium and can also restrict blood flow. Because blood flow to the brain is restricted, this can lead to a stroke and possibly death.

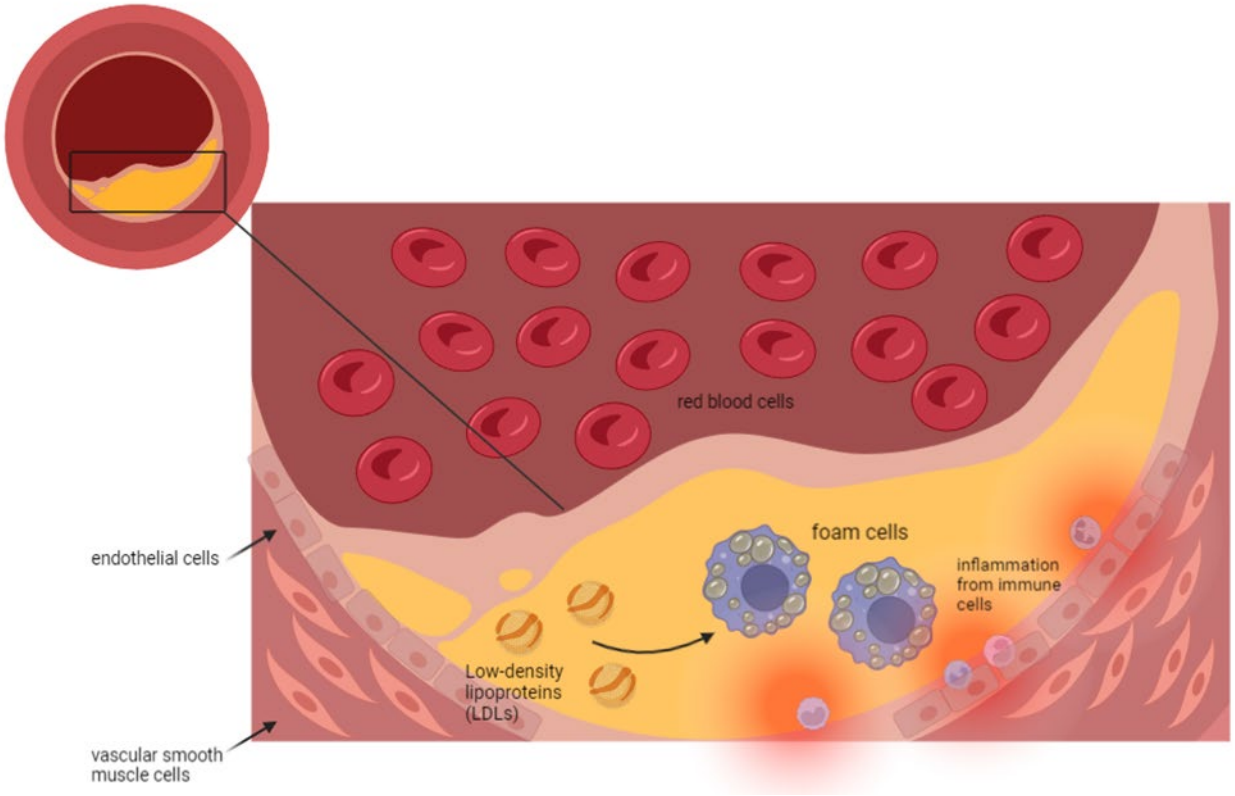

Figure 2. Diagram of how atherosclerosis develops in the arteries and what components are found in plaque. (figure made by Pramodani Arulkumar)

A study conducted in 2016 measured intraplaque carotid hemorrhage in Vitamin D deficient patients using carotid MR imaging and determined a negative correlation between the two. They used multivariable Poisson regression to determine a correlation between two carotid arteries and low Vitamin D levels. As the Vitamin D level increased, there was a significant decrease in the IPH volume in the carotid artery, with a p-value of 0.003, which is less than the alpha value of 0.05 (McNally et al. 2016). The figures show that Vitamin D decreases the IPH volume and the risk of cardiovascular disease and stroke since it is in the carotid artery. Therefore, plaque formation in the carotid artery is hazardous as it affects the brain.

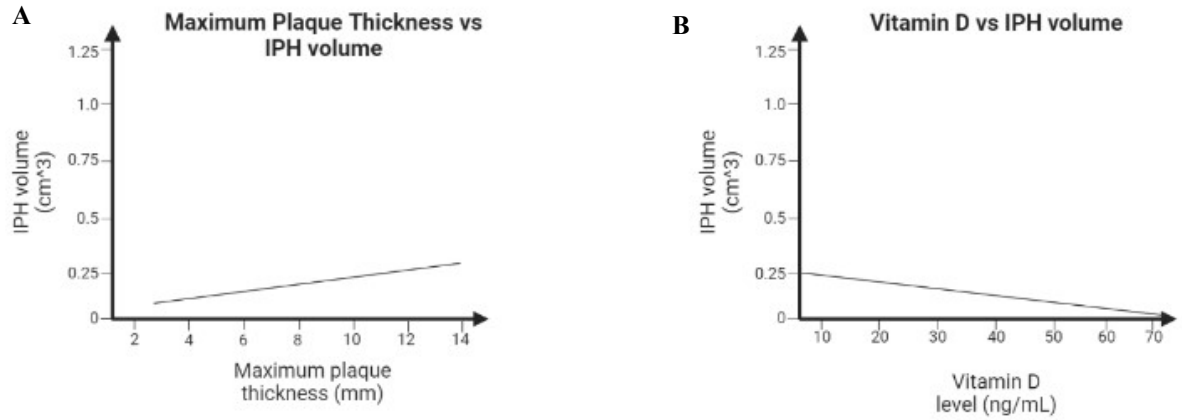

Figure 3. (A) Graph showing positive correlation between maximum plaque thickness and intraplaque hemorrhage (IPH) volume ($p < 0.001$). (B) Graph showing negative correlation between vitamin D level and IPH volume ($p = 0.003$). (Figure made by Pramodani Arulkumar)

Homocysteine

Homocysteine is a sulfhydryl-containing amino acid found in the bloodstream in the form of plasma. Homocysteine can be converted into cysteine, more commonly found in the body. There are four different forms of homocysteine (Hcy). About 80%-90% is in the form of protein-bound homocysteine. The rest are in the forms of free Hcy, oxidized Hcy, and Hcy-thiolactone. A healthy individual would have a homocysteine level between 5 and 15 µmol/L in the bloodstream. However, hyperhomocysteinemia causes homocysteine levels in the bloodstream to be above 15 µmol/L. High levels can lead to the formation of blood clots and damage the lining of the arteries, increasing the risk of cardiovascular disease. Hyperhomocysteinemia is caused by genetic defects in enzymes involved in homocysteine metabolism, the main one being 5,10-methylene tetrahydrofolate reductase. However, hyperhomocysteinemia can also be caused by a lack of folate, vitamin B6, and vitamin B12. In a patient with this condition, lipid and lipoprotein metabolism increases, increasing the risk of atherosclerosis (Ganguly et al. 2015). Vitamin D is responsible for incorporating fat and hydrolyzing triglycerides, decreasing lipoprotein metabolism (Aggarwal et al. 2016). Essentially, Vitamin D plays a role in decreasing hyperhomocysteinemia and therefore decreasing the risk of cardiovascular disease.

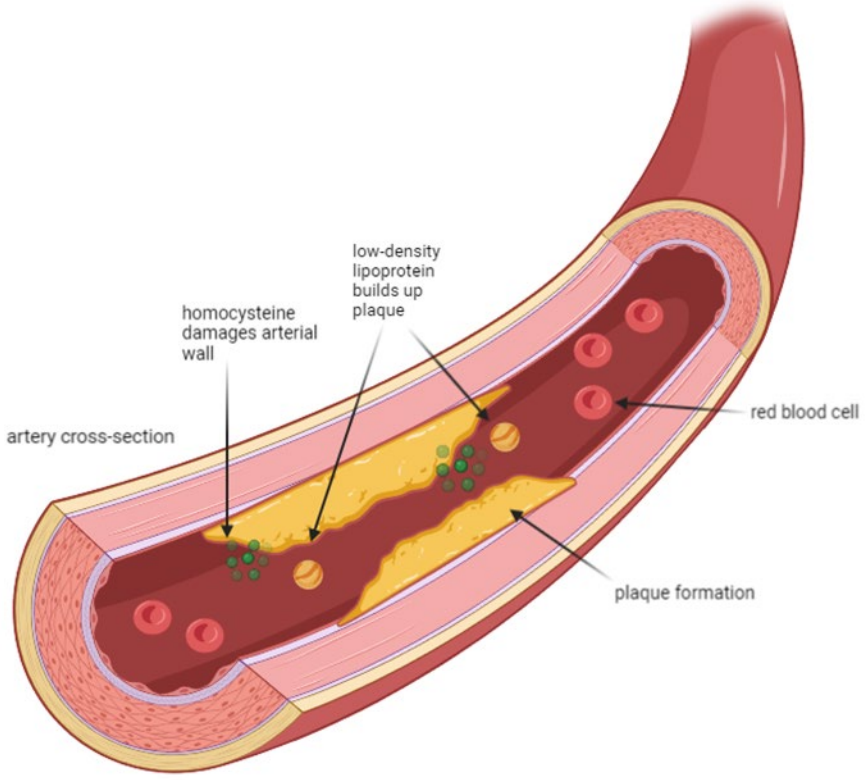

Figure 4. Diagram showing how homocysteine can damage the arterial lining and cause plaque formation. (Figure made by Pramodani Arulkumar)

In addition, homocysteine can play a role in increasing the risk of cardiovascular disease. Studies have shown that homocysteine induces mRNA and protein expressions of C-reactive protein (CRP), a protein in charge of acute inflammation at sites of infection, in vascular smooth muscle cells (Ganguly et al. 2015). Once the arterial lining becomes inflamed, atherosclerosis becomes more prominent and prevents further blood flow in the circulatory system. Therefore, high homocysteine levels induce atherosclerosis and increase the chances of coronary heart disease.

Research on the elderly helped identify an association between homocysteine and arterial stiffness. Arterial stiffness progressively worsens with age, a predictor of fatal cardiovascular disease. Using pulse wave velocity measurement (PWV), scientists can measure the aortic stiffness, specifically the carotid artery. The stronger the PWV, the more stiffness the artery has. A study done with elevated serum homocysteine levels shows a relationship between an increase in homocysteine and an increase in carotid-femoral stiffness (Zhang et al. 2014). They concluded that hyperhomocysteinemia might stimulate vascular smooth muscle cell proliferation, damaging the arterial lining and leading to further atherosclerosis.

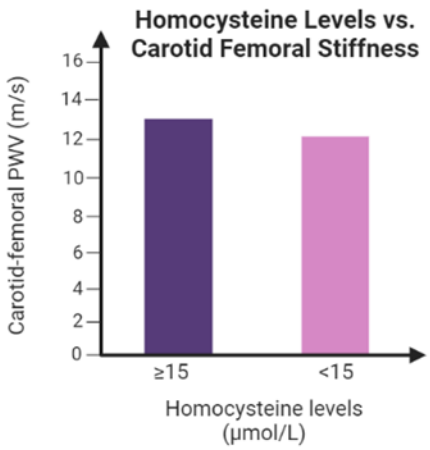

Figure 5. Graph shows how high levels of homocysteine can increase carotid stiffness (high homocysteine levels are defined as >= 15 μmol/L, normal homocysteine levels are defined as < 15 μmol/L). p = 0.01, alpha = 0.05. (Figure made by Pramodani Arulkumar)

Possible Treatment Options

Since Vitamin D has been known to decrease the risk of cardiovascular disease, it is important to investigate some potential treatment options. About 80% of vitamin D in the body is obtained from the direct UV rays in sunlight, while nutritional supplements such as fortified milk and fatty fish liver supply the other 20%. Cholecalciferol is more efficient in achieving sufficient 1,25 dihydroxyvitamin D levels. Patients with chronic liver disease are at a higher risk of cardiovascular disease; therefore, being vitamin D-deficient will only increase the chances of a heart attack. Therefore, calcitriol is the best treatment for those with a damaged liver or fat malabsorption, as calcitriol is the form of vitamin D produced by the liver. It can help improve fat absorption, reducing further risk of plaque formation, especially in the carotid artery. Finding ways to improve the function of the 25-hydroxylase enzyme that breaks down calcitriol into the bloodstream can help lower the risk of heart disease (Sizar et al. 2022).

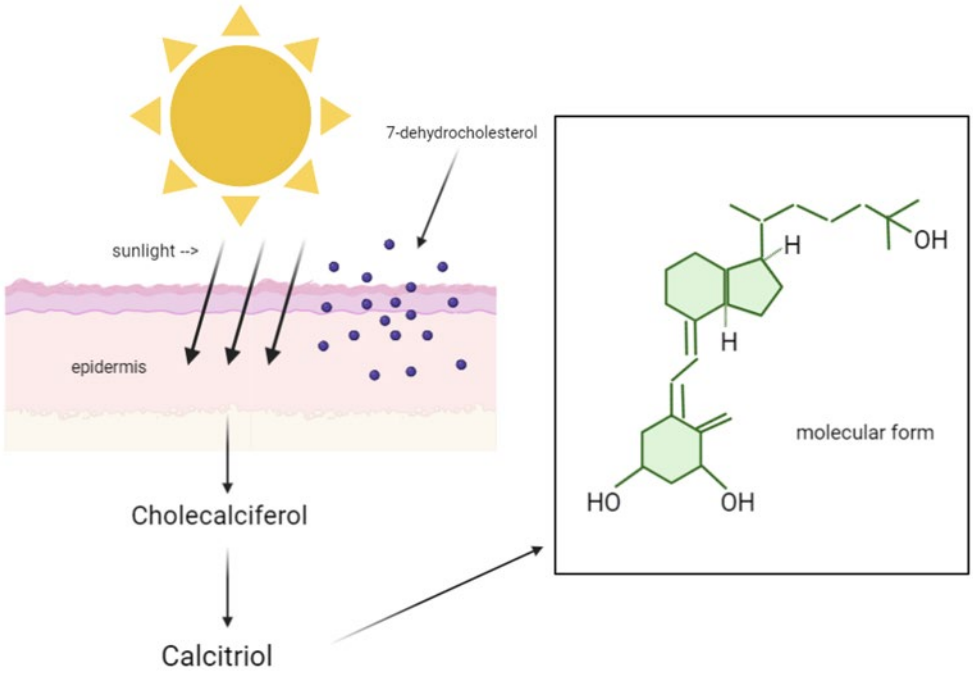

Figure 6. Diagram shows how sunlight gets converted into calcitriol, and the molecular form of calcitriol. (Figure made by Pramodani Arulkumar)

Conclusion

This research paper aimed to identify how Vitamin D can decrease the risk of coronary heart disease, including atherosclerosis, and damage to the arterial lining by inhibiting LDL uptake and helping the body absorb calcium and phosphorus. Factors such as homocysteine play a major role in providing essential substances to the body, but high levels can increase the risk of heart attacks. Heart attacks in the carotid artery can lead to stroke, brain damage, and possibly death. As heart attacks are one of the significant causes of death worldwide, and Vitamin D deficiency affects over one-seventh of the world's population, research can show the relationship between the two and provide ideas for possible treatment options. As the topic is relatively new in research and experiments have shown conflicting results, scientists can proceed with future studies and experimentations to determine if Vitamin D is beneficial and ways to develop Vitamin D into a treatment that can reduce the risk of coronary heart disease.

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