General

Benefit of Probiotics on Cardiovascular Health- A Narrative Review

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Coronary artery disease (CAD) is a leading cause of death globally and a prevalent cardiovascular disease (CVD) in which plaque buildup in artery walls results in inadequate blood flow. Risk factors for CAD include hypertension, inflammation, diabetes, and poor diet. In the past few decades, research has emerged on the employment of probiotics in cardiovascular health, particularly focused on methods for using probiotics as preventative measures for the risk factors of CAD. Probiotics can reduce hypertension and inflammation, improve insulin sensitivity, and possibly reduce salt levels in individuals with high-sodium diets. Still, more research needs to be done on the safety and considerations of administering probiotics and their underlying mechanisms since the evidence is predominantly experimental. Probiotics have proven to be a valuable research point given the urgency and incidence rates of coronary artery disease.

INTRODUCTION

Coronary artery disease (CAD) is a type of cardiovascular disease (CVD) in which plaque buildup in the artery walls leads to partially or fully blocked blood flow.[1,2] This results in the heart failing to receive adequate amounts of oxygenated blood, which can become a severe issue in situations of stress, oxygen level changes, etc where the amount and urgency of blood that the heart needs changes.[3]

Coronary artery disease is a prominent cause of death in the United States and many developing countries, and therefore is an important point of public health research.[4] CAD is present in approximately 10.9% of adults over the age of 45, and nearly four in 10 deaths resulting from cardiovascular disease are due to CAD. Many patients who are diagnosed with CAD have a history of smoking, obesity, stress, diabetes, hypertension, or diet concerns.[5] Fortunately, increasing awareness of treatments and risk factors for CAD has proven effective in decreasing related mortality rates.

A notable risk factor for CAD is a poor diet, especially since plaque buildup can result from a high-cholesterol diet.[1-3] Therefore, there has been increased research on probiotics and their use for CVD. Probiotics are live microorganisms, generally bacteria or yeast, that are consumed and believed to have health benefits for gut bacteria.[6] They were first discovered for their modern medical uses in the early 1900s, with the work of Louis Pasteur on analyzing the microorganisms involved in fermentation.[7]

When consumed, probiotics help to balance the gut microbiota, which is the collection of microorganisms colonizing the gut.[6] Although probiotics are often connected to gastrointestinal health, the condition of the gut microbiota can be a determining factor in cardiovascular health. For CAD specifically, many probiotics can reduce the risk factors of the disease such as inflammation, hypercholestremia, and hypertension, positively impacting the population and reducing the risk of CAD in the future.[8] Often, these probiotics are ingested in the form of fermented foods, such as yogurt, kimchi, and sauerkraut, and can be easily prepared.[8]

REVIEW

When conducting a narrative review on the available research for probiotics in preventing CAD, the databases utilized were PubMed and Google Scholar. The focal terminology included in this search consisted of “coronary artery disease,” “epidemiology of CAD,” “risk factors,” “probiotics,” “probiotics for CAD,” “gut microbiota,” “probiotic foods,” and “fermented.” Out of the resulting articles, ones that focused specifically on CAD as well as ones that gave details on the microbiology behind the body’s interactions with the probiotics were selected. In addition, articles that contained research studies in their title were chosen. These articles would allow for the creation of a review article that summarizes current studies on probiotics in CAD and allows for discussion of the mechanisms. After analyzing the resulting articles in English, the risk factors and causes of CAD were highlighted to determine which currently known causes were critical to consider for this review. Then, the probiotic-related search terms were used to locate research investigating the efficacy of probiotic strains to prevent and counter causes of CAD. Finally, a search was done on the safety and ethical concerns and the possible risks associated with probiotics in order to achieve a rounded overview

of the current state of knowledge of probiotics concerning CAD.

DISCUSSION

Due to the importance of a proper diet in preventing cardiovascular disease, probiotics are a promising non-invasive preventative measure for good cardiovascular health, and research on various probiotics exists. This review will discuss the leading research on probiotics that has shown to be beneficial in preventing the risk factors associated with CAD. It will also cover the risks and uncertainties associated with probiotics found in current research records.

Coronary artery disease is inflammatory, but, fortunately, a recent study using mice who were treated with a mixture of *Bifidobacterium* and *Lactobacillus* strains showed that certain probiotics can show anti-inflammatory properties within a few weeks.[9,10] It is important to note that there needs to be more research to pinpoint the mechanisms underlying the anti-inflammatory properties of microorganisms in probiotics; however, existing research has shown a correlation. For instance, some probiotic strains have shown a correlation between a reduction of pro-inflammatory cytokines, which are proteins that increase inflammation. *Bifidobacterium longum* and *Lactobacillus helveticus* are microorganisms that have exhibited these anti-inflammatory properties when tested in rats.[8,11,12]

Plaque buildup is also a significant indication of CAD. Research on mice has shown that microorganisms like *Lactobacillus rhamnosus*, when consumed orally, can remove plaque and cholesterol on artery walls and allow for better blood flow.[13] Bile salt hydrolases (BSH) are enzymes that break down bile salts and lead to a reduction of cholesterol absorption, thereby reducing cholesterol in the blood.[8,10] Fortunately, *Lactobacillus reuteri* and *Bifidobacterium longum* are microorganisms that were tested in a recent study and administered to mice with high cholesterol levels as probiotics to stimulate BSH and reduce cholesterol, reducing the risk of CAD in the future.[14] Specifically, lower-density lipoprotein (LDL) and triglycerides have shown reductions by probiotic strains in a study on 70 pregnant women who were given *Streptococcus thermophiles*, *Lactobacillus* strains, and *Bifidobacterium* strains.[8] This is promising because LDL is a harmful cholesterol that can lead to complications if present in high quantities.[15] However, cholesterol is not all bad; for example, it is crucial for keeping the plasma membrane of body cells intact. A study testing oral consumption of probiotics with *Lactobacillus*, *Enterococcus*, and *Bifidobacterium* strains observed that these can assimilate cholesterol so it will be present in plasma membranes instead of remaining in the blood.[16,17]

Hypertension, or high blood pressure, is another risk factor for coronary artery disease.[10] Microorganisms like *Enterococcus faecalis* found in fermented milk have shown a correlation in reducing blood pressure. Studies predict this could be through a mechanism of hindering an enzyme called angiotensin-converting enzyme (ACE), which activates vasoconstrictors and deactivates vasodilators in the body.[18,19] A study using cell culture of *Enterococcus faecalis* observed that a majority of the microorganisms led to the production of molecules that inhibit ACE.[20] Therefore, these probiotics could increase vasodilator activation in the body and thus expand the arteries, allowing for lower blood pressure and a reduced CAD risk. In addition, some probiotics can reduce high sodium levels, which decreases blood pressure. A study among 30 malnourished children observed reduced levels of sodium after treatment with probiotics.[21]

Recent research on coronary artery disease shows that proper diet management, like reducing cholesterol and salt consumption, is one of the most important guidelines for dealing with CAD.[22,23] One study tested nearly 50,000 post-menopausal women, and out of the women who underwent a dietary restriction, it was observed that while there was not a direct reduction in CAD risks, there was an effect on the risk factors.[23]

Another consideration for coronary artery disease is diabetes and similar diet-related concerns. Specifically, insulin sensitivity, or the ability of the body to absorb sugar from the blood, can be increased by probiotics like *Lactobacillus* and *Bifidobacterium,* as seen in studies where human participants were administered mixtures of these bacterial strains.[24] Using probiotics is a preventative measure for coronary artery disease because insulin resistance can lead to hypertension and endothelial dysfunction, which becomes another issue in causing CAD. The endothelium is an inner layer of blood vessels, and when it functions improperly, there is decreased vasodilation, or expansion of blood vessels, and therefore increased hypertension.[19, 25-27] For this reason, insulin sensitivity is crucial to prevent insulin resistance and reduce a patient's risk for coronary artery disease. However, regarding probiotics, there are mixed results and incomplete data on whether they can improve insulin sensitivity, as some studies mention that more detailed measurements would be beneficial.[27]

There are many ways people can incorporate probiotics into their daily lives, many of which include dairy products [Figure 1]. For instance, *lactobacillus* and *bifidobacterium* strains are found in fermented items like yogurt, cheese, and kefir.[28] Non-dairy foods like pickles, sauerkraut, natto, dosa, idli, tempeh, and miso are made from cereals, soybeans, and vegetables.[28] These foods also include lactic acid bacterial strains that benefit the heart and may prevent CAD.[28] Fortunately, fermentation does not require extensive resources and is common in numerous traditional cultures.[29]

Although it is valuable to discuss discoveries and innovations like using probiotics for CVD, it is crucial to acknowledge the risks and uncertainties associated with probiotic consumption according to current research. Probiotics contain nonpathogenic microorganisms, but studies have shown a risk of infection in pediatric patients — specifically low-weight infants.[6,30] There may be safety risks for patients who are immunosuppressed for a similar concern of infection.[30] For instance, *Lactobacillus*, a common bacterial strain in probiotic foods, has been seen to cause infection in numerous studies testing immunocompromised children, but the risk is considered rare.[30] In ad-

dition, some authors argue that it is necessary for those who are administering probiotic-based medications to consider how the bacteria are interacting with the host organism (for example, directly or indirectly) and overall take a mindful and analytic approach.[22,31] This is important since the evidence on probiotics is not yet solid, even though countless studies show positive results. In other words, there is insufficient knowledge on how the bacteria will act when consumed and whether it will have the claimed health benefits.

CONCLUSION

Probiotics are a promising solution for cardiovascular diseases, especially coronary artery disease. Current research focuses on probiotics as a non-invasive preventative measure, preventing hypertension, inflammation, cholesterol and plaque buildup, and insulin sensitivity. However, it is vital to note that there needs to be more research to get more solid research about the mechanisms and the host-microorganism relationship. Remaining cautious and attentive when administering probiotics for CVD is critical to prevent careless errors due to insufficient research. Probiotics have proven to moderate cholesterol and salt, among other risk factors, and with more research, they could become a strong option for CAD treatment and prevention. With more research pointing towards the efficacy of spreading awareness about preventative measures for CAD, probiotics are a critical step in improving the global diet and decreasing incidence rates.

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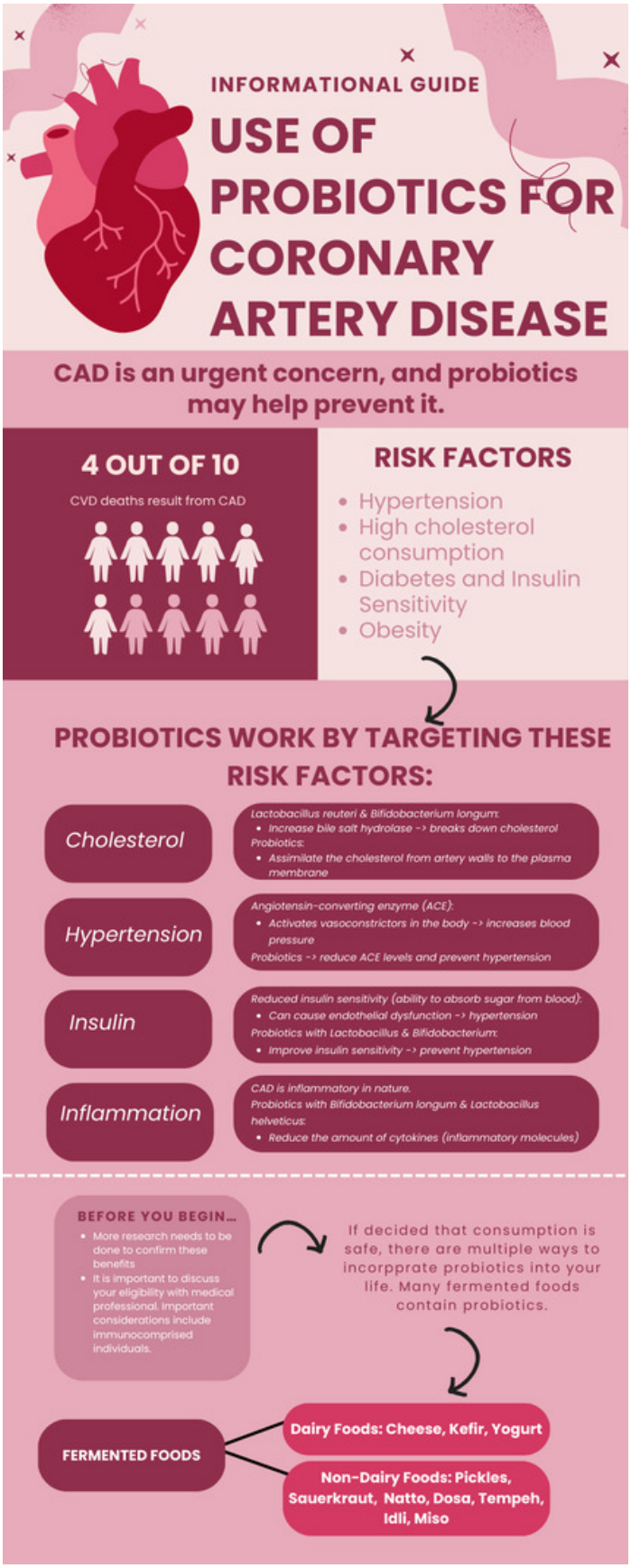
INFORMATIONAL GUIDE
USE OF PROBIOTICS FOR CORONARY ARTERY DISEASE
CAD is an urgent concern, and probiotics may help prevent it.
4 OUT OF 10
CVD deaths result from CAD
RISK FACTORS
Hypertension
High cholesterol consumption
Diabetes and Insulin Sensitivity
Obesity
PROBIOTICS WORK BY TARGETING THESE RISK FACTORS:
Cholesterol
Lactobacillus reuteri & Bifidobacterium longum:
Increase bile salt hydrolase -> breaks down cholesterol
Probiotics:
Assimilate the cholesterol from artery walls to the plasma membrane
Hypertension
Angiotensin-converting enzyme (ACE):
Activates vasoconstrictors in the body -> increases blood pressure
Probiotics -> reduce ACE levels and prevent hypertension
Insulin
Reduced insulin sensitivity (ability to absorb sugar from blood):
Can cause endothelial dysfunction -> hypertension
Probiotics with Lactobacillus & Bifidobacterium:
Improve insulin sensitivity -> prevent hypertension
Inflammation
CAD is inflammatory in nature.
Probiotics with Bifidobacterium longum & Lactobacillus helveticus:
Reduce the amount of cytokines (inflammatory molecules)
BEFORE YOU BEGIN...
More research needs to be done to confirm these benefits
It is important to discuss your eligibility with medical professional. Important considerations include immunocomprised individuals.
If decided that consumption is safe, there are multiple ways to incorpprate probiotics into your life. Many fermented foods contain probiotics.
FERMENTED FOODS
Dairy Foods: Cheese, Kefir, Yogurt
Non-Dairy Foods: Pickles, Sauerkraut, Natto, Dosa, Tempeh, Idli, Miso

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