

Review on Role of Nutraceuticals for Congenital Heart Disease

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ABSTRACT:

Congenital heart disease is a type of defect or malformation in one or more structures of the heart or blood vessels that occur in fetus. Researchers estimated that about 1 million US children and about 1.4 million US adults living with congenital heart disease. Over 2,00,000 children are estimated to be born with congenital heart disease in India every year. Higher mortality rates have been reported in males with congenital heart disease. However, mortality around surgery for congenital heart disease is higher in girls compared to boys. About 75% of babies born with a critical congenital heart disease are expected to survive to one year of age. About 69% of babies born with congenital heart disease are expected to survive to 18 years of age. Treatment for congenital heart disease depends on the type and severity of the defect. Current treatments like surgery, cardiac catheterization, heart transplants which includes many side effects like muscle pain, swelling, loss of appetite in surgery and bleeding, damage to artery, infection in cardiac catheterization. Whereas Nutraceuticals like omega-3-fattyacids, blue berries, beans, broccoli, tofu etc. can provide an alternative and beneficial pathway.

Keywords: Congenital heart disease, epidemiology, diagnosis, nutraceuticals, blueberries

I. INTRODUCTION:

Congenital heart disease, or a congenital heart defect, is a heart abnormality present at birth. The problem can affect the heart walls, heart valves, blood vessels. The disease usually occurs during early pregnancy when the baby's heart is forming (1). There are numerous types of congenital heart diseases. They can range from simple conditions that don't cause symptoms to complex problems that causes severe, life-threatening symptoms (2). Many doctors classify congenital heart diseases as either cyanotic congenital heart disease also known as critical congenital heart disease and noncyanotic

congenital heart disease (3). Critical congenital heart disease can be further classified into 3 different types of lesions namely right heart obstructive lesions, left heart obstructive lesions, mixing obstructive lesions (4). Common congenital heart disease includes ventricular septal defect, atrial septal defect (5). Globally, CHD constitutes the major cause of mortality among Children's, especially in developing countries. It also accounts for more than 20% of infant's death prenatally (6). The prevalence rate of CHD is estimated to be 8/1000 live births (7).

Etiology:

Congenital heart disease is caused when something disrupts the normal development of the heart (8). Scientists don't fully understand why that happens, but it may relate to drinking or smoking during pregnancy (or significant environmental exposures such as smoking), illnesses in the mother during pregnancy (diabetes, drug use, phenyl ketonuria or viral infections). congenital heart diseases are passed down through families (inherited) (9,10,11). It increases the risk of the condition, including downs syndrome, turner syndrome, Noonan syndrome, flu (influenza) (12,13). congenital heart disease can contribute to other health concerns later in life. Complications may occur years after a congenital heart defect is treated (14). Complications of congenital heart disease in adults include arrhythmias, endocarditis, stroke, pulmonary hypertension, heart failure (15,16,17).

Epidemiology:

Congenital heart disease affects 8 to 9 per 1000 live births, and approximately 25% are considered critical congenital heart disease (18,19,20). The birth prevalence of CHD is reported to be 8-12/1000 live birth (21,22). considering a rate of 9/1000, about 1.35million babies are born with CHD each year globally (23,24). Higher mortality rates have been reported in males (25,26,27). In china,90-150 thousand new

births with CHD were diagnosed every year, and infant mortality due to CHD reached 3.91 per ,1000 births in 2018 (28,29,30) (31,32). The prevalence of CHD in Jinan from 2005 to 2020 is 1,322,374 births and 5,180 CHD from 2005 to2020, and the prevalence was 3.92 per 1000 births (33,34,35). CHDs are diagnosed in 8 to 10 per 1000 live births in united states. In the US in 2004, CHDs accounted for >46000 hospitalizations among individuals of all ages and nearly \$1.4 billion in hospital costs (36,37,38,39).

Pathophysiology:

Ventricular septal defect:

This defect is based on the complex development of the ventricular septum during embryogenesis, involving the fusion of distinct septal components. The site of fusion of all components resides behind the tricuspid valve septal leaflet and below the valve of the aorta of the left ventricle outflow tract. The VSD of endocardial cushion is associated with insufficiency of atrioventricular valve, aortic insufficiently associated outflow defects, and complicated physiological lesions. The pathophysiology of VSD and ASD differs depending on the difference in the hemodynamic effects of VSD and ASD. In VSD the ventricular blood flow has two systolic pathways, usual out flow tract of ventricle and blood flow through the VSD to the outflow tract of the ventricle. The volume and direction of systolic blood flow across the VSD is determined by the ohm's law, by comparing the resistance of each pathway. For example, in patients having low resistance from the LV to the pulmonary artery compared with the resistance of low to the systemic circulation, leading to large left to right systolic blood flow across the defect. In case if the VDC is very small, then there will be high resistance at the defect limiting the shunt {left to right} with low pulmonary resistance. If resistance of pulmonary circulation is higher than the resistance of systemic circulation, there will be right-to-left shunt not depending on the defect size (40). Comparing the blood volume crossing a VSD in systole, the blood flow in diastole is very low.

The flow across the VSD in a diastole is much similar to that of across the ASD in systole (41,42).

Signs & symptoms:

Signs & symptoms for congenital heart diseases depend on the type and severity of the particular defect. Symptoms sometimes don't

develop until the teenage or early adulthood (43). Some defects might have few or no signs or symptoms. others might cause a baby to have following symptoms, blue tinted nails or lips, fast or troubled breathing, tiredness when feeding, sleepiness, cool, clammy skin, fainting, poor weight gain in infants, irritability and prolonged crying, swelling in legs, fatigue (44,45).

Diagnosis:

In many cases, congenital heart disease is diagnosed in a baby during pregnancy. However, a diagnosis may sometimes only be confirmed after birth (46). Tests to diagnose or confirm congenital heart disease in adults and children include:

- 1.Echocardiography
- 2.Electrocardiogram
- 3.Chest x-ray
- 4.Pulse oximetry
- 5.Cardiac catheterization
- 6.Hyperoxia test
- 7.Angiography
- 8.Transesophageal echocardiogram
- 9.Exercise tests or stress tests
- 10.Heart CT scan and heart MRI (47,48,49,50)

Treatment:

The treatment for a congenital heart defect depends on the type and severity of the defect. Some babies have mild heart defects that heal on their own with time (51). Others may have severe defects that require extensive treatment. In these cases, treatment may include the following (52):

- 1.Medications
- 2.Implantable heart devices
- 3.Catheter procedures
- 4.Open heart surgery
- 5.Heart transplant
- 6.Fetal cardiac intervention (53,54,55)

Nutraceuticals:

Nutraceuticals are products, which other than nutrition are also used as medicine (56). A nutraceutical product may be defined as a substance, which has physiological benefit or provides protection against diseases (57). The term "nutraceutical" combines the two words of "nutrient", which is a nourishing food component, and "pharmaceutical", which is a medical drug (58). The name was coined in 1989 by Stephen Derelict, founder and chairman of the foundation for innovation in medicine, which is an American organization located in Cranford, new jersey (59)

(60). Nutraceuticals may be used to improve health, delay the aging process, prevent chronic diseases, increase life expectancy, or support the structure or function of the body (61). Nutraceuticals can also be categorized as traditional nutraceuticals and non-traditional nutraceuticals.

Nowadays, nutraceuticals have received considerable interest due to potential nutritional, safety and therapeutic effects (62). Market research recently proposed that the worldwide nutraceuticals market is expanding and would reach US \$250 billion by 2018 (63). Recent studies have shown promising results for these compounds in various pathological complications such as diabetes, atherosclerosis, cardiovascular diseases, cancer and neurological disorders (64,65). A dietary supplement is considered as a product that bears or contains one or more of the following dietary ingredients; a mineral, a vitamin, an amino acid, a medical herbs or other botanical, a dietary substance for use by man to supplement the diet by increasing the total daily intake, or a concentrate, metabolite, constituent, extract, or combinations of these ingredients (66,67).

Nutraceuticals used in congenital heart diseases:

Broccoli:

Broccoli – *brassica oleracea L. var. italica* belongs to family Brassicaceae. The word “brassica” means to cut off the head. Broccoli is an Italian word from the Latin *brachium*, meaning an arm or branch (68). Broccoli is a rich source of carbohydrates, potassium, vitamin K, vitamin A, vitamin E, folate. Broccoli inflorescence is a good source of health promoting compounds since it contains Glucosinolates, flavonoids, hydroxycinnamic acids and other minor compounds (69). Dietary use of broccoli has encouraged scientists to test for wide range of biological activities including gastroprotective, antimicrobial, antioxidant, anticancer, cardioprotective, anti-obesity and immunomodulating activities. Broccoli exerts cardioprotective effects through various mechanisms such as (a) inhibition of phase 1 enzymes and DNA adducts; (b) induction of phase 2 antioxidant detoxifying enzyme; (c) antioxidant function; (d) induction of cell cycle arrest; (e) inhibition of angiogenesis; and anti-inflammatory properties and thus considered as a potential functional food (70).

Strawberries:

The strawberry (*Fragaria ananassa*) originated in Europe in the 18th century (71). It is a

hybrid of 2 wild strawberry species from north America and Chile (72). Strawberries are bright red, juicy, and sweet. The strawberry represents a relevant source of micronutrients, such as minerals, vitamin C, folate and phenolic substances, most of which are natural antioxidants and contribute to the high nutritional quality of the fruit (73,74). Strawberry consumption has also been proposed as a useful dietary complement to improve the overall utility of diets designed to lower coronary heart disease risk (75). The abundance of antioxidants and polyphenols in strawberries makes them the ideal food to protect your heart from ailments (76,77). Strawberries contain anthocyanins (the antioxidants responsible for their red hue), which protect the lining of the circulatory system, thereby shielding the arteries from plaque build-up and regulating the blood pressure (78,79). There is evidence that the addition of berries to the diet can positively affect risk factors for CVD by inhibiting platelet aggregation, improving the plasma lipid profile, increasing low density lipoprotein (LDL) resistance to oxidation (80,81).

Tofu:

Tofu also known as soy curd is generally obtained by coagulating soymilk. It is naturally gluten free and low in calories (82). The soybean has originated from China nearly 4000-5000 years ago. It is an important source of protein, isoflavones such as phytoestrogens. Isoflavones may have both estrogen agonist and estrogen antagonist properties (83). These may help protect against some cancers, heart disease, osteoporosis. The researcher found that those who ate tofu more than once a week lowered their risk of heart disease by 18% (84). The reduced risk was most pronounced in young women and postmenopausal women who were not taking hormones (85). The antioxidant and anti-inflammatory properties of soy peptides found in fermented soy food like tofu can help to protect the blood vessels from oxidative and inflammatory damage. Menopausal women can rely on tofu for production of estrogen (86).

Pea:

Pea (*Pisum sativum L.*), a nutritious agricultural commodity belongs to the Leguminosae family (87,88). The annual global production of green pea and dry pea seeds are approximately 14.5 million tons and 22 million tons, respectively (89,90). Pea seeds are well known for its pivotal nutrients that can be differentiated in mainly soluble and insoluble

fibers, proteins (tryptophan and lysine), complex carbohydrates, vitamin B, folate, minerals, low content of saturated fat (91,92,93,94,95). Green peas contain a decent amount of heart healthy minerals such as magnesium, potassium, and calcium (96,97). Diets high in these nutrients may be helpful for preventing heart disease (98). Inflammation and stress caused by free radicals(oxidation) can contribute to plaque formation along blood vessel walls (99). Omega-3 and omega-6 fatty acids found in peas help to reduce oxidation and inflammation and prevent plaques from forming (100,101,102).

Blueberries:

Blueberries are a widely distributed and widespread group of perennial flowering plant with blue or purple berries. They are classified in the section cyanococcus within the genus vaccinium (103). Among all fruits, berries have shown substantial cardio protective benefits due to their high polyphenol content (104). Blueberries are particularly high in polyphenolic flavonoids in addition to containing significant amounts of micronutrients and fiber. Blueberries contain a plant compound called anthocyanin (105). This gives blueberries both their blue color and many of their health benefits. Blueberries can help heart health, bone strength, skin health, blood pressure, diabetes, cancer prevention and mental health (106). The fiber, potassium, vitamin C, vitamin B6, and phytonutrient content in blueberries supports heart health (107). Fiber content helps to reduce the total amount of cholesterol in the blood and decrease the risk of heart disease (108). Vitamin B6 and folate prevent the build-up of a compound known as homocysteine. Excessive build-up of homocysteine in the body can damage blood vessels and lead to heart problem (109,110,111).

Omega-3 fatty acid:

Omega-3 fatty acids are a type of polyunsaturated fats with various health benefits including reducing the risk of heart disease (112), dementia (113), and alleviating inflammation in arthritis sufferers (114,115). high omega-3 foods include flaxseeds, chia seeds, fish, walnuts, avocados, navy beans, fish, brussels sprouts (116,117,118,119).

Avocados:

Avocados are a nutrient-dense fruit, containing dietary fiber, potassium, magnesium, MUFA, and polyunsaturated fatty acids as well as

phytonutrients and bioactive compounds, which have been independently associated with cardiovascular health (120,121,122). The primary monounsaturated fatty acid present in avocados is oleic acid healthy fat and it is suggested that it helps in reducing hypertension, inflammation, and insulin sensitivity (123,124,125). Avocados are a source of vitamins C, E, K, and B6 as well as riboflavin, niacin, folate, pantothenic acid. In every 100 g of avocado there are 76 milligrams of a natural plant sterol called beta sitosterol (126,127). Regularly consuming beta sitosterol and other plant sterols may help maintain healthy cholesterol levels, which are important for heart health. Folate is important for a healthy pregnancy (128,129). Adequate intake reduces the risk of miscarriage and neutral tube abnormalities. Avocados contain fatty acids that are integral to a healthy diet and fetal development (130,131,132).

Spinach:

Spinach(*spinaciaoleracea*) is a leafy green vegetable that originated in Persia. It belongs to the amaranth family and is related to beets and quinoa (133). Spinach is an extremely nutrient rich vegetable. It packs high amounts of carotenoids, vitamin C, vitamin K, folic acid, iron, and calcium (134). Folic acid also known as folate or vitamin B9, this compound is vital for pregnant women and essential for normal cellular function and tissue growth. Eating spinach may benefit eye health, reduce oxidative stress, help prevent cancer and heart diseases, and reduce blood pressure levels (135,136). Spinach contains several important plant compounds, including lutein, kaempferol, nitrates, quercetin, zeaxanthin. Spinach contains high amounts of nitrates, which may promote heart health (137).

II. CONCLUSION:

Nutraceuticals embody a novel and exhilarating research field for discovery of innovative health products with tremendous potentials of health benefits including safety, efficacy, and economy. Researches have realized the fact that proper nutrition and dietary supplements can prevent and cure chronic diseases like heart diseases, cancer. Several types of nutraceuticals have been isolated from foods, and massive quantities are produced using biotechnology and genetic engineering tools which provide pharmacoeconomic benefits. The association between folate supplementation and CHD has been confirmed by several studies though

experimental evidence is still lacking. If folic acid is proven to prevent CHD the public health impact is expected to exceed that of preventing NTDs. Nutraceuticals are better than other treatment because they are inexpensive and have no side effects.

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