Therapeutic applications of vitamins and coenzymes on heart disease and cardiomyopathy: A Review

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Abstracts: The present review is based mainly on papers published between 2000 and 2020 and gives information about the properties of the Vitamins and coenzymes in chemical and biological systems and its possible role in preventing cardiac diseases. The main aim of this report is to highlight its role as therapeutic applications of these in cardiomyopathy, also reported are bioactive properties that may influence the development of treatments and protection against cardiovascular cell damage. The paper will also examine recent observations in various fields.

COENZYMЕ Q10 AND ITS ASSOCIATION WITH HEART DISEASE

INTRODUCTION

Coenzyme Q10/Ubiquinone is mainly used as a supplementation with conventional therapy to improve heart functions in almost all cardiac diseases assisting improvements in several health functions such as improvement in ejection fraction etc as well as quality of life in patients postoperative period in patients during from heart ailments.

C-Q10 (2,3-dimethoxy-5-methyl-6-decaprenyl benzoquinone/ubiquinone) is a endogenously synthesized provitamin, lipid soluble which acts as an antioxidant in conjunction with Vit E with its primary use in as an adjunctive therapy (for short term and long term management) for Chronic Heart Failure(CHF) by influencing significant improvements in mean ejection fraction, Cardiac Output and mean Stroke Volume.

In the US, according to the statistics of 2016, 23% CVD death occurs below 70years of age, however in India CVD between 25-69 i.e. 24.8% of the population is getting affected which is a productive population. Although being endogenously synthesized the nutritional supplement of CO Q10 does not increase above normal in the tissues with impaired CO Q10 synthesis capacity. Several Heart Disease like cardiomyopathy is found to be associated with COQ10 deficiencies.

Heart Failure characterized by a loss of contractile function due to energy depletion status in the mitochondria due to deficiency in the endogenous level of COQ10 as it functions as a cofactor in mitochondria by transferring electrons from complex 1(succinyl)to complex 2 (NADH dehydrogenase) and 3 ultimately resulting in the formation of ATP by regulating cytochrome b-cl complex. CO Q10 is a naturally occurring fat soluble substance present in high concentration in tissues requiring high amounts of energy especially in the heart, liver, kidney and pancreas. Heart has the highest concentration of COQ10 as it has to perform several functions all of which are energy dependent like cardiac contraction and relaxation where COQ10 acts as a radical scavenger by transferring electrons in between complexes. Heart is highly sensitive to the deficiency of this coenzyme and has been found to contribute to both types of Cardiomyopathy: Dilated Cardiomyopathy and Hypertrophic Cardiomyopathy(HCM) where COQ10 is known to prevent resistant heart failure symptoms. Majority, up to 75% of all heart diseases are accompanied by low/deficient CO Q10 levels. Coenzyme COQ10 used a supplement drug shows wonderful effects in patient suffering from heart ailments like Chronic Heart Failure(CHF), Angina Pectoris, Hypertension, Ventricular arrhythmia, Cardiomyopathy, anthracycline antineoplastic therapy and even showed significant improvements in eliminating clinical symptoms, functional status and quality of life in patients with end stage Heart Failure, waiting for transplantation according to the surveyed clinical trial conducted all across globe.
This is supposed to be a supplement drug adjunct to standard therapy for the respective ailments. CO Q10 prevent oxidation of lipoproteins (LDL: cholesterol) and thereby inhibit atherosclerosis and disruption of plaque on heart walls and walls of arteries by improving ATP production, antioxidant activity and membrane stabilizing properties (due to phospholipid-protein interaction), improvement in endothelial function, cardiac bioenergetic, preservation of Na⁺/K⁺ pump, vasodilation, effect of aldosterone and angiotensin and anti-viscosity effect. Also, conditions of coronary artery disease, the rate of inactivation of Nitric Oxide to per-oxo nitrite by superoxide anions may be reduced by CO Q10. According to studies, normal safe dosage ranges up to 1200 mg/ml/person, even 3000 mg/ml/person did not cause any severe side-effect, with the goal of achieving serum concentrations of 2.0–3.0 µg/mL (normal concentrations are 0.7–1.0 µg/mL) in clinical trials and is well tolerated with only minor nausea, gastrointestinal effects in few patients and it cannot be overdosed. CO Q10 influences a number of genes of relevance to cardiovascular function, including those involved in fat metabolism and inflammation. 25% of COQ10 can be obtained through diet, daily requirement being 500 mg. Q-SYMBIO in powdered form studied in randomized clinical trial to determine efficacy of CO Q10 supplementation on comorbidity and mortality in case of several heart ailments like heart failure over a decade since introduction of ACE inhibitors, beta-blockers in a double blinded placebo control study. Studies yielded that COQ10 is a novel drug in supplementation with conventional therapies especially when it showed remarkable improvements in patients with heart failure as it eased energy production by heart muscles. The deficiency of endogenous CO Q10 is observed with aging, use of certain drugs before like statin, beta-blockers (as they share a common biosynthetic pathway) and several diseases of liver, kidney, etc.

KISEL-10 also another supplemental COQ10 showed significant improvements in patients suffering from Keshan's Disease, a cardiomyopathy endemic to regions of China with selenium depleted soils. Both, Q-SYMBIO and KISEL-10 have not shown any severe side effects and are considered safe for dosage according to studies. Regarding bioavailability of COQ10, CO Q10 manufactured by fermentation to a crystalline substance that cannot be absorbed via intestine therefore dispersible tablets are created from the crystals to facilitate absorption. Also, evidence supports COQ10 as a therapeutic agent in protection of ischemic tissue from reperfusion damage. CO Q10 also influences formation of a potent inhibitor for free radical formation, DT diaphorase. In rats cultured cardiomyocytes showed improved survival of cells pretreated with CO Q10 and subsequently rendered anoxic leading to a support of COQ10 as an ischemic modifier. CO Q10 also plays a role as an ischemia modifier.

CO Q10 may influence prostaglandin metabolism, specifically prostacyclin. The clinical response and survival of these patients to those found with patients on vasodilators and converting enzyme inhibitors. Pharmacokinetic studies revealed that Oral COQ10 supplement took 5-10 hours with mean $T_{\text{max}}$ of 6.5 hours to reach peak in the plasma following intake of 100 mg of dispersible tablet as slow absorption is observed possibly due to its high molecular weight. Excretion primarily through the biliary tract and a significant amount of COQ10 was traced in patients' faeces with chronic dosage. Being a natural substance with low toxicity and imparting major contribution in survival rate CO Q10 supplementation should be considered engineered with other combinations to attain a more successful combination for this drug to be a future drug for all heart ailments.

**Fig 1 shows the Role of CO Q10 in preventing Heart Disease: Atherosclerosis**
Clinical trials of CQ-10

Coenzyme Q10 Supplementation in Children with Idiopathic Dilated Cardiomyopathy: NCT02115581

The study was conducted as a randomized, double-blind, placebo-controlled trials aimed to determine the outcome of supplementation of Coenzyme Q10 in group of 38 children patient (17 in arm of known cases of Dilated Cardiomyopathy who received CO Q10 supplementation and 21 children in arm of known cases of cardiomyopathy who received control) below 18 years of age receiving conventional therapy of heart failure due to the condition of Idiopathic Dilated Cardiomyopathy at intervals of three, six and nine months of dosage (dose of 2 mg/kg/day in 2 or 3 divided doses and increased to the maximum dose of 10 mg/kg/day according to the patient's tolerance) as therapy. The primary outcome of the study was improvement in the left ventricular ejection fraction measured by echocardiography. Also, improvement of abnormal filling of the left ventricle is determined by doppler-derived trans-mitral blood flow and pulmonary venous blood flow data to assess the severity of abnormal diastolic filling. No adverse effect or side effects observed as such.

Coenzyme Q10 in post-cardiac arrest cerebral resuscitation: NCT01319110

The clinical trial constitutes a randomized, parallel assignment, quadruple masked, placebo controlled study in 10 patients (5 in each arm) aged 18 years or older receiving CO Q10 in a dosage of 200mg three times per day for 7 days (through pre-existing NG or OG tube mixed with 20ml of chocolate to blind certain investigators) until death/discharge to determine the levels of Co Q10 in post-cardiac arrest (CA) in serum as well as if the levels of COQ10 can be increased in post CA patients with administration of exogenous COQ10 with comparison to supplementation vs placebo. The results of the trial established low COQ10 levels compared to standard laboratory control values, quantitative comparison of serum COQ10 levels among those randomized to COQ10 supplementation and placebo. No adverse effect found as such during supplementation therapy.

Firefighter Aged Garlic Extract Investigation with Coenzyme Q10 as treatment for Heart Disease (FAITH): NCT00860847

A study conducted among 65 people with 32 with supplementation and 33 with only placebo kept as control (aged 35-84 years) who are firefighters in a randomized, parallel assignment, quadruply masked, placebo controlled intervention with supplementation of aged garlic extract and Coenzyme Q10 to assess risk of sudden death due to cardiovascular health issue amongst firefighter population. The objectives of the study was to observe if the combination was effective in slowing the progression of coronary artery disease (CAD) with pre-conditions of atherosclerosis (Coronary Artery Calcification) in firefighters who has never used statins or other cardiovascular risk factors as well as coronary stenosis. Dosage administered was 1200 mg of oral AGE and 120 mg of CO Q10 combination. Outcomes was observed as change in the Total Coronary Calcium Scores by computed tomography and evaluation of Total Plasma Cholesterol and Triglycerides (Total Plasma Lipid), LDL-Cholesterol, HDL-Cholesterol, and VLDL-Cholesterol assessed by the Precipitation Method; Endothelial Markers and Inflammation like C-reactive Protein and Homocysteine also GSH to understand the difference when compared with control. No adverse effect found as such.

Intervention with Selenium and Q10 in Cardiovascular Mortality and Cardiac Function in the Elderly Population in Sweden (KiSel 10): NCT01443780

A randomized, parallel-assignment, triply masked, double-blind placebo controlled study was conduction with Selenium and CO Q10 combined supplementation in a group of 443 patients (between ages of 70-87) for a period of 48 months intervention with routine checkups every 6 months by collecting blood samples, doing echocardiograms and cardiac natriuretic peptides were analyzed to determine the possible risk of cardiovascular mortality as well as cardiovascular health in the elderly. Q10 is known to produce several selenium containing enzymes that plays a central role in providing energy to the heart muscles for its pumping action. Dosage in individuals 200mg/day mg/day of coenzyme Q10 (Bio-Quinon 100 mg B.I.D, Pharma Nord, Vejle, Denmark) and 200 µg/day of organic selenium (SelenoPrecise 200 µg, Pharma Nord), or placebo in which sugar pills were given. No serious adverse effect as such.

Vitamin B and its derivatives in Heart disease and Cardiomyopathy

Introduction

Heart failure (HF)-associated mortality remains high, despite guideline-recommended medical therapies. Poor nutritional status and unintentional cachexia have been shown to have a strong association with worse survival in HF patients. Importantly, micronutrient deficiencies are potential contributing factors to the progression of HF.

This review aims to summarize contemporary evidence on the role of micronutrients in the pathophysiology and outcome of HF patients. Emphasis will be given to the most well studied micronutrients, specifically, vitamin D, vitamin B complex, coenzyme Q10 and L-carnitine.

Nutritional factors such as magnesium, folic acid, vitamin B12, vitamin B6, L-arginine, and polyunsaturated fatty acids (PUFAs) appear to be of significant benefit for patients with coronary heart disease, and in the prevention and arresting the progression of heart failure and cardiac arrhythmias. In addition, ingestion of an adequate amount of protein and maintaining normal concentrations of plasma albumin seem to be essential for these patients.
These nutrients closely interact with the metabolism of L-arginine-nitric oxide system, essential fatty acids and eicosanoids such that beneficial products such as nitric oxide, prostaglandin E1, prostacyclin, prostaglandin I3, lipoxins, resolvins, protectins and protectins are generated and synthesis of pro-inflammatory cytokines is suppressed that results in platelet anti-aggregation, vasodilatation, angiogenesis and prevention of coronary heart disease, cardiac arrhythmias and stabilization of heart failure.

This implies that subjects at high risk of coronary heart disease, cardiac arrhythmias and heart failure and those who have these diseases need to be screened for plasma levels of magnesium, folic acid, vitamin B12, vitamin B6, L-arginine, nitric oxide, various PUFAs, lipoxin A4, resolvins, protectins, asymmetrical dimethylarginine (ADMA—an endogenous inhibitor of nitric oxide), albumin, and various eicosanoids and cytokines and correct their abnormalities to restore normal physiology.

Thiamine was discovered in 1926 by two Dutch scientists, Drs Jansen and Donath, and was isolated in a pure form and synthesized in a laboratory by Dr Williams. Throughout history, thiamine has been given multiple names: vitamine, aneurin, and antineuritic vitamin.

The public health prominence of thiamine, however, predates its discovery. The disease caused by thiamine deficiency, beriberi, was widespread in the Asian countries as early as the 19th century. It was postulated even before the discovery of thiamine that beriberi was a nutritional deficiency that was caused by the ingestion of polished rice. The origin of the term beriberi is unclear. Two possible sources of the term may be from the Sinhalese meaning “I cannot” or from the Arabic meaning “sailor’s asthma.”

It was only in the 1950s that interventions to encourage the use of whole grains were developed. Thiamine deficiency was, at one time, widespread in the developing world as a result of the exclusive use of polished rice as a staple diet in many Asian countries. With the realization that polished rice could lead to thiamine deficiency, it was somewhat controlled. Until recently, thiamine deficiency was considered to be a disease of historical importance only in the developed world.

However, it is now realized that a large number of certain populations may be at high risk for developing this deficiency, including HF; therefore, the interest in thiamine and thiamine deficiency has recently been reemerging.

Cardiac Dysfunction Mechanism

B Vitamins

The B vitamins are water soluble vitamins that are critical coenzymes in the Krebs cycle necessary for the production of adenosine triphosphate (ATP) [19]. They include thiamine (B1), riboflavin (B2), pyridoxine (B6), folic acid (B9), cobalamin (B12), niacin (B3), and pantothenic acid and biotin, all of which are essential nutrients that require continued ingestion to maintain nutritionally healthy levels. The current recommended daily allowances for B vitamins in healthy individuals may not provide adequate amounts for patients with HF. In addition, the use of loop diuretics, in particular, increases renal losses of water soluble vitamins. The prevalence of thiamine deficiency in the setting of HF has been estimated to range between 13% and 33%. Risk factors that have been associated with thiamine deficiency include advancing age, malnutrition, hospitalization, and loop diuretics [20, 21].

Severe thiamine deficiency can result in high-output cardiac failure due to excessive vasodilation (wet beriberi); however, it is uncommon in the modern era. Small studies have demonstrated improvement in both LV function and cardiac output with thiamine supplementation. Seligman Metal. showed a mean improvement of 13% in LVEF and 10 mm Hg improvement in systolic blood pressure after 7 days of intravenous (IV) thiamine. Another study found that a combination of IV thiamine for 7 days followed by oral thiamine for 6 weeks resulted in a 22% improvement in LVEF in 90% of treated patients [29]. More recently, similar results were demonstrated by Schoenenberger et al. in a randomized, double-blind, crossover study that included nine patients with LVEF < 40%. After 4 weeks of thiamine supplementation, they observed an absolute increase of 3.9% in LVEF, from 29.5
% to 32.8%. Although these data indicate that thiamine supplementation may have some beneficial effects on surrogate endpoints of HF, large-scale studies are necessary to evaluate their impact on clinical outcomes.

Deficiencies in riboflavin, pyridoxine, folic acid and cobalamin have also been documented in the HF population]. Additionally, riboflavin, cobalamin and folic acid play a role in homocysteine metabolism, while cobalamin has been shown to improve endothelial function in patients with diabetes and HTN Results from a single center study suggested that cobalamin may be a potential biomarker of volume overload in patients with decompensated HF]. A recent study from Japan reported an inverse relationship between folic acid intake and risk for cardiovascular disease, including HF Overall, there is insufficient data to indicate a benefit of the B vitamins on HF outcomes.

Cardioprotective effects of vitamin B6 in Heart disease and Cardiomyopathy

Several studies have shown that vitamin B6 and its major metabolite, PLP, exert anti-ischemic effects in the heart. PLP has also been reported to reduce ischemic injury to the brain]. In a rat model of myocardial infarction, PLP has been demonstrated to reduce infarct size and improve cardiac function. A reduction of the ischemia-reperfusion (I/R) injury and infarct size was also seen in isolated rat hearts]. A phase II clinical trial, in which PLP was given to patients undergoing percutaneous coronary intervention, showed a decrease in infarct size 24 h after angioplasty. In 901 high-risk patients undergoing coronary artery bypass graft (CABG) surgery, PLP resulted in a significant decrease in preoperative myocardial infarction but did not affect the prespecified primary endpoint].

A reduction in cardiovascular death and myocardial infarction by PLP in the high-risk patients undergoing CABG was found to be independent of cross clamp time. However, in another study, in which 3023 intermediate- to high-risk patients undergoing CABG were used as subjects, PLP did not show any significant effect on cardiovascular death or non-fatal myocardial infarction Although the exact reason for the negative results of this study using intermediate- to high-risk patients for CABG is not clear, the clinical studies using high-risk patients for CABG as well as in patients following angioplasty show a high potential for PLP therapy in ischemic heart disease.

Vitamin C in Heart disease and Cardiomyopathy

Vitamin C is also known as ascorbic acid or ascorbate which is found in many food items like tomatoes, broccoli, etc. Vitamin C’s function as an antioxidant makes it important for cardiovascular diseases. Vitamin C most commonly prevents atherosclerosis. In atherosclerosis, fats, cholesterol accumulate on the walls of the arteries as plaques. These plaques are very unstable and can burst resulting in the damage of arteries and formation of blood clot thus restricting blood flow. This can result in myocardial infarction, cardiovascular death, etc. Several studies have been conducted across the globe to show the relation between vitamin C and cardiovascular diseases. Although some studies have shown no relation or positive relation but many other studies have shown an inverse relation between cardiovascular diseases and vitamin C. Its functions in respect to prevention of cardiovascular diseases are

Oxidative Low Density Lipoprotein (LDL) reduction: Reactive oxygen and nitrogen species are formed by endothelial cells which oxidize LDL to oxidized LDL which is highly reactive. These oxidized LDL are taken up by macrophages and they form foam cells which are full of cholesterol and lipid and which ultimately results in the formation of plaques. Vitamin C protects LDL from oxidation thus preventing it from forming foam cells. It also absorbs reactive oxygen and nitrogen species reducing their concentrations in the plasma. It also reduces the affinity of apolipoprotein B towards transition metal ions and as transition metal ions induces the oxidation of LDL thereby preventing oxidized LDL formation.

It inhibits oxidized LDL-related ICAM-I overexpression and monocyte adhesion thus reducing the atherogenic inflammatory response. It prevents apoptosis of macrophages.

NO is secreted by endothelial cells from L-arginine by NO synthase (NOS) in the presence of NOS cofactor BH4. This NO relaxes smooth muscles in the vessels thus allowing vasodilation and helps in smooth blood flow. It also prevents apoptosis of endothelial cells, adhesion of leukocytes to the interior wall of blood vessels. NAD(P)H oxidase produces superoxide which converts NO to peroxynitrite which oxidizes NOS cofactor thus resulting in uncoupling of NO synthase which then converts molecular oxygen to superoxide as a result of altered enzymatic activity thus initiating a chain reaction. This builds up an oxidative stress which results in the development of cardiovascular diseases. Vitamin C regenerates the NOS cofactor and also protects the cofactor from getting oxidized and it also attenuates the activity of NAD(P)H oxidase. It also increases the sensitivity of guanylyl cyclase to NO signaling. It also has a preservation action against NO synthase by preventing S-nitrosylation of the regulatory cysteine residues on the NO synthase.

In mice it is seen that Vitamin C deficiency results in structural deformity in the walls of the aorta which indicates defects in collagen and elastin synthesis.

A study on eighty healthy male volunteers showed that vitamin C reduces arterial stiffness and platelet aggregation thus it reduces the left ventricular load and mass and also reduces the risk of atheroma formation. This shows that Vitamin C reduces the risk of cardiovascular diseases. Another prospective, multipurpose, cohort study shows that vitamin C reduces the risk of cardiovascular mortality but not cardiovascular diseases. Clinical trials like Physicians Health Study II (PHS II) found no effect of vitamin C on cardiovascular events, stroke, myocardial infarction, cardiovascular mortality or total mortality.
Vitamin K in Heart disease and Cardiomyopathy

Vitamin K is a group of fat soluble vitamins found in foods or in supplements. Vitamin K was first invented by a Danish scientist Henrik Dam. Vitamin K mainly exists in 2 forms phylloquinone and menaquinone. Phylloquinone (Vitamin K1) is found in green leafy vegetables. Menaquinone (Vitamin K2) which is produced by bacteria is found in eggs, meat, natto etc. Vitamin K2 MK-7 is the most active form of vitamin K. Vitamin K is very important for good bone and heart health.

Calcium causes health problems like arterial calcification and arterial stiffening can be reduced or prevented by vitamin K. Osteoblasts are the cells that make the skeleton produce osteocalcin which takes calcium from blood and helps it to bind to the matrix of the bone.

Vitamin K2 plays the role of activating osteocalcin because osteocalcin is usually in the inactive form. Matrix Gla protein is a vitamin K dependent protein which is produced by vascular smooth muscle cells. It also helps in the prevention of accumulation of calcium on the walls of blood vessels thus preventing arterial calcification. Vitamin K is a cofactor for 1 enzyme, gamma-glutamyl carboxylase which gamma-carboxylates certain glutamic acid residues post translationally in a number of vitamin-K dependent proteins. Vitamin K also maintains blood homeostasis.

It also helps in blood coagulation as hepatic coagulation factors prothrombin and factor X are Vitamin K dependent protein.

A study on 16000 healthy women showed that higher intake of natural vitamin K2 is associated with lower risk of cardiovascular events.

Also it is seen that vitamin K and D had beneficial effects on the elastic properties of the vessel wall in postmenopausal women.

Vitamin E in Heart disease and Cardiomyopathy

Vitamin E is a group of eight fat soluble compounds four tocopherols and four tocotrienols. Vitamin E function as an antioxidant making it important for cardiovascular health. It interacts with lipid peroxyl radical and prevents it from forming a new radical and thus terminating the chain reaction. Studies have shown that vitamin E can reduce cardiovascular events but there are also studies that show that there is no association of vitamin E with cardiovascular events or increase of cardiovascular events due to vitamin E consumption.

In diabetic patients, atherosclerosis and endothelial dysfunction is a major problem. Haptoglobin is synthesized by hepatocytes and is an abundant plasma glycoprotein. There are two classes of functional alleles 1 and 2 with homozygous 1-1, 2-2 and heterozygous 2-1 genotypes possible. The two alleles differ in the antioxidant property of their protein product. Haptoglobin (Hp) helps to clear haemoglobin (Hb) by forming Hp-Hb complex and thereby reducing the oxidative stress exerted by the haemoglobin iron on blood vessels. Hp 2-2-Hb complexes are cleared less efficiently than Hp 1-1-Hb and Hp 2-1-Hb complexes mainly in diabetes mellitus (DM) patients.

This results in increased binding of Hp-Hb to Apo A1 on high density lipoprotein thereby attaching the pro-oxidative heme moiety to high density lipoprotein and as a result high density lipoprotein becomes unable to stimulate the reverse transfer of cholesterol from macrophages. Israel Cardiovascular Vitamin E (ICARE) study showed that Hp 2-2 individuals suffering from diabetes mellitus had a higher risk for cardiovascular mortality and vitamin E reduced this risk of cardiovascular mortality, stroke and myocardial infarction.

Clinical trials of Vitamin C, Vitamin K and Vitamin E in its Derivatives in heart disease and cardiomyopathy

Women's Health Study of Low-dose Aspirin and Vitamin E in Apparently Healthy Women:-

Trial ID: NCT00000479

This test was conducted on female candidates 45 years of age and older. This trial tested the effect of vitamin E and aspirin supplementation on important vascular events and in the incidence of total malignant neoplasms of epithelial cell origin. It is a randomized, double blind, placebo-controlled trial. The participants were under four arms aspirin and placebo, vitamin E, aspirin combined, vitamin E and placebo, and placebo and placebo. The results showed that though vitamin E reduced the number of major cardiovascular events and cardiovascular death but it didn’t reduce the number of strokes and myocardial infarction significantly compared to placebo treatment.

Vitamin K2 Supplementation and Effect on Arterial Stiffness Progression in the Renal Transplant Population:-

Trial ID: NCT02517580

This test was conducted on 60 candidates 18 years of age and older who have undergone renal graft. This trial tested the effect of vitamin K2 supplementation on the progression of arterial stiffness on stable renal transplant patients. It is a single arm, single centre trial. The participants were under vitamin K2. The results showed that vitamin K2 reduced the carotid femoral pulse wave velocity.
Pilot Study to Assess Effect of High Dose Ascorbic Acid (Vitamin C) on Inflammation Reduction in Cardiac Surgery Patients:
Trial ID: NCT02762331

This test was conducted on 6 candidates 18 to 70 years of age who are scheduled for elective non-emergent valve repair or replacement, or multivessel CABG surgery. This is a randomized parallel, placebo controlled trial. This trial tested the effect of vitamin C supplementation on the reduction of the post-operative atrial fibrillation. The participants were under vitamin C and placebo. The results don't show any significant outcomes.

Vitamin C in Atrial Fibrillation Ablation (VitC-AF):
Trial ID: NCT03148236

This test was conducted on 20 candidates 21 years of age and older who will undergo catheter-based ablation procedure for diagnosis of atrial fibrillation. This trial tested the presence of creatinine, hsCRP, IL-6, plasma ascorbic acid level and Von Willebrand factor. It is a randomized, double blind, placebo controlled, single centre trial. The participants were under two arms, vitamin C and placebo. The results showed that vitamin C reduced hsCRP level which is a biomarker of inflammation within a timeframe of baseline to 24 hours but overall it did not show any significant results.

Randomized Double Blind Study of Administration of Vitamin C for Prophylaxis of Post-operative Atrial Fibrillation in On-pump Cardiac Surgery Procedures:
Trial ID: NCT01107730

This test was conducted on 33 candidates 15 to 90 years of age who have undergone on pump cardiac surgery. This trial tested the effect of vitamin C on the treatment of postoperative atrial fibrillation. It is a randomized, double blind, placebo controlled, parallel trial. The participants were under three arms L-Carnitine, vitamin C and placebo. The results showed that vitamin C reduced the number of Postoperative Atrial Fibrillation patients but the results were not significant.

A Randomized Controlled Trial to Compare Prophylaxis With Oral Ascorbic Acid, Oral Amiodarone or Both in Combination With Beta Blockers to Reduce Postoperative Atrial Fibrillation After Cardiac Surgery:
Trial ID: NCT00953212

This test was conducted on 304 candidates 18 years of age and older who are all comers for open heart surgery. This trial tested the effect of ascorbic acid on the treatment of post-operative atrial fibrillation. It is a randomized, prospective, controlled trial. The participants were under four arms amiodarone, ascorbic acid and beta blockers, and amiodarone and beta blockers, and ascorbic acid and beta blockers, and only beta blocker. The results didn't show any significant outcomes.

Conclusion

Chemical and in vitro cell studies have shown preventive properties of these compounds, being a potent antioxidant, against a variety of ROS and RNS. In addition, the epidemiologic and immunopathological studies suggest that consumption of these compounds may lower multiple disease and cardiomyopathy risk. Such potential benefits have been ascribed in part to high concentrations of compounds in nutraceutical treatments. However, these findings have yet only been supported by a small number of intervention trials. By defining the right population and combining antioxidant and immunopathological potentials of these compounds with vitamins and other bioactive plant compounds, the beneficial role of them in other diseases that could be better clarified in future studies.
References


