ECRONICON OPEN ACCESS

EC MICROBIOLOGY
Review Article

Role of Tonics and Vitamins in Management of Patients with Chronic Diseases

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Received: January 08, 2021; **Published:** January 20, 2021

Abstract

Background: Vitamins and minerals are a diverse group of substances that play an enormous number of roles in the body. Vitamins (vital amines) are organic compounds that are required in trace amounts in the diet because they cannot be synthesized in sufficient quantities by an organism. Vitamins and their metabolites are essential for a large number of physiological processes, fulfilling diverse functions as hormones and antioxidants.

Aim: In this review, we will look into the role of tonics and vitamins in management of patients with chronic disease.

Conclusion: This review concluded that the vitamins had a role in management of chronic disease like cardiovascular die, cancer, diabetes and others. The most common vitamins reported were Vitamin A, Vitamin B, Vitamin C, Vitamin D and Vitamin E. It is important for physicians to identify patients with poor nutrition or other reasons for increased vitamin needs.

Keywords: *Vitamins; Vitamins and Chronic Diseases; Vitamins Importance; Management of Chronic Diseases with Vitamins*

Introduction

Vitamins and minerals are a diverse group of substances that play an enormous number of roles in the body [1]. Vitamins (vital amines) are organic compounds that are required in trace amounts in the diet because they cannot be synthesized in sufficient quantities by an organism [2]. Vitamins and their metabolites are essential for a large number of physiological processes, fulfilling diverse functions as hormones and antioxidants [2]. In addition, vitamins have a role in the immune system, which extends to both innate and adaptive immune responses.

Chronic conditions are diseases of long-term duration and may result from a combination of genetic, physiological, environmental, and behavioral factors [3]. It is the no. 1 cause of death and disability in the United States [4]. The main types of chronic disease include cardiovascular diseases (which account for 17.9 million deaths globally every year), cancers (which are responsible for 9 million deaths annually), chronic respiratory diseases (3.9 million deaths/year), and diabetes (1.6 million deaths/year) [3]. Also, mortality resulting from dementia more than doubled between 2000 and 2016, and it was the fifth leading cause of death worldwide in 2016 [5].

The role of nutrition in chronic disease management is particularly crucial as diet is a modifiable risk factor for most chronic conditions that exist either as single conditions or in comorbid states. Strategies for managing these chronic conditions are usually multidimensional, and at the center of these approaches are nutritional and/or dietary interventions, regular physical activity, and lifestyle modifications [6].

Suboptimal intake of some vitamins, above levels causing classic vitamin deficiency, is a risk factor for chronic diseases and common in the general population, especially the elderly. Recent evidence has shown that suboptimal levels of vitamins, even well above those causing deficiency syndromes, are risk factors for chronic diseases such as cardiovascular disease, cancer, and osteoporosis. For example, suboptimal folic acid levels, along with suboptimal levels of vitamins B6 and B12, are a risk factor for cardiovascular disease, neural tube defects, and colon and breast cancer; low levels of vitamin D contribute to osteopenia and fractures; and low levels of the antioxidant vitamins (vitamins A, E and C) may increase risk for several chronic diseases [7].

During the past four decades, emerging nutritional research on the efficacy of a complete diet and its role in disease prevention led to substantial pharmaceutical investments in the field of vitamins and dietary supplements [8]. As a result of data encouraging the use of nutritional additives, there was a worldwide trend of increasing consumption of these supplements since their introduction to the market. In 2012, a total of 13.1 billion USD was spent on multivitamin and mineral-containing supplements, of which an estimated 5.4 billion USD (40%) was spent on multi-vitamins alone [9].

However, the role of vitamin supplementation in prevention or reversal of many chronic diseases is less well established. Studies evaluating the effects of vitamin supplementation have been variable; randomized trials often fail to demonstrate the associations seen in observational studies. Additionally, methodological flaws, including lack of standardization of baseline vitamin status and dose, may contribute to inconsistent study results [10].

In this review, we will look into the role of tonics and vitamins in management of patients with chronic diseases.

Vitamin A

Vitamin A refers to a family of fat-soluble compounds called retinoids, which have vitamin A activity. The term vitamin A comprises various chemical components with a structural and functional similarity. The most active form is retinol, present in animal tissues, esterified with long chain fatty acids. Carotenes that are present in vegetable tissues are enzymatically hydrolyzed into retinal and converted to retinol in the enterocyte [11]. Vitamin A is obtained from the diet either as all-trans-retinol, retinyl esters or β-carotene. It and the similar compounds belonging to the retinoid family occur only in foods of animal origin, such as liver, butter, milk, and egg yolks [12].

Vitamin A participates in multiple metabolic processes such as genetic expression, cellular differentiation and growth, having a very important role in the immune system, it is critical in vision (particularly night vision), fetal development, taste, hearing, appetite and spermatogenesis. Retinoids have a very important function as antioxidants, thus helping to maintain the organism's homeostasis when subjected to various forms of stress with the potential to protect against inflammatory disease and atherosclerosis [13].

Vitamin A and cancer: Because of its effects on the epithelium and on immunity, retinol has been investigated as a chemo-protective agent for several cancers. Vitamin A may decrease the risk of bladder and breast cancers, but the evidence is weak [15]. Many groups have also examined the relationship between retinol intake and breast cancer. A previous review concluded that existing evidence supported a modest inverse relationship between vitamin A and breast cancer, although it was unclear whether carotenoids or retinol was the key nutrient [15]. Since that review, three prospective cohort studies have been published; two of them showed a modest decrease in risk for retinol or total vitamin A. However, another one showed no association [16].

Vitamin A and CVD: Numerous natural carotenoids are present in fresh fruits and vegetables, and some have been studied extensively in the prevention of coronary heart disease (CHD); early observational studies reported an association between a high dietary intake of β-carotene and a lowered incidence of CVD [17]. The evaluation of the relation between vegetable intake and CHD risk in the Physicians' Health Study concluded that the consumption of vegetables rich in carotenoids was associated with a reduced risk of CHD [18].

Vitamin A and the pancreas: Patients with chronic pancreatitis are at risk of deficiencies in the fat-soluble vitamins due to the loss of pancreatic exocrine function. Multiple clinical trials suggested that the use of a combined preparation of antioxidants, (including beta carotene), in patients with painful chronic pancreatitis significantly reduced pain and improved quality of life when compared to placebo [19].

B vitamins and folate

Thiamine, Riboflavin, Niacin, Pantothenic acid, Pyridoxine, Biotin, Cobalamin and Folic acid are usually grouped as B vitamins [11]. Folate (other interchangeable terms include folic acid and folacin) is a water-soluble B vitamin that is necessary in forming coenzymes for purine and pyrimidine synthesis, erythropoiesis, and methionine regeneration [20]. Vitamin B6 refers to a group of nitrogen-containing compounds with 3 primary forms: pyridoxine, pyridoxal, and pyridoxamine. They are water soluble and are found in a variety of plant and animal products [14]. It participates in more than 100 enzymatic reactions and is needed for protein metabolism, conversion of tryptophan to niacin, neurotransmitter formation and found in dietary sources include poultry, fish, meat, legumes, nuts, potatoes, and whole grains [21]. Vitamin B12 (cyanocobalamin) is water soluble and found in animal products only (meat, poultry, fish, eggs and milk). It acts as a coenzyme for fat and carbohydrate metabolism, protein synthesis, and hematopoiesis [14].

B vitamins and CHD: Thiamine supplementation is recommended for patients with refractory congestive heart failure (CHF), although its role in heart failure not related to proven thiamine deficiency remains controversial [22]. There may be a role for thiamine supplementation in preventing the cardiomyopathy sometimes seen with diabetes.

Many studies have reported increased risk of CHD or ischemic stroke associated with low folate intake or low blood folate levels. Higher dietary intakes of folate and vitamin B6 are associated with decreased risk of CHD. Several large clinical trials of folate, B6, and B12 are under way and will likely clarify the relationships of these vitamins to coronary disease [23].

Vitamin B and Cancer: Recently, interest has grown in the effects of folate supplementation in cancer prevention [24]. Higher dietary folate intake appears to reduce the risk of colon and breast cancer, particularly among moderate consumers of alcohol. A recent report from the National Health and Nutrition Examination Survey I (NHANES I) found a statistically significant 60% risk reduction in colon cancer in men and a similar nonsignificant effect in women [25]. Colon and breast cancers are among the most common cancers in Western societies, so folate's potential for helping to prevent these cancers is important.

Vitamins B6, B9, B12: Vitamin B6 may affect colorectal carcinogenesis via its role in DNA synthesis and methylation. Moreover, it was shown to inhibit angiogenesis, suppress nitric oxide and reduce oxidative stress in animal models [26].

Vitamin C

Vitamin C is a water-soluble vitamin that exists in the body primarily in its reduced form, ascorbic acid. The oxidized from of the vitamin, dehydroascorbic acid (DHA), also has antiscorbutic (scurvy preventive) activity because it is easily reduced intracellularly to ascorbic acid. It is also a strong antioxidant, food sources of vitamin C include citrus fruits, strawberries, melons, tomatoes, broccoli, and peppers [26], vitamin C also promotes hormone synthesis, wound healing, and iron absorption [14].

Vitamin C and coronary heart disease: Because of vitamin C's antioxidant effects, many studies of CHD prevention include vitamin C supplementation. Vitamin C, especially with tocopherol, inhibits low-density lipoprotein oxidation, a process that is believed to be involved in the formation of atherosclerotic plaques [27]. In several epidemiologic studies, plasma ascorbate levels were inversely associated with coronary vascular disease (CVD) and stroke. Many studies have shown beneficial effects of high doses of ascorbic acid on endothelial-dependent vasodilation [28]. Some beneficial effects of ascorbic acid supplements on thrombotic risk of CVD and impaired

endothelial function in women with pre-eclampsia have also been reported. Of two prospective serum vitamin C studies, one. Showed decreased cardiovascular mortality with increasing concentrations, but another showed no relationship [29].

Vitamin C and cancer: Most case-control studies have found an inverse association between vitamin C intake from fruits and vegetables and cancers of the oral cavity, larynx-pharynx, esophagus, lung, stomach, and colon-rectum [30]. Antioxidant action of ascorbic acid inhibits the formation of carcinogenic N-nitroso compounds that are implicated in gastric and lung cancer [30]. Results from several studies indicate that vitamin C supplementation of these patients' increases gastric ascorbate, decreases cancer biomarkers and oxidative damage in the gastric mucosa, and may decrease gastric cancer risk [31].

Of the hormone-dependent cancers, only breast cancer was inversely associated with vitamin C intake. A meta-analysis found decreased breast cancer risk (20% risk reduction) associated with high dietary vitamin C intake [32]. The evidence is moderately strong that diets high in vitamin C are associated with decreased risk of cancers of the oral cavity, esophagus, stomach, and breast. However, it remains unclear whether this decrease is because of high intake of fruits and vegetables (which offer a wide range of other nutrients) or whether vitamin C itself is the protective nutrient [14].

Vitamin C and gallstones: Clinical and experimental data suggested a potential protective effect of vitamin C on the formation of gallstones [33]. This might be attributed to the reduction in bile acid biogenesis and the supersaturation of bile with cholesterol due to the deficiency in cholesterol 7α-hydroxylation in cases of ascorbic acid deficiency.

Vitamin C and diabetes: Evidence suggests that oxidative stress has an important role in diabetic complications and increased oxidative stress and hyperglycemia may accelerate *in vivo* ascorbate destruction [34]. In one study, ascorbic acid supplementation resulted in improvement of glycemic control and vascular health and decreased glycosylated hemoglobin and erythrocyte sorbitol [35]. Also, results of another study suggest that supplementation with ascorbic acid may modulate insulin activity in diabetic patients [36].

Vitamin D

Vitamin D (calciferol) is not a true vitamin, since humans are able to synthesize it with adequate sunlight exposure. There are two main forms of Vitamin D, Vitamin D3 (cholecalciferol) and Vitamin D2 (ergocalciferol). It is derived from 7-dehydrocholesterol, which is converted in the skin by ultraviolet light band B (UVB) to Vitamin D3 (cholecalciferol), an inactive precursor. More than 90% of systemic Vitamin D originates from the skin and around 10% from food intake [37]. Vitamin D may also be ingested in the diet in the form of vitamin D3, a prohormone. Food sources include fortified milk, saltwater fish and fish-liver oil [14].

Vitamin D and cardiovascular diseases: Vitamin D receptors (VDR) are present in most tissues, including the endothelium, vascular smooth muscle and myocardium [11]. The role of vitamin D in the cardiovascular system is noticeable since the presence of its receptors not only the heart but also in the entire cardiovascular system. Vitamin D has well known effects in endothelial cells, where it stimulates nitric oxide (NO) production, protects against oxidative stress and prevent endothelial apoptosis, it may contribute for reversing atherosclerosis burden [38]. Vitamin D also seems to present an anticoagulant activity, through the regulation of the expression of pro-coagulant and ant fibrinolytic factors. Low levels of vitamin D have also been linked with the occurrence of fatal strokes, heart failure, sudden cardiac death and calcific aortic stenosis. Despite these findings, it is not clear what dosage of vitamin D is necessary for the prevention of CVD [39]. Prospective studies need to be performed to test whether vitamin D supplementation can actually prevent CVD.

Vitamin D and cancer: Vitamin D binding protein (VDBP) as a carrier of Vitamin D can be combined with Vitamin D and its metabolites to play a crucial role in transport to the cell. Studies have demonstrated that low level of VDBP is related to a variety of malignant tumors, including breast, prostate and colorectal [40]. The role of vitamin D in colorectal cancer (CRC) prevention due to the ability of vit D to inhibit cell proliferation and increase apoptosis *in vitro*. Many cell types, including colorectal epithelial cells, contain vitamin D receptors

(VDR). These cells are able to convert the circulating 25(OH) D into active 1,25(OH)D metabolites, which in turn bind to the cells' own VDR to produce an autocrine effect by inducing cell differentiation and by inhibiting proliferation, invasiveness, angiogenesis, and metastatic potential [41]. Also, A convincing explanation for vitamin D to be adequate is the study that postmenopausal women who increased their vitamin D intake by 1100 IU of vitamin D 3 decreased their relative cancer risk by 60 to 77 percent [42].

Vitamin D and the liver: Results from studies investigating the role of vitamin D plus calcium supplementation in preventing and treating hepatic osteodystrophy in patients with cholestatic liver disease were conflicting with heterogeneous designs and populations [43].

Vitamin D and diabetes: 25OHD deficiency has been shown to be related to the development of diabetes. 1, 25 (OH) 2 D3 can be combined with Vitamin D3 receptor on the islet β cells, increasing insulin sensitivity, inhibiting inflammatory factors, alleviating chronic inflammation process of the pancreas to improve the function of islet β cells also it also inhibits the action of the renin-angiotensin system, which promotes insulin secretion [44].

Vitamin E

Vitamin E is fat soluble and composed of a family of 8 related compounds, the tocopherols and the tocotrienols. The major chemical forms of vitamin E (based on the location of a methyl group) are the tocopherols α, β, Δ, and γ [14]. Vitamin E, like other antioxidants, prevent oxidative damage to lipid membranes and low-density lipoprotein (LDL). It is also needed in immune function, and supplementation enhances cell-mediated immunity in elderly patients [45].

Vitamin E and coronary heart disease: Vitamin E is postulated to prevent atherosclerotic disease not only by its antioxidant effects, but also by inhibitory effects upon smooth muscle proliferation and platelet adhesion [46]. The antioxidant and anticoagulant properties of vitamin E are believed to protect against MI and thrombotic stroke. The value of vitamin E in the prevention of atherosclerosis is the subject of an extensive review article [47].

Observational studies have reported that vitamin E is a protective factor for CHD [14]. In the Cambridge Heart Antioxidant Study (CHAOS), α-tocopherol at 267 to 533 mg/d (400 - 800 IU) reduced the 1-year rate of nonfatal myocardial infarctions among patients with known CHD by 80% but caused no reduction in cardiovascular mortality [48]. However, the observational studies showing a protective effect of vitamin E were all among lower-risk populations, and there are no trial data from similar populations. Generally, vitamin E may still be useful in primary prevention when taken throughout long periods.

Conclusion

This review concluded that the vitamins had a role in management of chronic disease like cardiovascular die, cancer, diabetes and others. The most common vitamins reported were Vitamin A, Vitamin B, Vitamin C, Vitamin D and Vitamin E. It is important for physicians to identify patients with poor nutrition or other reasons for increased vitamin needs.

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Volume 17 Issue 2 February 2021