

Review article:

Report on Recent Advances in Treatment Options through Vitamins

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Abstract

Vitamins are the essential dietary components that are required in trace amounts by our body for the proper functioning of its biochemical processes and to prevent the deficiency diseases. The case of an infant having epileptic seizures at birth is discussed, which was found to be pyridoxine (vitamin B6) - dependent. It has been discovered through recent researches that vitamin K is involved in the immunology, atherosclerosis, inflammation and bone mineralization. Vitamin C is found to act as an anti-tumor agent when used intravenously in high doses. Recent researches have led us to understand that vitamins have a broader spectrum of functions than they are anticipated to have in our body and can be used to treat much more diseases when used alone, in combination or via different routes or in different concentrations or doses.

Keywords: Vitamins; Supplementation; vitamins deficiency diseases; Treatment advances; Covid19

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Introduction

The celebrating moments after the birth of the fourth child turned into a shock for the family, when the new born started to have seizures. The father was unaware of being an asymptomatic carrier of the pyridoxine – dependent epilepsy. The child was a baby girl, healthy at birth but after an hour of her birth she had epileptic seizures, and was put on Phenobarbital (5-ethyl-5-phenylbarbituric acid.), but the seizures didn't stop completely and doctors gave her Carbamazepine, still the neonate was not stable then an amazing diagnosis was made and Pyridoxine (vitamin B6, Vita-6) was given to the infant and this did the spell and at last she was stable.

So, the above story makes it evident to us that a vitamin deficiency can be life threatening. In our society, it is a very common concept that vitamins are given to malnourished people¹ or might be given to the growing kids² for some extra energy or to the pregnant women³. But reality is quite different, vitamins in fact are not intended for just these

purposes because vitamins, as the name indicates, are the vital ingredients that are required by our body in very little amounts, for the proper functioning of its systems and the metabolic activities⁴. Nevertheless, this fact cannot be denied that they are the compounds that the nature has provided in our food in sufficient enough amounts to fulfill our body needs⁵, but there are several conditions to it. As we know that people don't take a balanced diet⁶, or are not much going in the sun, or sometimes our body is not able to convert the provitamin forms to their active vitamin form⁷⁻¹⁰ etc. So here arises the need for taking vitamin supplements as the deficiency of every vitamin may lead to potentially dangerous diseases.

There are various compounds that come under the heading of vitamins, though they all are different chemically and also, they have different metabolic functions, though they all are needed in very small amounts by our body and some are not synthesized in our body.

“To be considered a vitamin, a chemical compound

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should be necessary to be included in diet and its absence in diet should lead to a proper deficiency disease, that is cured or treated with the administration of that vitamin”¹¹.

So, now it is clear that vitamins are essential for the proper functioning of the biochemical processes in our body, though they are needed in just trace amounts¹².

Some of them are produced endogenously^{13, 14}, but whether they are produced or not by our body their quantity is most of the times not sufficient enough and they should have to be taken in diet to fulfill our needs.

The main functions and the sources of vitamins are shown in the following Table1.

Table1: Main Functions and the Sources of Vitamins		
Water-Soluble Vitamins		
Nutrient	Function	Sources
Thiamine (vitamin B1)	Coenzyme in pyruvate and 2-oxo-glutarate dehydrogenases and transketolase (metabolism of energy), regulation of Cl channel in nerve conduction	Whole grains, cereals, legumes, nuts, seeds.
Riboflavin (vitamin B2)	Coenzyme in oxidation and reduction reactions (metabolism of energy), maintains normal vision, healthy skin, prosthetic group of flavoproteins.	Leafy green vegetables, whole grains, cereal, milk and milk products.
Niacin Nicotinic acid Nicotinamide (vitamin B3)	Coenzyme in oxidation reduction reaction (metabolism of energy), functional part of NAD and NADP, maintains intracellular Ca, cell signaling, important for nervous system, digestive system and skin health.	Whole grains, cereals, mushrooms, asparagus, leafy green vegetables, peanut butter, meat, poultry and fish.
Pantothenic acid	Functional part of coenzyme A and acyl carrier protein (energy metabolism), fatty acid synthesis and metabolism.	Widespread in foods
Biotin (vitamin H)	Coenzyme in carboxylation reactions in gluconeogenesis and fatty acid synthesis, regulation of cell cycle.	Widespread in foods also produced by intestinal bacteria.
Pyridoxine Pyridoxal Pyridoxamine (vitamin B6)	Coenzyme in transamination and decarboxylation of amino acids and glycogen phosphorylase (protein metabolism), modulation of steroid hormone action, helps in red blood cells synthesis.	Fruits, vegetables, meat, fish, poultry.
Folic acid	Coenzyme in transfer of one carbon fragments (synthesis of DNA and RBC's)	Legumes, seeds, orange juice, liver, refined grains, leafy green vegetables.
Cobalamin (vitamin B12)	Coenzyme in transfer of one carbon fragments (synthesis of DNA and RBC's) and metabolism of folic acid, nerve function.	Seafood, eggs, milk, milk products, meat, poultry, fish. Not found in plant foods.
Ascorbic acid (vitamin C)	Coenzyme in hydroxylation of proline and lysine in collagen synthesis (protein metabolism), antioxidant, enhances absorption of iron, important for immune system health.	Fruits, vegetables: especially citrus fruits, cabbage, cantaloupe, strawberry, peppers, tomatoes, potatoes, lettuce, papaya, mango, kiwi fruit.
Fat-Soluble Vitamins		
Retinol (vitamin A) β-carotene (precursor of vitamin A)	Needed for colored vision and night time vision, required for the gene expression, cell differentiation, healthy skin and mucous membranes, bone and tooth growth and healthy immune system. β-carotene acts as an antioxidant.	Vitamin A(Retinol) comes from animals: milk, cheese, cream, butter, eggs, liver. β-carotene comes plants, green leafy vegetables, orange(dark) fruits (cantaloupe, apricot), carrots, winter squash, sweet potatoes, pumpkin)
Calciferol (vitamin D)	Needed to maintain Ca ²⁺ balance and its absorption from intestine, regulation of gene expression and cell differentiation.	Milk, fatty fish, liver, egg yolk, skin synthesize vitamin D in presence of sunlight.
Tocopherols Tocotrienols (vitamin E)	Antioxidant, functions in cell signaling, protects cell wall.	Leafy green vegetables, wheat germ, whole grains, liver, egg yolks, nuts, seeds, polyunsaturated plant oils (soybean, corn etc.)
Phylloquinone Menaquinones (vitamin K)	Acts as coenzyme in the process of blood clotting and bone matrix.	Green vegetables like kale, collard greens, spinach, broccoli, Brussels' sprouts, and asparagus. Also produced by intestinal bacteria.

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It is of utmost importance to mention here that two of the vitamins i.e., vitamin D and niacin should have been excluded from the list of vitamins, due to the fact that the amounts of these two vitamins produced endogenously is indeed enough to meet the requirements under normal conditions. Nevertheless, they are considered as vitamins, only due to the reason that they were discovered as a result of research on the deficiency diseases pellagra and rickets².

The functions and deficiency states of vitamins shown in Table 1, give us a brief idea about the possible hazards of vitamin deficiencies and the important role of vitamins in the biochemical processes of our body.

With the advancement in technology and research, treatment strategies are also becoming advanced and new researches are continuously done to cure ailments with novel approaches in order to get the maximum benefit for the society. With the advent in technologies available for research it is also discovered that vitamins can be useful in the treatment of many other diseases other than the assigned deficiency diseases¹⁵⁻¹⁷, and they are used alone, in combinations with other medications or vitamins and also they are given via different routes of administration¹⁸⁻²⁰.

Several advances are there almost in every field of treatment options and for cure of diseases. Few of the latest advancements done on the treatment options through vitamins includes a research done on vitamin D, that which form of vitamin D is more potent in humans it was found that vitamin D3 is 87% more potent to achieve the serum concentrations of the active form of vitamin D [25(OH)D] than vitamin D2, also it produces about 2-3-fold greater storage of vitamin D than does vitamin D2. This study proved that due to its more potency and low cost vitamin D3 must be preferred over D2 for the treatment of the deficiency diseases²¹. Similarly, it has been discovered in several studies that vitamin C, which was once used as a treatment or to prevent scurvy, a deficiency state of vitamin C, can successfully be used to treat various types of cancers if used in high doses intravenously²²⁻²⁸. A study on the recent advances in vitamin K- dependent Gla(gamma-carboxylated glutamic acid)containing proteins was done^{11,29}. This study was also comprised of the vitamin K's nutritional benefits other than curing its deficiency diseases. The synergistic effects of vitamin K and D are discussed in this study as they both are involved in the osteocalcin production and activation which is very important for the extracellular

mineralization, and in turn bone health. Breakthrough regarding vitamin K dependent proteins' functions in immunology, inflammation and atherosclerosis have been achieved³⁰. Research studies reveals the use of micronutrients like vitamins, minerals, antioxidants etc. for the prevention and treatment of cardiovascular diseases and hypertension³¹. Vitamin D3 is considered and known for its strong calcemic activity but it also has antitumor properties. Therefore, vitamin D3 analogues have been developed with enhanced antitumor activity and reduced calcemic activity. These vitamin D3 analogues are used alone or in combination with antiestrogen tamoxifen for the treatment of breast cancer³². Similarly, Albuminuria in the patients of diabetes (type2) has been studied and the effects of combined treatment with vitamin C and E have been evaluated for its treatment³³. A study was carried out to evaluate the effects of the combined therapy with vitamin A and zinc to treat gastrointestinal parasitic infections in Mexican children³⁴. A study was conducted to establish the fact that 25(OH)D is washed out during hemodialysis and there is a deficiency of vitamin D which may be the cause of rapid worsening of the clinical condition of chronic kidney disease patients³⁵. It appears that after hemodialysis, because of abrupt decline in 25(OH)D, there is rapid intracellular environment fluctuations at molecular level. Perhaps, these fluctuations may be the cause of rapid clinical deterioration³⁵. Another study was done to indicate the consequence of genetically controlled folate cycle deficiency in children with autism spectrum disorders (ASD) and the results of the study revealed the cause of immunodeficiency in children with folate cycle disorder. According to the results of this study, it could be expected that the folate cycle is responsible for the development of a special immunodeficiency, in which NK and NKT cells (lymphocytes i.e. natural killer and natural killer T-cells) can severely diminish resistance to intracellular microorganisms, tumors, and an affinity to develop autoimmune reaction and delayed type hypersensitivity³⁶. A research was conducted to evaluate if, serum 25(OH)D level is related with hemoglobin levels, RBC counts and hematocrit in aged people with anemia of inflammation and non-inflammation. This study demonstrates that vitamin D metabolites may influence anemia, through inflammation pathway³⁷.

The world is under a stressful condition due to the current COVID19 pandemic. A lot of research had been done and is still being done to find treatments, prevention and to stop its spread. As like other drugs,

few researches and studies has been conducted with the use of vitamins and many are in progress. Number of studies were done on the supplementation of vitamin D to the COVID19 patients or the persons who are at risk of getting it. These studies include the uses of vitamin D against respiratory tract infections, various types of influenza, epidemiology of COVID and how vitamin D would prove beneficial in its treatment and prevention³⁸⁻⁴³. Studies have also been done on the role of vitamin C in the prevention and treatment of COVID19 as vitamin C has antioxidant properties. High doses of vitamin C were given intravenously to the individuals in this study⁴⁴. A study done on the vitamin D deficiency and its relation with the current corona virus disease and according to this study, although the current situation requires the individuals to stay at home as much as possible and this refrains them from getting enough sunlight and thus vitamin D, so due to this they must take vitamin D supplementation (or by food) as per requirements (and not in excessive amounts) to avoid being deficient of this vitamin but there is no evidence that the deficiency of vitamin D makes people prone of getting corona infected, and also no evidence that

vitamin D is a treatment for the disease⁴⁵. Another research was conducted to determine the anticipated importance of vitamin D in the clinical management of COVID-19 and the results proved that this is just a myth and vitamin D role in the management of COVID19 stays vague⁴⁶. COVID19 patients in China and US were given high intravenous dose of vitamin C for short term which showed good results and improvement with no adverse effects. Vitamin C due to its pharmacological properties and safety profile on high dose administration can thus be used in the management protocol of COVID19 along with other drugs but not as a sole agent for its treatment, though further research is required to be done in this regard^{47, 48}.

Conclusion

Keeping in mind the current situation of the world and the new infections and diseases that are arising every day, the need for research and development of novel drugs is getting inevitable. The researches in this regard include the discovery of vitamin D3's antitumor effects, use of vitamins and other micronutrients in cardiovascular diseases, discovery

Table 2: Recent advancements in treatment options through vitamins

Vitamin	Function	Deficiency	Advancement in treatment
Vitamin A (Retinol) (β – carotene)	Visual pigments in retina, regulation of gene expression, cell differentiation, antioxidant.	Night blindness, xerophthalmia, Keratinization of skin.	Use of vitamin A in the treatment and prevention of cancer ⁴⁹ Combined therapy of vitamin A and zinc to treat gastrointestinal parasitic infections in Mexican children ¹⁵
Vitamin D (Calciferol)	Maintenance of calcium balance and increases the intestinal reabsorption of Ca ²⁺ , gene expression, cell differentiation.	Rickets Osteomalacia	Vitamin D3 is more potent than vitamin D2 ³ , Vitamin D3 has antitumor activity ¹³ , Vitamin D can be used in the treatment and prevention of respiratory tract infections like COVID ¹⁶⁻²² . Treatment with vitamin D in chronic kidney disease ⁵⁰ Treatment with vitamin D of prostate cancer patients ⁵¹ Vitamin D in the treatment of coronary heart disease ⁵²
Vitamin C (Ascorbic acid)	Co enzyme in collagen synthesis, antioxidant, enhances absorption of iron.	Scurvy	Acts as anticancer agent if used in high doses intravenously ⁴⁻¹⁰ , Used in the treatment of albuminuria in type2 diabetes in combination with vitamin E ¹⁴ , Prevention and treatment of COVID ²³⁻²⁴ .
Vitamin K (Phyllo Quinone) (Mena Quinone)	Blood clotting, Bone matrix formation	Impaired blood clotting, hemorrhagic diseases	Vitamin K dependent proteins functions in immunology, atherosclerosis and inflammation ¹¹ .
Vitamin B12(Cobalamin)	Co enzyme in transfer of one-carbon fragments and metabolism of Folic acid	Pernicious anemia	Supplementation with vitamin B12, Folic acid and sunlight exposure improves vitiligo ⁵³

of the combined treatment of vitamin C and E in the treatment of albuminuria in diabetes patients, role of vitamin B6 in epilepsy, role of vitamin K dependent proteins in immunology, atherosclerosis and inflammation was also revealed and there is a long list of researches and experimentations leading to the new discoveries about novel uses of vitamins. The role of vitamins in the treatment of the corona virus infection is quite controversial and needs further research, though the pharmacological properties and role of vitamins in the vital biochemical functions of the body approves this theory that they may be helpful in the management protocol of COVID19 along with other drugs but they cannot be used solely

for the treatment of this infection, though they can be helpful in increasing immunity and keeping the other infections at bay which might be supportive in the treatment strategies or for the prevention of corona virus infection as well as other infections.

Therefore, as a medicinal chemist, it's our duty to keep researching for better derivatives and searching for new drugs. Vitamins are indeed essential dietary components, but now with research and technology it getting more and more evident that they are much more than that and they can be useful against a number of life-threatening maladies, but for that lots of experimentation and exploration will be required to be done to make this world a better place to live.

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