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Review Article

Vitamin C in dermatology and cosmetology: a review

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ABSTRACT

Vitamin C is a very powerful water-soluble antioxidant with various potential benefits for patients with skin diseases. The chemically active form of vitamin C is L-ascorbic acid (LAA) and thus is used extensively in medical practices. Due to an active transport mechanism, the absorption of vitamin C in the gut is limited, thereby reducing the amount of drug absorbed orally despite a high dosage, which in turn reduces the bioavailability of vitamin C in the skin. Therefore, topical use of vitamin C is usually preferred in dermatology practice. The function of vitamin C is mostly linked to its electron-donating property. Several processes such as reduction of iron in the gastrointestinal tract, synthesis of carnitine, gene transcription, protection against reactive oxygen species (ROS), demethylation of DNA, Hydroxylation of transcription factors, tRNA, and ribosomal proteins, collagen, and hormonal synthesis are carried out due to the active participation of vitamin C in the body. Scurvy usually occurs due to inadequate consumption of vitamin C through a regular diet or inability to absorb the vitamin C in the body. 90% of ascorbic acid comes from fresh fruits and vegetable consumption, failure of which can lead to scurvy.

Keywords: Vitamin C, Scurvy, Antioxidant, RDA

INTRODUCTION

Ascorbic acid, also known as vitamin C is a powerful antioxidant and a micronutrient, that is nowadays highly prescribed in dermatology as well as cosmeceuticals for its enhanced collagen production and ultraviolet (UV)-induced damage protection properties. Vitamin C is present in higher concentrations in normal human skin, however, various studies indicated that vitamin C levels drastically dropped in naturally aged and/or photoaged skin.[1] The chemically active form of vitamin C is LAA and thus is used extensively in medical practices. Due to an active transport mechanism, the absorption of vitamin C in the gut is limited, thereby reducing the amount of drug absorbed orally despite a high dosage, which in turn reduces the bioavailability of vitamin C in the skin. Therefore, topical use of vitamin C is usually preferred in dermatology practice.[2-4]

The unavailability of L-glucono-gamma lactone oxidase, the primary enzyme required for *in vivo* synthesis of vitamin C in the human body makes it necessary to acquire vitamin C from other natural sources like citrus fruits, strawberries, broccoli, papaya, and green leafy vegetables.[3,4]

RECOMMENDED INTAKE OF VITAMIN C

The dietary reference intakes (DRIs) an organization constituted by the food and nutrition board (FNB) provide basic intake recommendations for vitamin C.[5] Table 1 indicates the recommended dietary allowance (RDAs) for various age and gender groups, which is vastly based on its antioxidant and physiological properties in the white blood cells. Also, it indicated the appropriate quantity required for the prevention of any deficiencies.[5-7]

Table 1: RDAs for vitamin C.[5]

Age (In years)	Male (mg)	Female (mg)	Pregnancy (mg)	Lactation (mg)
0-6 months	40*	40*		
7-12 months	50*	50*		
1-3	15	15		
4-8	25	25		
9-13	45	45		
14-18	75	65	80	115
19+	90	75	85	120

Smokers individuals who smoke require 35 mg/day more vitamin C than nonsmokers; *Adequate Intake (AI).

Physiological function of vitamin C

The function of vitamin C is mostly linked to its electron-donating property.[8] Several processes such as reduction of iron in the gastrointestinal tract, synthesis of carnitine, gene transcription, protection against ROS, demethylation of DNA, hydroxylation of transcription factors, tRNA and ribosomal proteins, collagen and hormonal synthesis are carried out due to the active participation of vitamin C in the body (Figure 1).

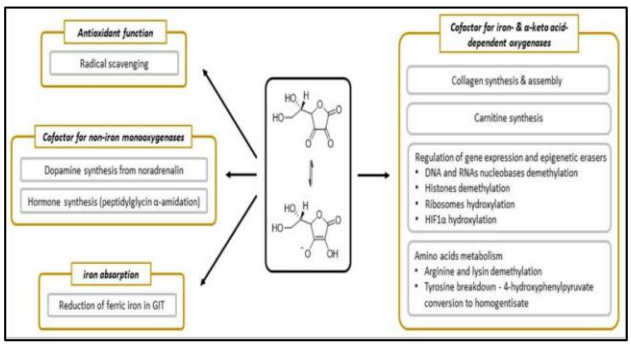

Figure 1: The summary of physiological functions of vitamin C.[8]

PHYSIOLOGICAL FUNCTIONS OF VITAMIN C CONCERNING DERMATOLOGY AND COSMETOLOGY

ROS and skin damage: vitamin C photoprotection properties

UV light generates ROS when the skin is exposed to it. These ROS radicals surge the process of cell damage, which in turn can cause alteration in the DNA, cell membrane and cell proteins like collagen.[3] Antioxidants can help neutralize the effects of ROS. Vitamin C helps in providing UV protection by not enabling the UV light to penetrate the skin, thereby reducing absorption of the UV light.[9] It is important to note that, vitamin C is equally effective against both UVB (290-320 nm) and UVA (320-400 nm).[2]

Collagen synthesis

Vitamin C stimulated both qualitative and quantitative aspects of collagen, by changing the collagen molecule as well as collagen synthesis respectively. Collagen gene expression is invigorated when vitamin C revives lipid restoration, thereby producing malondialdehyde as the by-product.[10] Collagen synthesis transcription as well as stabilization of procollagen mRNA are both activated due to vitamin C which ultimately helps in collagen synthesis.

Anti-inflammatory action

Vitamin C when used in moderate amounts can reduce inflammation. It was concluded that the hs-CRP and IL-6 levels as well as the FBG levels were reduced in hypertensive and/or diabetic patients when using vitamin C conducted by a study done by Ellulu et al.[11] The anti-inflammatory properties of vitamin C can also be used for treating skin conditions like rosacea and the acne vulgaris.[10]

De-pigmenting agent

Vitamin C suppresses the tyrosinase enzyme activity, thereby inhibiting melanin synthesis.[12] Therefore, vitamin C is widely used in dermatology as well as cosmetology as a depigmentation treatment for hyperpigmented spots on the skin. It is also helpful in reducing hyperpigmentation of gingival melanin.[13]

Differentiation of keratinocytes promotion

The differentiation of keratinocytes can affect the integrity of the skin barrier, resulting in various skin diseases. Vitamin C can delay the differentiation of keratinocytes which helps in managing oxidative stress and maintaining overall skin health by preventing the skin water loss.[14]

Iron absorption

Vitamin C can effectively reduce ferric ions to ferrous ions, resulting in an increase in iron absorption in the body even with a low amount of vitamin C consumption.[15,16]

VITAMIN C DEFICIENCY OR SCURVY

Scurvy was first discussed and described in 1550 BC in an Egyptian medical scroll, Eber's papyrus, after several sailors and soldiers due to the minimal access to fruits and vegetables started to develop signs and symptoms of vitamin C deficiency.[17] The overall prevalence of scurvy in the US is around 5.9%, as per the National health and nutrition examination survey (NHANES) survey of 2017-2018 with a mean serum level of less than 11.4 µmol/l considered as a vitamin C deficient individual.[18] Scurvy usually occurs due to inadequate consumption of vitamin C through a regular diet or inability to absorb the vitamin

C in the body. 90% of ascorbic acid comes from fresh fruits and vegetable consumption, failure of which can lead to scurvy.[19]

Risk factors for developing scurvy

In the US, scurvy diagnosis is more common in babies, children, and geriatrics who struggle to get enough vitamin C through their diets. Common risk factors include: not having enough fresh fruits and vegetables; alcohol/drug dependency; pregnant/breastfeeding mothers; type 1 diabetes, inflammatory bowel disease patients; smokers; restrictive diet due to food allergies; kids and geriatrics; and dialysis patients.

Manifestations of scurvy

The first signs and symptoms of vitamin C deficiency appear after four to twelve (4-12) weeks of getting insufficient vitamin C in the diet.[20] Fatigue, anorexia, and irritated behavior are some of the non-specific symptoms that start to occur when the serum ascorbic level in the body goes below 20 µmol/l. More aggravated symptoms start to appear after a dip in serum level by the lower than 11.4 µmol/l.[21]

Dermatological manifestations

Various manifestations of vitamin C deficiency include xerosis, petechiae, follicular hyperkeratosis, corkscrew hairs and perifollicular hemorrhage. Due to a decrease in vitamin C in the body, it also leads to inhibition of melanin synthesis, resulting in skin discoloration. Manifestations in the nail included splinter hemorrhages and koilonychia.[22]

Gastrointestinal manifestations

Various recently done studies have linked vitamin C to vascular function in the body.[23] Antunes et al in a study described a case of a 40-year-old who had a history of alcoholism and poor diet and developed polyarthralgia, bleeding gums, and hematochezia episodes.[24] Vitamin C deficiency has been reported to cause gastrointestinal bleeding in many cases. Various other gastrointestinal manifestations include submucosal hemorrhages in the stomach, duodenum, and colon.

Vitamin C has been known to provide vasorelaxation and increase nitric oxide synthesis which in turn modulate the inflammatory response.[25]

Musculoskeletal manifestations

Arthalgias of the knee, ankles, and wrists along with muscle pain, muscular hematomas, hemarthosis are some of the common musculoskeletal manifestations associated with vitamin C deficiency. Due to low levels of vitamin C in the body, the collagen structure undergoes alterations, leading to deficient osteoid matrix formation and increased bone resorption. The muscle pain maybe due to bleeding into the muscles or periosteum.[26]

Diagnosis

Clinical presentation, plain radiographic findings of long bones, medical history, and history of poor diet are the primary diagnosis tools.[27] The physician will assess all the risk factors and ask detailed questions about the daily diet of the patient. Swollen and bleeding gums, skin bruising with discoloration, delay in wound healing are some of the signs that should be looked upon while performing a physical examination. Laboratory test usually helps to confirm a case of scurvy. A routine blood test measuring the vitamin C levels in plasma and leucocytes is one of the confirming factors for the diagnosis of scurvy. If plasma concentration falls below 0.2 mg/dl, it is a clear indication of scurvy.[24] As scurvy disrupts in normal bone formation in paediatrics, an X-ray of the knees, ribs and wrists can also be performed for any relevant damage in those areas.

Treatment

Vitamin C supplements and providing relief for those conditions that led to the deficiency is the ultimate therapy for scurvy, 100 mg ascorbic acid three times a day for at least 1 week till the patient is fully recovered is the prescribed dosage for children. Adults usually can take a dosage of 300-1000 mg/day depending on the severity of the disease.[28]

Toxicity

Overprescribing or overconsumption of vitamin C can have its fair share of side effects as well. Various studies indicate an increase in vitamin C consumption to be linked to oxalate kidney stones, primarily in males.[29] Fatal cardiac arrhythmias due to iron overload in the body has also been reported in many studies, which is directly linked to increased ascorbic acid levels in the body. This usually happens due to oxidative injury The LOVIT (lessening organ dysfunction with vitamin C) trial concluded that ICU patients who received a 4-day course of IV vitamin C had a higher susceptibility of death or organ damage than those who received a placebo.[30]

CONCLUSION

Vitamin C is a very powerful water-soluble antioxidant with various potential benefits for patients with skin diseases like photo-aging, skin pigmentation, tissue inflammation, tissue healing, and collagen synthesis. However, the pharmacological use of vitamin C should be done with a lot of caution as there are some risks associated with overconsumption of vitamin C as well. In these modern times, the occurrence of vitamin C deficiency is rare, yet not uncommon. Proper diet, vitamin C supplementation, and following the RDA vitamin C dosage, vitamin C can serve as a boon for

overall health improvement. However, clinicians and healthcare professionals have to be on the lookout for any vitamin C toxicity complications, therefore proper monitoring should be enabled.

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