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Vitamin C deficiency is an under-diagnosed contributor to degenerative disc disease in the elderly

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SUMMARY

The human aging process is often accompanied by significant increases in degenerative spine disease. The pathophysiology of intervertebral disc degeneration has been extensively studied, but the etiology of this aging-related problem remains poorly understood. The elderly often have lower daily vitamin C intakes and circulating ascorbic acid values than younger people because of problems with poor dentition or mobility, and also are more likely to have underlying sub-clinical diseases that can reduce plasma ascorbate concentrations. Ascorbate is essential for collagen production, and vitamin C deficiency will result in defective connective tissue, including reductions in collagen synthesis and structural stability. It is hypothesised that vitamin C deficiencies may be a key contributing factor in the development of degenerative disk disease (DDD) in the elderly. Once degenerative disc disease has begun, the tissue inflammation that accompanies DDD may further increase vitamin C requirements in the affected patient, thereby creating a cascade of positive feedbacks that potentially accelerates and contributes to further disc degeneration and low-back pain. Aggressive monitoring of patient ascorbate status, as well as more finely-calibrated RDAs for vitamin C that explicitly take into account the patient's age, may be required if aging-related degenerative disk disease is to be minimised.

Introduction

Recent increases in average human life span have unfortunately been accompanied by significant increases in degenerative spine disease in the elderly [1,2], and chronic low-back pain is a common and debilitating problem in older adults [3]. Back problems are a leading cause of disability, with the prevalence of lumbar intervertebral disc degeneration growing steadily from early adulthood onwards, and the prevalence of low-back pain incidence increasing linearly to reach its highest levels after age 45 [4]. In a recent study of 270 adults ranging from 51 to 86 years old, Hangai et al. [5] reported that aging correlated significantly with lumbar intervertebral disc degeneration of L1/2, L2/3, L3/4, and L4/5. The presence of degenerative disc and facet pathology in older adults is ubiquitous, regardless of clinical status, with >90% demonstrating some level of degeneration [6].

While the pathophysiology of intervertebral disc degeneration has been studied extensively, pivotal questions remain unresolved [7]. Hadjipavlou [8] concluded that most evidence points to an age-related process, influenced primarily by mechanical and genetic factors. Here I hypothesise that a vitamin C deficiency may be a key contributing factor in the development of degenerative disk disease (DDD) in the elderly.

Age-related physiological changes – whether associated with disease or not – have a marked impact not only on health in general, but also on nutrient requirements and food preferences in the elderly [9]. As stressed by Richard and Roussel [10], it is important to recognize that a close relationship exists between health and nutrition in the elderly, particularly with regards to the provision of key micronutrients. Nutrient deficiencies are frequent in older populations, and a wide variety of nutrients may be involved, including ascorbic acid, or vitamin C [11]. Humans cannot efficiently synthesize this chemically unstable micronutrient, and on average, the human body loses ca. 3% of its vitamin C content per day [12].

Dietary vitamin C is indispensable in humans, who lack the enzyme gulonolactone synthetase needed for its biosynthesis [13]. Vitamin C is an essential nutrient for the conversion of dopamine to norepinephrine, as well as for the biosynthesis of L-carnitine and collagen [14]. Ascorbate is needed for collagen production because this vitamin is an important cofactor for the activity of prolyl hydroxylase, the enzyme that hydroxylates prolyl residues in procollagen, elastin, and other proteins having collagenous domains [15]. A minimum of 35% of the prolyl residues in collagen must be hydroxylated for collagen to maintain its normal triple-helical conformation at normal physiological temperatures [15]. Hypovitaminosis C thus results in defective connective tissue, including reductions in the synthesis and structural stability of collagen [16].

I propose here that inadequate body contents of vitamin C contribute significantly to the development of DDD in the elderly,

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especially among elderly smokers. A similar hypothesis was raised more than 50 years ago by McCormick [17] based upon his extensive clinical experience as a nutritionist:

> "From a carefully correlated study of the nutritional background of subjects of intervertebral-disc lesions, and from the records of analogous post-mortem findings regarding the condition of cartilaginous structures in scurvy, as cited by Lind in his classical treatise on this subject (1753), the writer is convinced that deficiency of vitamin C plays an important etiological role in these lesions." –W.J. McCormick

Effects of aging on ascorbate levels

During the years since McCormick's publication, a trend towards lower levels of ascorbic acid with aging has been documented by a number of researchers [e.g., 18,19]; see also similar citations in Ref. [14]. However, other studies of apparently healthy, well-nourished elderly populations in the United States have found no evidence of a greater incidence of vitamin C deficiency among the elderly compared to young adults and no decrease in plasma ascorbate with advancing age [14]. While the reasons for these contrasting results remain unclear, the elderly nonetheless can often have lower daily vitamin C intakes and circulating ascorbic acid values than younger people because of problems with poor dentition or mobility, and the elderly also are more likely to have underlying sub-clinical diseases that can influence plasma ascorbate concentrations [20]. Moreover, humans generally tend to experience an overall decline in nutrient intake from food as they age [21]. It is thus important to note here that the NAS [14] report states that "older adults have similar *or lower* **[emphasis added]** plasma ascorbate concentrations than young adults".

Low vitamin C status in the elderly can be further exacerbated by patient-specific conditions. For example, susceptibility to both sub-clinical and clinical vitamin C deficiency is partly genetically determined: despite a nominally adequate dietary supply, vitamin C is markedly lower in concentration and is particularly prone to *in vivo* oxidation in individuals exhibiting the human plasma protein haptoglobin phenotype Hp 2–2 [22]. In addition, smoking can significantly reduce plasma ascorbic acid (AA) concentrations [23]: active smokers have on average more than a 25% lower circulating concentration of AA than non-smokers [24], and their AA levels are inversely related to cigarette consumption rates [25]. Additional risk factors for vitamin C deficiency include male gender, being retired, excessive alcohol intake, and the presence of infectious disease [26].

Cascading interactions in DDD

In addition to the factors mentioned above, plasma vitamin C levels are inversely correlated with high-sensitive C-reactive protein (hs-CRP) concentrations, a marker of sub-clinical inflammation [12]. With regards to DDD, systemic levels of C-reactive protein are higher in patients with sciatica than in controls, and disc cells are capable of expressing pro-inflammatory molecules such as TNF-α [27]. Moreover, hs-CRP concentrations are increased in patients with chronic low-back pain and Modic I lesions, reflecting local inflammation phenomena occurring at the vertebral endplate level [28]. Once degenerative disc disease has begun, I hypothesise that the tissue inflammation that accompanies DDD will further increase vitamin C requirements in the affected patient, thereby creating a cascade of positive feedbacks that potentially accelerates and contributes to further disc degeneration and low-back pain.

Conclusions

> "The medical profession itself took a very narrow and very wrong view. Lack of ascorbic acid caused scurvy, so if there was no scurvy there was no lack of ascorbic acid. Nothing could be clearer than this. The only trouble was that scurvy is not a first symptom of a lack but a final collapse, a premortal syndrome and there is a very wide gap between scurvy and full health." – Nobel Prize winner Albert Szent-Gyorgyi

Li and Schellhorn [29], remarking upon the above quote, emphasized that our growing understanding of the mechanisms of vitamin C transport, its newly-described physiological roles, and the potential involvement of ascorbate in cancer and heart disease have led to calls for reappraisal of the dietary requirements for this vitamin. I wish to add here to these calls.

In principle, unless underlying pathologies are present that would markedly compromise the body's absorption and retention of ascorbate, it has generally been concluded that the vitamin C requirements of the elderly should not differ substantially from those of younger people [e.g., 14]. Consistent with this conclusion, it has been recommended that the estimated requirement for vitamin C for individuals 51 years and older remain the same as that of the younger adult [14]. However, vitamin C nutrition may be more important for people with certain diseases or conditions [30].

Specifically with regards to DDD, I conclude that much more aggressive monitoring of patient ascorbate status as well as more finely-calibrated RDAs for vitamin C that explicitly take into account the patient's age status, may be required if aging-related degenerative disk disease is to be minimised. I hypothesise here that unless compensatory increases in dietary vitamin C intake are put into effect, vitamin C deficiency may contribute significantly to the development and pathophysiology of intervertebral disc disease during the normal human aging process.

Direct tests of this hypothesis would be straightforward, using established cohort methods that have been extensively used to examine the effects of patient nutrition and nutrient status on specific health states [e.g., 31]. The frequency and intensity of low-back pain and sciatic pain, as well as Modic changes, in the study population can be scored using existing criteria [e.g., 32]. Critically-important parallel measurements of patient vitamin C status in these same test subjects can be made using the recently-developed FRASC method [33,34], which provides a rapid, reliable and sensitive tool for plasma ascorbate analyses. Moreover, explicit but non-invasive tests for hypothesised linkages between vitamin C status and the hydroxylation status/structural stability of collagen in the study population may potentially be monitored using pyridinoline:deoxypyridinoline ratios in the study patients' urinary degradation products [35; see also 36].

Conflict of interest

I have no financial and personal relationships with other people or organisations that could inappropriately influence this work.

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