

INSIGHTS INTO THE ROLE OF ASCORBIC ACID IN PAIN MANAGEMENT; A COMPREHENSIVE REVIEW

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Abstract : In this review, we focus on human studies investigating the role of vitamin C in orthopedic, viral, cancer, and postoperative pain. Preclinical pain models are not always directly comparable to clinical pain scenarios. However, we will discuss some preclinical studies although these were conducted in animals that can synthesize their own vitamin C and as such are not ideal models for the demanding vitamin C situation of humans. Vitamin C has several important functions in the body, mainly acting as a cofactor for a family of biosynthetic and regulatory metalloenzymes. These functions include the synthesis of neurotransmitters and peptide hormones and the regulation of transcription factors and gene expression.

1. INTRODUCTION

Over the last three decades, access to pain and its relief has been an important area of focus. In the 1990s, inadequate assessments and treatment of pain was identified as a health problem and later designated as the “fifth vital sign”. To improve pain management and the emergence of new forms of medication, over-the-counter opioid prescription ultimately led to the national opioid crisis. In response, research and guidelines have sought to identify alternative approaches to pain management. Recent guidelines and best practice reports have recommended individualized, multimodal and multidisciplinary pain management that includes medications, corrective therapies, interventional procedures, and behavioral health approaches and complementary and integrative medicine. However, one of the limitations of these articles is the lack of discussion of the role of vitamins and minerals in pain. According to a 2002 study, more than one-third of Americans use complementary and alternative medicine. Because pharmacists are often the only health professionals who can answer consumer questions about over-the-counter medications, it is important to understand the potential role of drug therapy of these substances to relieve pain.

1.1 PAIN

Pain is defined as “an unpleasant sensory and emotional experience associated with or described by actual or potential tissue damage” [1]. Pain taxonomy developed through the work of the International Association for the Study of Pain and includes broad classifications related to pain etiology, such as nociceptive (pain caused by injury) and neuropathic (neuropathic pain or pain in response to pain, nerve damage), as well as certain signs of pain such as allodynia (increased sensitivity of neurons) and hyperalgesia (increased sensitivity to pain). Temporal effects such as chronic and acute are also considered. The main pain organ is the brain. After noxious stimuli are emitted, they are sent as nociceptive signals to the central nervous system via the spinal cord and ascend to higher centers. Here, the experience of pain is perceived and experienced in a complex and dynamic interaction between both advanced and primitive brain regions. Pain is a transdiagnostic symptom, and although somatic pathology plays a role in the activation of pain pathways, psychosocial, cultural and environmental factors influence the experience of pain over time [2].

1.2 NOCICEPTION

Nociception is defined as “the neural processes that encode and process noxious stimuli.” A noxious stimulus is an “actual or potential tissue-damaging event”, usually physical (mechanical, thermal, electromagnetic) or chemical energy. It is interesting to note that not all noxious stimuli (such as X-rays) cause tissue damage, and even if they do (such as a slow-growing liver or brain tumor), they do not always activate nociceptors and cause pain [3]. A nociceptor is a “sensory receptor, able to transform and code noxious stimuli”. In other words, nociceptors transform “tissue damage energy” (mechanical, thermal or chemical) into electrical nerve energy. Transmission, just as the rods and cones of the eye convert electromagnetic energy light pulses. Nociceptive “traffic”

ascends from tissues via nociceptive neurons, the dorsal horn and various spinal cords/into the brainstem, midbrain, thalamus and various cortical regions, and is modulated by descending inhibitory and facilitatory pathways. Technically speaking, there are no "pain pathways", but rather nociceptive transmission pathways[4]. In other words, the spinothalamic pathway does not actually transmit "pain". Neurophysiological processes that "enhance" nociception produce sensitization, which can be defined as "increased nociceptive efficiency with a given input".

1.3 NOCICEPTION AND PAIN ARE NOT THE SAME

Basic knowledge of neuroscience over the last 30 years, including functional brain imaging. Explanatory notes accompanying the definition indicate that pain and nociception are not the same thing; "Pain is a subjective phenomenon, while nociception is an object of sensory physiology." Nociception (due to tissue damage) is a sensory process that most often (but not only) "triggers" multidimensional and conscious pain (classic). "pain as disturbance" paradigm). Pain can still occur in the absence of nociception (tissue damage) (eg, phantom pain or allodynia) and nociception can occur without a "trigger" (tissue nociception without local anesthesia or unconsciousness\during surgery under general anesthesia)[5]. Pain is an absolute function of consciousness, while nociception is not. There is no "pain center" in the brain, and strictly speaking, there are no "pain pathways". Pain does not cause changes in the nervous system, although these processes, such as fMRI cortical changes, are associated with pain. To find a sensory metaphor, nociception is comparable to the process of converting sound energy of nerve impulses in the inner ear which are transmitted to the auditory cortex[6]. Hearing is the conscious experience of such auditory stimuli, and pain is more like "music," a complex sensory and emotional experience. Like pain, you can experience music without any sensory (auditory) input (like a note playing in your head)[7].

2. CLASSIFICATION

2.1 TEMPORAL CLASSIFICATION

ACUTE PAIN

The IASP lacks a definition of acute pain, which is defined as "pain of recent onset and probably of limited duration; usually with an identifiable temporal and causal relationship to an injury or disease".

CHRONIC (ONGOING) PAIN

Although there is a notable lack of a definition of "chronic pain" in the IASP, it is usually defined as "pain that lasts longer than 3 or 6 months or pain that lasts beyond normal (tissue) healing time[8] the latter definition does not reflect diseases such as chronic inflammatory arthritis (rheumatoid arthritis), neuropathic pain or hyperalgesia. Temporal definitions of pain are relatively artificial, and acute pain is generally considered adaptive or "physiological". proximate cause and chronic pain as "maladaptive", often without clear\discontinuous pathology. There is considerable overlap between these concepts and they probably exist along a temporal and pathophysiological continuum.

2.2 DISEASE-BASED CLASSIFICATIONS

ICD 10 classifies pain only as a symptom of disease states in various organ systems. If the pain is not related to an organ system, region, or disease, it is defined as "pain not elsewhere classified," which in turn can be acute, chronic, intractable, or "pain other wise unspecified. The IASP has pain coded. A 5-axis taxonomy to describe chronic pain disorders based on body region, organ system, temporal characteristics, intensity, and etiology[9].

3. VITAMIN C

Vitamin C, also known as ascorbic acid (AA), is an essential nutrient for many multicellular organisms, especially humans. Ascorbic acid is a watersoluble vitamin found in varying amounts in fruits and vegetables and in the muscles of organs (such as liver and kidneys). Vitamin C deficiency causes scurvy, generalized connective tissue weakness and capillary fragility[10]. Among chemists, it is used as a reagent in the production of fine chemicals, enzymatic reagents and nanomaterials. Therefore, the detection and quantification of ascorbic acid in food samples, products and foodstuffs becomes crucial for researchers, clinicians, as well as the pharmaceutical and food industries[11]. It is also an incredible nutrient used to repair damaged tissues and produce important neurotransmitters that play a key role in the proper functioning of the immune system. It is used as a cofactor for the enzyme needed to hydroxylate lysine and proline in the formation of collagen[12]. This vitamin, discovered in 1912, is on the Model List of Essential Medicines of the World Health Organization. Incredible vitamins for its wide range of health benefits.

4. FUNCTIONS OF VITAMIN C

Vitamin C, also known as ascorbic acid, is essential for the growth, development and repair of all body tissues. It is involved in many body functions, such as collagen formation, iron absorption, proper functioning of the immune system, wound healing and maintenance of cartilage, bones and teeth[13]. Vitamin C is one of the many antioxidants that protect against this harmful molecules such as free radicals and toxins caused by damage caused by chemicals and pollutants such as cigarette smoke. Free radicals can build up and contribute to health conditions such as cancer, heart disease and arthritis[14, 15,16]. The body does not store vitamin C, so an overdose is not a concern. But it's still important not to exceed the safe upper limit of 2,000 milligrams per day to avoid stomach upset and diarrhea. Vitamin C is one of the water-soluble vitamins. Since your body does not store them, you must keep them in your diet at all times to maintain healthy levels. Eat fruits and vegetables rich in vitamin C raw or boil them in a small amount of water so that you don't lose some of the water-soluble vitamin in the cooking water. Vitamin C is easily absorbed from both food and water. Available in tablet form and can improve iron absorption when the two are taken together[17].

5. VITAMIN C IN PAIN MANAGEMENT

Vitamin C deficiency (plasma concentrations <11 $\mu\text{mol/L}$) shows as scurvy-related myalgia and arthralgia within the knees, wrists, and lower legs due to dying inside these areas[18]. Insufficiency of this vitamin is uncommon in developed nations, but the populaces basically influenced are hospitalized elderly patients, cancer patients, and basically sick patients. The utilize of vitamin C has been appeared to be successful in a few perspectives of torment administration.

Complex Territorial Torment Disorder (CRPS):

Numerous randomized, controlled trials have illustrated that vitamin C supplementation decreased the rate of CRPS in wrist- and ankle surgery patients, with the foremost useful measurement being 0.5 g or more per day[19,20]. The same dose was moreover managed prophylactically for osteoarthritis in joint-replacement patients, Who were at that point found to have no frequency of CRPS.

5.1 Rheumatoid Joint pain and Osteoarthritis:

It has been famous that patients with rheumatoid joint pain display with normal vitamin C levels less than half the level in sound controls[21]. One think about detailed a add up to decrease of torment in a single rheumatoid joint pain understanding taking after twice- weekly implantations of high-dose vitamin C, and a think about in Osteoarthritis patients given 1 g of verbal calcium ascorbate per day found that the decrease in torment was less than half of that detailed for nonsteroidal anti-inflammatory drugs[22,23]. These information may too propose more adequacy with parenteral versus verbal organization in patients with joint pain.

5.2 Orthopaedic Torment:

Vitamin C shows administrative impacts on bone and collagen formation. A think about of 16 patients with Pagetas malady appeared a lessening in bone torment taking after organization of 3 g of vitamin C per day for 2 weeks. In any case, the torment diminishment was not more noteworthy than that watched with normal calcitonin treatment for the illness.

5.3 PHN:

Serum levels of vitamin C are much lower in shingles patients than in sound people, and this has been found to extend the hazard of PHN.23 Randomized controlled trials have appeared a decreased rate of PHN and diminished long-term torment taking after parenteral vitamin C.

5.4 Cancer Torment:

Cancer patients ordinarily have expanded vitamin C prerequisites and lower circulating levels than solid individuals[24]. Questionnaire-based ponders analysing quality of life appeared noteworthy advancements(>30%) due to diminished torment taking after vitamin C managed orally or parenterally.

5.5 Diminished Opioid Necessities:

Patients getting opioids have been found to display diminished withdrawal side effects with coadministration of vitamin C. A few ponders have too watched that these patients required less morphine counterparts of opioids compared with patients who did not get vitamin C coadministration[25].

6. CONCLUSION

Pain is a complex and multifaceted disease that affects different people differently. Although several pharmacological treatments are available for pain relief, no single treatment regimen works for all patients. Vitamins and minerals can be an alternative for pain relief, how especially in the treatment of neuropathic and chronic pain. Although the evidence for the use of vitamins and minerals is limited, pharmacists are well positioned to help patients make informed decisions about the use of these nutrients.

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