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Protective Role of Ascorbic Acid in Bronchial Asthma: Review

Nagdeote AN[1], Basutkar DG.[2] Lanje MJ[3], Deokar P[4]

[1]*Associate Professor in Biochemistry, ESIPGIMSR, Andheri E, Mumbai*
[2]*Professor in Biochemistry, ESIPGIMSR, Andheri, Mumbai*
[3]*Assistant Professor in Biochemistry, ESIPGIMSR, Andheri, Mumbai*
[4]*Senior Resident in Biochemistry, ESIPGIMSR, Andheri, Mumbai*

Corresponding Author:
Dr Abhay N. Nagdeote
Dept of Biochemistry
ESIPGIMSR, Central Road, MIDC
Andheri E Mumbai 400093.

Abstract:

Ascorbic acid is an important aqueous antioxidant of pulmonary tissue and is most abundant water soluble antioxidant present in lung than elsewhere in the human body. Evidence is reviewed which indicate that ascorbic acid can influence the pulmonary smooth muscle contractility directly or indirectly. It has been pointed out that a diet low in vitamin C is a risk factor for asthma. Abnormality in pulmonary smooth muscle contractility is associated with oxidant exposure. Ascorbic acid is present in the extracellular fluid lining of the lung, where it could be important in protecting against both endogenous and exogenous oxidants. Ascorbic acid is also known to improve the immunological response and produces the bronchodilator prostaglandins PGE 2, thus producing the beneficial effects. Supplementation of vitamin C rich diet or maintenance of therapeutic sufficiency of ascorbic acid should be considered, important while treating bronchial asthma

Key words: asthma, ascorbic acid, antioxidants,

INTRODUCTION:

Scurvy is well-recognized consequence of ascorbic acid deficiency. Many studies have aroused interest in the possible role of ascorbic acid in preventing other diseases. Pauling[1] suggested that a high intake of vitamin C might prevent colds and influenza. Other studies have suggested that vitamin C protects against cardiovascular diseases[2]. Many studies pointed out the protective role of ascorbic acid in bronchial asthma directly or indirectly.

Lung is the most extensive of all the body tissue which, interface directly between human being and their environment[3]. The entire respiratory tract acts act as a defense organ against noxious foreign agent to perform its task of gas exchange adequately. Defense mechanisms that involve lungs include filterative clearance, mucocilliary clearance, coughing reflexes, phagocytic clearance, mucosal protein and local immunity[4].

As there is increase prevalence of asthma worldwide, diet and environment pollutants can be doubted as one of the major causes. Increased interest generated in the recent past in antioxidants, which may be attributed to the fact that oxidants and mutagens are commonly found in food and air and are endogenously produced[5]. The main focus is on ascorbic acid because it is thought to be the most abundant antioxidant substance in the extracellular fluid lining of the lung[6] and it appears to play a dual role as water soluble antioxidant which may act directly as well as restore the antioxidant properties of fat soluble vitamin E[7].

Oxidant Injury and Asthma

It has been suggested that, oxygen radicals are capable of causing tissue injury and promoting tissue inflammation, and have been implicated in the pathogenesis of disease. Airway inflammation is the important characteristic of asthma, and the metabolism of oxygen radical is enhanced in symptomatic asthma in relation to clinical disease activity[8].

There is an increase in oxygen species generation in blood monocytes[9] of asthmatic patients, which suggested that asthma can be caused by free radical or it can aggravate the preexisting disease. It has also been suggested that there is overproduction of oxidants by leukocytes in asthma. Eosinophils, appears to play an important role in asthma because their presence in bronchoalveolar lavage and blood is closely linked with bronchial hyperresponsiveness. Eosinophils, alveolar macrophages, and neutrophils of asthmatic patients produce more oxygen species than those from normal subjects. Reactive oxygen species directly contract airway smooth muscle preparation and this effect is enhanced when the epithelium is injured or removed. Reactive oxygen species also appears to directly stimulate histamine release from mast cell and mucous secretion from airway epithelium[10].

Ascorbic acid and Asthma:

The relation between ascorbic acid and asthma was initially observed in 1803, when Reississen[11] noted convulsive asthma in the sailors with scurvy. Studies done on the trachea of guinea pigs deficient in vitamin C revealed that ascorbic acid antagonized prostaglandins (PGF2 alpha) induced bronchoconstriction[12/13]. Several studies have been conducted regarding the possible role of ascorbic acid in asthma include the effect of ascorbic acid on variety of bronchial provocation tests with exercise, allergens,

histamine[14] and methacholine[15]. Studies at cellular level include effect of ascorbic acid on non-specific (leukocyte function) and specific (humoral and cellular) immune systems. Majority of studies show beneficial effects of ascorbic acid in asthma, ranging from antibronchospastic action to improvement of immune system of the body[16/17/18]. Only few studies do not show the beneficial effect of ascorbic acid[19, 20].

In cross sectional analysis it has been pointed out that ingestion of citrus and kiwi fruit and diet supplements rich in ascorbic acid have a significant role against wheezing effect of asthma especially in children[21]. Biltagi el al concluded that there is improvement of pulmonary function tests in children with moderately persistent bronchial asthma by supplementing vitamin C zinc and omega-3 fatty acid either singly or in combination [22]. Low intake of oranges and other fruit juices, which are the largest source of vitamin C, were associated with deficits in the pulmonary function in children[23]. Vitamin C [24] may have a protective effect on airway hyperreactivity in some patients with exercise induced asthma. Important role of ascorbic acid in the maintenance of pulmonary function has been reported by McNally[25] who showed that the administration of ascorbic acid cause pulmonary dilation and that urinary excretion of vitamin during the acute episode of asthma were significantly reduced. This would suggest that during the asthmatic episodes, ascorbic acid was being actively metabolized probably at the bronchial mucosal surface, thus reducing onto its depletion in plasma content to the level below the renal threshold.

DISCUSSION:

Ascorbic acid can be useful in asthma in different ways

1. Ascorbic acid and antioxidant action:

Asthmatic patient show increased superoxide generation from leukocytes, increased total nitrites and nitrates, increased protein carbonyls, increased lipid peroxidation products and decreased protein sulfhydrils in plasma indicating increased oxidative stress[26]. Ascorbic acid is an important antioxidant[27]that directly neutralizes free radicals. It is also a part of glutathione peroxidase pathway for repairing oxidative damage to the lipid membrane and act as a regenerating agent for vitamin E [28]. Since free radical injury is one of the features of asthma, ascorbic acid helps in scavenging the free radicals thereby producing the beneficial effect. Hatch[29] has suggested that ascorbic acid is the major antioxidant present in the airway surface liquid of the lung, and it may protect against endogenous oxidant as well as exogenous agents such as cigarette smoke and environmental air pollutants. It has also been suggested that [30], ascorbic acid prevents lipid peroxidation and protects the antioxidant systems. Olusi et al[31] examined plasma and white blood cell ascorbic acid concentration in 62 asthmatic subjects and 57 normal controls. These investigations found that both treated and untreated asthmatic had significantly lower plasma and white blood cell ascorbic acid concentration compared to normal controls. The decreased ascorbic acid concentration in asthmatics could be attributed to its normal physiological function, increase utilization to overcome continuous generation of oxidant radical and also to neutralize the exogenous oxidant. Kongerud. et al[32], Aderele et al[33] and akinkube et al[34] also observed similar results in their studies. Kongerud J. et al[32] suggested that ascorbic acid deficiency might be either` an underlying factor in the pathophysiology of asthma or a response to asthmatic airway inflammation. Aderele et al[33] and Akinkube et al[34], attributed such kind of lowering in plasma ascorbic acid is due to its utilization in the maintenance of defense mechanism, tissue integrity and replacement process. Destruction of respiratory mucous membrane during common cold and resulting reduction of the tissue ascorbic may further delay the healing of mucous membrane surface leading to prolonged symptoms in asthma[35]. Some studies have observed the beneficial role of ascorbic acid in common cold[36/37].

2. Ascorbic acid and immunity:

Anderson R[17] found that there is improvement in the primary immunological abnormalities in the patient of bronchial asthma. In 10 patients, the effect of ascorbic acid on exercise induced bronchoconstriction, were assessed. Those, patient who received antiasthma chemoprophylaxis along with ascorbic acid, significant improved polymorphonuclear leukocyte motility, decreased ASO (antisteptolysin) level are observed. The stimulatory effect of ascorbate has been found to be related entirely to inhibition of autooxidative effect of the myeloperoxidase/hydrogen peroxide/halide system. In animal, ascorbate deprivation results in T-cell and phagocyte deficiency, which can be corrected by vitamin C supplements. Furthermore, the high doses, of ascorbic acid have been shown to stimulate T-lymphocyte response in normal subjects[38].

3. Ascorbic acid and prostaglandin biosynthesis:

The study of Kalayci O et al [39]showed that antioxidant vitamins are decreased in sera of asthmatic patients even during the asymptomatic period of the disease, and that this decrease is not totally dependent on the increased oxidative stress as reflected by lipid peroxidation products. This can be proved by the fact that ascorbic acid induces relaxation of the tracheal smooth muscle in vitro due to significant release of prostaglandin E2 by tracheal smooth muscle cells[13]. The protective role of ascorbic acid on airways is not only against PGF2 alpha but have also has been observed against 5-hydrotryptamine and histamine. Dawson and west[40] indicated that the protective effect of ascorbic acid is probably direct. In order to test the protective role of ascorbic acid, the guinea pigs were maintained on ascorbic acid free diet. Tracheal preparation obtained from animals affected by scurvy released lower amount of PGE2 and a significant higher quantity of PGF2 alpha. These result indicated that ascorbic acid increase the formation and release of PGE2, which causes relaxation of the tracheal smooth muscle, whereas ascorbic acid insufficiency can effectively prevent the formation of PGE2 and allow reduction of endoperoxide to form PGF2 alpha, which cause contraction of trachea[13]. The above contention can be proved by the study of Mohsenin[15] who

observed that indomethacin, an inhibitor of prostaglandins synthesis, reversed the protective effects of ascorbic acid in asthmatic subject.

CONCLUSION:

It can be concluded that ascorbic acid is found to produce a positive response in bronchial asthma by three different mechanisms as antioxidant, causing improved immunity and by producing the bronchodilator prostaglandin PGE2. Since many studies indicated lowering of ascorbic acid in asthmatic patients, supplementation of vitamin C rich diet or maintenance sufficiency of this vitamin in the treatment of asthma should be considered important along with standard anti asthmatic therapy.

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