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Nutritional Protocol for Asthma

Emmett James Hughes

University of Bridgeport, Bridgeport, CT, USA

Corresponding author:
Emmett James Hughes

ehughes@bridgeport.edu

University of Bridgeport, Bridgeport, CT, USA.

Tel: (632) 988-6445
Fax: (203) 576-4351

Abstract

Asthma is characterized by hypersensitivity of the bronchioles, leading to bronchospasm, oedema of the mucosa and increased secretion of mucous, usually more viscous. This leads to a deficiency in ventilation. There are several factors that are involved, including the release of inflammatory mediators from mast cells (particularly leukotrienes), pollution, stress, pollen, insect and food allergens/sensitivities, animal hair/fur/dander, food additives, obesity, and genetically modified plants (leading to increased allergens in foods).

Keywords: Asthma; Leukotrienes; Oxidative stress; T helper cells

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Introduction

Asthma is a common disorder that is currently managed with suppression of symptoms. This review looks at mitigating some of the physiological mechanism that leads to this complex and sometimes difficult to control disease. Additionally, it has been demonstrated that a deficiency in the glutathione S-transferase M1 gene predisposed an individual to becoming asthmatic due to increased oxidative stress. Ozone, tobacco smoke exposure and diesel exhaust particles are particularly damaging to the lungs in the absence of this gene [1]. According to the CDC the incidence of asthma is 8.6 per cent in children, and 7.4 per cent of adults. Approximately 1.8 million emergency department visits per year are due to asthma attacks. Although not common, deaths from asthma in the U.S. in 2013 were 3,630.

Asthma is divided into two main categories, intrinsic and extrinsic. Intrinsic asthma is due to hypersensitivity of the airways independent of antibodies. These sensitivities can include chemicals, exercise, complement activation, cold air, infection, and emotional stress. Extrinsic asthma is due to increased levels of IgE in the plasma.

An imbalance between TH1 and TH2 (two subsets of T helper cells) seems to be one of the mechanisms of airway inflammation mediated by the immune system [2]. An increase in TH2 cells causes in increase in interleukins 4, 6, 9 and 13, IgE, and eosinophils, as well as increased plasma cell formation and antibody production. Ferulic acid (found in the seeds of peanut, coffee, artichoke, apple, and orange, as well as in both seeds and cell walls of Chinese water chestnut (Eleocharis dulcis), rice, wheat, oats, and pineapple) has been demonstrated to restore this balance by influencing antigen-presentation via dendritic cell function [3].

The extrinsic and intrinsic factors induced by TH2 cells trigger the release of cytokines from mast cells. Both preformed and de novo mediators are involved. Preformed mediators include histamine, eosinophilia chemotactic factor, proteases, neutrophilic chemotactic factor, gycosidases, and heparin. De novo factors include eicosanoids derived from the fatty acids present in the phosolipid bilayer of the plasma membrane of the mast cells. Prostaglandins, thromboxane's, and slow-reacting substance of anaphylaxis (leukotrienes LTC4, LTD4 and LTE4), are the resulting cytokines [4]. These inflammatory mediators are responsible for the majority of the signs and symptoms of asthma. These include smooth muscle constriction in the bronchioles, oedema of the airway mucosa, inflammatory cell infiltration, and the breakdown of the epithelium via glycosidases and proteases. Chronic asthma results in the remodelling of the airways and permanent damage, causing thickening of the airways and more pronounced airway restriction.

Autonomic Nervous System

Stimulation of the vagus nerve (parasympathetic) causes the release of Ach and the formation of cGMP (cyclic guanosine monophosphate) and constriction of the airways. Conversely, sympathetic stimulation of beta$_2$ adrenergic receptors (localized in the lungs) and the formation of cAMP, leads to bronchodilation. A relative deficiency of cAMP, or the overproduction of cGMP or both, leads to airway constriction and degranulation of mast cells.

The adrenal gland plays a critical role in this balance between parasympathetic and sympathetic stimulation of the airways.

Cortisol has an effect of increasing the sensitivity of beta$_2$ adrenergic receptors, and epinephrine is the prime stimulators of these receptors. It is thought that during an asthma attack, there is a deficiency of both, leading to the predominance of cGMP and an underproduction of cAMP leading to bronchiole constriction.

Increased Intestinal Permeability

Also known as leak-gut syndrome, increased intestinal permeability is a contributing factor to the development of food allergies and sensitivities. An increase in gut permeability leads to an increase in antigens, thus increase the likelihood of developing additional allergies [5].

Melatonin

While melatonin has been well-established as a potent antioxidant, there is some concern that it increases bronchial sensitivity [6]. This may be especially problematic for patients with nocturnal asthma. However, melatonin has been shown to decrease mucus production in experimental animal models of asthma [7]. Since those with nocturnal asthma where shown to have an inverse correlation with melatonin levels and FEV_1, it is possible that supplementing with melatonin would prevent the late peak of melatonin and possibly mitigate the night time symptoms.

Diet

It has been clearly established that a diet rich in fruits and vegetables lowers the risk of developing chronic respiratory problems [8]. Increased flavonoids, antioxidants, plant sterols, fibre, and omega-3 fatty acids from fruits and vegetables have all been shown to reduce the risk of asthma as well as improve symptoms in those with asthma. A vegan diet has been suggested to reduce the symptoms of asthma and has been shown to reduce the need for medication [9]. Identifying food allergies and sensitivities is especially important in mitigating the symptoms and complication of chronic asthma. Immediate (Type I) hypersensitivity reactions are most often due to eggs, fish, shellfish, nuts, and peanuts. Delayed onset (Type IV) hypersensitivity reactions are most often due to the consumption of milk, chocolate, wheat, citrus, and food colourings [10]. The recognition of food allergies and sensitivities is crucial when attempting to improve symptoms in asthma patients. This food list is not exhaustive. Other suspects include nightshades (white potatoes, bell peppers, eggplant, and tomatoes), corn, rye, triticale, spelt, barley, dairy, beef, alcohol, food preservatives, and soy. These all need to be eliminated from the diet for six weeks and then reintroduced one at a time. Careful monitoring of symptoms is crucial to identify food triggers.

Antibiotics/probiotics

A combined study that involved more than 12,000 children, the researchers looked at the incidence of asthma in children who had been treated with antibiotics in the first year of life. It was discovered that when compared to non-treated children, there was more than a two-fold increase in asthma in the treated children [11]. Other studies have confirmed these results. Mothers taking antibiotics during pregnancy have an increased risk of the child developing asthma by age 7. Supplementing with probiotics, especially *Lactobacillus* and *Bifidobacterium*, has been shown to lower the risk of asthma [12].

Supplements

Omega-3 fatty acids

Increased intake of omega-3 fatty acids has been clearly demonstrated to lead to anti-inflammatory eicosanoids (prostaglandins, leukotrienes, thromboxanes) thereby leading to overall improvements in asthma [13]. Supplementing with flax seed oil at 3000 mg t.i.d. along with 400 IU of vitamin E/day is the suggested dosage. There are no known side effects at these dosages for either supplement.

Pyridoxine (Vitamin B_6)

Pyridoxine may have a direct benefit in asthmatics. These patients have been shown to have consistently lower plasma levels of pyridoxine phosphate levels when compared to normal. Supplementing with pyridoxine decreases the production of inflammatory eicosanoids [14]. In patients being treated with theophylline for asthma, pyridoxine supplementation is recommended. Theophylline reduces pyridoxal-5-phosphate levels significantly. Additionally, B6 supplements have been demonstrated to reduce the side-effects of theophylline (nausea, headaches, sleep disorders, and irritability) [15]. In one reported case, dosages of 200 mg caused peripheral neuropathies. Normally 2–5 g over several months is required to produce this effect. The recommended dose is 100 mg/day.

Antioxidants

The intake of vitamins C, E beta-carotene, as well as the minerals zinc, selenium and copper have all declined in the past 30 years due to drastic alterations in diet. Increasing antioxidant-rich foods is beneficial in asthma patients [16]. Carotenes are known to positively affect epithelium, especially in the bronchioles [17]. Through nuclear Retinoic Acid Receptor (RAR) and retinoid X receptor (RXR) activation, carotenes help to repair damaged epithelium. Vitamin E acts as an antioxidant for lipid-based substances as well as inhibits the formation of inflammatory leukotrienes [18]. Asthmatics have reduced plasma levels of selenium. Since glutathione peroxidase (a selenium-dependent enzyme) is needed to reduce leukotriene synthesis, supplementing with selenium in asthmatics is warranted.

Other vitamins/minerals

Magnesium has been well-established as a muscle relaxer. This is true regarding the smooth muscle of the bronchioles as well [19]. Magnesium is used intravenously and inhaled through a nebulizer [20,21]. Oral doses should be given to bowel tolerance, usually in the range of 600–1000 mg/day. Too much magnesium can cause diarrhoea, and in severe cases respiratory depression. Vitamin D deficiency is associated with increased bronchiole reactivity [22-24]. Vitamin D is known to block the formation of a variety of inflammatory mediators in the lung. It also raises the

levels of interleukin-10, which has an anti-inflammatory effect. Additionally, vitamin D prevents the remodelling of airways seen in chronic asthma [25]. The recommended dose is 1200-1500 IU/day. There are no known side effects in this range.

Herbs

The most popular herb used to treat asthma was *Ephedra sinensis*, used in traditional Chinese medicine under the name Ma huang. Unfortunately, due to abuses of Ephedra that resulted in a number of deaths, it is now illegal to sell any products that contain ephedra in the U.S. as of April 12, 2004. Many of the constituents of ephedra have proven bronchodilation effects [26,27].

Hedera helix (ivy) has a long history of use for the treatment of asthma in Europe [28,29]. It is known to increase levels of TH1 and decrease TH2 activity.

Zizyphi fructus (jujube plum) is used in traditional Chinese medicine (TCM) for allergies and asthma. There are constituents that act as beta-adrenergic receptors leading to increased c-AMP levels. It is known to stimulate ciliary action in the bronchiole due to increases in nitric oxide levels [30]. Saponins extracted from the seeds of the jujube plum have demonstrated the ability to prevent histamine release from mast cells [31].

Tylophora asthmatica has been used in Ayurvedic medicine for disorders of the respiratory system. It has been shown to stimulate the release of epinephrine from the adrenal cortex [32]. It is also thought to have anti-spasmodic and antihistamine effects as well.

Glycyrrhiza glabra (licorice root) has been used for many years to treat inflammation and allergies. Glycyrrhetinic acid, the primary active ingredient in licorice root, has been demonstrated to inhibit phospholipase A2, inhibiting eicosanoid synthesis [33]. It has also exhibited activity as an expectorant. When combined with other herbs, crow-dipper, astragali, and angelica, it has been demonstrated to be more effective than pharmaceuticals alone [34].

Boswellia serrata is an ayurvedic herb known to inhibit the synthesis of inflammatory mediators. Casperome®, a purified extract of boswellic acids, has been demonstrated to be beneficial as a treatment in asthma [35]. There are multiple effects of boswellic acids on the immune system, including down regulation of TNF-alpha and decrease of IL-1, IL-2, IL-4, IL-6 and IFN-gamma, which are proinflammatory cytokines [36].

Since asthma is a multifactorial disorder, successful treatment involves a multi-pronged approach. Elimination of environmental triggers, such as airborne allergens can be difficult. However, decreasing the exposure to these allergens is a worthwhile endeavour. Recognition and elimination of food sensitivities and allergies is another key factor in improving a patient's symptoms. These two steps are critical before embarking on a protocol of supplements to treat asthma.

Conclusion

Asthma is a common disease that can have a significant impact on a person's overall health and well-being. The current approach to treating asthma is the use pharmaceuticals that manage or supress the symptoms rather than positively affect the pathophysiology of the disease. These pharmaceuticals are not without risk. Adding anti-inflammatory agents along with additional natural substances can have a positive effect on the development of asthma, as well as the pathological changes observed in the respiratory tract of patients with chronic asthma.

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