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Vitamin E in children with asthma: A review

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ABSTRACT

Asthma is a chronic inflammatory airway disorder and the most common chronic disease among children characterized by frequent and chronic cough, wheezing, and dyspnea. Asthma is defined as an inflammatory process in response to T- Helper 2 cells. Vitamin E as a Lipid soluble vitamin; containing 4 isomers α, β, γ, δ, with α- tocopherol as the most important isomer is an important defensive agent against epithelial tissue damages caused by antioxidants in human. The results of animal studies showed vitamins C and E cause decreased and modulation of pulmonary responses to oxidant agents such as O3 or NO2. A few studies showed an association between reduced intake of vitamin E by mothers during pregnancy and wheezing in children aged 2 years old. Some studies showed significant declines in serum vitamin E level in asthmatic children compared to non-asthmatic. However, in another study no significant relationship was observed between serum level of vitamin E and risk of asthma. There are controversies on the effect of vitamin E in children with asthma. This study aimed to investigate the role of vitamin E in children with asthma.

Introduction

Asthma is a chronic inflammatory airway disorder and the most common chronic disease among children characterized by frequent and chronic cough, wheezing and dyspnea.[1] The prevalence of asthma is different worldwide with an increasing trend

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in recent decades which imposes considerable financial and sociocultural burden on patients' families. More than 300 million patients are suffering from asthma around the world. The exact cause of asthma is not known yet. But, multi-factorial causes, such as genetic and environmental factors are involved.[2,3] Also, asthma is a complex disease that multiple factors such as autonomic system, immunology, infections, endocrine and psychological agents play an important role in the development of the disease.[4] Common environmental factors are infections, different allergens and pollutants that cause inflammation of respiratory tract and respiratory symptoms by effect on cell mediated immunity and producing different cytokines. Asthma is defined as an inflammatory process in response to T-Helper (TH2) cells. Cytokines like IL4, 5 and 13 that produce IgE can lead to realizing of mediators.[5]

For instance, viral agents increase production of fibroblast, neutrophils, eosinophils and monocytes by increasing Inter Cellular Adhesion Molecule 1 (ICAM-1) via nuclear factor kappa-light-chain-enhancer of activated B cells (NK-Fβ) and stimulating TH2 cells and increasing production of cytokine 4,6,8 and 16.[3] In recent years, there has been increasing interests in the role of nutrition in severity of asthma. This interest is more focused on the role of antioxidants such as vitamins A, C, E, and carotenoids. Some reports on development of asthma signified the role of insufficient levels of antioxidants such as vitamins and minerals following low intake of green plants (thus reduced level of vitamin E) and increase in consumption of foods containing free radicals.[6-9] Peripheral blood inflammatory cells and Bronchoalveolar lavage (BAL) fluid produce more anion superoxide in asthmatic patients compared to control group which led to increasing of antioxidant consumption.[10-12] Steroids reduce oxygen free- radicals produced by these cells.[13] These antioxidants agents cause respiratory tract smooth muscle contraction, increasing of secretion, and sheering of epithelium. Reactive oxidant species (ROS) result in production of cytokines and chemokines.[14, 15] which proves the role of nutrition in development and severity of asthma. Vitamin E was used to decrease the symptoms of asthma and improving respiratory status of asthmatic patients.[6] It decreased or prevented toxicity of oxidant agents on respiratory system.[6, 16-18] There is a paucity of information regarding the effect of vitamin E on pediatric asthma, therefore, this study aimed to review the effect of vitamin E on pediatric asthma.

Vitamin E

Vitamin E is the major Lipid soluble vitamin which is also an important defensive agent against epithelial tissue damages caused by antioxidants in human. It contains 4 isomers including α, β, γ, б, amongst which α-tocopherol is the most important isomer. This vitamin causes break down of pre-oxidase chain of fat and also decreasing production of prostaglandin E2 following peroxidation of fat in pulmonary epithelial cells after contact with Ozone (O3).[19] Antioxidant agents are the first defensive line against oxygen free-radicals. Fluid existence in respiratory tracts is containing antioxidants agents such as vitamin C, uric acid, glutathione peroxidase, α-tocopherol (vitamin E), catalase, dismutase superoxide, thioredoxin reductase, seruloplasmin and transferrin. These agents are found in nutrients like fruits and vegetables.[14, 16] These agents have a role in clearance of free radicals and act as sacrificial targets for O3. They also restrict the interaction between oxidants with lipid and

proteins secreted by respiratory tract lining fluid.[20] Vitamin E is an important anti-oxidant in cell membrane containing tocopherol and tocotrinol that inhibits oxidation of components such as unsaturated fatty acid, even it can stimulate poly-unsaturated fatty acid against antioxidants.[4, 21] In addition, this vitamin causes improvement of T-cells and granulocytes functions.[21] Oxidant are agents causing suppression of TH1 and increase in production of TH2. Previous studies showed an increase in the level of vitamin E in lung following consumption of vitamin E supplements compared to non-users. So that, vitamin E moves to the lung in oxidative stress situations.[22] vitamin E suppresses IgE response due to allergic agents during allergic diseases like asthma.[23] It also improves the blood supply and tissue repair.[4] Vitamin C was reported to be effective in clearance of free radicals in combination with vitamin E.[4] It seems vitamin E consumption is decreased in recent years. For example, in 1950 the intake of vitamin E was 13-15mg/day that decreased to 10.66mg/day in 2005- 2006. The cause of vitamin E deficiency is low intake of green vegetables, cereals and whole grains.[24-26] In children, vegetables may decrease wheezing.[27] However, a study in England revealed no considerable change in the prevalence and severity of asthma in school-age children who received fruits more than 1.3-2 serving/d.[28]

Animal studies

The results of animal studies showed the role of vitamins C and E in decreasing and modulation of pulmonary responses to anti-oxidant agents such as O3 or NO2. [29,30] Vitamin E deficiency and decrease in levels of vitamin E lead to production of pro-inflammatory markers, decrease in surfactant lipid synthesis in type II alveolar cells and epithelial tissue damage due to air pollution.[31] Elsayed showed that level of vitamin E in animal receiving vitamin E supplements was higher in pulmonary tissue after contact with Ozone than the animal which did not receive the supplements.[32]

Human studies

In another study mononuclear cells of cord blood in mothers of neonates who had higher intake of vitamin E during pregnancy demonstrated lower response to antigen stimulation compared to mothers with lower consumption of vitamin E.[33]

A study on children with asthma who were exposed to air pollution and received vitamin C and E supplements, found a considerable decrease in IL6 and IL8 level of nasal secretion compared to children who received placebo.[34] This result revealed the protective effect of antioxidant against the side effects of O3 on pulmonary function in children with asthma suffering from mild vitamins deficiency in dietary intake.[16] In some controlled studies in human, using vitamin C and E supplements with different dosages caused protection against acute Ozone effects on lung fuction.[35,36]

In a study conducted by Romiew in children with asthma who received vitamin C 250mg/d combined with vitamin E 50mg/d, exposure to air pollution such as NO2 and Ozone (particle mass less than 10 μm or PM10) showed the protective role of the supplements against acute Ozone effects on lung function. These effects were found to more in individuals with moderate asthma than those with mild asthma.[16] Other studies showed a relationship between intake of vitamin E and risk of asthma, and two even confirmed its protective effect.[37-40] A cohort study by devereux which was performed in 5-year-old children showed a reverse correlation between receiving vitamin E during pregnancy by their mothers and

wheezing and asthma as a present illness and the symptoms presented in one year ago.[21]

In a study by Nada Omar, there was a significant decline in serum vitamin E level in asthma children compared to non-asthmatic.[4] Similar findings were reported by others.[41-43] While, the result of another study was not similar.[44] The cause of different results reported by different studies could be due to several factors such as severity of asthma, diet and statistical techniques. For instance, Nada Omar indicated that decrease in levels of vitamin E in children was associated with more severe asthma which was reported by the others. Also, the levels of malondialdehyde (MDA) and ROS increased in asthmatic children.[45, 46]

The result of another study showed no significant relationship between serum level of vitamin E and risk of asthma. The serum level of vitamin E in children with asthma was not significantly different from that of the healthy individuals. [47] In a report, there was a significant relationship between decrease in consumption of vitamin E and FEF25-75. This finding is indicated that vitamin E plays a protective role on small respiratory tract function, but changing in FEV1 was not significant and was less sensitive.[48] An investigation in Saudi Arabia, showed that inadequate intake of vitamin E was associated with increased asthma attack.[49] Another study showed that severe asthma was associated with vitamin E intake, but it was not related to asthmatic status.[50] Several studies have been found correlations between higher intake of fruity vegetables, citrus and kiwi fruits and wheezing in children. Mediterranean foods due to rich in vegetables and fruits were associated with decreasing asthma and wheezing.[51-54] In another investigation Gilliland et al. showed that decreasing intake of vitamins A, C and E was associated with decline of spirometry parameters including FVC, FEV1, FEF25-75.[48] Decreasing pulmonary function caused by low intake of vitamins was reported in other studies too.[44,47] Receiving high dose of antioxidants develop wheezing in children aged 2 years.[55] In a study by shock et al, α-tocopherol level in BAL fluid was assessed in children with atopic asthma and healthy control group and no difference was found between the two groups. But, the results of other studies showed that the level of BAL fluid decreased in presence of gaseous pollutants such as Ozone, NO2 and small particles,[44,56-58] Consumption of vegetables and fruits could decrease systemic inflammation specially decline in CRP concentration.[59] In pearson's study, vitamin E had no effect on pediatric asthma.[18] Other studies found that consuming antioxidant vitamins or vegetables and fruits improve pulmonary function or may decrease wheezing.[60-63]

Study on mothers

In a survey performed in USA, low consumption of vitamin by mothers during pregnancy was associated with wheezing in children aged 2 years old. Same results were also found in Japan, where increased level of wheezing was observed in children aged 16-24 months.[64,65]

Also, decreased α-tocopherol (vitamin E) during pregnancy was associated with failure to thrive in pregnancy, decreased pulmonary function and increasing asthma in 5 year-old children.[21] But, a study showed high dose of vitamin E consumption in pregnant women with preeclampsia was not associated with decreasing wheezing and asthma in children.[65] In a study by Devereux, receiving vitamin E during pregnancy was associated with reduced proliferative response of mononuclear cells to allergens like grass and

mites compared to individuals who had low vitamin intake. Wheezing was also decreased in first group.[33,66] Similar results were also obtained for mites and coakroch.[67] Augusto in an investigation showed that higher antioxidants intake such as vitamin E and Zinc during pregnancy alleviates wheezing in children at 2 years of age, while it had no effect on eczema.[55]

Martindale et al. showed that consumption of vitamin E by mothers resulted in decreased level of wheezing in children aged 2 years old and atopic eczema.[66] In a study by Clark, the risk of asthma reduced in children whose mother received vitamin E 15mg/d during pregnancy.[68] In Anne's study, pregnant women at risk of preeclampsia, consumption of vitamin C and E had no effect on prevalence of asthma in their children aged 2 years old, unless, causes

increasing cost and health care utilisation.[65]

Conclusion

Although there were not many studies on the consumption of antioxidants such as vitamin E, vegetables and fruits in children with asthma and/ or pregnant women, but most of them indicated the positive effect of antioxidants intake such as vitamin E which found in most vegetables and fruits to relieve the prevalence of asthma or improving the symptoms of the disease and spirometry parameters among the patients.[6,16,35-40] However, some studies did not confirm this positive effect.[47,48,50] Therefore, further investigations and clinical trials are needed to confirm the effect of antioxidants such as vitamin E on asthma in children.

Conflict of Interest

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