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REVIEW

Deficiency of vitamin D and vitamin C in the pathogenesis of bronchial asthma

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ABSTRACT

Epidemiology of bronchial asthma (BA) indicates a marked paradox: rapid rise in the prevalence.Simultaneous decline in mortality is mostly related to improvement in the diagnosis and therapy. In many economically developed countries the BA affects more than 10 per cent of the population, while mortality related to this respiratory disorder is below 1/100,000. Factors favorably influencing mortality of BA include new more effective medications, decline in smoking and also improved nutrition, based on awareness of protective role of vitamins. Vitamin D deficiency has a number of biological effects that are potentially instrumental in the pathogenesis and severity of BA. Increased number of randomized, controlled, interventional studies is showing positive effects of vitamin D supplementation in pediatric and in adult BA. Oxidative stress is potentially an important pathogenic factor in the progression of BA. Vitamin C (ascorbic acid) belongs to the most effective nutritional antioxidants. By counteracting oxidants, reducing generation of reactive oxygen species, vitamin C may inhibit external attacks in the respiratory tract, thus modulating the development of BA *(Fig. 2, Ref. 15)*. Text in PDF *www.elis.sk.*

KEY WORDS: bronchial astma prevalence and mortality, nutritional deficiency, vitamin D immune modulation, oxidative stress, vitamin C antioxidant.

Bronchial asthma (BA) is a significant public health problem and a high economic burden disease for which prevention is partly possible (1). The strongest risk factors for developing BA are a combination of genetic predisposition with environmental exposure to inhaled substances that may provoke allergic reactions. Deficiency of protective nutrients also contributes. Effective new medications are available to help in maintaining the quality of life, avoiding disability and death.

Proportion of patients with BA is on a continuous rise. Worldwide, there are close to 300 million asthmatics. This makes the BA one of the most frequent chronic disorders. In children, BA is the most frequent non-contagious disease. In Slovakia, there were diagnosed in the past 15 years more than 63 thousand new cases of BA.

Figure 1 illustrates the prevalence of BA in Europe. There is a very high incidence of BA in Scandinavia, Great Britain and France, where more than 10 per cent of the population is affected.

The purpose of this review is to critically evaluate the role of vitamin deficiency in BA, with particular focus on the vitamin D and vitamin C.

Fig. 1. Prevalence of adult asthma in Europe. According to European Lung Foundation, UK, 2015.

Vitamin D

Vitamin D deficiency is highly prevalent worldwide and plays a role in asthma pathogenesis (2,3). Vitamin D has been demonstrated to possess potent immunomodulatory effects, affecting the T and B cells. This immunomodulation may lead to BA-specific clinical benefits in terms of decreased infections, altered airway smooth muscle-remodeling and -function as well as modulation of response to standard anti-asthma therapy by glucocorticoids and to immunotherapy.

Vitamin D plays an important role in immune regulation through interactions between 1,25-dihydroxyvitamin D and vitamin D receptors (2) .Thus, vitamin D deficiency has a number of biological effects that are potentially important in altering the pathogenesis and severity of BA. Data from an increasing number of randomized, controlled, interventional studies of vitamin D supplementation in pediatric and adult BA are being published (4, 5). Asthmatic children with low blood vitamin D levels may have a greater risk of suffering severe asthma attacks.

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Although the role of vitamin D in bone health is well established, compelling data also support the extraskeletal effects, including epithelial integrity and prevention of infection (6).

Vitamin C

Inflammatory abnormalities exist in subjects suffering from BA, in whom an inflammatory state is often associated with increased generation of reactive oxygen species and the damaging effect of free radicals. For this reason oxidative stress may be an important pathogenic factor in the progression of the BA.

Vitamin C is one of the most effective nutritional antioxidants by inhibiting the generation of reactive oxygen species. By counteracting oxidants and reducing external attacks (bacteria, viruses, toxins, xenobiotics)in the lung, vitamin C may modulate the development of BA and the impairment of pulmonary function. Vitamin C deficiency participates in the relation between oxidative stress, bronchial inflammation,reduction of cellular functions and the development of BA symptoms.

Vitamin C intervention may reduce oxidative stress and prevent or minimize asthmatic symptoms both in children and adults (7, 8). Decreased concentrations of vitamin C in plasma are associated with BA (9). Ascorbic acid supplementation attenuates exercise-induced bronchoconstriction in patients with BA (10, 11).

Another study tested if mild BA and airway responsiveness may be ameliorated by vitamin C supplementation using excessive amount of 3 grams per day, then 1 gram/day for 2 weeks (12). Bronchial hyperresponsiveness after methacholine challenge was not significantly affected. Another report stated that it may be „reasonable“ in patients with BA exacerbated by common cold, to use vitamin C (13). This effect of vitamin C was less obvious when the same individuals with BA did not suffer from the common cold. Data from adults participating in the National Health and Nutrition Examination (14) reported no significant decrease in respiratory function in individuals with low vitamin C intake. It was concluded that there may be a synergistic effect of all antioxidants to improve lung function. Supplementation with an individual antioxidant may be of no benefit.

Most reports on potential benefit of vitamin C in BA are based on observational studies, describing association of low vitamin C saturation (plasma level) in BA patients who had multifactorial health disorders. For critical evaluation and convincing evidence, there is a need for strictly controlled randomized studies that would eliminate potential confounders.

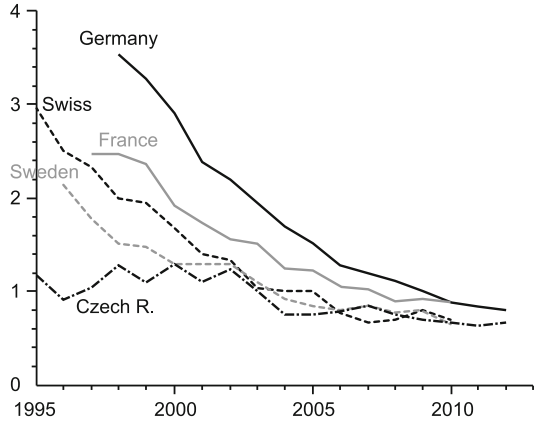

Fig. 2. Decrease of asthma mortality in Europe. According to WHO, European Mortality Database 2014.

Conclusion

Figure 2 illustrates an epidemiologic paradox: impressive decline of mortality due to BA when there is a remarkable increase in the prevalence of this disorder. It suggests that pathogenic causes of BA are mostly multifactorial. Atopy (allergic sensitization) is common in individuals with BA, especially in children.Causes of global BA epidemic remain largely unidentified. Contaminants in the industrialized world are an obvious target. Alarming has been a pronounced increment in prevalence of BA in many non-industrialized countries.

The role of nutrition is an interesting modifying factor. A number of observational studies reported potential relation between vitamins A, D, E, K and C in BA. Preventive and therapeutic potential, especially of vitamin D and vitamin C, deserves careful exploration. Extraskeletal role of vitamin D in immunomodulation and in epithelium protection appears to be well established. Vitamin C antioxidant influence, at least in theory, may be beneficial for individuals with BA. However, scientific evidence here is less solid than that for vitamin D.

The literature on this subject is replete with poorly controlled observational studies. More convincing are randomized controlled trials (RCT), however these are relatively rare. Most of the evidence is insufficient to endorse other vitamins to prevent or manage BA (15).

In general, dietary factors may play a prominent role in BA. Adequate intake of protective nutrients is highly desirable also in BA.

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