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Editorial

Potential Mechanisms for Obesity-Asthma Link

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Obesity and asthma prevalence have rapidly increased worldwide. Clinical and epidemiological studies support a strong positive relationship between these two chronic diseases, which are associated with inflammation. It is interesting to note that overweight and obese children are at higher risk for asthma. Obesity probably has an effect on asthma development through several different mechanisms [1,2].

Asthma and obesity are likely to be connected in a multifactorial fashion. Environmental and lifestyle changes (diet, physical activity, and early life exposures) as well as the presence of genetic susceptibilities are important, previously known factors contributing to the increase in their prevalence over the past few decades and have altered the occurrence and expression of asthma and obesity [1].

In recent years, there has been an accumulating body of evidence related to other possible mechanisms participating potentially in the link established between obesity and asthma. The biological mechanisms behind the link between body mass index (BMI) increase and asthma may be summarized in the following manner:

Anthropometric measurements are considered along with fat measurements for the evaluation of obese subjects. These parameters generally are not determined during the physical examination of asthmatic individuals. So far, waist circumference was found as the only measure that correlated with increased IgE levels and allergic rhinitis [3].

The mechanisms underlying the association between obesity and asthma severity may be related to a decreased immunological tolerance induced by a defective function of regulatory T cells (Tregs), which are responsible from the maintenance of peripheral tolerance [4-6]. Association between rapid weight gain in infancy and asthma or obesity development is suggested [6,7]. Tregs are the key players that prevent allergy development [8]. In a recently published article, significantly reduced Tregs were observed in obese, asthmatic and asthmatic obese children. Obesity and asthma are characterized by chronic and systemic inflammation, and reduction in Tregs may initiate inflammatory processes and cause obesity, which is higher in children with asthma [6].

Type of infant feeding has been matter of discussion for a long time. Effects of artificial formula feeding upon weight gain were pointed out years ago [9]. Pronounced early weight gain during infancy appears to be an important predictor for childhood asthma, particularly within the first 6 years of life [10]. Artificial formula feeding was introduced into infant nutrition before mammalian target of rapamycin (mTOR), cell's master regulator of cell growth and proliferation, has been extensively studied. There is a direct link between amino acid availability and mTOR-driven cell growth [11].

Activation and generation of T cells are associated with the central role of mTOR activity [12]. Abundant amount of amino acids by excess protein intake due to artificial formula feeding within the postnatal period may lead to overstimulation of mTOR in many immune cells including T cells. High protein infant formula feeding overstimulating insulin finally activates mTOR [11,13]. mTOR signalling plays a role also during asthma. Inhibition of mTOR has been shown to alleviate cardinal asthmatic features, including airway hyperresponsiveness and eosinophilic inflammation. Increased mTOR signalling by high protein formula feeding may interfere with postnatal mTOR-mediated immune cell programming [11,14,15].

Increased expression of some proinflammatory cytokines such as tumor necrosis factor (TNF)-α has been introduced as a common factor in asthma and obesity and possibly an important target for obesity-related asthma in some experimental studies [16,17]. Restoring normal body weight has

been suggested as an appropriate strategy for reducing TNF-α levels, and controlling inflammation, which may help improving asthma control in obesity-related asthma [16].

Adipocyte-derived parameters have recently gained importance. Besides proinflammatory parameters such as leptin, resistin and visfatin, adiponectin, with its antiinflammatory aspects, have recently contributed to the matter. Leptin is increased in obesity and leads to increased neutrophil recruitment to the lungs. Leptin signalling negatively modulates Tregs function. The increased asthma severity in obesity might be caused by decreased immunological tolerance induced by a decreased function of Tregs mediated by leptin [4]. Elevated leptin, resistin and visfatin levels accompanying diminished concentration of adiponectin have been reported in asthmatic obese children and systemic inflammatory biomarkers are found to be correlated with BMI values [18,19]. The leptin-adiponectin balance is disturbed in obese individuals and this may cause neutrophilic airway inflammation [20].

Adipokines can also affect the survival and function of eosinophils. Leptin has proinflammatory systemic activities that may contribute, at least in part, to asthma. Leptin activates eosinophils and thus may serve as an important eosinophil survival factor through anti-apoptotic activity. The links between eosinophilic activity and leptin suggest that leptin is involved in enhanced eosinophil accumulation into the airways of obese individuals [21].

Obesity is commonly associated with hypertriglyceridemia, hypercholesterolemia and insulin resistance. Since dyslipidemia and hyperinsulinemia are also involved in the development of airway inflammation, they may help to explain the link between obesity and asthma [1, 2,22]

Obesity in childhood is also a significant predictor of obesity in adulthood. Particularly, asthmatic obese children should be handled with utmost care because this is an expanding area on which studies must be focused.

Studies must be organized in both adult and pediatric population to observe the similarities and differences in terms of mechanisms. Due to changes, including hormones, associated with puberty, particularly alterations in insulin sensitivity, the adolescence period must be evaluated individually as prepubertal and postpubertal periods. Gender differences are also to be taken into account. Distribution of body fat must also be considered.

Studies on molecular and cellular medicine aspects of this topic must also be performed, because apoptosis, phagocytosis and efferocytosis are the processes, which are known to contribute to the establishment and progression of such chronic inflammatory diseases.

Wide-scoped, case-controlled, multi-centered and longitudinal studies considering nutritional aspects, adipotropins as well as hormones derived from adipocytes, proinflammatory cytokines, T cells, mTOR and also genetic and environmental factors are indispensable to solve this sophisticated problem and to clear this rather enigmatic relationship between these two diseases of the age. Advancement in understanding associations of obesity with asthma will allow advancement in developing more effective, straightforward and complete therapeutic solutions.

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