Obesity-Associated Asthma: a Literature Review of Its Pathophysiology and Treatment Options

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Abstract
Obesity, a complex heterogeneous chronic disease, is a well-established risk factor for development of asthma. Several factors were described in association with obesity. Those include hormonal development of asthma. Several factors were described in association with obesity. Those include hormonal imbalance, behavioral, nutritional, genetics diet and lifestyle factors. Those same factors are attributed to obesity-associated asthma. This article reviews current literature regarding multifactorial factors contributing to obesity-associated asthma and potential therapeutic agents.

Keywords
Obesity; Obesity-associated asthma; association with obesity

Introduction
Obesity has been described as a risk factor for development of asthma. Several studies described the pathophysiology of obesity-associated asthma. It is believed that obesity results in a chronic inflammatory state that lead to airway hyper-reactivity [1]. Hyperinsulinemia, a state that is both associated with and is a consequence of obesity, is show to be associated with airway hyper responsiveness [2-4] arginine metabolism and mitochondrial dysfunctions were also reported to be associated with obesity-related asthma [5-6] Moreover, diet,including maternal diet rich in omega-6 during pregnancy, has been shown to be associated with obesity [7].

Obesity and asthma are closely related conditions. Many of the proposed treatment options apply to both conditons. Diet that is a rich in anti-oxidant have been recommended for obese asthmatics [5] Vitamin D supplementation has also advised for both obese and asthmatic patients [7]. Pharmacotherapy with metformin is hypothesized to be beneficial in the treatment of obesity-associated asthma [8].

Pathophysiology
Obesity leads to Chronic inflammatory state, Inflammatory cytokines interleukin-4(IL-4) and IL-13 are associated with asthma. It has been hypothesized that those inflammatory cytokines induce mitochondrial dysfunction by upregulation of oxidized linoleic that to mitochondrial loss [5].

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Few studies reported that hyperalimentation postnatally may contribute to early-onset pulmonary dysregulation. A study by dinger k, et al. showed that offspring mice with postnatal hyperalimentation developed leptin and insulin resistance and showed increased expression of interleukins and tumor necrosis alpha, the study suggested possible early metabolic programming of obesity-related asthma [1]. An article by Raphaelle V. reported a hypothesis of increased intake of proinflammatory omega-6 polyunsaturated fatty acid coupled with decreased intake of omega-3 polyunsaturated fatty acid to be associated with asthma [7].

Several other studies demonstrated association of diet with development of both asthma and obesity. A study by Singh VP, et al showed that normal weight mice who were fed high fructose diet developed arginine dysfunction and asthma-like features. The study hypothesized that diet, such as fructose, that caused metabolic syndrome without necessarily causing obesity may result in nitric oxide metabolic dysfunction [6]. However, high fructose is well known to be highly associated with obesity. The article by Raphaelle reported that diet deficient in vitamins E and D, zinc and omega-3 polyunsaturated fatty acids during pregnancy is associated with wheezing early in life [7].

A state that is well known to be associated with obesity, is thought to cause lung changes characteristic of asthma via growth factor-like effects. It was postulated that insulin may induce vagally-mediated bronchoconstriction effect. In addition, it is believed that insulin have effect on the central nervous system increasing airway reactivity [9, 10]. Another related metabolic hormone, leptin is believed to regular airway diameter via parasympathetic signaling [11]. Both hyperinsulinemia and decreased insulin level are associated with obesity and asthma.

**Discussion**

Obesity-related asthma is a unique variant in that it tends to be difficult to manage. Likewise obesity, body maladaptation is likely contributing factor for its challenging management. The chronic pathophysiological changes attribute to obesity play a role in worsening asthma. A clear understanding of all associated factor is crucial for optimal management. Metformin is well-known medication for the treatment of hyperinsulinemia. Up to data, it has never been used for sole treatment of asthma. A study by calixto MC, et al. Compared eosinophil cell numbers in bronchoalveolar lavage (BAL) fluid in lung of obese mice versus lean mice in response to metformin. Obese mice BAL fluid initially had significantly higher number of cosinophils and insulin resistance. Metformin revered insulin resistance in those mice and also significantly decrease number of eosinophil cells [8]. Statin, other pharmacologic agent often taking by obese patients. Was shown to inhibit L-arginine degradation by arginase, hence restoration nitric oxide metabolism [5]. Human studies are needed to evaluate pharmacologic benefits of metformin, leptin and statin in the management of asthma. Since asthma is closely related, it seems logical to start to start medication early with modest increase in body mass index (BMI).

Diet has always been the mainstay of treatment and management of obesity and asthma is no exception. Studies showed benefits of exogenous antioxidants such coenzyme Q10 on restoration mitochondrial function [5]. Other antioxidants such

As vitamin A,E and C were shown to have protective effect on lung tissues. Few studies found low vitamin D in obese individuals [7]. A study by taylor SK showed that inhaled 25-hydroxy-vitamin D 1,25-hydroxy-vitamin D resulted in enhanced lung maturation in mice [12]. More studies are needed in human to show benefit of routine vitamin D suplementation to newborns. Other studies showed importance of maternal diet on postnatal health and long-term metabolic program [7]. Further research is need to comeup with recommendation on starting healthy life in utero to assure longevity and decreased morbidities.

**Conclusion**

Obesity is a state of chronic inflammation. The same inflammatory response seen in obese individuals thought to be contributing to pulmonary dysfunction. It is suggested that obesity-mediated proinflammatory state leads to airway hyperresponsiveness and mitochondrial loss. Many studies showed promising benefits of anti-inflammatory medications, that are used in the treatment of Obesity, in decreased pulmonary inflammation. However, human clinical trials are lacking to validate or recommend their routine use in asthma.

**Reference**


7. Raphaelle V, Camargo Jr CA, Diet and asthma: need to account for asthma type and level of prevention.


