PROCEEDINGS REPORT

Influence of obesity on the prevalence and clinical features of asthma

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Abstract

Obesity has been associated with an increased prevalence of asthma and poorer control of this disease. However, the mechanisms by which obesity can influence airway function and make asthma more difficult to control remain uncertain. The physiological changes associated with obesity can contribute to respiratory symptoms and these should be differentiated from those caused by asthma. Obesity can possibly influence the development of asthma through genetic, developmental, hormonal, neurogenic or mechanical influences. Breathing at low lung volumes and changes in the pattern of breathing in obese subjects may alter airway smooth muscle plasticity and airway function. The release by adipocytes of various cytokines and mediators such as Interleukin-6, TNF- α , eotaxin, and leptin, and the reduction of anti-inflammatory adipokines in obese subjects may possibly contribute to the development or increased clinical expression of asthma in promoting airway inflammation. Reduced asthma control and impaired response to asthma therapy have been reported in obese patients. Obesity-related co-morbidities such as Sleep Apnea and Gastroesophageal reflux may also contribute to this poor control. Weight loss improves asthma control and reduces medication needs. Research is needed to better define the optimal management of obese asthmatic patients.

Prevalence of asthma and obesity

Asthma and obesity are two common health problems.^{1,2} Recent data show that close to 60% of Canadians are overweight or obese with a body mass index (BMI) of 25 kg/m² or more, about one in 4 Canadians being obese (BMI $\geq$ 30 kg/m²).³ Asthma prevalence has increased in most countries in the last decades and the World Health Organization considers that there are at least 300 million individuals suffering from asthma worldwide.⁴ In Canada, about 10% of the population is considered to have asthma.⁵

A relationship between asthma and obesity was suggested in an early study published by Camargo et al. in 1999.⁶ In this prospective cohort from the Nurses' Health Study II on 85911 participants aged 26 to 46 yr, BMI had a strong positive association with risk of adult-onset asthma. In another large study looking at the association between asthma and BMI between 1963 and 2002 in 135,000 Norwegians aged 14-60 yr followed on average for 21 yr, the risk of asthma increased steadily with BMI.⁷ More recently, Beuther et al analyzed seven prospective studies (n = 333,102 subjects), evaluating BMI and incident asthma in adults⁸; compared with normal weight sub-

jects, those with a BMI ≥ 25 had an odds ratio for incident asthma of 1.51 and a dose-response effect of elevated BMI on asthma incidence was observed. An increased prevalence of physicians' diagnosed and self-reported asthma has also been observed in obese subjects in other studies, particularly in women.⁹⁻¹¹ However, despite the evidence of an association between obesity and asthma in most studies, the specific nature of this relationship remains to be better defined.

How can obesity contribute to the development of asthma ?

Although asthma may promote weight gain through increased sedentary life style and occasional use of oral corticosteroids, this does not fully explain the association of asthma and obesity in the majority of patients. How obesity can influence the development of asthma is still a matter of debate and various hypotheses have been proposed, involving genetic, developmental, hormonal, neurogenic or mechanical influences.^{12;13}

Common genetic influences promoting the development of both asthma and obesity have been suggested.^{14;15} In this regard, Hallstrand et al. analyzed data obtained from 1001 monozygotic and 383 dizygotic same-sex twin pairs included in the University of Washington Twin Registry, looking at the presence of a self-reported physician diagnosis of asthma in obese subjects (with a BMI of 30 or greater).¹⁶ In this last study, a strong association between asthma and BMI was identified in this population and significant heritability was detected for asthma (53%) and obesity (77%), suggesting additive genetic influences on each disorder.

In regard to alterations in lung function, an excellent review of the various effects of obesity on pulmonary function has been published.¹⁷ Among those changes, we may note that marked obesity can be associated with a restrictive pattern, with a mild reduction in total lung capacity (TLC) although the most frequent finding in the obese is a reduced expira-

tory reserve volume (ERV), and an altered pattern of breathing, particularly on exertion, with higher breathing frequencies and reduced tidal volumes. Furthermore, we have previously reported that obese non-asthmatic subjects have lost the protective effect of a deep inspiration observed in non-obese non-asthmatic subjects.¹⁸ Although the importance of this finding is unknown, it could possibly enhance the effect of processes leading to increased airway responsiveness. In this regard however, the often reported relationship between the presence of airway hyperresponsiveness (AHR) and obesity has been questioned in studies showing a relationship between obesity and asthma, but none between obesity and increased airway responsiveness.^{11,13,19}

Obesity is also considered a pro-inflammatory state and increases in various inflammatory cytokines and mediators such as tumor necrosis factor- α , interleukin-6, as well as C-reactive protein and leptin have been observed in obese subjects.^{20;21} Levels of the pro-inflammatory hormone leptin are higher and those of the anti-inflammatory adiponectine are lower in obese asthmatic subjects.^{22;23} It has been suggested that leptin could be involved in the pathogenesis of asthma in obese subjects through its influence on interferon- γ .

An elevated BMI has been proposed as a risk factor for atopy, a major risk factor for asthma, although studies looking at the prevalence of asthma in obese atopic subjects, including one of our recent reports, suggest that the association between asthma and obesity is not mainly mediated through atopy.²⁴⁻²⁶ In this regard, Chen et al. had previously reported that obesity was more likely associated with nonallergic rather than to allergic asthma in adults,²⁷ and Appleton et al. had found an association between central obesity and increased risk of nonatopic asthma only.²⁸

Influence of obesity on asthma control: response to asthma therapy

The main goal of asthma treatment is to achieve adequate control of the disease, as reflected by minimal symptoms and rescue bronchodilator use, no night-time symptoms, normal daily activities, rare and mild exacerbations and optimal pulmonary function.^{29,30} This goal can be achieved, in most patients, with appropriate asthma education, environmental measures, individualized pharmacotherapy and regular follow-up. Asthma has been however reported to be more difficult to control in obese patients compared to individuals with a normal weight.³¹⁻³⁴

This reduced asthma control may be related to the effects of obesity *per se* on asthmatic airways, to the contribution of obesity-related co-morbid conditions, or reduced response to medication. Obesity is associated with an increased work of breathing and this, in addition to the previously described changes in lung function, may possibly enhance asthma symptoms induced by the airway inflammatory process and smooth muscle contraction in asthmatic airways. Obese subjects also have an increased prevalence of co-morbid conditions that may influence asthma control, such as gastroesophageal reflux and sleep apnea.^{35,36} Finally, increased BMI is associated with a reduced response to asthma medications such as inhaled corticosteroids (ICS), as well as, particularly in presence of morbid obesity, to the association of an ICS and a long-acting bronchodilator.^{34,37} Leukotriene receptor antagonists may be less affected by obesity but this remains to be further explored.³⁷ The mechanisms underlying this reduced response to various medications remain to be determined.

Effects of weight loss on asthma

Weight loss, even modest, has been universally found to improve asthma control and reduce its severity, as assessed mainly by medication needs.^{38,39} Weight reduction from diet and exercise has been found to improve asthma symptoms, reduce peak expiratory flow

variation and improve spirometric values but the most striking changes have been reported in morbidly obese asthmatic subjects following bariatric surgery.⁴⁰

Conclusion

Asthma and obesity are frequently associated, and obesity may contribute to the development and/or severity of asthma through various influences, probably in most patients, of multifactorial origin. Asthma in the obese may represent a specific phenotype and this should be better defined, as should be the influence not only of BMI but of the pattern of distribution of fat in the body on airway function. Furthermore, more research is needed to determine what is the optimal management of asthma in obese patients. It is, nevertheless, important to confirm the asthma diagnosis in the obese, try to assess the respective contribution of obesity and asthma to respiratory symptoms, and carefully assess the effects of therapy, while emphasizing the importance of weight loss. In this regard, the recent recommendations of the Canadian Medical Association guidelines on the management of obesity will be helpful to establish appropriate weight loss strategies.⁴¹

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