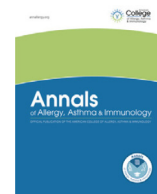




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Letters

Obesity in asthma Intricately linked and often overlooked

In December 2020, the National Asthma Education and Prevention Program Coordinating Committee (coordinated by the National Heart, Lung, and Blood Institute) published a much-anticipated update to the Asthma Management Guidelines.¹ Previously updated in 2007, the guidelines inform evidence-based care for clinicians caring for adults and children with asthma. Primary topics discussed in the recent update include the following: use of fractional exhaled nitric oxide testing, indoor allergen mitigation, use of intermittent inhaled corticosteroids and long-acting muscarinic antagonists, and adjunctive treatment modalities (eg, immunotherapy). These updates address the needs of clinicians and fill knowledge gaps through inclusion of emerging evidence.

Obesity and its relevance to asthma is one topic of critical importance that was not addressed in the updated guidelines. Although the mechanisms underlying the connection between asthma and obesity are not fully understood, these 2 conditions are interrelated. Obesity is a risk factor for the development of asthma, affecting approximately 60% of adults with severe asthma and increases the risk of asthma by 26% to 38% in children.^{2,3} Children and adults with obesity are more likely to experience poor health outcomes related to asthma compared with individuals with a healthy weight, including more frequent exacerbations, poorer symptom control, and lower quality of life.² Although most evidence suggests that obesity augments asthma outcomes, in some instances, asthma (and some of its therapies) may also predispose to obesity.

Differences in asthma-related health outcomes may be due in part to heterogeneity in asthma, which was noted as an emerging topic in the 2020 update.¹ A unique obese-asthma phenotype has been described in previous literature.² The underlying reasons for this asthma phenotype are likely multifactorial, encompassing demographic, environmental, and biological factors. For instance, important physiological differences exist in individuals with obesity. Obesity is associated with heightened levels of inflammation and inflammatory biomarkers, which may play a key role in development of asthma. Children and adults with obesity are also known to display differences in lung function. Several mechanisms have been explored to explain these differences in lung function. Excessive truncal adiposity may cause a mass effect resulting in a decreased functional residual capacity, potentially affecting bronchial smooth muscle stretch. Children with obesity may also have higher absolute value forced expiratory volume and forced vital capacity and lower forced expiratory volume and forced vital capacity ratios, which may lead to an increased risk of severe exacerbations.⁴

Pharmacokinetic and pharmacodynamic differences also affect patients with obesity, indicating a potential need for drug dosing

adjustments. In one study, children with obesity receiving identical doses of albuterol had less response as measured by both pulmonary function testing and symptom relief.⁵ Patients with obesity may also have decreased responsiveness to inhaled corticosteroids, putting them at increased risk of experiencing exacerbations. Other studies have postulated that dosing adjustments (likely increases) for systemic corticosteroids may be necessary owing to the baseline elevation in endogenous corticosteroid production in obesity which may affect the overall response to exogenous corticosteroids.⁶ Excess body weight may also have implications for the efficacy of magnesium sulfate used in the setting of acute asthma exacerbations. One pharmacokinetic study found that weight was the only factor that predicted serum magnesium levels in children being treated for asthma exacerbation; weight was associated with increased volume of distribution and magnesium clearance, indicating a potential need for increased doses for patients with higher weights.⁷

When considering the mounting evidence supporting a specific obese-asthma phenotype, it is clearly necessary to address the issue of comorbid obesity within asthma clinical guidelines. Currently, owing to a lack of evidence to support adjustment of screening, testing, and optimal treatment approaches in this population, clinicians are left to adjust therapies and determine management strategies without obesity-specific guidance. Creating evidence-based guidance remains difficult given these substantial gaps in research. Consequently, drawing on the expertise of experts in the field and integrating the best available evidence are necessary. Waiting until substantial evidence is available to address obesity in clinical guidelines for asthma is not without risk. If this approach continues, high-risk subpopulations with asthma and comorbid obesity are likely to continue to experience increased asthma morbidity.

Adequately addressing asthma in the context of obesity will require a strategic shift in the focus of future research. Ideally, studies should investigate on how modifications to typical therapy may be more effective in patients with obesity. Prospective or pragmatic trials using standardized asthma outcomes may be beneficial in developing evidence-based guidelines that address whether dosing adjustments for typically prescribed inhaled and systemic drugs are warranted. Pharmacokinetic and pharmacodynamic studies would also provide necessary background for drug dose-escalation studies.

Although knowledge accumulates on optimal treatment strategies for asthma in the context of obesity, future clinical guidelines may also be enriched by addressing obesity-related comorbidities contributing to asthma morbidity. For example, drugs used to address metabolic syndrome (eg, statins) may be beneficial for asthma owing to anti-inflammatory effects.⁸ Adults with obstructive sleep apnea treated with continuous positive airway pressure had improvements in asthma control and lung function⁹ and children with asthma and obstructive sleep apnea had improvement in asthma-related

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symptoms after adenotonsillectomy.¹⁰ Considering obesity-related changes in lung function which may be present independent of asthma (eg, decreased functional residual capacity), weight reduction interventions have been promising with regard to asthma outcomes in children and adults, though variability in results exists. Although more research is needed to quantify the asthma-related benefits of these interventions, the possibility of improvement would be of interest to clinicians managing patients with obesity and asthma.

Failing to explicitly address obesity as a significant asthma comorbidity in national guidelines will have implications in the clinical care of obese patients with asthma and may perpetuate oversight of this as an important factor contributing to asthma control. Individuals planning future research and interventions may be less likely to recognize and prioritize obesity-related work in populations with asthma. Institutions may also be less inclined to support such work. Individuals with obesity make up a substantial proportion of patients with severe asthma, and this high-risk population warrants special consideration in guideline development and in scholarly work to expeditiously identify best practices and effective treatment regimens.

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